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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Form 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2020

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: 001-37539

Global Blood Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**27-4825712**
(State of other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
181 Oyster Point Boulevard, South San Francisco, California	**94080**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (650) 741-7700

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, $0.001 par value	**GBT**	**The NASDAQ Global Select Market**

Securities registered under 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 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 definitions 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. ☒

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 was approximately $1,606.1 million as of June 30, 2020 based upon the closing sale price on the NASDAQ Global Select Market reported for such date. Shares of common stock held by each executive officer and director have been excluded in that such persons may be deemed to be affiliates of the registrant. Shares of common stock held by other persons, including certain holders of more than 10% of the outstanding shares of common stock, have not been excluded in that such persons are not deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of February 18, 2021, the registrant had 62,156,860 shares of common stock, par value $0.001, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement for the registrant's 2021 Annual Meeting of Stockholders, to be filed subsequent to the date hereof with the Securities and Exchange Commission, or SEC, are incorporated by reference into Part III of this report. Such proxy statement will be filed with the SEC not later than 120 days after the end of the registrant's fiscal year ended December 31, 2020.

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

Statements made in this Annual Report on Form 10-K that are not statements of historical information are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. These forward-looking statements include, but are not limited to, statements regarding:

- our ability to successfully commercialize our approved product, Oxbryta® (voxelotor) tablets as well as inclacumab or any other product candidate we may identify and pursue, if approved;
- the potential market opportunity for, and rate and degree of market acceptance of, Oxbryta, inclacumab or any other product candidate we may identify and pursue, if approved;
- the benefits of the use of Oxbryta, inclacumab or any other product candidate we may identify and develop;
- the limitations of current treatment options for sickle cell disease, or SCD;
- our ability to successfully maintain a sales force and commercial infrastructure and to commercialize Oxbryta and any other approved products (if any) effectively and in compliance with complex compliance and other requirements;
- our ability to compete with companies currently commercializing or engaged in the clinical development of treatments for the disease indications that we pursue;
- our ability to manufacture Oxbryta for commercial sale and clinical development in conformity with the FDA and other applicable requirements;
- our reliance on third-party contract manufacturers to manufacture and supply Oxbryta and our product candidates;
- our expectations regarding government and third-party payor coverage and reimbursement;
- the timing and results of our continued development of Oxbryta, including, but not limited to, ongoing or planned clinical studies to satisfy post-approval confirmatory study requirements or to seek to expand approved product labeling;
- the timing and results of our preclinical studies and clinical trials of inclacumab and any other product candidate we may develop;
- our ability to leverage the safety data from prior clinical studies of inclacumab, which were not in patients with SCD, in our development of inclacumab;
- our ability to enroll patients in and complete our clinical trials at the pace we project;
- whether the results of our preclinical studies and clinical trials will be sufficient to support any or full domestic or foreign regulatory approvals for Oxbryta, inclacumab or any other product candidate we may develop;
- our ability to obtain, including under any expedited development or review programs, and maintain any or full regulatory approval of Oxbryta, inclacumab or any other product candidates we may develop;
- our ability to advance any other programs through preclinical and clinical development, and the timing and scope of these development activities;
- our ability to maintain, or to recognize the anticipated benefits of, orphan drug designation for Oxbryta or to obtain orphan drug designation for any product candidate we may identify and pursue in the United States, Europe or any other jurisdiction;
- our ability to maintain, or to recognize the anticipated benefits of, access to accelerated development and review programs through the FDA, such as the fast track and breakthrough therapy programs, or through the EMA's PRIME program, for Oxbryta or any product candidate we may identify and pursue;

- our reliance on third parties to conduct our clinical trials;
- our ability to retain and recruit key personnel;
- our ability to obtain and maintain intellectual property protection for Oxbryta or any product candidate we may identify and pursue;
- our estimates of our expenses, ongoing losses, future revenue, capital requirements, sufficiency of capital resources and our needs for or ability to obtain additional financing;
- our financial performance;
- developments and projections relating to our competitors or our industry;
- our plans to explore strategic transactions to broaden our pipeline; and
- our ability to implement our strategic plans for our business and technology.

We have made these statements in reliance on the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These statements are subject to certain risks and uncertainties, which could cause actual results to differ materially from those projected or anticipated. Although we believe our assumptions underlying our forward-looking statements are reasonable as of the date of this report, we cannot assure you that the forward-looking statements set out in this report will prove to be accurate. In some cases, you can identify forward-looking statements by words such as “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “seek,” “should,” “target,” “will,” “would,” or the negative of these words or other comparable terminology. Some of the factors that could cause our actual results to differ materially from our expectations or beliefs are disclosed under the caption “Risk Factors,” as well as other sections of this report that include, without limitation: risks and uncertainties relating to the COVID-19 pandemic, including the extent and duration of the impact on our business, the results of our commercialization of Oxbryta, the potential safety, efficacy or other therapeutic benefits of Oxbryta and our product candidates, our capital resources, commercial market estimates, the timing for initiation of, availability of data from, and completion of, our ongoing and planned clinical trials and the results of these clinical trials, the pathways for regulatory approval of Oxbryta and our product candidates, our ongoing and future research and development efforts, patent protection, effects of healthcare reform, government and third-party payor actions, reliance on third parties, and other risks set forth below. All forward-looking statements speak only as of the date on which they are made and we disclaim any intent to update forward-looking statements to reflect subsequent developments or actual results. Except as required by law, we assume no obligation to update any forward-looking statements publicly, or to revise any forward-looking statement to reflect events or developments occurring after the date of this report, even if new information becomes available in the future. Thus, you should not assume that our silence over time means that actual events are bearing out as previously expressed or implied in any such forward-looking statement.

This Annual Report on Form 10-K also contains estimates, projections and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market, and other data from reports, research surveys, studies, and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data, and similar sources.

In this Annual Report on Form 10-K, unless the context requires otherwise, “GBT,” “Company,” “we,” “our,” and “us” means Global Blood Therapeutics, Inc., together with our consolidated subsidiaries. Oxbryta, GBT Source Solutions and GBT Source are trademarks of GBT. This Form 10-K also contains trademarks of third parties, and any such trademark is the property of its owner.

SUMMARY OF RISK FACTORS

Below is a summary of the principal factors that make an investment in our common stock speculative or risky. This summary does not address all of the risks that we face. Additional discussion of the risks summarized in this risk factor summary, and other risks that we face, can be found below under the heading "Risk Factors" and should be carefully considered, together with other information in this Annual Report on Form 10-K and our other filings with the Securities and Exchange Commission, or SEC, before making investment decisions regarding our common stock.

- Our business is substantially dependent on our ability to successfully commercialize our first approved product, Oxbryta, which will depend upon the degree of market acceptance by the medical community and marketplace.
- If our sales and marketing capabilities for Oxbryta or any future product candidate for which we receive regulatory approval are not effective, we may not succeed in our commercialization efforts.
- Our profitability depends on our ability to sell sufficient amounts of product at competitive prices and on the availability of adequate coverage and reimbursement through governmental or private third-party payors, the status of which is subject to significant uncertainty.
- Our future growth may depend on our ability to penetrate foreign markets, which would subject us to additional regulatory burdens and other risks and uncertainties.
- We will be subject to ongoing regulatory obligations and scrutiny for Oxbryta and any other product candidate for which we receive approval, which may include restrictions on product labeling, distribution or other post-marketing activities.
- Our business operations and relationships with third parties are subject to various laws and regulations, and any failure to comply with such laws and regulations could adversely affect our business.
- We face intense competition and rapid technological change and the possibility that our competitors may develop therapies that render our only approved product, Oxbryta, or product candidates uneconomical or obsolete, which could adversely affect our development programs, commercialization activities and financial condition.
- If the market for Oxbryta or our product candidates is smaller than expected, our business and financial condition may be adversely affected.
- We have a limited operating history, with only one drug approved for marketing, and expect to continue to incur losses for the foreseeable future.
- We may require substantial additional funds to achieve our business goals, and any inability to obtain such funds may force us to delay, limit or terminate our commercialization of Oxbryta or our other product development efforts and operations.
- We are party to a loan and security agreement that contains operating covenants and obligations that may restrict our business and financing activities.
- If we are unable to obtain regulatory approval in additional jurisdictions for Oxbryta or in any jurisdictions for other product candidates, our business will be substantially harmed.
- All of our programs other than Oxbryta are still in earlier development stages, so we remain very reliant on the potential success of Oxbryta in the clinic and in the marketplace.
- Expedited development and regulatory approval programs for Oxbryta or other product candidates may not lead to a faster development or regulatory review or approval process, or to a timely approval, if at all.
- The development of Oxbryta represents a novel therapeutic approach, and the outcomes of our clinical trials may not support any label expansion or any decision to seek, grant or maintain any regulatory approval.

- Results of earlier studies may not be predictive of future clinical trial results, and initial studies may not establish or maintain an adequate safety or efficacy profile for Oxbryta or a product candidate to justify proceeding to advanced clinical trials or an application for regulatory approval.
- We may encounter substantial delays in conducting or completing our clinical trials, including due to difficulties in enrolling patients or maintaining compliance with trial protocols, or the occurrence of serious adverse events or unacceptable side effects.
- We may not realize the expected benefits of the orphan drug designations we have received for Oxbryta, and we may not receive orphan drug designation for any product candidate.
- If the third parties upon which we rely to conduct our clinical trials, nonclinical studies, manufacturing and other activities related to the development and commercialization of Oxbryta and our product candidates fail to meet regulatory requirements or otherwise do not perform in a satisfactory manner, our business will be harmed.
- If we or our licensors are unable to obtain and maintain intellectual property protection that is adequate in scope and duration for Oxbryta or our product candidates, our ability to successfully commercialize Oxbryta and other product candidates will be impaired.
- We may become subject to litigation, claims and investigations, including healthcare compliance claims, product liability claims or claims alleging infringement of third parties' proprietary rights and/or seeking to invalidate our patents, which would be costly and could impair our development and commercialization efforts.
- If we are unable to protect the confidentiality of our trade secrets or other confidential information, our business would be harmed.
- The COVID-19 pandemic has adversely impacted, and may continue to adversely impact, our business, including our commercialization activities, clinical trials and preclinical studies.
- Our success depends on our ability to retain key employees, consultants and advisors and to attract, retain and motivate qualified personnel, including an adequate sales force, as well as managing our growth.
- If we are not successful in discovering, developing, acquiring or commercializing additional product candidates, our ability to expand our business and achieve our strategic objectives could be impaired.
- Any collaboration, license, distribution or other arrangements that we are a party to or may enter into in the future may not be successful.
- Our operating results may fluctuate significantly, which makes our future operating results difficult to predict.
- We do not currently intend to pay dividends on our common stock, and, consequently, our stockholders' ability to achieve a return on their investment will depend on appreciation in the price of our common stock.

PART I

Item 1. *Business*

Overview

We are a biopharmaceutical company dedicated to the discovery, development and delivery of life-changing treatments that provide hope to underserved patient communities. Founded in 2011, our goal is to transform the treatment and care of sickle cell disease, or SCD, a lifelong, devastating inherited blood disorder that is marked by red blood cell, or RBC, destruction and occluded blood flow and hypoxia, which leads to anemia, stroke, multi-organ failure, severe pain crises, and shortened patient life span. Our mission is driven by the historical lack of understanding, investment and attention given to SCD. Although the fundamental cause of SCD has been understood for decades, therapeutic innovation and access to care have significantly lagged compared to many other rare diseases. For example, there are approximately three times more individuals in the United States living with SCD than cystic fibrosis, or CF. However, since the enactment of the Orphan Drug Act passed in 1983, only four drugs have been approved for SCD compared to 15 drugs approved for CF. As a result of the lack of treatment options, patients with SCD suffer serious morbidity and premature mortality.

Given the estimated prevalence of SCD in our current focus areas of the U.S., Europe, the Gulf Cooperation Council, or GCC, region and Latin America, we believe there is an opportunity to bring our first medicine, Oxbryta® (voxelotor) tablets, to more than 350,000 people living with SCD in the next several years. Worldwide, there are millions of people living with SCD, which occurs predominantly in populations of African, Middle Eastern and South Asian descent and has an estimated global incidence of 250,000 to 300,000 births annually.

In November 2019, the U.S. Food and Drug Administration, or FDA, granted accelerated approval for Oxbryta for the treatment of SCD in adults and children 12 years of age and older. Oxbryta, an oral therapy taken once daily, is the first FDA-approved treatment that directly inhibits sickle hemoglobin, or HbS, polymerization, the root cause of SCD.

The accelerated approval of Oxbryta was based on clinically meaningful and statistically significant improvements in hemoglobin levels, accompanied by reductions in RBC destruction (hemolysis). Data from our Phase 3 HOPE (Hemoglobin Oxygen Affinity Modulation to Inhibit HbS PolymErization) Study of 274 patients 12 years of age and older with SCD showed that, after 24 weeks of treatment, 51.1% of patients receiving the 1500 mg dose of Oxbryta, which is the approved dose, achieved a greater than 1 g/dL increase in hemoglobin compared with 6.5% receiving placebo ($p<0.001$), and Oxbryta had a favorable safety and tolerability profile.

By early December 2019, we began to make Oxbryta available to patients through our specialty pharmacy partner network. In addition, we established GBT Source Solutions®, a comprehensive program for patients who are prescribed Oxbryta that provides a wide range of practical, educational and financial support customized to each patient's needs. In addition, we have focused on securing reimbursement and expanding patient access. By the end of September 2020, one quarter ahead of our goal, we secured broad Oxbryta reimbursement coverage for 90% of lives covered by payers either through published policies or verified patient adjudication. We also secured fee-for-service Medicaid coverage in 44 states, including all 17 priority states where most SCD patients live.

We have a number of ongoing clinical trials of Oxbryta. The Phase 2a HOPE-KIDS 1 Study, an open-label, single- and multiple-dose trial, is evaluating the safety, tolerability, pharmacokinetics and exploratory treatment effect of Oxbryta in pediatric patients aged 4 to 17 years with SCD. The Phase 3 HOPE-KIDS 2 Study, a post-approval confirmatory study we initiated in December 2019 as a condition of the accelerated approval of Oxbryta in the United States, uses transcranial Doppler, or TCD, flow velocity to seek to demonstrate a decrease in stroke risk in children 2 to 15 years of age. The ActIVe Phase 4 study, a pilot, open-label, single-arm study, aims to evaluate the effect of Oxbryta on exercise capacity, as measured by cardiopulmonary exercise testing (CPET) in

patients 12 years of age and older with SCD. We also expect to conduct additional clinical studies of Oxbryta, including to seek to expand the potential approved product label into younger pediatric populations as well as to study further the efficacy and safety profile of Oxbryta for SCD patients.

In January 2021, the European Medicines Agency, or EMA, accepted for review our Marketing Authorization Application, or MAA, seeking full marketing authorization of Oxbryta to treat hemolytic anemia (which is low hemoglobin due to red blood cell destruction) in SCD patients ages 12 years and older, and the MAA is undergoing standard review by the EMA. In addition, we plan to submit by mid-2021 a supplemental New Drug Application, or sNDA, to expand the current Oxbryta label to include treatment of SCD in children ages 4 to 11 years, under the FDA's accelerated approval pathway. Thereafter, we also plan to submit a New Drug Application, or NDA, for a new age-appropriate formulation for this patient population. To provide early access prior to potentially receiving additional marketing approval, we have established an expanded access protocol for eligible SCD patients in the United States and an early access program for eligible SCD patients outside the United States. In addition, we have entered into an exclusive agreement with Biopharma-Middle East and Africa, or Biopharma-MEA, to distribute Oxbryta in the six countries that make up the GCC region (Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, and the United Arab Emirates), where the U.S. approval of Oxbryta can be referenced to allow for access to the medicine while health authorities conduct their reviews.

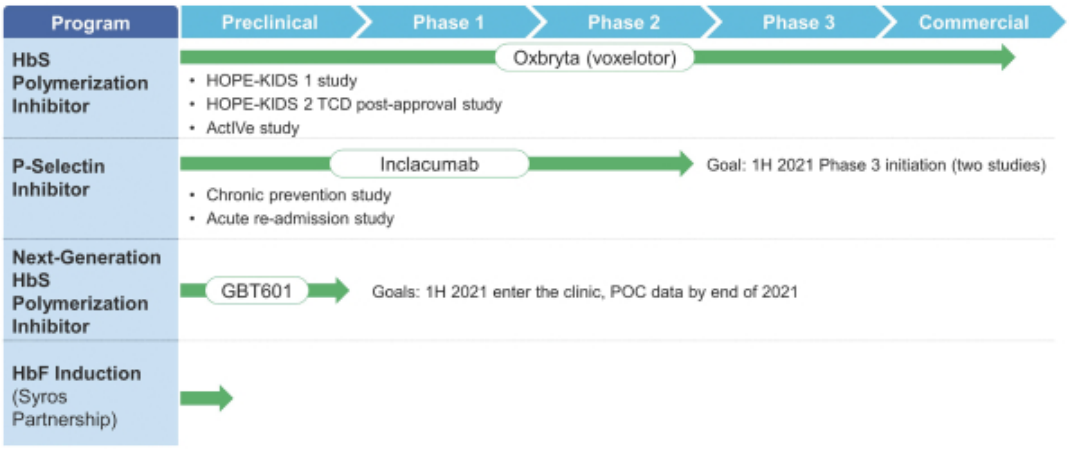
Beyond Oxbryta, we are engaged in other research and development activities, including working on new targets to potentially develop next generation of treatments for SCD, including inclacumab, a P-selectin inhibitor, which is a clinically validated target in SCD, known to reduce the incidence of vaso-occlusive crises, or VOCs, and our next generation hemoglobin polymerization inhibitor, GBT021601, or GBT601. As part of our efforts to build our pipeline, we regularly evaluate opportunities to in-license, acquire or invest in new business, technology or assets or engage in related discussions with other business entities.

In March 2020, the Centers for Disease Control and Prevention, or CDC, declared a global pandemic related to SARS-CoV-2, the virus that causes coronavirus disease 2019, or COVID-19, and the pandemic has impacted our business, including our commercialization of Oxbryta and our research and development activities. For example, we implemented a temporary work from home policy; temporarily suspended our field team from most in-person interactions, including visits to physician offices, clinics and hospitals as well as in-person meetings with payors; and temporarily delayed or paused certain research and development activities, including screening and enrollment in all clinical studies sponsored by us. As we continue to monitor and work toward resumption of all trial activities, we are continuing with administrative trial-start up activities (such as contracting and Institutional Review Board, or IRB, and Ethics Committee, or EC, approvals). Notably, the COVID-19 pandemic has not significantly impacted our supply of Oxbryta. We continue to believe we have an adequate supply of Oxbryta to sustain estimated patient need through 2021, and we are continuing to produce Oxbryta tablets.

We have seen a significant decrease in weekly new patient prescriptions for Oxbryta from a peak in early March 2020, and we expect the rate of new patient prescriptions may remain lower, depending on the course of the pandemic. While we intend to resume normal operations as soon as practicable, we do not know for certain the extent or duration of these and other disruptions or the long-term impact on our business. Since mid-March 2020, when we made the decision to suspend in-person visits to health professionals by our field teams, we have been engaging with healthcare professionals, or HCPs, and payors through increased use of digital and internet-based education and outreach, as well as limited face-to-face engagements in some settings following appropriate COVID-19 protocols.

Product Pipeline

The following table summarizes our approved product and our most advanced research and development programs:



Our lead development candidate is inclacumab, a novel fully human monoclonal antibody against P-selectin, which is a clinically validated target in SCD, known to reduce the incidence of VOCs. We licensed inclacumab from F. Hoffmann-La Roche Ltd. and Hoffmann-La Roche Inc. (together, "Roche") in August 2018. Prior to licensing inclacumab to us, Roche conducted clinical studies that enrolled more than 700 non-SCD patients and demonstrated an encouraging pharmacokinetic, safety, and tolerability profile for inclacumab. We expect to be able to leverage the safety data from Roche's prior clinical studies, as we proceed with our development of inclacumab as a potential treatment to reduce the frequency of VOCs in patients with SCD and to reduce the hospital VOC readmission rate for patients that require inpatient treatment for an initial VOC episode. We expect to initiate two pivotal clinical trials by the end of the first half of 2021. One study will be a chronic prevention study with an endpoint of the reduction in VOCs over a 48-week treatment period, and the other study will focus on hospital readmissions with an endpoint of the reduction of the rate of readmission to hospitals for VOC within 90 days following an initial hospitalization for VOC.

Also in development is our next generation hemoglobin polymerization inhibitor, GBT601, a molecule discovered and designed by scientists at GBT. Preclinical data presented at the 62nd American Society of Hematology (ASH) Annual Meeting & Exposition and our annual Analyst and Investor Day in December 2020, showed why we believe GBT601 has the potential to be a potent hemoglobin S polymerization inhibitor and functional cure of SCD. GBT601 has the same mechanism of action as Oxbryta, but with the potential for greater efficacy by achieving higher hemoglobin occupancy at significantly lower doses. The preclinical data presented at ASH showed that GBT601 improved hemolysis and normalized hemoglobin, and also improved red blood cell survival, health and organ function. In December 2020, we initiated a Phase 1 clinical trial of GBT601 in normal healthy volunteers, and we expect to initiate by mid-2021 a Phase 1 clinical trial on the safety and tolerability of GBT601 in SCD patients.

While still in early stages, we have an ongoing collaboration with Syros Pharmaceuticals, Inc., or Syros, under License and Collaboration Agreement, or the Syros Agreement, entered into in December 2019, to discover, develop and commercialize novel therapies for SCD and beta thalassemia. We are currently exploring orally available, small molecule drugs designed to upregulate fetal hemoglobin. An increase in fetal hemoglobin by 10% to 30% can dilute the concentration of deoxygenated hemoglobin S, which can participate in polymerization, and prevent hemoglobin polymers from forming. Upregulating levels of fetal hemoglobin could be pharmacologically curative for SCD as well as beta thalassemia. Under the Syros Agreement, we have an option to obtain an exclusive worldwide license to develop, manufacture and commercialize any compounds or products resulting from the collaboration, subject to Syros' option to co-promote the first product in the United States.

Strategy

Our mission is to discover, develop and deliver life-changing treatments for people living with grievous blood-based disorders, starting with SCD. We believe that with our first approved medicine, Oxbryta, along with our innovative patient support program, GBT Source Solutions, we have established a strong track record of execution and have made an even stronger commitment to supporting the SCD community. Looking forward, we are working to build on the U.S. launch of Oxbryta with the potential expansion of our FDA label to treat younger patients in the United States, regulatory approval and launch in Europe and the Middle East, and to expand to Latin America. We also have a strong pipeline of potential best-in-class therapies with inclacumab and GBT601, and we actively seek new innovations to complement our portfolio. We are a dedicated leader in SCD, and every day we pursue our goal of making SCD a well-managed chronic condition and to profoundly impact the disparities in healthcare these patients face. Key elements of our strategy are to:

Build on the U.S. launch of Oxbryta and Address Impact of COVID-19.

We launched Oxbryta in the United States in December 2019 and by the end of 2020, thousands of SCD patients were using this first-in-class oral therapy. The growing body of real-world experience suggests that patients have improved overall health while taking Oxbryta. We expect the demand for Oxbryta to continue throughout 2021 and have several ongoing and planned initiatives to build on the ongoing launch:

- We are deploying a variety of patient and healthcare provider marketing materials in support of the Oxbryta launch. Given our accelerated approval in the United States, all marketing materials are required to undergo FDA review before use. Several of our materials have already been approved or are currently under review. These materials include advertisements, social media campaigns, patient starter kits, guides and brochures.
- GBT Source Solutions, our comprehensive program for patients, provides support by reviewing insurance coverage options and explaining benefits, working with the specialty pharmacy partner
- network to coordinate delivery of Oxbryta to wherever the patient chooses, helping with financial and co-pay assistance for eligible patients, and helping patients stay on treatment as prescribed by their treating physicians with a nurse support team. GBT Source Solutions is supported by a team of highly trained professionals and regional, field-based patient navigators that will help patients and provide resources to help HCPs understand insurance requirements and other administrative details when prescribing Oxbryta. The program features a high-touch model, including early contact to introduce the program, explain how the patient will interact with team members, and provide patient starter kits and adherence tools. Those tools include a treatment journal, a side effects management tip sheet, and bottle and app-linked reminders for daily dosing. We believe these tools will help patients better navigate the start of their treatments and help overall adherence.
- Our field team, which consists of approximately 60 Sickle Cell Therapeutic Specialists and 10 Regional Business Directors, continues to engage with nearly 5,000 targeted HCPs to educate them on Oxbryta's broad label.
- We are introducing new education materials with information on the 72-week HOPE Study data presented at the ASH Annual Meeting & Exposition in December 2020, as well as the favorable safety and tolerability and durable efficacy seen with sustained use of Oxbryta.

Shortly after COVID-19 was declared a global pandemic in March 2020, many states where SCD is prevalent were effectively shut down and, in a matter of a few days, we pulled our salesforce from the field for their safety and that of HCPs and patients. We immediately began the process of adapting our sales approach to virtual engagements, and we reengaged HCPs via telephone and video meetings.

In June 2020, the CDC identified SCD as one of a few underlying medical conditions that place adults of any age at increased risk of severe illness and death from the virus that causes COVID-19. We believe the

pandemic directly decreased SCD patient visits to HCPs, with SCD patient visits decreasing sharply early in the second quarter of 2020 and then recovering somewhat to remain for the rest of 2020 at about 70% to 80% of the pre-COVID-19 pandemic baseline. In addition, the weekly number of hospital inpatient admissions for VOCs decreased by 20-50% in the second and third quarters of 2020 as compared to baseline at the beginning of 2020.

The COVID-19 pandemic also impacted new prescriptions of Oxbryta. In the first quarter of 2020, we reported 1,650 new prescriptions. Despite the increasing impact of COVID-19 starting at the end of the first quarter, we added approximately 1,000 new prescriptions in each of the remaining three quarters of 2020. We believe this is an indicator of the underlying demand for Oxbryta. It also reflects increases in the use of telemedicine by HCPs, and our field team's virtual engagements and in-person visits, with safety protocols in place, in the geographies that allowed in-person interaction.

When the pandemic subsides, we expect that, over time, the number of new Oxbryta prescriptions will grow and surpass pre-COVID-19 pandemic levels. We also expect that our initiatives will help improve patient adherence to Oxbryta, which is an important lever for chronic therapies.

Expand clinical data and potential approved product labeling supporting Oxbryta.

We have a comprehensive plan to continue to build clinical evidence supporting the safety and efficacy of Oxbryta, now that our Phase 3 HOPE Study that provided the support for accelerated approval of the product has concluded. This plan includes studies designed to demonstrate that improving hemoglobin and reducing hemolysis leads to an improvement in organ dysfunction (as assessed in various organs) and exercise capacity.

We are continuing to study Oxbryta in the ongoing Phase 2a HOPE-KIDS 1 Study, an open-label, single- and multiple-dose trial evaluating the safety, tolerability, pharmacokinetics and exploratory treatment effect of Oxbryta in pediatric patients aged 4 to 17 years with SCD, and our HOPE-KIDS 2 Study, a Phase 3 clinical trial that we intend to satisfy the FDA's requirement for us to complete at least one post-approval confirmatory study. Initiated in December 2019, our HOPE-KIDS 2 Study is using TCD flow velocity to seek to demonstrate a decrease in stroke risk in children 2 to 15 years of age. The ActIVe Phase 4 study, a pilot, open-label, single-arm study, aims to evaluate the effect of Oxbryta on activity levels and sleep quality, as measured by actigraphy in patients 12 years of age and older with SCD. In addition, we are planning a comprehensive program to gather and evaluate real world evidence and historical data to further review the long-term connection between improvements in hemoglobin and organ damage and longer-term outcomes, with an initial focus on stroke and silent infarct. We also plan to study the potential effects of Oxbryta on leg ulcer healing, blood flow within the brain and neurocognitive function and we plan to assess pulmonary hypertension and resting oxygen saturation. These and other aspects of our overall clinical development program for Oxbryta are also intended to position us to be able to seek potential approval over time for product labeling for Oxbryta for patients younger than the current age limit (12 years old), down to as young as 9 months of age.

By mid-2021, we plan to submit a sNDA to expand the current Oxbryta label to include treatment of SCD in children ages 4 to 11 years, under the FDA's accelerated approval pathway, which submission will include clinical data from our Phase 2a HOPE-KIDS 1 study. Thereafter, we also plan to submit an NDA for a new age-appropriate formulation for this patient population. In addition, we initiated a multi-center expanded access protocol in the United States for pediatric patients to provide access to treatment with Oxbryta prior to potential market authorization for children ages 4 to 11 years who, in the judgment of their treating physician, have an urgent need for treatment for their SCD, have no comparable or satisfactory treatment options and are unable to participate in our clinical trials.

Expand the approved use of Oxbryta in Europe, the Middle East and Latin America.

In Europe, there are approximately 52,000 SCD patients, the majority of whom are in two countries, France and the United Kingdom. In December 2020, we initiated an early access program in Europe and other regions

outside the United States, for the treatment of hemolytic anemia in SCD patients ages 12 years and older. Through the program, physicians in countries with an early access regulatory and legal pathway may be able to request voxelotor for eligible SCD patients who do not have access to the medicine as part of a clinical trial.

In January 2021, the EMA accepted for review our MAA seeking full marketing authorization of Oxbryta to treat hemolytic anemia (which is low hemoglobin due to red blood cell destruction) in SCD patients ages 12 years and older. The MAA is undergoing standard review by the EMA, and we could potentially secure approval as early as first or second quarter of 2022. The MAA is based on data from our Phase 3 HOPE Study and our Phase 2 HOPE-KIDS 1 Study, both of which enrolled patients at clinical sites in Europe. The EMA has included Oxbryta in its Priority Medicines (PRIME) program, and the European Commission, or EC, has designated Oxbryta as an orphan medicinal product for the treatment of patients with SCD. In addition, we currently plan to submit a separate application for the potential approval of Oxbryta in Great Britain that would rely on the decision, if positive, taken by the EC on our current MAA, as described below under “Regulatory Path for Oxbryta in International Markets.”

In the GCC region, where there are estimated to be more than 100,000 SCD patients age 12 years and older, we established an exclusive agreement with Biopharma-MEA to potentially secure regulatory approvals and distribute Oxbryta in the GCC region. In the GCC region, the U.S. approval of Oxbryta can be referenced to allow for access to the medicine while health authorities conduct their reviews.

In Latin America, where there are approximately 100,000 SCD patients, mostly in Brazil, we plan to establish a distribution agreement with a local partner to potentially secure regulatory approvals and distribute Oxbryta in this market.

Advance our innovative pipeline: inclacumab, GBT601 and other next-generation treatments.

Our strategy includes the expansion of our product pipeline through the discovery and development of novel therapeutic approaches for SCD and grievous blood disorders, including with our internal programs of inclacumab and GBT601 and under our collaboration with Syros. In addition, our drug discovery and business development teams actively work on an ongoing basis on new opportunities to expand our product pipeline.

Improve care for SCD patients worldwide.

The majority of the global SCD patient population is outside of the United States, including more than 75% of the global incidence in sub-Saharan Africa and large populations in India, the Middle East, and Latin America. Each of these regions represent unique challenges to providing access due to complex healthcare systems and will require a customizable approach that meets the needs of the local community. Our clinical programs include sites outside of the United States, and participants in our clinical trials will have an opportunity to continue to receive Oxbryta until it is available in their countries. We are developing strategies to make Oxbryta available to all patients in these regions in a manner that is sustainable for us over the long term.

Key 2020 Highlights

Regulatory/Commercial

- In 2020, we executed the commercial launch of Oxbryta in the United States, leveraging our field team and GBT Source Solutions to educate HCPs, payors and other stakeholders on Oxbryta. Over the course of the year, we secured FDA approval for patient and healthcare provider marketing materials in support of the Oxbryta launch.
- In March 2020, we adapted our commercial launch of Oxbryta to the challenging environment created by the COVID-19 pandemic through proactive measures to reduce the risk of spreading the COVID-19 virus among our employees, customers, business partners and local communities.
- In June 2020, we announced plans to seek the potential expansion of the use of Oxbryta for the treatment of SCD in children ages 4 to 11 years.

- In June 2020, we announced plans to submit an MAA to the EMA for Oxbryta to treat hemolytic anemia in SCD patients ages 12 years and older by mid-2021, and, in January 2021, we were notified that the EMA has completed the validation of the MAA we submitted and has started its standard review process.
- In September 2020, we announced our entry into an exclusive agreement with Biopharma-MEA to distribute Oxbryta in the GCC region.
- As of the end of September 2020 (a quarter ahead of our goal), we achieved broad payer coverage for Oxbryta in the United States, defined as 90% of lives covered by payers either through published policies or verified patient adjudication.
- In December 2020, we initiated two early access programs for Oxbryta. One is in Europe and other regions outside the United States, for the treatment of hemolytic anemia in eligible SCD patients ages 12 years and older, and the other is a multi-center expanded access protocol in the United States for eligible pediatric SCD patients to provide access prior to potential market authorization for children ages 4 to 11 who have no alternative treatment options.

SCD Community

- In March 2020, as a response to the COVID-19 pandemic and its impact on the SCD community, we created the GBT Community Fund, under which we provided $150,000 in grants to support the acute needs of SCD patients and families during the pandemic. At that time, we also made a donation of $100,000 to the Sickle Cell Disease Association of America (SCDAA) in response to its urgent call for its COVID-19 Emergency Fund, and employees and members of our Board of Directors contributed more than $100,000 to support the SCD community during the pandemic.
- In June 2020, we awarded a total of $250,000 in grants to five non-profit organizations through our Access to Excellent Care for Sickle Cell Patients (ACCEL) Grant Program. The program provides grant funding to support novel projects aimed at improving access to high-quality healthcare for individuals with SCD.
- In September 2020, we hosted the 9th Annual Sickle Cell Disease Therapeutics Conference, which featured discussions about the latest advances and future trends in the treatment of SCD, and the impact of COVID-19 on this vulnerable patient population.
- In December 2020, as part of the GBT Gives Back initiative, GBT employees donated more than $40,500 to sickle cell organizations across the globe.

Medical Meeting Presentations and Publications

- In June 2020, we presented four abstracts at the virtual edition of the 25th Annual European Hematology Association Congress. This included a retrospective analysis of data from the landmark STOP 2 study (Stroke Prevention in Sickle Cell Anemia) linking higher Hb levels to lower TCD flow velocity, a predictor of stroke risk in children with SCD, and three encore presentations of the pivotal Phase 3 HOPE Study that reinforced key attributes of Oxbryta.
- In October 2020, we presented two abstracts that provide greater insight into the safety and efficacy of Oxbryta at the 15th Annual Scientific Conference on Sickle Cell and Thalassemia (ASCAT) and 1st EHA European Sickle Cell Conference.
- In December 2020, we presented nine abstracts related to our SCD programs at ASH, including the 72-week analysis of the completed Phase 3 HOPE Study of Oxbryta, real-world evidence supporting the use of Oxbryta, and new research on our pipeline programs, inclacumab and GBT601.

Corporate

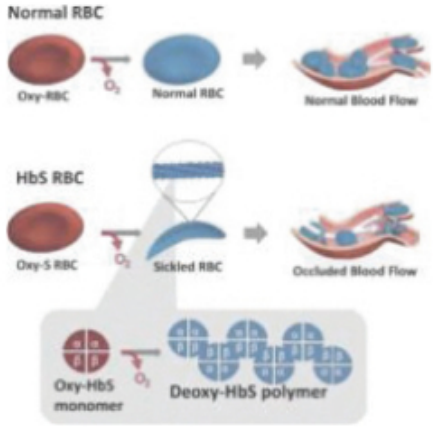
- We announced the appointment of a head of research and development who is expected to join us in May 2021 and, in August 2020, we added a chief medical officer to our senior management team.
- In October 2020, we received the 2020 Rare Impact Award® for Industry Innovation for Oxbryta from the National Organization for Rare Disorders (NORD); in addition, Oxbryta was selected as Breakthrough Drug of the Year by the 2020 National Xconomy Awards.

Further Details on SCD

SCD is a devastating and rare inherited blood disorder that impacts hemoglobin, a protein carried by RBCs that delivers oxygen to tissues and organs throughout the body. It attacks every organ in the body and causes a wide range of complications, including inflammation, multi-organ damage and failure and early death. Many of these start with anemia and hemolysis. Beginning in childhood, patients can suffer unpredictable and recurrent episodes or crises of severe pain due to blocked blood flow to organs, which often lead to physical and psychosocial disability. In addition, the constant destruction of RBCs and the release of their contents into the blood often leads to damaged or diseased blood vessels, which further exacerbate blood flow obstruction and multi-organ damage. Consequences of SCD can manifest in early childhood and may include stroke, spleen failure, pulmonary hypertension, acute chest syndrome, liver disease, kidney failure, leg ulcers, priapism, which is a medical emergency due to refractory penile erection, and premature death. In the United States, SCD has been estimated to shorten patient life expectancy by approximately 30 years even with available medical care.

SCD is a genetic blood disorder caused by a single gene mutation in the beta-chain of hemoglobin, which results in mutant hemoglobin known as HbS. Hemoglobin is the protein in RBCs that carries oxygen from the lungs to the body's tissues, releases oxygen at the tissues, and returns carbon dioxide from the tissues back to the lungs. Hemoglobin accomplishes this by binding and then releasing oxygen through allosterism, which means the hemoglobin molecule changes its shape to have a high affinity for oxygen in the lungs, where oxygen is abundant, and to have a low affinity for oxygen in the tissues, where oxygen must be released. Oxyhemoglobin, the high oxygen affinity form of hemoglobin, is formed in the lungs during respiration, when oxygen binds to the hemoglobin molecule. Deoxyhemoglobin, the low oxygen affinity form of hemoglobin, is formed when oxygen molecules are removed from the binding site as blood flows from the lungs to the tissues in the body. In patients with SCD, deoxygenated HbS molecules polymerize to form long, rigid rods within an RBC, much like a "sword within a balloon." As a consequence, the normally round and flexible RBC becomes rigid and elongates into a "sickled" shape. Sickled RBCs do not flow properly in the bloodstream; they clog small blood vessels and reduce blood flow to the organs. This results in inadequate oxygen delivery, or hypoxia, to all body tissues, which can lead to multi-organ failure and premature death.

The following graphic illustrates the process by which sickling occurs in SCD patients as a result of the polymerization of deoxygenated HbS in an RBC, leading to occluded blood flow, in contrast to a normal RBC:



SCD manifests in individuals who inherit at least one HbS gene from a parent and an additional mutation on the second beta globin gene from the other parent. There are several different genotypes of SCD, including the following major genotypes:

- HbSS, or sickle cell anemia, where both genes are HbS;
- HbSC, where one gene is HbS, and the other is HbC (inherited from a non-SCD impacted parent); and
- HbS/ßthal, where one gene is HbS, and the other is Beta thalassemia.

SCD Patient and Community Impact

The Centers for Disease Control and Prevention, or CDC, estimates the prevalence of SCD at more than 100,000 individuals in the United States. The incidence of SCD is estimated at approximately 1 in 2,000 to 2,500 newborns in the United States. In addition, there an estimated 52,000 individuals in Europe, more than 100,000 people age 12 years and older in the GCC region and approximately 100,000 individuals in Latin America, primarily in Brazil, living with the disease. SCD occurs predominantly in populations of African, Middle Eastern and South Asian descent, and the global incidence of is estimated to be 250,000 to 300,000 births annually. While newborn screening is mandatory in the United States, Brazil, Costa Rica, France, United Kingdom, Spain and Netherlands, it remains inconsistent in countries throughout other regions of the world including Europe, Latin America, Middle East, South Asia and sub-Saharan Africa.

Of SCD patients in the United States, approximately 45% are under the age of 18, and approximately 60% to 65% have the HbSS genotype, which is often referred to as sickle cell anemia, with the remaining 35% to 40% having other genotypes. In all genotypes of SCD, the mechanism that leads to the consequences of the disease involves the polymerization of HbS in its deoxygenated state, which results in RBC sickling. Our Phase 3 HOPE Study included SCD patients with all genotypes of SCD, and showed Oxbryta is active across all SCD genotypes. As a result, Oxbryta is approved for use with all SCD genotypes.

SCD is associated with a high healthcare utilization and economic burden. It is estimated that in the United States, the annual cost of medical care for an SCD patient with complications is up to $286,000 and that end-organ damage drives major healthcare utilization, with an average SCD patient receiving healthcare services for 30 to 54 days per year. In addition, there is potential for a significant financial burden on patients and society: it is estimated that SCD patients are deprived of approximately $700,000 in lost lifetime income, not including the impact on caregiver productivity. As a result, we believe that a safe, effective and convenient oral treatment for SCD has the potential to be well received by patients, physicians and payors.

Nearly 50% of SCD patients will experience one or more VOCs in a year. At least 80% of all hospitalizations of SCD patients are for a VOC, and in around 50% of these cases, the patient will be readmitted within 90 days for another VOC, adding to the cost of the index hospitalization. As a result, we believe that a safe, effective and convenient treatment that can reduce the frequency of VOCs and related hospital readmissions has the potential to be well received by patients, physicians and payors.

Other Current Treatment Options

There has historically been limited innovation in the development of SCD therapies and there remains a significant unmet medical need for SCD patients. In recent years this has begun to change, including the FDA approval of Oxbryta in November 2019, and a significant increase in orphan drug approvals by the FDA. However, there are limitations to other currently approved treatment options.

The first drug approved to treat SCD, known as hydroxyurea, which was initially approved as a chemotherapy drug, was approved by the FDA in 1998 for the treatment of sickle cell anemia in adults with three or more painful crises per year. The use of hydroxyurea is significantly limited by its side effect profile, variable patient responses and concerns regarding long-term toxicity. Hydroxyurea's side effects include impairment of fertility, suppression of white blood cells, or neutropenia, and suppression of platelets, or thrombocytopenia, which place patients at risk for infection and bleeding.

In July 2017, the FDA approved L-glutamine oral powder for patients age five and older with SCD to reduce severe complications associated with the disorder. In January 2018, Emmaus Life Sciences, Inc., the marketer for Endari® (L-glutamine oral powder) announced the availability of the product to patients. Endari is supplied to patients as powder that requires a large volume administration (5 grams—15 grams) mixed with liquid or food twice a day.

In November 2019, the FDA approved Adakveo® (crizanlizumab) to reduce the frequency of VOCs, or pain crises, in adult and pediatric patients aged 16 years and older with SCD, and it was made available to patients before the end of 2019. Crizanlizumab is administered via a 30-minute intravenous, or IV, infusion given once per month by a health care provider.

In addition to treatment with hydroxyurea, L-glutamine and crizanlizumab, transfusions with normal blood are an option to help alleviate anemia, which is a common symptom of SCD, and reduce sickling of RBCs. Blood transfusions have a number of limitations, including the expense of treatment, lack of uniform accessibility and risks ranging from allergic reactions to serious complications such as blood-borne infection and iron overload, which can cause organ damage. The only potentially curative treatment currently available for SCD patients is bone marrow transplantation, which requires a suitable matching donor and carries significant risks, including an approximately 5% mortality rate. Despite these other current treatment options, blood transfusion and palliative therapy for acute pain attacks, patients with SCD continue to suffer serious morbidity and premature mortality.

In light of the devastating effects of SCD on patients and the high costs of care for these patients, there has been a significant unmet need for a treatment that:

- inhibits abnormal hemoglobin polymer formation, the underlying mechanism of RBC sickling;
- stops inappropriate RBC destruction and improves blood flow and oxygen delivery to tissues;
- reduces hemolytic anemia that leads to chronic organ damage and early mortality in patients with SCD;
- prevents or reduces the episodes or crises of severe pain associated with SCD;
- modifies the long-term course of the disease;
- is effective in all SCD genotypes and in both children and adults;

- has a more favorable side effect profile than currently available therapies; and
- is available as a convenient, oral therapy.

In addition, while there have been therapies approved to treat patients with VOCs, or pain crises, there remains an opportunity to improve care with a treatment that:

- similar to crizanlizumab, reduces the frequency of VOCs, but with a more convenient dosing schedule; and
- reduces the hospital re-admission rate due to VOCs in patients that are admitted to the hospital for a VOC.

Oxbryta – *Mechanism, Development and Approval*

In November 2019, we received FDA accelerated approval for Oxbryta for the treatment of SCD in adults and children 12 years of age and older. Oxbryta, an oral, once-daily therapy, is the first FDA-approved treatment that directly inhibits sickle hemoglobin polymerization, the root cause of SCD. We believe the label for Oxbryta highlights several important attributes for physicians and patients, including:

- A broad indication for use with no hemoglobin level restrictions and no clinically significant differences in the pharmacokinetics based on age, sex, body weight or mild to severe renal impairment;
- A specific description of Oxbryta as a hemoglobin S polymerization inhibitor that may inhibit RBC sickling, improve RBC deformability, and reduce whole blood viscosity;
- No restriction on use with or without hydroxyurea; and
- Clinical data highlights from the HOPE Study, including the subject-level change from baseline in hemoglobin at week 24 in patients who completed 24 weeks of treatment with Oxbryta 1500 mg dose or placebo.

Overview of Hemoglobin Biology and Oxbryta's Mechanism of Action

Hemoglobin transports oxygen from the lungs to the body's tissues, releases oxygen into the tissues, and returns carbon dioxide from the tissues back to the lungs by changing its shape to be high affinity for oxygen in the lungs, where oxygen is abundant, and low affinity for oxygen in the tissues, where oxygen must be released. An important tool for assessing how readily hemoglobin acquires and binds oxygen in the lungs and releases oxygen into the tissues is the oxygen equilibrium curve, or OEC. The OEC represents the proportion of oxyhemoglobin, measured as the percentage of oxygen saturation (O_2 % saturation) on the vertical axis relative to the amount of oxygen dissolved in blood, indicated as the oxygen tension, or partial pressure of oxygen (pO_2) measured in millimeters of mercury (mmHg), on the horizontal axis.

We have demonstrated in preclinical models that our novel hemoglobin modifiers, including Oxbryta, bind to hemoglobin, resulting in increased oxygen affinity. The effect of Oxbryta on the measured OEC is a shift of the curve to the left. In other words, at a given prevailing oxygen tension in the blood, we have observed a higher percentage of oxygen saturation, or a higher proportion of oxyhemoglobin in the blood, following the administration of Oxbryta.

In several preclinical studies of SCD, scientists have demonstrated that hemoglobin in the oxygenated state is a potent inhibitor of HbS polymerization. Since HbS polymerization occurs in the deoxygenated state, we believe that increasing the proportion of oxyhemoglobin, or "left-shifting" the OEC, should delay the polymerization of HbS and prevent the sickling of RBCs, which may ameliorate many of the clinical manifestations of SCD. Importantly, we are able to measure the proportion of hemoglobin modification (%HbMOD), which is expressed as the percentage of hemoglobin molecules occupied or bound by Oxbryta.

HbF, which is present during fetal development and persists for up to six to nine months in infants until it is replaced by adult hemoglobin, has an inherent high affinity for oxygen, which is critical for a developing fetus to capture oxygen from the mother's blood. Newborns with SCD do not experience RBC sickling until approximately six to nine months of age, after which HbF is no longer expressed. Additionally, it has been observed that rare individuals who have inherited the HbS mutation and a gene modification that allows them to continue to express 10% to 30% HbF in their RBCs into adulthood do not exhibit the clinical manifestations of SCD, despite expressing up to 90% HbS in their blood. HbF dilutes the concentration of deoxygenated HbS that can participate in polymerization, and, thereby, prevents hemoglobin polymer from forming.

Based on these observations, during our development of Oxbryta we posited that to delay polymerization of HbS, Oxbryta would need to bind to only approximately 10% to 30% of the total hemoglobin in a patient's blood. One theoretical concern regarding increasing the affinity of hemoglobin for oxygen is that excessive oxygen affinity could prevent hemoglobin from releasing oxygen into the tissues, thus causing hypoxia. However, we have not observed any findings from our clinical programs that demonstrated any evidence of such tissue impairment. Based on HbF data, our animal toxicology studies, and our clinical studies, we believe our target modification of the total hemoglobin in a patient's blood does not adversely compromise oxygen delivery to the tissues. This is supported by exercise testing we have performed in SCD patients and healthy volunteers showing normal oxygen consumption and the absence of a dose level or exposure related increase in erythropoietin levels in patients enrolled in the HOPE Study.

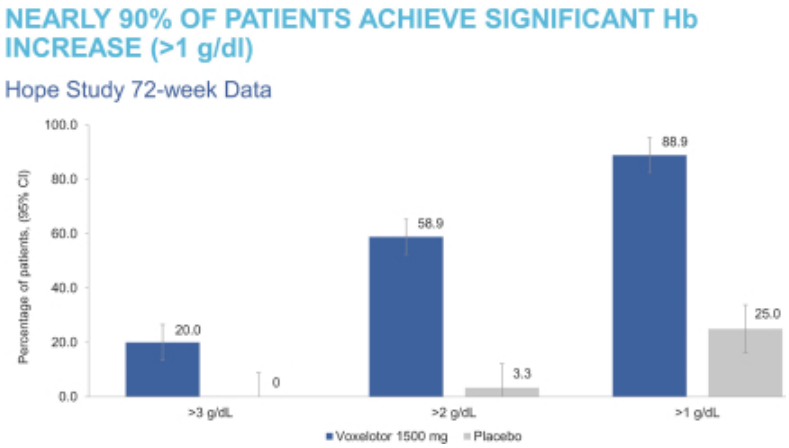
Oxbryta increases hemoglobin's affinity for oxygen by binding to the alpha-chain of hemoglobin. Oxbryta has been demonstrated keep a proportion of HbS in its oxygenated state so it cannot participate in polymerization. Similar to HbF, by diluting total HbS with a proportion of Oxbryta-bound hemoglobin, Oxbryta prevents hemoglobin polymer formation. Based on its mechanism of action, we believe that Oxbryta can reduce the physical and clinical manifestations of SCD.

Overview of Phase 3 and Other Oxbryta Clinical Trials

Phase 3 HOPE Study

We completed a randomized, double-blind, placebo-controlled, multi-national Phase 3 clinical trial of Oxbryta in adult and adolescent patients with SCD that we refer to as the HOPE (Hemoglobin Oxygen Affinity Modulation to Inhibit HbS PolymErization) Study, the interim results of which we used as the basis for our accelerated approval under Subpart H of FDA's NDA regulations. Data from the Phase 3 HOPE Study of 274 patients 12 years of age and older with SCD showed that the HOPE Study met its primary endpoint of an improvement in hemoglobin greater than 1 g/dL at 24 weeks with Oxbryta 1500 mg compared with placebo: After 24 weeks of treatment, 51.1% of patients receiving Oxbryta achieved a greater than 1 g/dL increase in hemoglobin compared with 6.5% receiving placebo ($p<0.001$). In addition, the data demonstrated corresponding improvements in other markers of hemolysis as well as a favorable safety and tolerability profile for Oxbryta. These interim Phase 3 HOPE data were published in the June 2019 issue of the *New England Journal of Medicine*.

In connection with the accelerated approval of Oxbryta, we submitted the final study report for the Phase 3 HOPE Study to the FDA in September 2020. This report included completed long-term results from the Phase 3 HOPE Study, which demonstrated that Oxbryta at 1500 mg resulted in durable improvements in hemoglobin levels and markers of hemolysis up to 72 weeks of treatment. As shown in the following graph, a large majority of patients (approximately 90%) achieved a Hb improvement of >1 g/dL from baseline at one or more time points during the study as compared to placebo (approximately 25%). The study also found significant improvements in markers of hemolysis in indirect bilirubin and reticulocyte percentage. Consistent with the 24-week data, treatment with Oxbryta remained well tolerated. The most common side effects reported were headache, diarrhea, abdominal pain, nausea, arthralgia, rash and pyrexia.



Hb, hemoglobin
Source: Long-Term Efficacy and Safety of Voxelator in Adolescents and Adults with Sickle Cell Disease: HOPE Trial 72-Week Analysis, ASH 2020 Poster #1716

As presented at the ASH Annual Meeting & Exposition in December 2020, the annualized incidence rates of VOCs were numerically lower in patients receiving Oxbryta 1500 mg (2.4) than placebo (2.8); and this numerical difference was greater in patients who had experienced two or more VOCs in the year prior to the study. In addition, a post-hoc analysis of the long-term results from the Phase 3 HOPE Study found that higher hemoglobin levels achieved with Oxbryta were associated with a lower incidence of VOCs over 72 weeks. Patients with the highest average hemoglobin levels over 72 weeks experienced the fewest VOCs with Oxbryta, with a stepwise reduction in VOC rate as hemoglobin levels increased. While the Phase 3 HOPE Study was not designed or powered to show an effect on VOCs, these results suggest the importance of reducing hemolysis and raising hemoglobin in individuals with SCD through inhibition of polymerization.

Another analysis of the long-term results from the Phase 3 HOPE Study used the Clinical Global Impression of Change (CGI-C) scale, a validated outcomes measure that provides a holistic assessment of the effect of treatment. Results showed that treatment with Oxbryta compared to placebo resulted in a statistically significant higher rating of improved overall patient health status after 72 weeks by the treating physician.

As part of the accelerated approval for Oxbryta, we agreed with the FDA to complete at least five years of follow-up for all patients on treatment and submit to the FDA interim reports each year in June from 2021 to 2025.

Real-World Use Studies

Data and analyses from real-world experience with Oxbryta were presented at the ASH Annual Meeting & Exposition in December 2020, including:

- An analysis evaluating Symphony Health claims data from a subset of 1,275 SCD patients ages 12 and older treated with Oxbryta, which showed statistically significant reductions in annualized transfusion rates and a reduced annual rate of VOC events following the initiation of Oxbryta therapy.
- A study from a single-center case series showed that both patients and clinicians observed improved health status based on the Patient Global Impression – Improvement (PGI-I) and the Clinical Global Impression – Improvement (CGI-I) scales to examine patient and clinician perception of health status in patients treated with Oxbryta. In addition, while cases of gastrointestinal side effects were reported at a rate of incidence similar to that as the HOPE Study, patients were successfully managed with adjustments to dosing regimens and persisted on treatment.

Additional Studies

We are conducting and plan to conduct additional clinical trials of Oxbryta, including our ongoing Phase 2a HOPE-KIDS 1 Study, our recently initiated Phase 3 HOPE-KIDS 2 Study a dose optimization study, and the ActIVe Phase 4 study. The HOPE-KIDS 1 Study, the HOPE-KIDS 2 Study and other aspects of our overall clinical development program for Oxbryta are also intended to position us to be able to seek approval over time for product labeling for Oxbryta for patients younger than the current age limit (12 years old), down to as young as 9 months of age.

Phase 2a HOPE-KIDS 1 Study

We are continuing to evaluate the safety and pharmacokinetics of single and multiple doses of Oxbryta in adolescent and pediatric patients with SCD in an ongoing Phase 2a clinical trial, which we call the HOPE-KIDS 1 Study. Initiated in August 2016, our ongoing HOPE-KIDS 1 Study is an open-label, single- and multiple-dose Phase 2a study that is evaluating the safety, tolerability, pharmacokinetics and exploratory treatment effect of Oxbryta in pediatric patients aged 4 to 17 years with SCD. Part A of the study evaluated a single 600 mg dose of Oxbryta in 13 patients aged 6 to 17 years, while Part B was designed to explore Oxbryta at doses of 900 mg and 1500 mg per day administered to 40 patients ages 12 to 17 for 24 weeks. Part C of the study is evaluating Oxbryta at a single 1500 mg dose (or weight-based equivalent) in patients age 4 to 17 years for up to 48 weeks, and Part D of the study is evaluating the safety of Oxbryta at the weight based equivalent of 1500 mg in patients age 9 months to under 4 years as measured by Treatment Emergent Adverse Events, or TEAEs, and Serious Adverse Events, or SAEs.

Part A pharmacokinetics, or PK, data in adolescents (12 to 17 years) demonstrated that the PK and half-life of Oxbryta were similar in adolescents and adults with results supporting once-daily dosing. Part A data for pediatric patients (6 to 11 years) demonstrated that PK exposures were higher in children compared with adolescents and adults, which informed dose selection for future pediatric studies in children under 12 years of age.

The primary objective of Part B was to assess the effect of Oxbryta on anemia. Secondary objectives include effect on clinical measures of hemolysis and PK profile. Additionally, we were able to assess the exploratory endpoint of TCD flow velocity measures in this study as TCD is a measure of stroke risk in pediatric and adolescent SCD patients. TCD measurement was not a primary or secondary endpoint or eligibility criteria in the HOPE KIDS-1 Study. Part B demonstrated a hematologic response to Oxbryta therapy, as evidenced by improvements in one or more markers of hemolysis and anemia (hemoglobin, unconjugated bilirubin and percentage reticulocyte counts).

Part C is currently enrolling patients age 4 to 17 years and will assess, as its primary endpoint, change in cerebral blood flow as measured by TCD flow velocity. Secondary measures include effect on clinical measures of hemolysis, change in cerebral blood flow and PK profile. We currently expect to complete the study in 2022.

Part D began enrolling patients age 9 months to under 4 years in 2020, and will assess, as its primary endpoint, the safety of a weight based equivalent of 1500 mg. Secondary measures include effect on clinical measures of hemolysis and PK profile.

Phase 3 HOPE-KIDS 2 Study

As a condition of accelerated approval of Oxbryta in the United States, and to potentially obtain full regulatory approval for Oxbryta, we will continue to study Oxbryta in the HOPE-KIDS 2 Study, a post-approval confirmatory study we initiated in December 2019 that is using TCD flow velocity to seek to demonstrate a decrease in stroke risk in children 2 to 15 years of age. HOPE-KIDS 2 is a randomized, placebo-controlled Phase 3 trial that will enroll approximately 220 patients with conditional TCD flow velocity (170-199 cm/sec) at about 50 sites in the United States, Europe and Africa. The primary objective of the study is to evaluate the effect of

Oxbryta on reducing the risk of stroke in children with SCD at 24 weeks months using mean change in TCD levels. Key secondary measures include conversion to normal or abnormal TCD at 96 weeks, change in hemoglobin over time and effect on clinical measures of hemolysis.

HOPE-KIDS 2 trial activities are ongoing and screening of participants has begun. We continue to focus on site training in the United States, Africa and MENA region, and enrollment of the first patient is planned for the first quarter of 2021. The overall treatment period will be 96 weeks, and, in connection with the accelerated approval of Oxbryta, we have agreed with the FDA to submit the interim study report by July 2025, complete the trial by March 2026 and to submit the final study report by September 2026.

Dose Optimization Study

As part of our overall life cycle management for Oxbryta, we have initiated a Phase 2 clinical trial to assess higher doses of Oxbryta, up to 3000 mg per day.

ActIVe Study

In order to demonstrate that Oxbryta provides a clinical benefit, we recently initiated the Phase 4 ActIVe (Actigraphy Improvement with Voxelotor) Study to evaluate daily physical activity in SCD patients 12 years of age and older who are on Oxbryta therapy.

Sales and Marketing

We assembled our commercial team and infrastructure, including up to approximately 75 internal sales personnel, key payer account management, marketing and patient and distribution support, ahead of our FDA approval of Oxbryta as part of our plan to commercialize Oxbryta as soon as practicable after approval. As such, we were able to make Oxbryta available in early December 2019. We plan to continue to efficiently support the commercial launch of Oxbryta with this targeted commercial organization, given the number of SCD patients in the United States and their geographic concentration primarily in only 17 states. In addition, the prescribing audience is concentrated as many SCD patients receive care from a hematologist or another sickle cell care provider.

We are also providing a comprehensive patient support program, called GBT Source Solutions, to support our commercialization. This high-touch support program helps patients through the entire process by (i) reviewing insurance coverage options and explaining benefits; (ii) working with the specialty pharmacy partner network to coordinate delivery of Oxbryta to wherever the patient chooses; (iii) helping with financial and copay assistance for eligible patients; and (iv) helping patients stay on treatment as prescribed by their treating physicians with a nurse support team.

With respect to commercializing Oxbryta outside of the United States, we are beginning to build a small team and additional capabilities that may be necessary to effectively support such potential commercialization, subject to any required approval. These capabilities will likely focus on a limited number of core European markets, where SCD is prevalent. Where appropriate, we may also utilize strategic partners, distributors or contract sales forces to expand the commercial availability of Oxbryta.

We currently do not expect that we will require large pharmaceutical partners for the commercialization of Oxbryta or our product candidates, although we may consider partnering in certain territories, New Molecular Entities, or NMEs, or indications for other strategic purposes. We intend to continue to evaluate our commercialization strategy as we advance our programs.

Competition

The biopharmaceutical industry is highly competitive. There are many public and private biopharmaceutical companies, universities, governmental agencies and other research organizations actively engaged in the research and development of products that may be similar to our product candidates or address similar markets. In addition, the number of companies seeking to develop and commercialize products and therapies similar to Oxbryta and our product candidates is likely to increase.

With respect to Oxbryta, inclacumab and GBT601, we face competition from the three currently FDA-approved treatments: hydroxyurea (marketed under several brand names, including Siklos® by Medunik USA, Inc., and Droxia® by Bristol-Myers Squibb Company, as well as in generic form), approved to reduce the frequency of painful crises and need for blood transfusions in patients with sickle cell anemia for the treatment of adults and pediatric patients age two years and older with SCD; Endari® (marketed by Emmaus Medical, Inc.), approved to reduce acute complications of SCD in patients age five years and older; and Adakveo (marketed by Novartis Pharmaceuticals Corporation), approved to reduce the frequency of VOCs in adult and pediatric patients age 16 years and older with SCD. Multiple companies are developing product candidates for chronic treatment in SCD, and several other companies are in early clinical trials to investigate new mechanisms of action for the chronic treatment of SCD. For example, Forma Therapeutics Holdings, LLC, with FT-4202, and Agios Pharmaceuticals, Inc. with mitapivat, are separately evaluating pyruvate kinase-R, or PKR, activators in clinical development for the potential treatment of SCD. We may also face competition from one-time therapies for patients with severe SCD, including hematopoietic stem cell transplantation, gene therapy and gene editing. For example, bluebird bio, Inc., is currently engaged in the clinical development of LentiGlobin, which aims to treat SCD by inserting a functional human beta-globin gene into the patient's own hematopoietic stem cells, or HSCs, ex vivo and then transplanting the modified stem cells into the patient's bloodstream. Bluebird has indicated its plans to pursue an accelerated development and approval pathway for its gene therapy product in SCD. In addition, gene editing, which is the process of altering specific sequences of genomic DNA, is being investigated by multiple companies for the potential treatment of SCD. For example, CRISPR Therapeutics AG is currently engaged in the clinical development of CTX001 for the potential treatment of SCD, under its collaboration with Vertex Pharmaceuticals Incorporated that is focused on the use of CRISPR's CRISPR/Cas9 gene-editing technology to discover and develop potential new treatments aimed at the underlying genetic causes of human disease. In addition, several agents are in development for the treatment of VOC in patients with SCD.

Some of our potential competitors, alone or with their strategic partners, have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of treatments and the commercialization of those treatments. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, are more convenient or are less expensive than any products that we may develop. Our competitors may also obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market.

Regulatory Path for Oxbryta in International Markets

In January 2021, the EMA validated our MAA, submitted under the Centralized Procedure, seeking full marketing authorization, or MA, of Oxbryta to treat hemolytic anemia in SCD patients ages 12 years and older. The MAA is under a standard review by the EMA and we could potentially secure regulatory approval as early as the first or second quarter of 2022.

Now that the UK (which includes Great Britain and Northern Ireland) has exited the European Union, or EU, often referred to as Brexit, Great Britain will no longer be covered by centralized MAs granted by the EC,

which, if granted, will include our MA for Oxbryta (while, under the Northern Irish Protocol, centralized MAs will continue to be recognized in Northern Ireland). As such, potential regulatory approval of Oxbryta in Great Britain will now require an application to the UK medicines regulator, the Medicines and Healthcare products Regulatory Agency, or MHRA. For a period of two years from January 1, 2021, the MHRA may rely on a decision taken by the EC to grant an MA under the Centralized Procedure to potentially more quickly grant a new Great Britain MA, and we currently plan to utilize this pathway to seek potential approval for Oxbryta in Great Britain. A separate application will, however, still be required.

Prior to filing our MAA, in November 2016, the EC granted Orphan Drug Designation status in the EU for Oxbryta for the treatment of SCD, and, in June 2017, the EMA granted PRIME designation for Oxbryta for the treatment of SCD. The PRIME program is a regulatory mechanism that provides for early and proactive EMA support to medicine developers to help patients benefit as early as possible from innovative new products that have demonstrated the potential to significantly address an unmet medical need. In addition, we have initiated an early access program in Europe for patients and physicians who may need access to Oxbryta prior to potential marketing authorization.

In September 2020, we entered into an exclusive agreement with Biopharma-MEA to distribute Oxbryta in the GCC region. Biopharm-MEA is responsible for registering Oxbryta with the relevant regulatory authorities in each of the countries to potentially make it broadly available. While this process is ongoing, the U.S. approval of Oxbryta can be referenced to allow for access to the medicine in the GCC region while regulatory authorities conduct their reviews.

Manufacturing

We are commercializing a solid oral formulation of a tablet form of Oxbryta, and we believe we have obtained an adequate supply of Oxbryta to satisfy our immediate commercial, clinical and nonclinical demands. We are also developing a pediatric formulation of Oxbryta for use in clinical trials and to include in our planned pediatric NDA submission for Oxbryta.

With respect to manufacturing, we do not own or operate or have any plans to establish any manufacturing facilities. We currently depend on third-party contract manufacturing organizations, or CMOs, for all of our requirements of raw materials, drug substance and drug product for our commercial, clinical and nonclinical activities for our portfolio, and we have entered into commercial manufacturing agreements with some of our CMOs to support Oxbryta commercialization. We intend to continue to rely on CMOs for the commercialization as well as continued development of Oxbryta, as well as the development and commercialization of any other product candidates, including inclacumab. Although we rely on CMOs, we have personnel and third-party consultants with extensive manufacturing experience to oversee the relationships with our contract manufacturers.

To decrease the risk of an interruption to our drug supply, when we believe it is reasonable for us to do so, we source materials from multiple suppliers so that, in general, the loss of any one source of supply should not have a material adverse effect on commercial production, project timelines or inventory of supplies for our studies or clinical trials. However, currently we have only one or a limited number of suppliers for some of these materials for Oxbryta and for other programs, and the loss of a primary source of supply could potentially delay the availability of Oxbryta or delay our development programs. We intend to maintain a safety stock of certain materials to help avoid delays in production, but we do not know whether such stock will be sufficient. In addition, we have established a second source for commercial drug substance and have identified potential second sources for finished drug product for Oxbryta commercial supply. There is no guarantee as to if or when we may establish the additional sources or whether they will be adequate in all circumstances we may encounter.

Drug Discovery and Development

Our goal is to build a robust product pipeline focused on the discovery and development of novel therapeutic approaches for SCD and grievous blood disorders. Our research and development pipeline targets

multiple pathologies, including vascular occlusion and hemoglobin polymerization, and our most advanced development programs are for inclacumab and GBT601.

We have an active business development strategy that may provide new opportunities to expand our product pipeline with next-generation treatments for SCD. To this end, we have entered into agreements with Roche and Syros.

License Agreement with F. Hoffmann-La Roche Ltd. and Hoffmann-La Roche Inc.

In August 2018, we entered into the License Agreement, or Roche Agreement, with Roche pursuant to which Roche granted us an exclusive and sublicensable worldwide license under certain patent rights and know-how to develop and commercialize inclacumab, including any modified compounds targeting P-selectin and derived from inclacumab, for all indications and uses, except diagnostic use. Roche retained a non-exclusive, worldwide, perpetual, royalty-free license to inclacumab solely for any diagnostic use.

We are developing inclacumab as a treatment for VOCs in patients with SCD, and we expect to be able to leverage the safety data from Roche's prior clinical studies, which were not in patients with SCD, as we proceed with our development of inclacumab. We have submitted an Investigational New Drug application, or IND, to the FDA for inclacumab to initiate two pivotal Phase 3 clinical studies in the first half of 2021. The two global, randomized, double-blind, placebo-controlled pivotal Phase 3 trials will evaluate the safety and efficacy of inclacumab. One study is designed to measure the reduction in frequency of VOCs over one year in patients with SCD when treated with inclacumab (30 mg/kg) or placebo every 12 weeks. The second study will evaluate inclacumab based on a primary endpoint of 90-day hospital readmission rates for VOC following an initial VOC hospitalization. Participants in that trial will receive either a single dose of inclacumab (30 mg/kg) or placebo, peri-discharge following a VOC hospitalization.

Under the Roche Agreement, we paid Roche an upfront payment of $2.0 million, and we will pay Roche up to an aggregate of $125.5 million in milestone payments for the SCD indication, including up to $40.5 million based on achievement of certain clinical development and regulatory milestones for inclacumab in the sickle cell disease indication, and up to $85.0 million based on achievement of certain thresholds for annual net sales of inclacumab. We will also pay Roche up to an additional $6.4 million in milestone payments, which are owed to a third party, based on achievement of such clinical development and regulatory milestones for inclacumab. As of December 31, 2020, we have recognized a $2.0 million clinical development milestone payment in our research and development costs for year ended December 31, 2020. We will also pay Roche up to $19.25 million in milestone payments based on achievement of certain clinical development and regulatory milestones for inclacumab for any other indication than the SCD indication. We have the right to sublicense our rights under the Roche Agreement to our affiliates without Roche's consent. Subject to certain conditions and limitations, including Roche's right of first negotiation described below, we will also have the right to sublicense our rights under the Roche Agreement to non-affiliates pursuant to partner agreements with Roche's prior written consent, which will not be unreasonably withheld or delayed. If at any time prior to the expiration of royalty or other payment obligations under the Roche Agreement, or the earlier termination of the Roche Agreement, we intend to enter into a partner agreement to sublicense rights to inclacumab, then Roche will have a right of first negotiation during an exclusivity period to negotiate in good faith with us the terms and conditions of such proposed transaction.

Collaboration with Syros Pharmaceuticals, Inc.

In December 2019, we entered into the Syros Agreement to discover, develop and commercialize novel therapies for SCD and beta thalassemia. Under the agreement, Syros will use its leading gene control platform to identify therapeutic targets and discover small molecule drugs that potentially induce fetal hemoglobin, and we have an option to obtain an exclusive worldwide license, with the right to sublicense, under relevant intellectual property rights and know-how of Syros arising from the collaboration, to develop, manufacture and

commercialize any compounds or products resulting from the collaboration, subject to Syros' option to co-promote the first product in the United States. If we exercise the option, we will be responsible for all development, manufacture, regulatory activities and commercialization of the compound or product. Syros and we will be responsible for our own costs incurred to conduct research activities, except that we will fund up to $40.0 million in preclinical research for at least three years. Unless earlier terminated or extended, the research program under the agreement will end on the third anniversary of the agreement.

Under the Syros Agreement, we paid Syros an upfront payment of $20.0 million, and, if we exercise the option, we may be obligated to pay Syros up to $315.0 million in option exercise, development, regulatory, commercialization and sales-based milestones per product candidate and product resulting from the collaboration. We will also be obligated to pay Syros, subject to certain reductions, tiered mid- to high-single digit royalties as percentages of calendar year net sales on any product resulting from the collaboration.

Social, Governance and Human Capital

Diversity & Inclusion

Since our founding, we have recognized that having a more diverse, inclusive, and equitable environment leads to increased performance, better decision making, increased productivity, and greater motivation. Our team represents a broad range of cultural and professional backgrounds that enrich our culture and drive our future growth and success. We are committed to fostering workplace development, diversity, and inclusion, or WDDI, at our company and across the biotechnology industry. We are dedicated to being at the forefront of efforts to develop a diverse and talented global workforce. We pledge to do our part to foster diversity and inclusion among our employees, customers and patients.

Human Capital Resources

As of December 31, 2020, we employed 389 full-time employees globally, including 154 in research and development and 235 in selling, general and administrative, which includes our commercial team. We have and expect to continue to retain consultants from time to time if required in connection with our business.

We consider our employees to be an essential factor in our ability to serve our customers and achieve our goal to transform the treatment of SCD, which depends on our ability to continue to attract, hire, and retain qualified personnel. We believe our employee turnover has historically been relatively low and below the average for life science companies, but with our recent headcount growth and evolution into a commercial-stage company, as well as the impact of the COVID-19 pandemic, we have experienced an increase in the number of employees leaving the company. Given our financial resources and our track record, we continue to be able to fill the vacated positions and grow our headcount in support of our mission.

To help attract, hire and retain skilled personnel, we offer a stimulating work environment, regular performance feedback, development opportunities, potential for career advancement, and a workplace culture focused on our mission and the wellbeing of our employees. In addition, we also monitor and periodically adjust our compensation programs with the goal of providing a competitive mix of compensation (including salary, incentive bonus and equity) and benefits packages.

We have never had a work stoppage, and none of our employees is represented by a labor organization or under any collective-bargaining arrangements. We consider our employee relations to be good.

Intellectual Property

We strive to protect the proprietary technology that we believe is important to our business, including seeking and maintaining patents and patent applications intended to cover Oxbryta and our product candidates

and compositions, their methods of use and processes for their manufacture, and any other aspects of inventions that are commercially important to the development of our business. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

We plan to continue to expand our intellectual property portfolio. We endeavor to promptly file domestic and international patent applications for new commercially valuable inventions, including applications directed to compositions and methods of treatment created or identified from our ongoing development of our product candidates. Our success will depend in part on our ability to obtain and maintain patent and other proprietary rights protecting our commercially important technology, inventions and know-how related to our business, defend and enforce our current and future issued patents, if any, preserve the confidentiality of our trade secrets and operate without infringing the valid and enforceable patents and proprietary rights of third parties. We also rely on know-how, continuing technological innovation and potential in-licensing opportunities to develop and maintain our intellectual property portfolio.

The patent positions of biopharmaceutical companies like us are generally uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent, if any, is issued, and patent scope can be reinterpreted by the courts after issuance. Moreover, many jurisdictions permit third parties to challenge issued patents in administrative proceedings, which may result in further narrowing or even cancellation of patent claims. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any patents, if issued, will provide sufficient protection from competitors for our business.

Because patent applications in the United States and certain other jurisdictions are maintained in secrecy for 18 months or potentially even longer, and since publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain of the priority of inventions covered by pending patent applications. Moreover, we may have to participate in interference proceedings or derivation proceedings declared by the United States Patent and Trademark Office, or USPTO, to determine the priority of inventions.

Patents

Our patent portfolio includes multiple issued U.S. and foreign patents, as well as multiple U.S. and foreign patent applications in various stages of prosecution or allowance. Our primary patents and patent applications relate to our general HbS intellectual property portfolio, which includes Oxbryta and its analogs.

Our HbS intellectual property portfolio is comprised of multiple patent families of patents and patent applications relating to Oxbryta and/or analogs that inhibit Hb polymerization. These patent families include patents and patent applications specifically related to Oxbryta, covering certain compositions of matter, methods of use, method of manufacture, commercial formulations, and polymorphs of Oxbryta and analogs. The pending patent applications are in a variety of jurisdictions, including the United States, jurisdictions under the Patent Cooperation Treaty and other countries.

With regard to Oxbryta specifically, we are the sole owner of issued U.S. patents covering Oxbryta, including its composition of matter, methods of use, formulations and polymorphs of Oxbryta. These issued U.S. patents covering Oxbryta are listed in the FDA Orange Book and will expire between 2032 and 2037, absent any applicable patent term extensions. Also with regard to Oxbryta specifically, we are the sole owner of issued composition of matter patents in Europe and certain other foreign jurisdictions. Any patents that may issue from our pending patent applications relating to Oxbryta in the United States or from corresponding foreign patent applications, if issued, are expected to expire between 2032 and 2037, absent any applicable patent term extensions. Some of these pending patent applications are jointly owned by us and Regents of the University of California, or the Regents, as described below.

Our other patents in our HbS intellectual property portfolio are comprised of additional issued U.S. patents covering Oxbryta analogs. These patents, and any patents that may issue from our pending patent applications

relating to Oxbryta analogs in the United States or from corresponding foreign patent applications, if issued, are currently expected to expire between 2032 and 2039, absent any applicable patent term extensions. Some of these pending patent applications are jointly owned by us and the Regents, as described below. With regard to GBT601 specifically, we are the sole owner of an issued U.S. patent covering its composition of matter, which will expire in 2039, absent any applicable patent term extensions. Any foreign patents, if issued from the same patent family, are expected to expire in 2039, absent any applicable patent term extensions.

With regard to inclacumab, we are the exclusive worldwide licensee of Roche's patent portfolio relating to inclacumab, which includes issued U.S. and foreign patents and pending applications covering the composition of matter of inclacumab. We expect inclacumab to be eligible for regulatory exclusivity (e.g., data exclusivity for biologics and orphan drug exclusivity) in various jurisdictions such as the U.S. and Europe, which exclusivities may extend beyond patent expiry. For example, we expect inclacumab, if approved, would be eligible for regulatory exclusivity (e.g., data exclusivity for biologics and orphan drug exclusivity) in various jurisdictions such as the U.S. and Europe, which exclusivities may extend beyond patent expiry in the case of inclacumab.

In addition, we have exclusively licensed from the Regents worldwide patent rights covering Oxbryta and certain Oxbryta analogs, some of which patent rights we jointly own with the Regents. In exchange for our exclusive license, we have agreed to pay a royalty to the Regents of less than 1% on future net sales and to use commercially reasonable efforts to develop, manufacture, market and sell the products covered by the licensed patents. The risks associated with joint ownership of patent rights are more fully discussed under "Risk Factors—Risks Related to Our Intellectual Property."

Beyond our HbS intellectual property portfolio, we own other issued U.S. and foreign patents, seek to obtain additional issued patents, and file patent applications relating to our other research and development programs over time.

Patent term

The base term of a U.S. patent is 20 years from the filing date of the earliest-filed non-provisional patent application from which the patent claims priority, assuming that all maintenance fees are paid. The term of a U.S. patent can be lengthened by patent term adjustment, which compensates the owner of the patent for administrative delays at the USPTO, the extent of which is offset by delays by the patent owner before the USPTO in obtaining the patent. In some cases, the term of a U.S. patent is shortened by a terminal disclaimer that reduces its term to that of an earlier-expiring patent. The term of a U.S. patent may be eligible for patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act, to account for at least some of the time the drug is under development and regulatory review after the patent is granted. With regard to a drug for which FDA approval is the first permitted marketing of the active ingredient, the Hatch-Waxman Act allows for extension of the term of one U.S. patent that includes at least one claim covering the composition of matter of an FDA-approved drug, an FDA-approved method of treatment using the drug and/or a method of manufacturing the FDA-approved drug. The extended patent term cannot exceed the shorter of five years beyond the non-extended expiration of the patent or 14 years from the date of the FDA approval of the drug. Some foreign jurisdictions, including Europe and Japan, have analogous patent term extension provisions, which allow for extension of the term of a patent that covers a drug approved by the applicable foreign regulatory agency. Following the FDA approval of Oxbryta, we applied for patent term extension Oxbryta, and we would expect to do the same for any other eligible product candidate that receives FDA approval in the future.

Trade secrets

In addition to patents, we rely on trade secrets and know-how to develop and maintain our competitive position. We typically rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. We protect trade secrets and know-how by establishing

confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors and contractors. These agreements generally provide that all confidential information developed or made known during the course of an individual or entities' relationship with us must be kept confidential during and after the relationship. These agreements also typically provide that all inventions resulting from work performed for us or relating to our business and conceived or completed during the period of employment or assignment, as applicable, shall be our exclusive property. In addition, we take other appropriate precautions, such as physical and technological security measures, to guard against misappropriation of our proprietary information by third parties.

Government Regulation

Government authorities in the United States at the federal, state and local level and in other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of drug products. Pricing of such products is also subject to regulation in many countries. Generally, before a new drug can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific to each regulatory authority, submitted for review and approved by the regulatory authority.

U.S. drug development

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. Drugs are also subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, untitled or warning letters, voluntary product recalls or withdrawals from the market, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

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

- completion of extensive nonclinical studies in accordance with applicable regulations, including the FDA's GLP regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, or ethics committee at each clinical trial site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with applicable IND regulations, good clinical practices, or GCPs, and other clinical-trial related regulations to establish the safety and efficacy of the investigational drug for each proposed indication;
- submission to the FDA of an NDA for a new drug;
- a determination by the FDA within 60 days of its receipt of an NDA whether to accept it for filing and review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities where the drug is produced to assess compliance with current good manufacturing practices, or

cGMPs, to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;

- potential FDA audit of the nonclinical study and/or clinical trial sites that generated the data in support of the NDA; and
- FDA review and approval of the NDA, including consideration of the views of any FDA advisory committee, prior to any commercial marketing or sale of the drug in the United States.

The nonclinical and clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for any of our product candidates, will be granted on a timely basis, or at all. The data required to support an NDA are generated in two distinct development stages: nonclinical and clinical. The nonclinical development stage generally involves synthesizing the active component, developing the formulation and determining the manufacturing process, as well as carrying out non-human toxicology, pharmacology and drug metabolism studies in the laboratory, which support subsequent clinical testing in humans. As the drug sponsor, we must submit the results of the nonclinical studies, 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. An IND is a request for authorization from the FDA to administer an investigational drug product to humans and must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions regarding the proposed clinical trial and places the IND on clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. The FDA also may impose a partial clinical hold that would limit a trial, for example, to certain doses or for a certain length of time or to a certain number of subjects.

The clinical stage of development involves the administration of the drug candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under 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 and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Further, each clinical trial must be reviewed and approved by an independent IRB for each institution at which the clinical trial will be conducted to ensure that the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries.

Clinical trials

Clinical trials are generally conducted in three sequential phases, known as Phase 1, Phase 2 and Phase 3 trials, which may overlap.

- Phase 1 clinical trials generally involve a small number of healthy volunteers who are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action, side effect tolerability and safety of the product candidate.
- Phase 2 clinical trials typically involve studies in disease-affected patients to determine the dose of the product candidate required to produce the desired benefits. At the same time, safety and further pharmacokinetic and pharmacodynamic information is collected, possible adverse effects and safety risks are identified, and a preliminary evaluation of efficacy is conducted.

- Phase 3 clinical trials generally involve large numbers of patients at multiple sites and are designed to provide the data necessary to demonstrate the effectiveness of the product candidate for its intended use, its safety in use, and to establish the overall benefit/risk relationship of the product candidate and provide an adequate basis for product approval. Phase 3 clinical trials may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a product during marketing.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval, to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA. In addition, as part of an accelerated approval such as we received for Oxbryta under the FDA's Subpart H regulations, at least one post-marketing study to verify clinical benefit is required.

As the drug sponsor, we must submit progress reports detailing the results of the clinical trials and other information at least annually to the FDA, as well as written IND safety reports to the FDA and the study investigators for serious and unexpected suspected adverse events, findings from other studies or animal or in vitro testing suggesting a significant risk to humans exposed to the drug and 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. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access to certain data from the trial. Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product 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, must include 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.

A manufacturer of an investigational drug for a serious disease or condition is required to make available, such as by posting on its website, its policy on evaluating and responding to requests for individual patient access to such investigational drug. This requirement applies on the earlier of the first initiation of a Phase 2 or Phase 3 trial of the investigational drug or, as applicable, 15 days after the drug receives a designation as a breakthrough therapy, fast track product or regenerative advanced therapy.

NDA and FDA review process

The results of nonclinical studies and clinical trials, together with other detailed information, including extensive manufacturing information and information on the composition of the drug and proposed labeling, are submitted to the FDA in the form of an NDA requesting approval to market the drug for one or more specified indications. The FDA reviews an NDA to determine, among other things, whether a drug is safe and effective for its intended use and whether the product is being manufactured in accordance with cGMP requirements to assure and preserve the product's identity, strength, quality and purity. FDA approval of an NDA must be obtained before a drug may be legally marketed in the United States.

Under PDUFA, each NDA is typically accompanied by a user fee (adjusted on an annual basis). According to the FDA's fee schedule, effective through September 30, 2021, the user fee for an NDA is $2,875,842. PDUFA also imposes an annual prescription drug product program fee for human drugs ($336,432). 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 having fewer than 500 employees. Additionally, an application for a product that has been designated as a drug for a rare disease or condition (referred to as an orphan drug) under section 526 of the FDCA is not subject to an application fee unless the application includes an indication for other than a rare disease or condition. Oxbryta for the treatment of SCD has been granted orphan drug designation by the FDA and by the EC.

The FDA reviews all NDAs submitted before it accepts them for filing and may request additional information rather than accepting an NDA for filing. The FDA is supposed to make a decision on accepting an NDA for filing within 60 days of receipt of the submission. Once the NDA is accepted for filing, the FDA begins an in-depth review of the NDA. Under the goals and policies agreed to by the FDA under PDUFA, the FDA is supposed to complete its initial review of an NDA that it has accepted for review and respond to the applicant within stated periods (within 10 months for a standard NDA and six months for an NDA designated by the agency for priority review). However, the FDA does not always meet its PDUFA goal dates for standard and priority NDAs, and the review process is often significantly extended by FDA requests for additional information or clarification.

Before approving an NDA, the FDA will conduct a pre-approval inspection of the manufacturing facilities for the new product (including the facilities of contract manufacturers, if applicable) to determine whether they comply with cGMP requirements. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The FDA may also audit data from clinical trials to ensure compliance with GCP requirements. Additionally, the FDA may refer applications for novel drug products or drug products which 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. There are likely to be extensive discussions between the FDA and the applicant during the review process. The review and evaluation of an NDA by the FDA is very comprehensive and time consuming and may take longer than originally planned to complete.

In addition, under Subpart H of the FDA's NDA regulations, which governs accelerated approval, the FDA may approve an NDA for a new drug product on the basis of adequate and well-controlled clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity. The FDA grants accelerated approval under Subpart H for new drugs that address serious or life-threatening illnesses and that provide meaningful therapeutic benefit to patients over existing treatments, and the NDA for Oxbryta was approved by the FDA under Subpart H. Drugs approved under Subpart H, such as Oxbryta, are required to be further evaluated in at least one post-marketing study to verify clinical benefit. As a condition of accelerated approval, the FDA may also impose marketing restrictions to limit distribution or use to assure safe use of the drug, although the FDA did not impose any such requirements for the accelerated approval of Oxbryta. Pursuing accelerated approval under Subpart H does not ensure faster development timelines or ensure regulatory approval.

After the FDA evaluates an NDA, it will issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A complete response letter indicates that the review cycle of the application is complete and the application will not be approved in its present form, and usually describes all of the specific deficiencies in the NDA identified by the FDA. The complete response letter may require additional clinical data and/or additional clinical trial(s), and/

or other significant and time-consuming requirements related to clinical trials, nonclinical studies or manufacturing. If a complete response letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, withdraw the application, or request a hearing. Even if such data and information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval.

United States Orphan drug designation

We were granted orphan drug designation by the FDA in 2015 for Oxbryta for the treatment of SCD. Under the Orphan Drug Act in the United States, the FDA may grant orphan designation to a drug product intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States (or more than 200,000 individuals in the United States when there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will be recovered from sales in the United States of such drug). Orphan product designation must be requested before submitting an NDA. After the FDA grants orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process, but does confer other potential development and commercialization benefits as described below.

Our NDA seeking approval for Oxbryta for the treatment of SCD qualified for the orphan user fee exemption from the PDUFA application fee. In addition, we should qualify for additional incentives, including tax credits for qualifying clinical trials of Oxbryta, and Oxbryta also qualified for a substantial period of regulatory market exclusivity, which will expire on November 25, 2026. If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication for seven years from the date of such approval, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity by means of greater effectiveness, greater safety, or by providing a major contribution to patient care. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity and may obtain approval for the same product for a different indication than that for which the orphan product has exclusivity. A competitor could also block the approval of one of our products for seven years by obtaining orphan product exclusivity for the same product (or a competitor product that contains our product candidate) for the same indication we are seeking. If a drug designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity. Orphan drug status in the EU has similar, but not identical, requirements and benefits.

Expedited development and review programs

In addition to the US orphan drug designation, Oxbryta received a Fast Track designation from the FDA for the potential treatment of SCD. The FDA's Fast Track program is intended to expedite or facilitate the process for reviewing new drugs that are intended to treat a serious or life threatening condition, where nonclinical or clinical data demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to both the product and the specific indication for which it is being studied.

Any product submitted to the FDA for marketing, including under a Fast Track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval under Subpart H. Any product is eligible for priority review if it treats a serious or life-threatening condition and, if approved, would provide a significant improvement in safety and effectiveness compared to available therapies. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug designated for priority review. Our NDA for Oxbryta was reviewed by the FDA pursuant to priority review and received accelerated approval under Subpart H.

Additionally, Oxbryta also received a breakthrough therapy designation from the FDA for the potential treatment of SCD. The benefits of breakthrough therapy designation include the same benefits as a Fast Track

designation, in addition to intensive guidance from the FDA to ensure an efficient drug development program. Fast Track designation, priority review, accelerated approval and breakthrough designation do not change the standards for approval but may expedite the development or approval process.

Pediatric information

Under the Pediatric Research Equity Act, or PREA, as amended, an NDA or supplement to an NDA must contain data to assess the safety and efficacy of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of pediatric data or full or partial waivers. A sponsor who is planning to submit a marketing application for a drug that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration is required to submit an initial Pediatric Study Plan, or PSP, within sixty days of an end-of-Phase 2 meeting or, if there is no end-of-Phase 2 meeting as early as practicable before the initiation of the Phase 3 or Phase 2/3 study. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from nonclinical studies, early phase clinical trials, and/or other clinical development programs. Generally, a drug product that has an indication for which orphan drug designation has been granted is exempt from the requirement to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients. Thus, our NDA for Oxbryta was not required to have this PREA assessment.

Post-marketing requirements

Following approval of a new product, a pharmaceutical company and the approved product are subject to continuing regulation by the FDA, including, monitoring and recordkeeping activities, submission of an NDA annual report, reporting of adverse experiences, product sampling and distribution requirements, and complying with complex promotion and advertising requirements, which include restrictions on promoting drugs for uses or for patient populations for which the drug was not approved (known as “off-label use”), and limitations on industry-sponsored scientific and educational activities and on interactions with healthcare providers. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such off-label uses. Prescription drug promotional materials must be submitted to the FDA in conjunction with the first use of these materials, and may be required to be reviewed in advance in certain circumstances such as a new product launch, including for drugs such as Oxbryta that are approved pursuant to the FDA’s Subpart H accelerated approval regulations. After 120 days following marketing approval, promotional materials for accelerated approval drugs must be submitted 30 days prior to use. Further, if there are any modifications to the drug, including changes in indications, labeling, or manufacturing processes or facilities, the pharmaceutical company may be required to submit and obtain FDA approval of a new NDA or NDA supplement, which may require additional data or the conduct of additional nonclinical studies and clinical trials. Newly discovered or developed safety or effectiveness data may require changes to a drug’s approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures, including a Risk Evaluation and Mitigation Strategy, or REMS, or the conduct of post-marketing studies to assess a newly discovered safety issue. The FDA has authority to require post-market studies, in certain circumstances, on reduced effectiveness of a drug and the FDA may require labeling changes related to new reduced effectiveness information.

Any distribution of prescription drug products and pharmaceutical samples must comply with the U.S. Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states.

Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution. The Drug Supply Chain Security Act, or DSCSA, was enacted in 2013 with the aim of building an electronic system to identify and trace certain prescription drugs distributed in the United States. The DSCSA mandates phased-in and resource-intensive obligations for pharmaceutical manufacturers, wholesale distributors, and dispensers over a 10-year period that is expected to culminate in November 2023. The law's requirements include the quarantine and prompt investigation of a suspect product, to determine if it is illegitimate, and notifying trading partners and the FDA of any illegitimate product. Drug manufacturers and their collaborators are also required to place a unique product identifier on prescription drug packages. This identifier consists of the National Drug Code, serial number, lot number and expiration date, in the form of a two dimensional data matrix barcode that can be read by humans and machines.

FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMP requirements. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products in accordance with cGMP requirements. Our third party manufacturers must comply with cGMP requirements that require among other things, quality control and quality assurance, the maintenance of records and documentation, and the obligation to investigate and correct any deviations from cGMP. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP requirements and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. The discovery of violative conditions, including failure to conform to cGMP requirements, could result in enforcement actions, and the discovery of problems with a product after approval may result in restrictions on a product, manufacturer or holder of an approved NDA, including recall.

Orange Book Listing

Section 505 of the FDCA describes three types of marketing applications that may be submitted to the FDA to request marketing authorization for a new drug. A Section 505(b)(1) NDA is an application that contains full reports of investigations of safety and efficacy. A Section 505(b)(2) NDA is an application in which the applicant, in part, relies on investigations that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted. Section 505(j) establishes an abbreviated approval process for a generic version of approved drug products through the submission of an Abbreviated New Drug Application, or ANDA. An ANDA provides for marketing of a generic drug product that has the same active ingredients, dosage form, strength, route of administration, labeling, performance characteristics and intended use, among other things, to a previously approved product. Limited changes must be preapproved by the FDA via a suitability petition. ANDAs are termed "abbreviated" because they are generally not required to include nonclinical and clinical data to establish safety and efficacy. Instead, generic applicants must scientifically demonstrate that their product is bioequivalent to, or performs in the same manner as, the innovator drug through *in vitro*, *in vivo*, or other testing. The generic version must deliver the same amount of active ingredients into a subject's bloodstream in the same amount of time as the innovator drug and can often be substituted by pharmacists under prescriptions written for the reference listed drug.

In seeking approval for a drug through an NDA, including a 505(b)(2) NDA, applicants are required to list with the FDA certain patents having claims that cover the applicant's product and method of use. Upon approval of an NDA, each of the patents listed in the application for the drug is then published in Approved Drug Products with Therapeutic Equivalence Evaluations, also known as the Orange Book. These products may be cited by potential competitors in support of approval of an ANDA or 505(b)(2) NDA.

Any applicant who files an ANDA seeking approval of a generic equivalent version of a drug listed in the Orange Book or a 505(b)(2) NDA referencing a drug listed in the Orange Book must make patent certifications

to the FDA relating to patents submitted to the FDA for the reference product: (1) that no patent information on the reference drug or method of use that is the subject of the application has been submitted to the FDA; (2) that any and all such patents submitted to the FDA have expired; (3) the date on which any such patent will expire and that ANDA approval will not be sought until after such patent expiration; or (4) that any such patent is invalid or will not be infringed upon by the manufacture, use, or sale of the drug product for which the ANDA is submitted. The last certification is known as a paragraph IV certification. Generally, the ANDA or 505(b)(2) NDA cannot be approved until all listed patents have expired, except where the ANDA or 505(b)(2) NDA applicant challenges a listed patent through a paragraph IV certification or if the applicant is not seeking approval of a patented method of use. If the applicant does not challenge the listed patents or does not indicate that it is not seeking approval of a patented method of use, the ANDA or 505(b)(2) NDA application will not be approved until all of the listed patents claiming the referenced product have expired.

If the competitor has provided a paragraph IV certification to the FDA, the competitor must also send notice of the paragraph IV certification to the holder of the NDA for the reference listed drug and the patent owner within 20 days after the application has been accepted for filing by the FDA. The NDA holder or patent owner may then initiate a patent infringement lawsuit in response to the notice of the paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a paragraph IV certification notice prevents the FDA from approving the ANDA or 505(b)(2) application until the earlier of 30 months from the date of the lawsuit, expiration of the patent, settlement of the lawsuit, a decision in the infringement case that is favorable to the applicant or such shorter or longer period as may be ordered by a court. This prohibition is generally referred to as the 30-month stay.

In instances where an ANDA or 505(b)(2) NDA applicant files a paragraph IV certification, the NDA holder or patent owners regularly take action to trigger the 30-month stay, recognizing that the related patent litigation may take many months or years to resolve. Thus, approval of an ANDA or 505(b)(2) NDA could be delayed for a significant period of time depending on the patent certification the applicant makes and the reference drug sponsor’s decision to initiate patent litigation.

In connection with the NDA submission and approval of the NDA for Oxbryta, we have listed six patents in the Orange Book for Oxbryta.

United States patent term restoration and marketing exclusivity and biosimilars in the U.S. and EU

Depending upon the timing, duration and specifics of the FDA approval of Oxbryta and any of our drug candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product’s approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the approval of that application, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved drug is eligible for the patent term extension and the application for the extension must be submitted prior to the expiration of the patent. The United States Patent and Trademark Office, or USPTO, in consultation with the FDA, reviews and approves any application for patent term extension or restoration. Following the FDA approval of Oxbryta, we applied for restoration of patent term (also referred to as patent term extension) for Oxbryta.

Marketing exclusivity provisions under the FDCA provide a five-year period of non-patent marketing exclusivity within the United States to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the

exclusivity period, the FDA may not accept for review an ANDA or a 505(b)(2) NDA submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovator drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator who holds the NDA for the active agent. The FDA has granted Oxbryta five-year marketing exclusivity, which will expire on November 25, 2024.

The FDCA also provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA for a drug product that contains an active moiety that has been previously approved if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example for new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the active agent for the original indication or condition of use.

Five-year and three-year exclusivity will not delay the submission or approval of a full NDA by a competitor. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the nonclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and efficacy. Pediatric exclusivity is another type of regulatory market exclusivity in the United States which, if granted, adds six months to the end of existing exclusivity periods and patent terms, and may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued pre-approval written request for such a pediatric trial where information relating to the use of the product candidate in a pediatric population may produce health benefits in that population.

In addition, in the United States, the Biologics Price Competition and Innovation Act of 2009 created an abbreviated approval pathway for biological products that are demonstrated to be “highly similar” or “biosimilar” to or “interchangeable” with an FDA approved biological product. This pathway allows competitors to reference the FDA’s prior approvals regarding innovative biological products and data submitted with a BLA to obtain approval of a biosimilar application twelve years after the time of approval of the innovative biological product. The twelve-year exclusivity period runs from the initial approval of the innovator product and not from approval of a later new indication, if any. In addition, the twelve-year exclusivity period does not prevent another company from independently developing a product that is highly similar to the innovative product, generating all the data necessary for and seeking approval under a full BLA. Further, it is possible that a biosimilar applicant could obtain approval for one or more of the indications approved for the innovator product by extrapolating clinical data from one indication to support approval for other indications. In the European Union, the European Commission has similarly granted marketing authorizations for biosimilars once the marketing exclusivity rights for the innovator product have expired. The EMA has published general and product class-specific guidelines to assist biosimilar developers in preparing marketing authorization applications for biosimilars. An applicant for a marketing authorization for a biosimilar in the European Union is required to demonstrate through comparability studies with the ‘reference’ biological medicine that: (i) their biological medicine is highly similar to the reference medicine, notwithstanding natural variability inherent to all biological medicines; and (ii) there are no clinically meaningful differences between the biosimilar and the reference medicine in terms of safety, quality and efficacy. Both the United States and the EU provide pathways for biologics competitors to seek approval for biosimilar products at the end of the relevant exclusivity period or, in some circumstances, before such period expires (for example, if a biosimilar applicant obtains approval for one or more of the indications approved for the innovator product by extrapolating clinical data from one indication to support approval for other indications). We are aware of many pharmaceutical and biotechnology and other companies that are actively engaged in research and development of biosimilars or interchangeable products.

Federal, state and foreign healthcare laws, including anti-kickback, fraud and abuse and health information privacy and security laws

Manufacturing, sales, promotion and other activities following product approval are also subject to regulation by numerous regulatory authorities in addition to the FDA, including, in the United States, the Centers for Medicare & Medicaid Services, or CMS, other divisions of the Department of Health and Human Services, or HHS, the United States Department of Justice, the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments.

Although we do not provide healthcare services, submit claims for third-party reimbursement, or receive payments directly from Medicare, Medicaid or other third-party payors for our products, we are subject to broadly applicable healthcare fraud and abuse regulation and enforcement by federal and state governments. Additionally, healthcare providers and third-party payors play a primary role in the recommendation of drugs and other medical items and services. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, reporting of payments to physicians and teaching hospitals and patient privacy laws and regulations and other healthcare laws.

Healthcare fraud and abuse and health information privacy and security laws potentially applicable to our operations include:

- the federal Anti-Kickback Law, which makes it illegal for any person to knowingly and willfully solicit, receive, offer or pay any remuneration (including any kickback, bribe or certain rebates), directly or indirectly, overtly or covertly, in cash or in kind, or in return for, that is intended to induce or reward referrals, including the purchase, recommendation, order or prescription of a particular drug, for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. A person or entity need not have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it in order to have committed a violation. Violations are subject to civil and criminal fines and penalties for each violation, plus imprisonment and exclusion from government healthcare programs. In addition, the government may assert that a claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act, or FCA. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. This law applies to our marketing practices, educational programs, pricing policies and relationships with healthcare providers, by prohibiting, among other things, soliciting, receiving, offering or providing remuneration intended to induce the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare or Medicaid programs;
- federal civil and criminal false claims laws, including the FCA, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval that are false, fictitious or fraudulent; knowingly making, using or causing to be made or used, a false statement or record material to a false or fraudulent claim or obligation to pay or transmit money or property to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims. The government may deem manufacturers to have “caused” the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label. Companies that submit claims directly to payors may also be liable under the FCA for the direct submission of such claims. In addition, our future activities relating to the reporting of wholesaler or estimated retail prices for our products, the reporting of prices used to calculate Medicaid rebate information

and other information affecting federal, state, and third-party reimbursement for our products, and the sale and marketing of our products, are subject to scrutiny under this law. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery. When an entity is determined to have violated the FCA, the government may impose civil fines and penalties for each false claim, plus treble damages, and exclude the entity from participation in Medicare, Medicaid and other federal healthcare programs;

- the federal civil monetary penalties laws, which impose civil fines for, among other things, the offering or transfer of remuneration to a Medicare or state healthcare program beneficiary if the person knows or should know it is likely to influence the beneficiary's selection of a particular provider, practitioner, or supplier of services reimbursable by Medicare or a state health care program, unless an exception applies;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, and its implementing regulations, which created additional federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity can be found guilty of violating HIPAA without actual knowledge of the statute or specific intent to violate it;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, there may be additional federal, state and non-U.S. laws which govern the privacy and security of health and other personal information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts;
- federal "sunshine" requirements imposed by the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the ACA, on drug, device, biological and medical supply manufacturers when payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to HHS under the Open Payments Program, information regarding any payment or other "transfer of value" made or distributed to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit required information may result in civil monetary penalties for all payments, transfers of value or ownership or investment interests that are not timely, accurately, and completely reported in an annual submission. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners;

- federal price reporting laws, which require manufacturers to calculate and report complex pricing metrics to government programs, where such reported prices may be used in the calculation of reimbursement and/or discounts on approved products;
- the Foreign Corrupt Practices Act, or FCPA, prohibits any United States individual or business from paying, offering, or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party, or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. Activities that violate the FCPA, even if they occur wholly outside the United States, can result in criminal and civil fines, imprisonment, disgorgement, oversight, and debarment from government contracts; and
- analogous state and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers or patients; state laws that require pharmaceutical companies to comply with the industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state and local laws that require the licensure of sales representatives; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and pricing information; data privacy and security laws and regulations in foreign jurisdictions that may be more stringent than those in the United States (such as the European Union, which adopted the General Data Protection Regulation, or GDPR, which became effective in May 2018); state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect; and state laws related to insurance fraud in the case of claims involving private insurers.

Additionally, pricing and rebate programs must comply with the Medicaid rebate requirements of the U.S. Omnibus Budget Reconciliation Act of 1990 and more recent requirements in the ACA. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. The handling of any controlled substances must comply with the U.S. Controlled Substances Act and Controlled Substances Import and Export Act. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. Manufacturing, sales, promotion and other activities are also potentially subject to federal and state consumer protection and unfair competition laws.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the voluntary recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

Regulations governing data collection and the use, processing and cross-border transfer of personal information

We have subsidiaries, employees and operations in Europe, which subject us to additional privacy restrictions, including in relation to employee information. We have also conducted, and expect to continue to conduct, clinical trials or continue to enroll subjects in our ongoing or future clinical trials in certain jurisdictions in which we may be subject to additional privacy restrictions. The collection, use, storage, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the

GDPR, which became effective in May 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR includes restrictions on cross-border data transfers. The GDPR has increased our responsibility and liability in relation to personal data that we process where such processing is subject to the GDPR, and we may be required to put in place additional mechanisms to ensure compliance with the GDPR, including as implemented by individual countries. Compliance with the GDPR will continue to be a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our European activities. Further, the United Kingdom's exit from the EU, often referred to as Brexit, has created uncertainty with regard to data protection regulation in the United Kingdom. In particular, it is unclear how data transfers to and from the United Kingdom will be regulated.

California recently enacted the California Consumer Privacy Act, or CCPA, which creates new individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. Effective as of January 2020, the CCPA requires covered companies to provide certain disclosures to consumers about its data collection, use and sharing practices, and to provide affected California residents with ways to opt out of certain sales or transfers of personal information, and also regulates employee information. Further, a new California privacy law, the California Privacy Rights Act, or CPRA, was passed by California voters in November 2020. The CPRA will create additional obligations with respect to processing and storing personal information that are scheduled to take effect on January 1, 2023 (with certain provisions having retroactive effect to January 1, 2022). While there is currently an exception in the CCPA and CPRA for protected health information that is subject to HIPAA, the CCPA and CPRA do and will impact our business activities. Other U.S. states also are considering omnibus privacy legislation and industry organizations regularly adopt and advocate for new standards in these areas.

European Union drug development, Orphan Drug and PRIME designations

In the EU, our product candidates may also be subject to extensive regulatory requirements. As in the United States, medicinal products can only be marketed if a marketing authorization from the competent regulatory authorities has been obtained.

Similar to the United States, the various phases of nonclinical and clinical research in the EU are subject to significant regulatory controls. Although the EU Clinical Trials Directive 2001/20/EC, or Directive, has sought to harmonize the EU clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the EU, the EU Member States have transposed and applied the provisions of the Directive differently. This has led to significant variations in the Member State regimes. Under the current regime, before a clinical trial can be initiated it must be approved in each of the EU countries where the trial is to be conducted by two distinct bodies: the National Competent Authority, or NCA, and one or more Ethics Committees, or ECs. Under the current regime all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial have to be reported to the NCA and ECs of the Member State where they occurred.

In April 2014, the EU adopted a new Clinical Trials Regulation (EU) No 536/2014, or Regulation. which is set to replace the current Clinical Trials Directive 2001/20/EC. It will overhaul the current system of approvals for clinical trials in the EU. Specifically, the new Regulation, which will be directly applicable in all Member States, aims at simplifying and streamlining the approval of clinical trials in the EU. For instance, the new Regulation provides for a streamlined application procedure via a single entry point and strictly defined deadlines for the assessment of clinical trial applications. It is expected that the new Regulation will apply following confirmation of full functionality of the Clinical Trials Information System, the centralized EU portal and database for clinical trials foreseen by the regulation, through an independent audit, which is currently anticipated to occur in December 2021.

In November 2016, the EC, acting on a positive recommendation from the Committee for Orphan Medicinal Products, or COMP, of the EMA, designated Oxbryta as an orphan medicinal product for the treatment of SCD. Orphan drug status in the EU has similar, but not identical, requirements and benefits to US orphan drug status, including 10 years of marketing exclusivity from the approval of the marketing authorization, designated product-specific consultation by the EMA, and certain reductions or exemptions in regulatory fees.

In June 2017, the EMA granted PRIME designation for Oxbryta for the treatment of SCD. The PRIME program is a new regulatory mechanism that provides for early and proactive EMA support to medicine developers to help patients benefit as early as possible from innovative new products that have demonstrated the potential to significantly address an unmet medical need, where there is no satisfactory method of diagnosis, prevention or treatment in the EU or, if there is, the new medicine will bring a major therapeutic advantage. It is intended to build upon the scientific advice scheme and accelerated assessment procedure offered by EMA. The scheme is voluntary, and eligibility criteria must be met for a medicine to qualify for PRIME. The PRIME scheme is open to medicines under development and for which the applicant intends to make an initial marketing authorization application through the Centralized Procedure. If a medicine is selected for the PRIME scheme, the EMA:

- appoints a rapporteur from the Committee for Medicinal Products for Human Use, or CHMP, or from the Committee for Advanced Therapies, or CAT, to provide continuous support and to build up knowledge of the medicine in advance of the filing of a marketing authorization application;
- issues guidance on the applicant’s overall development plan and regulatory strategy;
- organizes a kick-off meeting with the rapporteur and experts from relevant EMA committees and working groups;
- provides a dedicated EMA contact person; and
- provides scientific advice at key development milestones, involving additional stakeholders, such as health technology assessment bodies and patients, as needed.

Medicines that are selected for the PRIME scheme are also expected to benefit from the EMA’s accelerated assessment procedure at the time of application for a marketing authorization. Where, during the course of development, a medicine no longer meets the eligibility criteria, support under the PRIME scheme may be withdrawn.

European Union drug review and approval

In the European Economic Area, or EEA, which is currently comprised of the Member States of the EU plus Norway, Iceland and Liechtenstein, medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of marketing authorizations:

The centralized MA is issued by the EC through the Centralized Procedure, based on the opinion of the CHMP, and is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, advanced-

therapy medicines (gene-therapy, somatic cell-therapy or tissue-engineered medicines), and medicinal products containing a new active substance indicated for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions, and viral diseases. This mandatory Centralized Procedure applies in the case of Oxbryta for SCD, in light of the 2016 designation of Oxbryta as an orphan medicinal product for the treatment of SCD.

The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

Under the Centralized Procedure the maximum timeframe for the evaluation of an MAA by the EMA is generally 210 days, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. Clock stops may extend the timeframe of evaluation of a MAA considerably beyond 210 days. Where the CHMP gives a positive opinion, it provides the opinion together with supporting documentation to the EC, who make the final decision to grant a marketing authorization, which is issued within 67 days of receipt of the EMA's recommendation. Accelerated assessment might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of major public health interest, particularly from the point of view of therapeutic innovation. The timeframe for the evaluation of a MAA under the accelerated assessment procedure is generally 150 days, but it is possible that the CHMP may revert to the standard time limit for the Centralized Procedure if it determines that the application is no longer appropriate to conduct an accelerated assessment.

National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in other Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. Under the Decentralized Procedure an identical dossier is submitted to the competent authorities of each of the Member States in which an MA is sought, one of which is selected by the applicant as the Reference Member State, or RMS. The competent authority of the RMS prepares a draft assessment report, a draft summary of the product characteristics, or SmPC, and a draft of the labeling and package leaflet, which are sent to the other Member States (referred to as the Concerned Member States) for their approval. If the Concerned Member States raise no objections, based on a potential serious risk to public health, to the assessment, SmPC, labeling, or packaging proposed by the RMS, the product is subsequently granted a National MA in all the relevant Member States (i.e., in the RMS and the Concerned Member States).

Under the above-described procedures, before granting an MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Now that the UK (which includes Great Britain and Northern Ireland) has left the EU, Great Britain will no longer be covered by centralized MAs (while under the Northern Irish Protocol, centralized MAs will continue to be recognized in Northern Ireland). All medicinal products with a current centralized MA were automatically converted to Great Britain MAs on January 1, 2021. For a period of two years from January 1, 2021, the MHRA may rely on a decision taken by the EC on the approval of a new MAA in the Centralized Procedure to more quickly grant a new Great Britain MA. A separate application will, however, still be required. The MHRA also has the power to have regard to MAs approved in EEA Member States through Decentralized or Mutual Recognition Procedures with a view to more quickly granting an MA in the UK or Great Britain.

European Union market and data exclusivity

In the EEA, innovative medicinal products, qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. The data exclusivity, if granted, prevents generic or biosimilar applicants from referencing the innovator's pre-clinical or clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar MA in the EEA. During the additional two-year period of market exclusivity, a generic or biosimilar marketing authorization application can be submitted, and the innovator's data may be referenced, but no generic or biosimilar product can be marketed until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are determined to bring a significant clinical benefit in comparison with existing therapies. However, even if an innovative medicinal product gains the prescribed period of data exclusivity, another company may market another version of the product if such company obtained an MA based on a MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

European Union orphan designation and exclusivity

In the EEA, the EC, after reviewing the opinion of the EMA's Committee for Orphan Medicinal Products, grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions and either (i) such condition affects not more than 5 in 10,000 persons in the EEA, or (ii) it is unlikely that the development of the medicine would generate sufficient return to justify the necessary investment in its development. In either case, the applicant must also demonstrate that no satisfactory method of diagnosis, prevention, or treatment for the condition has been authorized (or, if a method exists, the product would be a significant benefit to those affected compared to the product available).

In the EEA, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity is granted following marketing authorization approval. During this market exclusivity period, neither the EMA nor the EC nor any of the competent authorities in the EEA Members States can accept an application or grant a marketing authorization for a "similar medicinal product." A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. Market exclusivity may also be revoked in very select cases, such as if (i) it is established that a similar medicinal product is safer, more effective or otherwise clinically superior to the authorized product; (ii) the marketing authorization holder consents to such revocation; or (iii) the marketing authorization holder cannot supply enough orphan medicinal product. Orphan drug designation must be requested before submitting an application for marketing approval. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. In November 2016, we were granted orphan drug designation in the EU for Oxbryta for the potential treatment of SCD.

From January 1, 2021, a separate process for orphan drug designation applies in Great Britain. There is no pre-marketing authorization orphan designation (as there is in the EEA) and the application for orphan designation will be reviewed by the MHRA at the time of the marketing authorization application. The criteria are the same as in the EEA, except that they apply to Great Britain only (i.e., there must be no satisfactory method of diagnosis, prevention or treatment of the condition concerned in Great Britain).

Brexit and the Regulatory Framework in the UK

In June 2016, the electorate in the UK voted in favor of leaving the EU (commonly referred to as Brexit). Thereafter, in March 2017, the country formally notified the EU of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. The UK formally left the EU at the end of January 2020, with a transition period from February through December 2020 during which EU pharmaceutical law remained applicable to the UK. It remains to be seen how Brexit will impact regulatory requirements for medicinal products and devices in the UK in the long-term. The MHRA has recently published detailed guidance for industry and organizations to follow now the transition period is over, which will be updated as the UK's regulatory position on medicinal products evolves over time.

Rest of the world regulation

For other countries outside of the EU and the United States, such as countries in the GCC region, Latin America, Eastern Europe, or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. Additionally, the clinical trials must be conducted in accordance with GCP requirements and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we or our partners fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Reimbursement

Sales of our products will depend, in part, on the extent to which our products will be covered by third-party payors, such as government health programs (e.g., Medicare and Medicaid), commercial insurance and managed healthcare organizations, as well as the level of reimbursement such third-party payors provide for our products. Patients and providers are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. In the United States, no uniform policy of coverage and reimbursement for drug products exists, and one payor's determination to provide coverage and adequate reimbursement for a product does not assure that other payors will make a similar determination. Accordingly, decisions regarding the extent of coverage and amount of reimbursement to be provided for any of our products will be made on a payor-by-payor basis. Many private payors, however, use coverage decisions and payment amounts determined by CMS as guidelines in setting their coverage and reimbursement policies. The coverage determination process is often time-consuming and costly and is likely to require us to provide scientific and clinical support for the use of our product candidates to each payor individually, with no assurance that coverage and adequate reimbursement will be obtained.

The United States government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price-controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. For example, the ACA contains provisions that may reduce the profitability of drug products through increased rebates for drugs reimbursed by Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, and mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs. Adoption of general controls and measures, coupled with the tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceutical drugs.

The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of HHS as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. Effective in 2010, the ACA made several

changes to the Medicaid Drug Rebate Program, including increasing pharmaceutical manufacturers' rebate liability by raising the minimum basic Medicaid rebate on most branded prescription drugs from 15.1% of average manufacturer price, or AMP, to 23.1% of AMP, and adding a new rebate calculation for "line extensions" (i.e., new formulations, such as extended release formulations) of solid oral dosage forms of branded products, creating a new methodology by which rebates are calculated for drugs that are inhaled, infused, instilled, implanted or injected, as well as potentially impacting their rebate liability by modifying the statutory definition of AMP. The ACA also expanded the universe of Medicaid utilization subject to drug rebates by requiring pharmaceutical manufacturers to pay rebates on Medicaid managed care utilization as of 2010 and by expanding the population potentially eligible for Medicaid drug benefits (phased-in by 2014). Pricing and rebate programs must also comply with the Medicaid rebate requirements of the U.S. Omnibus Budget Reconciliation Act of 1990.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, established the Medicare Part D program to provide a voluntary prescription drug benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs. Unlike Medicare Parts A and B, Part D coverage is not standardized. While all Medicare drug plans must give at least a standard level of coverage set by Medicare, Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for drugs for which we obtain marketing approval. Any negotiated prices for any of our products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

For a drug product to receive federal reimbursement under the Medicaid or Medicare Part B programs or to be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B drug pricing program. The required 340B discount on a given product is calculated based on the AMP and Medicaid rebate amounts reported by the manufacturer. As of 2010, the ACA expanded the types of entities eligible to receive discounted 340B pricing, although under the current state of the law these newly eligible entities (with the exception of children's hospitals) will not be eligible to receive discounted 340B pricing on orphan drugs. As 340B drug pricing is determined based on AMP and Medicaid rebate data, the revisions to the Medicaid rebate formula and AMP definition described above could cause the required 340B discount to increase.

The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. The plan for the research was published in 2012 by HHS, the Agency for Healthcare Research and Quality and the National Institutes for Health, and periodic reports on the status of the research and related expenditures are made to Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, it is not clear what effect, if any, the research will have on the sales of Oxbryta or our product candidates, if any such drug or the condition that they are intended to treat are the subject of such research. It is also possible that comparative effectiveness research demonstrating benefits in a competitor's drug could adversely affect the sales of Oxbryta or our product candidates. If third-party payors do not consider our drugs to be cost-effective compared to other available therapies, they may not cover our drugs after approval as a benefit under their plans or, if they do, the level of payment or utilization may not be sufficient to allow us to sell our drugs on a profitable basis.

In recent years, additional laws have resulted in direct or indirect reimbursement reductions for certain Medicare providers, including:

- 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. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments, are suspended until March 31, 2021, and are currently scheduled to remain in effect through 2030 unless additional Congressional action is taken.
- The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

These laws, and future state and federal healthcare reform measures may be adopted in the future, any of which may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

As noted above, the marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. We expect that an increasing emphasis on cost containment measures in the United States will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

In many foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country. For example, the EU provides options for its member states to restrict the range of medicinal products, for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. Historically, products launched in the EU do not follow price structures of the United States and generally prices tend to be significantly lower. It can also take a significant period of time after any regulatory approval to obtain various pricing and reimbursement approvals in various member states. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products, if approved.

U.S. Healthcare Reform and regulatory changes

The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that could affect our ability to profitably sell our products. In the United States, there have been and continue to be laws enacted by the federal government, state governments, regulators and third-party payers to control healthcare costs, and generally, to reform the healthcare system in the United States. For example, the ACA was passed in March 2010 and has substantially changed the way healthcare is delivered and financed by both governmental and private insurers. The ACA expanded coverage for the uninsured while at the same time containing overall healthcare costs. With regard to pharmaceutical products, the ACA, among other things, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and

extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs, and a Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% 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. The required discount was increased to 70% on January 1, 2019 pursuant to subsequent legislation.

Some of the provisions of the ACA have yet to be fully implemented, while certain provisions have been subject to judicial and Congressional challenges. The full impact of the ACA, any law repealing, replacing, or modifying elements of it, and the political uncertainty surrounding its repeal, replacement, or modification on our business remains unclear. We expect that additional federal healthcare reform measures may be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare drugs and services, and in turn could significantly reduce the projected value of certain development projects and reduce our profitability and may increase our regulatory burdens and operating costs.

There has been increasing legislative and enforcement interest in the United States with respect to drug pricing practices, including for specialty drugs. For example, there have been several recent federal Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration's budget proposal for fiscal year 2021 includes a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. Additionally, the Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out-of-pocket costs of drug products paid by consumers. HHS has already started the process of soliciting feedback on some of these measures and, at the same time, is immediately implementing others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage Plans the option of using step therapy, a type of prior authorization, for Part B drugs beginning in January 2020, codifying an earlier CMS policy change.

During 2020, President Trump announced several executive orders related to prescription drug pricing that seek to implement several of the administration's proposals. Further, in November 2020, CMS issued an Interim Final Rule implementing the Most Favored Nation, or MFN, Model under which Medicare Part B reimbursement rates will be calculated for certain drugs and biologics based on the lowest price drug manufacturers receive in Organization for Economic Cooperation and Development countries with a similar gross domestic product per capita. The MFN Model regulations mandate participation by identified Part B providers and will apply in all U.S. states and territories for a seven-year period from 2021 through 2027. However, the Interim Final Rule was not finalized and has been challenged in court and enjoined from implementation. Additionally, in November 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also created a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Although a number of these, and other proposed measures may require authorization through additional legislation to become effective, and the Biden administration may reverse or otherwise change these measures, Congress has indicated that it will continue to seek new legislative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical 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.

Finally, in May 2018, the Right to Try Act was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

Research and Development

Research and development expenses were $155.1 million for the year ended December 31, 2020, $174.6 million for the year ended December 31, 2019 and $131.3 million for the year ended December 31, 2018.

Financial Information about Segments

We operate in a single accounting segment—dedicated to discovering, developing and commercializing novel therapeutics to treat grievous blood-based disorders. Refer to Note 1, “Organization and Basis of Presentation” in the Notes to Consolidated Financial Statements included elsewhere in this report.

Corporate Information

We were incorporated in Delaware in February 2011 and commenced operations in May 2012. Our principal executive offices are located at 181 Oyster Point Blvd., South San Francisco, California 94080. Our telephone number is (650) 741-7700 and our e-mail address is investor@gbt.com. Our Internet website address is www.gbt.com. No portion of our website is incorporated by reference into this Annual Report on Form 10-K.

You are advised to read this Annual Report on Form 10-K in conjunction with other reports and documents that we file from time to time with the Securities and Exchange Commission, or SEC. In particular, please read our Quarterly Reports on Form 10-Q and any Current Reports on Form 8-K that we may file from time to time. You may obtain copies of these reports directly from us or from the SEC. In addition, the SEC maintains information for electronic filers (including Global Blood Therapeutics, Inc.) at its website at www.sec.gov. We make our periodic and current reports available on our internet website, free of charge, as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC.

Item 1A. *Risk Factors*

This Annual Report on Form 10-K contains forward-looking information based on our current expectations. Because our business is subject to many risks and our actual results may differ materially from any forward-looking statements made by or on behalf of us, this section includes a discussion of important factors that could affect our business, operating results, financial condition and the trading price of our common stock. You should carefully consider these risk factors, together with all of the other information included in this Annual Report on Form 10-K as well as our other publicly available filings with the SEC.

Risks Related to Commercialization

Our business is substantially dependent on our ability to successfully commercialize Oxbryta, and the commercial success of Oxbryta or any future drug we may develop or obtain will depend upon the degree of market acceptance by physicians, patients, third-party payors and others in the medical community and marketplace.

Our business depends heavily on our ability to successfully commercialize our first approved product, Oxbryta, for the treatment of sickle cell disease, or SCD. Oxbryta or any future drug of ours approved for commercial sale may fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community and marketplace. If Oxbryta or any other approved drug does not achieve an adequate level of acceptance, we may not generate significant revenue from drug sales and we may not become profitable. Before granting reimbursement approval, healthcare payors may require us to demonstrate that the drug, in addition to treating the target indication, also provides incremental health benefits to patients. For example, there have been numerous instances of government and private payors placing restrictions on coverage for products approved by the U.S. Food and Drug Administration, or FDA, under the FDA's Subpart H regulations, or Subpart H. Our efforts to educate the medical community and third-party payors about the benefits of Oxbryta or any future drug approved for commercial sale will require significant resources and may never be successful. The degree of market acceptance of Oxbryta and any other approved drugs that we may pursue will depend on a wide range of factors, including:

- the demonstrated efficacy and potential advantages of our drugs compared to alternative treatments;
- our ability to offer our drugs for sale at competitive prices;
- the availability of third-party coverage and adequate reimbursement;
- the convenience and ease of administration of our drugs compared to alternative current and future treatments;
- the willingness of the SCD or other target patient populations to try new therapies and of physicians to prescribe these therapies;
- the availability of our drugs and our ability to meet market demand, including a reliable supply for long-term chronic treatment;
- the strength of labeling, marketing and distribution support;
- the clinical indications and approved labeling for which the drug is approved, including labeling restrictions for drugs approved under Subpart H, such as Oxbryta;
- the prevalence and severity of any side effects and overall safety profile of the drug; and
- any restrictions on the use of the drug, including together with other medications.

For example, shortly after we launched Oxbryta, the outbreak of the novel coronavirus, SARS-CoV-2, which causes coronavirus disease 2019 (COVID-19), evolved into a global pandemic that has significantly impacted people and entities throughout the world. In light of the COVID-19 pandemic, we temporarily

suspended our field team from most in-person interactions, including visits to physician offices, clinics and hospitals as well as in-person meetings with payors. The COVID-19 pandemic has also reduced our ability to engage with the medical and investor communities. These and other measures have impacted our ability to commercialize Oxbryta and may significantly impact our business in general, and we may continue to experience disruptions to our commercial efforts as well as other disruptions that could materially impact our business.

If our sales and marketing capabilities for Oxbryta in the United States are not effective, or we are unable to establish or secure effective sales and marketing capabilities for any future drug approved for commercial sale in the United States or another geographic market, we may be unsuccessful in our commercial efforts.

In 2019, we established the infrastructure we believed was adequate for the commercial launch of Oxbryta in the United States, which occurred in December 2019. This included establishing a sales and marketing organization with technical expertise and supporting distribution capabilities to commercialize Oxbryta in the United States. Our commercialization of Oxbryta in the United States will continue to be expensive, difficult, risky and time consuming, and we may not deploy or have adequate resources over time to support the successful commercialization of Oxbryta. Any failures or delays in our commercial efforts, including with respect to any changes in related resources or activities following launch, could adversely impact the commercialization of Oxbryta or any other products, if any are approved.

Although many of our employees have experience with commercializing products while employed at other companies, our 2019 launch of Oxbryta is our first experience marketing and selling a drug together as a management team. To successfully commercialize Oxbryta or any other drugs we may develop or obtain, we will need to continue to develop and strengthen our commercial capabilities, either on our own or with others. Our initial estimate of the size of the required sales force may be materially more or less than the size of the sales force actually required to effectively commercialize Oxbryta or any other product candidates, if any. For example, we may have hired substantially more sales representatives than required and may incur excess costs as a result.

In light of the COVID-19 pandemic, we have temporarily suspended our field team from most in-person interactions, including visits to physician offices, clinics and hospitals as well as in-person meetings with payors. While we are continuing to engage with healthcare professionals and payors through digital and internet-based education and outreach, the impact of temporarily suspending our field force from in-person interactions is unknown. We have seen a significant decrease in weekly new patient prescriptions for Oxbryta from a peak in early March, and we expect the rate of new patient prescriptions may remain lower, depending on the course of the pandemic.

Another potential challenge for our commercial efforts is frequency of doctor visits by SCD patients. We believe that nearly half of Medicaid and Medicare patients living with SCD do not see a hematologist at least once per year. This infrequency of doctor visits, which has been exacerbated during the COVID-19 pandemic, may impede prescriptions for Oxbryta.

With respect to certain geographical markets, we may seek to enter into collaborations with other entities to utilize their local marketing and distribution capabilities, but we may be unable to enter into such agreements on favorable terms, if at all. If our future collaborators do not commit sufficient resources to commercialize Oxbryta or future drugs, if any, and we are unable to develop the necessary marketing capabilities on our own, we will be unable to generate sufficient product revenue to sustain our business. We may also be competing with companies that currently have extensive and well-funded marketing and sales operations. For example, in November 2019, the FDA approved Novartis' biologic, crizanlizumab, for the reduction of the frequency of vaso-occlusive crises, or VOCs, in patients with SCD, and, in October 2020, Novartis announced that the European Commission approved crizanlizumab for the prevention of recurrent VOCs in patients with SCD. Without an effective internal team or the support of a third party to perform marketing and sales functions, we would be unable to compete successfully against more established companies, and our commercial efforts and ability to generate revenues would be impaired.

Our profitability will depend significantly on our ability to sell sufficient amounts of product at competitive prices and on the availability of adequate coverage and reimbursement through governmental or private third-party payors. The insurance coverage and reimbursement status of newly approved products is uncertain in the United States and elsewhere, and failure to obtain or maintain adequate coverage and reimbursement for Oxbryta or any other products we may develop due to price controls, resource constraints or reimbursement limitations could limit our ability to market those products and impair our ability to generate revenue.

Our target patient populations are small, and, accordingly, the pricing, coverage and reimbursement of Oxbryta or any of our product candidates, if approved, must be adequate to support our commercial infrastructure. To achieve profitability, our per-patient prices must be sufficient to recover our development and manufacturing costs, and we must be able to sell sufficient amounts of product at these prices. Additionally, the availability of government funded or private insurance coverage for Oxbryta and any other product candidates for any approved indications, if any, and the extent of reimbursement by governmental and private payors, will be essential for most patients to be able to afford Oxbryta or any of our other specialty products, if approved. In particular, the list price for Oxbryta in the United States is $125,000 per year, and a significant percentage of patients with SCD in the United States rely on government programs, such as Medicare and Medicaid, for their coverage of drugs and other medical care, so the availability of federal and state coverage of Oxbryta is critical to the success of our commercialization efforts for Oxbryta in the United States. Sales of Oxbryta or any future drug we may develop or obtain will depend substantially, both domestically and abroad, on the extent to which the costs of such drugs will be paid by third party payors, like private health insurers, including health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, and government health administration programs. If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize Oxbryta or any future drug we may develop or obtain. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved drug products, and even more uncertainty related to the insurance coverage for products, such as Oxbryta, that receive accelerated approval by the FDA under Subpart H (including in the period before required post-marketing confirmatory studies to verify clinical benefit). The process for determining whether a third-party payor will provide coverage for a product may be separate from the process for setting the reimbursement rate that the payor will pay for the product. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the FDA-approved products for a particular indication. Moreover, a third-party payor’s decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. For example, the payor’s reimbursement payment rate may not be adequate or may require co-payments that patients find unacceptably high. Additionally, coverage and reimbursement for products can differ significantly from payor to payor.

In the United States, significant decisions about reimbursement for new medicines are made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, as CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare, and federal and state programs enter into contracts with drug manufacturers for discounted drug prices for Medicare, VA/Federal Supply Schedule, 340B and Medicaid under the Medicaid Drug Rebate Program, among others. The practices and requirements relating to these arrangements are highly complex and subject to differing regulatory requirements and time frames, which will impact the commercialization of Oxbryta. For example, payment of rebates by drug manufacturers for Medicaid purchases are determined by each state, and in some cases, if a company does not enter into a rebate agreement, its Medicaid sales will be subjected to a “prior authorization” procedure that requires state agency approval to qualify a doctor’s prescription for reimbursement. Limitations could also come from entities such as local Medicare carriers, fiscal intermediaries, or Medicare Administrative Contractors. Further, Medicare Part D, which provides a pharmacy benefit to certain Medicare patients, does not require participating prescription drug plans to cover all drugs within a class of products. Our business could be materially adversely affected if private or governmental payors, including Medicare Part D prescription drug plans, were to limit access to, or deny or limit reimbursement of, Oxbryta or any of our product candidates, if approved.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada, and other countries has and will continue to put pressure on the potential pricing and usage of Oxbryta and any future drugs we may develop or obtain. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems, and changes to these regulations over time contribute to uncertainty regarding the ability to obtain pricing and usage approvals for our product candidates outside of the United States. In addition, the prices of medicines under such systems are, in general, substantially lower than in the United States. Other countries allow companies to fix their own prices for medicines, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates outside of the United States. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenues and profits.

In many non-U.S. jurisdictions, including some countries in the European Union, or EU, the proposed pricing for a drug must be approved before it may be lawfully marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted and reimbursement may in some cases be unavailable. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, which may negatively impact the revenues we are able to generate from the sale of the product in that country. The requirements governing drug pricing vary widely from country to country and products may be subject to continuing governmental control following approval. For example, reimbursement in the European Union, or EU, must be negotiated on a country-by-country basis and, in many countries, the product cannot be commercially launched until reimbursement is approved. Furthermore, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use, including by approving a specific price for the medicinal product or adopting a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. In addition, to obtain coverage and reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies, or to meet other criteria for pricing approval. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products or product candidates.

Moreover, increasing efforts by governmental and third-party payors, in the United States and abroad, to cap or reduce healthcare costs may cause such organizations to limit both coverage and levels of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for Oxbryta or our product candidates. We expect to experience pricing pressures in connection with the sale of Oxbryta and any future drugs we may develop or obtain, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative and political changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. For example, third-party payors are increasingly requiring higher levels of evidence of the benefits and clinical outcomes of new technologies, benchmarking against other therapies, seeking performance-based discounts, and challenging the prices charged. We cannot be sure that coverage will be available for Oxbryta or any other product we commercialize and, if available, that the reimbursement rates will be adequate, as increasingly high barriers are being erected to the entry of new products. In addition, drug prices are under significant scrutiny in the markets in which our products are or may be sold, and drug pricing and other healthcare costs continue to be subject to intense political and social pressures that we anticipate will continue and escalate on a global basis.

Our future profitability will depend, in part, on our ability to commercialize and obtain reimbursement for Oxbryta and our product candidates in markets within and outside of the United States and Europe. If reimbursement for Oxbryta, or our product candidates, if approved, is unavailable or limited in scope or amount,

or if pricing is set at unsatisfactory levels, in the United States or, based on the large population of patients with SCD who reside in foreign countries, abroad, our business and operations may be harmed, our stock price may be adversely impacted and experience periods of volatility, we may have difficulty raising funds and our results of operations may be adversely impacted.

Our future growth may depend, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.

Our current plans include the pursuit of commercialization for Oxbryta in Europe, the Gulf Cooperation Council, or GCC, region and Latin America. If we commercialize Oxbryta and any future drugs we may develop or obtain in foreign markets, we would be subject to additional risks and uncertainties, including:

- the burden of complying with complex and changing foreign regulatory, tax, accounting, compliance and legal requirements;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- import or export licensing requirements;
- longer accounts receivable collection times;
- longer lead times for shipping;
- language barriers for technical training;
- reduced protection of intellectual property rights in some foreign countries, and related prevalence of bioequivalent or generic alternatives to therapeutics;
- foreign currency exchange rate fluctuations;
- potential resource constraints, including with respect to patients' ability to obtain reimbursement for our products in foreign markets; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

Any of these factors could impair our ability to commercialize Oxbryta and any future drugs we may develop or obtain outside the United States, which could have a material adverse effect on our business and results of operations.

With the FDA approval of Oxbryta, and with respect to any other product candidate that receives regulatory approval in any jurisdiction, we will be subject to ongoing regulatory obligations and scrutiny, which may include significant restrictions relating to product labeling, distribution or other post-marketing requirements.

Even if a product candidate is approved, regulatory authorities may still impose significant restrictions on its indicated uses, approved labeling, distribution or marketing or may impose ongoing requirements for potentially costly post-marketing studies. For example, because the FDA approved Oxbryta under the accelerated approval pathway under Subpart H, we must conduct at least one post-marketing confirmatory study to verify clinical risk/benefit, which we intend to satisfy through our HOPE-KIDS 2 Study, and we may not be able to successfully and timely complete this study or any other post-marketing confirmatory study as required to maintain approval or achieve full approval. Also, the FDA has restricted the indicated use of Oxbryta under the approved label to patients 12 years and older. While we plan to conduct additional studies to potentially lower the indicated age range to 9 months of age, failure to reach agreement with the FDA on these studies, failure to obtain adequate results from them, or disagreements with regulatory authorities over the interpretation of the results may prevent expansion of the age range within our approved label.

Furthermore, any new legislation addressing drug safety or other drug related issues could result in delays or increased costs to assure compliance. With respect to Oxbryta and any other product candidate that is approved, at a minimum, they will each be subject to current standard ongoing regulatory requirements for labeling, packaging, storage, advertising, promotion, sampling, record-keeping and submission of safety and other post-market information, including both federal and state requirements in the United States. In addition, regulatory agencies may not approve labeling claims that are necessary or desirable for the successful commercialization of Oxbryta, inclacumab or any other product candidates.

For example, the development of Oxbryta for the prophylactic treatment of SCD in pediatric patients is an important part of our current business strategy, and if we are unable to obtain regulatory approval for Oxbryta for the desired age ranges or other key labeling parameters, our business is likely to suffer.

In addition, manufacturers and their facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to current good manufacturing practices, or cGMPs. For Oxbryta, inclacumab and any other product candidates we may pursue, we are wholly reliant on third party contract manufacturers for clinical as well as any commercial supplies of product candidates and products. As such, we and our contract manufacturers are subject to continual review and periodic inspections to assess compliance with cGMP requirements and must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, and quality control. We are also required to report certain adverse reactions and production problems, if any, to the FDA and comparable foreign regulatory authorities, and to comply with requirements concerning advertising and promotion for Oxbryta and any future products. In addition, we are subject to very rapid reporting obligations relating to any adverse events or serious adverse events relating to Oxbryta and our product candidates. Our failure to report adverse events we become aware of within the prescribed timeframes could have serious negative consequences for our commercialization, development programs, business and operations. In addition, any promotional communications or materials for prescription drugs are subject to a variety of complex legal and regulatory restrictions, including, but not limited to, consistency with the approved product's approved label. Failure to obey these standard marketing requirements for Oxbryta or any other approved product, if any, could have serious negative consequences for our commercialization activities, business and operations.

If the FDA or any comparable foreign regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with a sponsor's activities relating to the promotion, marketing, or labeling of a product, these regulatory agencies may impose restrictions or sanctions on that product or us, including requiring withdrawal of the product from the market. In addition, in the United States, a wide range of commercialization and pre-launch activities relating to a drug candidate are subject to potential for significant civil and/or criminal liability and sanctions under federal anti-kickback and fraud and abuse statutes and regulations. If we fail to comply with any of these complex applicable regulatory requirements, a regulatory agency or enforcement authority may:

- issue untitled or warning letters;
- impose civil or criminal penalties;
- impose injunctions;
- impose fines;
- impose additional specialized restrictions on the company's activities and practices;
- suspend regulatory approval;
- suspend ongoing clinical trials;
- seek voluntary product recalls and impose publicity requirements;

- refuse to approve pending applications or supplements to approved applications submitted by us;
- impose restrictions on our operations, including closing our contract manufacturers' facilities; or
- seize or detain products.

As a company, we have limited experience with obtaining approval for, launching or commercializing any product candidates or products, or with complying with most of these complex ongoing regulatory requirements. It will continue to take significant effort and management attention to address compliance with these requirements with respect to Oxbryta in the United States and in any jurisdiction for which we seek to commercialize Oxbryta or any other product candidate, if approved. Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity even if significant liabilities do not result. Any failure to comply with these complex ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenues from Oxbryta or to obtain approval for, launch, commercialize and generate revenues from inclacumab or any future product candidates. If we are subject to regulatory sanctions or if regulatory approval for our product candidates is withdrawn or limited, our business, prospects, financial condition and results of operations would be significantly harmed.

Our business operations and current and future relationships with investigators, health care professionals, consultants, third-party payors and customers are or will be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, health information privacy and security laws, and other healthcare laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

Our current and future operations are or will be directly, or indirectly through our prescribers, customers and third-party payors, subject to various U.S. federal and state healthcare laws and regulations. These laws may impact, among other things, our current business operations, including our sales, marketing, distribution, commercialization, medical and educational programs and our clinical research activities, and they may constrain our business and financial arrangements and relationships with healthcare providers, physicians and other parties through which we market, sell and distribute Oxbryta and any future drugs we may develop or obtain. We may also be subject to additional healthcare, statutory and regulatory requirements and enforcement by foreign regulatory authorities in jurisdictions in which we conduct our business. The laws that may affect our ability to operate include the federal Anti-Kickback Statute, the federal False Claims laws, the U.S. Federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, the Physician Payment Sunshine Act, and analogous state laws and regulations such as state anti-kickback and false claims laws and analogous non-U.S. fraud and abuse laws and regulations, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors.

Ensuring that our business activities (including our operations and arrangements with third parties) comply with applicable healthcare laws and regulations is complex, time-consuming, costly and could materially impact our operations. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse, price reporting or other healthcare laws and regulations.

Although an effective compliance program can mitigate the risk of investigation and prosecution for violations of these requirements, these risks cannot be entirely eliminated. Moreover, achieving and sustaining compliance with applicable federal, state and foreign privacy, security, and fraud requirements is costly. Any action against us for violation of these requirements, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from our business and operations, and could negatively impact the price of our common stock.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform and other factors. Federal and state enforcement bodies in the United States regularly pursue a large number of investigations, prosecutions, convictions and settlements in the healthcare industry, and in the EU, enforcement of the General Data Protection Regulation 2016/679, known as GDPR, is increasing. Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion of products or individuals from U.S. government funded healthcare programs, such as Medicare and Medicaid, or similar programs in other countries or jurisdictions, disgorgement, individual imprisonment, 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, contractual damages, reputational harm, diminished profits, and the curtailment or restructuring of our operations. Further, defending against any such actions can be costly, time-consuming and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. If any of the physicians or other providers or entities with whom we expect to do business is found to not be in compliance with applicable requirements, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment. If any of the above occur, it could adversely affect our ability to operate our business and our results of operations.

Healthcare legislative reform measures may have a material adverse effect on our business and results of operations.

In the United States, there have been and continue to be a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could restrict or regulate post-approval activities, affect our ability to profitably sell Oxbryta and any other drug candidates for which we obtain marketing approval, and prevent or delay marketing approval of our drug candidates. For example, in 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or the Affordable Care Act or ACA, was passed, which substantially changes the way health care is financed by both governmental and private insurers, and significantly impacts the U.S. pharmaceutical industry. Since its enactment, there have been many judicial, executive and legislative challenges to numerous aspects of the ACA. The full impact on our business of the ACA, the potential impacts of any challenges, including any laws repealing and/or replacing elements of it, as well as the political uncertainty surrounding any repeal or replacement legislation, remain unclear.

Additionally, at the federal level, statutes and regulations routinely impact a variety of parameters relating to federal programs and Medicaid. For example, CMS’s final rule regarding the Medicaid drug rebate program, issued in 2016, revised the manner in which the “average manufacturer price” is to be calculated by manufacturers participating in the program. At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical 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. The full impact of these federal and state laws and regulations, as well as other new laws and reform measures that may be proposed and adopted in the future, remains uncertain, but may result in additional reductions in Medicaid and other health care funding, or higher production costs which could have a material adverse effect on our customers and, accordingly, our financial operations.

There have been multiple recent U.S. congressional inquiries and proposed and adopted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship

between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs and biologics. In addition, Congress and multiple presidential administrations have indicated that they will continue to seek new legislative and/or administrative measures to control drug costs.

At the state level, legislatures are increasingly passing legislation and implementing 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 addition, regional health care authorities are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for Oxbryta and our drug candidates, once approved, or put pressure on our product pricing over time.

Moreover, there have been a number of other legislative and regulatory changes in recent years aimed at the biopharmaceutical industry. For instance, the Drug Quality and Security Act imposes obligations on manufacturers of biopharmaceutical products related to product tracking and tracing. Among the requirements of this legislation, manufacturers are required to provide certain information regarding the product to individuals and entities to which product ownership is transferred, will be required to label products with a product identifier, and are required keep certain records regarding the product. The transfer of information to subsequent product owners by manufacturers will eventually be required to be done electronically. Manufacturers are also required to verify that purchasers of the manufacturers' products are appropriately licensed. Further, manufacturers have product investigation, quarantine, disposition, and FDA and trading partner notification responsibilities related to counterfeit, diverted, stolen, and intentionally adulterated products that would result in serious adverse health consequences or death to humans, as well as products that are the subject of fraudulent transactions or which are otherwise unfit for distribution such that they would be reasonably likely to result in serious health consequences or death.

We expect federal and state healthcare reform measures that may be adopted in the future in the United States may result in more rigorous coverage criteria, increased regulatory burdens and operating costs, decreased net revenue from our pharmaceutical products and additional downward pressure on the price that we receive for Oxbryta and any of our drug candidates approved for use. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. These legislative and executive efforts have significantly increased uncertainty regarding the availability of healthcare programs, insurance coverage and reimbursement as a general matter as well as for Oxbryta and our product candidates, and we cannot predict how these events will impact our business or operations. Accordingly, at this time it is difficult to determine the full impact of these efforts on our business. In the United States, many patients with SCD participate in the Medicaid program, and the impact of uncertainty or changes relating to the ACA or healthcare programs, insurance coverage or reimbursement generally have a particularly significant impact on our business or results of operations.

We face intense competition and rapid technological change and the possibility that our competitors may develop therapies that are similar, more advanced, or more effective than ours, which may adversely affect our financial condition and our ability to successfully commercialize Oxbryta and our product candidates.

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. We are currently aware of various existing therapies and development candidates that are or may compete with Oxbryta and inclacumab for the potential treatment of SCD. For example, the FDA approved Novartis' crizanlizumab in November 2019. Both crizanlizumab and inclacumab are human monoclonal antibodies against P-selectin for the treatment of VOCs in patients with SCD. The FDA's approval of crizanlizumab resulted in another new and innovative SCD product entering the United States SCD

market approximately one week earlier than Oxbryta, and substantially earlier than any potential approval of our inclacumab product candidate (which could be a direct competitor to crizanlizumab). As a result, the commercialization of crizanlizumab may also impact our commercialization of Oxbryta in the United States, as well as inclacumab if we are successful in developing and obtaining approval for it for SCD patients. In addition, Novartis announced in October 2020 that the European Commission approved crizanlizumab for the prevention of recurrent VOCs in patients with SCD.

We have competitors both in the United States and internationally, including major multinational pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies. Many of our competitors have substantially greater financial, technical, and other resources, such as larger research and development, marketing and manufacturing organizations. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. As a result, these companies may obtain regulatory approval more rapidly than we are able to and may be more effective in selling and marketing their products as well. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or licensing on an exclusive basis, products that are more effective or less costly than any product candidate that we may develop, or achieve earlier patent protection, regulatory approval, product commercialization and market penetration than we do. Additionally, technologies developed by our competitors may render Oxbryta or our product candidates uneconomical or obsolete, and we may not be successful in marketing any drugs or product candidates against competitors.

If the market opportunities for Oxbryta or our product candidates are smaller than we believe they are, our revenue may be adversely affected, and our business may suffer. Our ability to successfully identify patients and acquire a significant market share will be necessary for us to achieve profitability and growth.

Our initial development and commercialization efforts are focused on the potential of Oxbryta to treat SCD. Our projections of both the number of people who have SCD, as well as the subset of people with SCD who have the potential to benefit from treatment with Oxbryta, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including the scientific literature, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of SCD. The number of patients may turn out to be lower than expected. The effort to identify patients with diseases we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. Additionally, the potential addressable patient population for Oxbryta and our product candidates may be limited or may not be amenable to treatment with Oxbryta or our product candidates, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business. Restrictions on labeling of any approved product, including any restrictions that may be imposed in connection with any approval under Subpart H, may also limit the size of the potential market for Oxbryta and our product candidates. Further, even if we obtain significant market share for Oxbryta or any other drug we may develop or obtain, because the potential target populations are small, we may never achieve profitability despite obtaining such significant market share.

Risks Related to Our Financial Position and Need for Additional Capital

We are a biopharmaceutical company with only one drug approved for marketing in the United States and with a limited operating history. We have incurred significant losses since our inception and anticipate that we will continue to incur losses for the foreseeable future. We have generated limited revenue since our inception, which, together with our limited operating history, may make it difficult for you to assess our future viability.

We are a biopharmaceutical company with only one drug, Oxbryta, approved for marketing, and such approval is only for the United States. We also have a limited operating history upon which you can evaluate our business and prospects. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. To date, we have focused principally on developing Oxbryta, and our current clinical development activities are focused on Oxbryta and our drug candidates. In August 2018, we entered into an exclusive worldwide license agreement with F. Hoffman-LaRoche and Hoffman-La Roche Inc., collectively, Roche, for the development and commercialization of inclacumab.

We are not profitable and have incurred losses in each year since our inception in February 2011 and the commencement of our principal operations in May 2012. Our net losses for the years ended December 31, 2020, 2019, and 2018 were $247.6 million, $266.8 million, and $174.2 million, respectively. As of December 31, 2020, we had an accumulated deficit of $986.5 million. We only begun to generate revenues with the December 2019 commercial launch of Oxbryta, and have financed our operations primarily through the sale of equity securities. We continue to incur significant research and development and other expenses related to our ongoing operations and expect to incur losses for the foreseeable future. We anticipate these losses will increase as we:

- commercialize Oxbryta and continue related clinical development, including conducting (i) our Phase 2a HOPE-KIDS 1 Study of Oxbryta, (ii) our Phase 3 HOPE-KIDS 2 Study, which we intend to serve as our post-confirmatory study of Oxbryta in SCD (and any other post-marketing studies that may be required by regulatory authorities, if any), and (iii) any additional clinical trials of Oxbryta we may conduct now or in the future in SCD patients or for any other indications for Oxbryta, inclacumab or any other product candidates, if any;
- establish and maintain manufacturing and supply relationships with third parties that can provide adequate supplies (in amount and quality) of Oxbryta, inclacumab or any other product candidates to support commercialization and further clinical development;
- seek and obtain additional regulatory and marketing approvals for Oxbryta for SCD, including for younger pediatric patient populations, or any potential approvals we may pursue;
- maintain a sales and marketing organization and enter into selected collaborations to commercialize Oxbryta for SCD or any other approved indication, as well as for any other product candidates;
- maintain a medical affairs organization to advance our engagement with healthcare providers and stakeholders;
- advance our other programs, including inclacumab and any other product candidates, through nonclinical and clinical development and commence development activities for any additional product candidates we may identify and pursue; and
- expand our organization to support our commercialization, research, development and medical activities and our operations as a public company.

Prior to the December 2019 commercial launch of Oxbryta, we had never generated any revenues from product sales, and we may never be able to achieve significant revenues or profitability. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our failure to maintain adequate cash reserves to commercialize Oxbryta, advance our development programs or achieve approval to commercialize any other products, or our failure to achieve sustained profitability, would depress the value of our company and could impair our ability to raise capital, expand our business, market Oxbryta,

diversify our research and development pipeline, market any other product candidates we may identify and pursue (if approved), or continue our operations. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital.

We may require substantial additional funds to achieve our business goals. If we are unable to obtain such funds when needed and on acceptable terms, we could be forced to delay, limit or terminate our commercialization activities for Oxbryta, our product development efforts or other operations. Raising additional capital may subject us to unfavorable terms, cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to Oxbryta, our product candidates or technologies.

We are currently commercializing Oxbryta and investigating Oxbryta in clinical development to support its potential full approval by the FDA and opportunities for potential label expansion. Among other activities, we are evaluating the safety and pharmacokinetics of single and multiple doses of Oxbryta in our HOPE-KIDS 1 Study, a Phase 2a clinical trial in adolescent and pediatric patients with SCD. Our clinical program for Oxbryta also includes our HOPE-KIDS 2 Study, which is our TCD post- confirmatory study of Oxbryta in SCD (to potentially satisfy the FDA's requirement for a post-confirmatory study under Subpart H). In light of the COVID-19 pandemic, we temporarily delayed or paused our research and development activities, including temporarily pausing screening and enrollment in all GBT-sponsored clinical studies (including our HOPE-KIDS 2 Study). Activities on our clinical trials have now resumed, with appropriate measures in place. Assessment of the long-term impact of COVID-19 on our clinical trials is ongoing. In addition, we have initiated and plan to initiate clinical trials on our product candidates, inclacumab and GBT601, and we are conducting nonclinical research activities in other programs.

Discovering, developing and commercializing biopharmaceutical products is expensive and time-consuming, and we expect our selling, general and administrative and research and development expenses to increase substantially in connection with our ongoing activities, particularly as we continue to commercialize Oxbryta and engage in research and development efforts for Oxbryta, inclacumab and other product candidates that we may identify and pursue in clinical trials. As of December 31, 2020 and December 31, 2019, we had working capital of $553.1 million and $556.5 million, respectively, and capital resources consisting of cash and cash equivalents and short and long-term marketable securities totaling $560.9 million and $695.0 million, respectively. We expect that our existing capital resources consisting of cash and cash equivalents and marketable securities will be sufficient to fund our operations for at least the next twelve months. Because the outcome of commercialization, reimbursement and any clinical development and regulatory approval process is highly uncertain, we cannot reasonably estimate the actual capital amounts necessary to successfully commercialize Oxbryta and complete our ongoing and planned additional development of activities for Oxbryta or any other future product candidates.

Our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings or other sources, such as strategic collaborations or license and development agreements. Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize Oxbryta, inclacumab or any other product candidates that we may identify and pursue. Moreover, such financing may result in dilution to stockholders, imposition of debt covenants and repayment obligations, or other restrictions that may affect our business. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans.

Our future funding requirements will depend on many factors, including, but not limited to:

- our ability to successfully commercialize Oxbryta, inclacumab and any other product candidates we may identify and develop in any territories;
- the manufacturing, selling, and marketing costs associated with the commercialization of Oxbryta and the potential commercialization of inclacumab and any other product candidates we may

identify and develop, including the cost and timing of establishing or maintaining our sales and marketing capabilities in any territory(ies);

- the amount and timing of sales and other revenues from Oxbryta, inclacumab and any other product candidates we may identify and develop, including the sales price and the availability of adequate third-party reimbursement;
- the time and cost necessary to conduct and complete multiple ongoing studies (including our HOPE-KIDS 1 Study, our Phase 3 HOPE-KIDS 2 Study and other studies);
- the time and cost necessary to conduct and complete any additional clinical studies required to pursue additional regulatory approvals for Oxbryta for SCD, including our Phase 3 HOPE-KIDS 2 Study (which is necessary to move from our current Subpart H approval to a full approval) and any studies to support potential label expansions into younger SCD pediatric populations, or any other post-marketing studies for Oxbryta for SCD;
- the progress, data and results of clinical trials of Oxbryta and product candidates;
- the progress, timing, scope and costs of our nonclinical studies, our clinical trials and other related activities, including our ability to enroll subjects in a timely manner for our ongoing and future clinical trials of Oxbryta, inclacumab or any other product candidate that we may identify and develop;
- the costs of obtaining clinical and commercial supplies of Oxbryta, inclacumab and any other product candidates we may identify and develop;
- our ability to advance our development programs, including for Oxbryta, inclacumab and any other potential product candidate programs we may identify and pursue, the timing and scope of these development activities, and the availability of approval for any of our other product candidates;
- our ability to successfully obtain any additional regulatory approvals from any regulatory authorities, and the scope of any such regulatory approvals, to market and sell Oxbryta, inclacumab and any other product candidates we may identify and develop in any territory(ies);
- the cash requirements of any future acquisitions or discovery of product candidates;
- the time and cost necessary to respond to technological and market developments;
- the extent to which we may acquire or in-license other product candidates and technologies, and the costs and timing associated with any such acquisitions or in-licenses;
- our ability to attract, hire, and retain qualified personnel; and
- the costs of maintaining, expanding, and protecting our intellectual property portfolio.

Additional funds may not be available when we need them, on terms that are acceptable to us, or at all. If adequate funds are not available to us on a timely basis, we may be required to delay, limit or terminate our development or commercialization activities for Oxbryta, inclacumab or for any other product candidates we may identify and pursue, or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially and adversely affect our business, prospects, financial condition and results of operations.

We are party to a loan and security agreement that contains operating and financial covenants that may restrict our business and financing activities.

In December 2019, we entered into a loan agreement, or Term Loan, with funds managed by Pharmakon Advisors LP, which are BioPharma Credit PLC, as collateral agent, Biopharma Credit Investments V (Master)

LP, as a lender, and BPCR Limited Partnership, as a lender, for a senior secured credit facility under which we were extended an initial term loan of $75.0 million upon execution of the loan agreement and an additional term loan of $75.0 million in November 2020. Borrowings under the Term Loan are secured by a first priority security interest in and a lien on substantially all of our assets, subject to certain exceptions.

The Term Loan restricts our ability, among other things, to:

- sell, transfer or otherwise dispose of any of our business or property, subject to limited exceptions;
- make certain changes to our organizational structure;
- consolidate or merge with other entities or acquire other entities;
- incur additional indebtedness or create encumbrances on our assets;
- pay dividends, other than dividends paid solely in shares of our common stock, or make distributions on and, in certain cases, repurchase our stock;
- repay subordinated indebtedness; or
- make certain investments.

In addition, we are required under the Term Loan to comply with various operating covenants and default clauses that may restrict our ability to finance our operations, engage in business activities or expand or fully pursue our business strategies. A breach of any of these covenants or clauses could result in a default under the Term Loan, which could cause all of the outstanding indebtedness under the facility to become immediately due and payable.

If we are unable to generate sufficient cash to repay our debt obligations when they become due and payable, we may not be able to obtain additional debt or equity financing on favorable terms, if at all, which may negatively affect our business operations and financial condition.

Risks Related to Our Business and the Clinical Development, Regulatory Review and Approval of Our Product Candidates

If we are unable to obtain regulatory approval in additional jurisdictions for Oxbryta or one or more jurisdictions for inclacumab or any future product candidates that we may identify and develop, our business will be substantially harmed.

We cannot commercialize a product until the appropriate regulatory authorities have reviewed and approved the product candidate. Approval by the FDA and comparable foreign regulatory authorities such as the European Medicines Agency, or EMA, is lengthy and unpredictable and depends upon numerous factors. Approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions, which may cause delays in the approval or the decision not to approve an application. We have only obtained regulatory approval for Oxbryta in the United States. In January 2021, the EMA accepted for review our Marketing Authorization Application, or MAA, seeking full marketing authorization of Oxbryta to treat hemolytic anemia in SCD patients ages 12 years and older, and the MAA is undergoing standard review by the EMA. We also plan to submit by mid-2021 a supplemental New Drug Application, or sNDA, to expand the current Oxbryta label to include treatment of SCD in children ages 4 to 11 years, under the FDA's accelerated approval pathway. Thereafter, we also plan to submit a New Drug Application, or NDA, for a new age-appropriate formulation for this patient population. In addition, Great Britain will no longer be covered by centralized MAs, which, if granted, will include our MA for Oxbryta, as a result of the UK's exit from the EU (often referred to as Brexit). We, therefore, plan to utilize the decision reliance procedure available for a period of two years from January 1, 2021, to seek approval of Oxbryta in Great Britain by the Medicines and Healthcare products Regulatory Agency, or MHRA, if our MA is granted by the EMA. While utilizing such decision reliance procedure may significantly accelerate the potential regulatory approval of Oxbryta in Great Britain as compared to making a completely separate

application in parallel to our EMA MAA, we will still need to make a separate application to the MHRA and there is no guarantee as to if or when the MHRA will approve such application. It is possible that we will never obtain these or any other regulatory approvals for Oxbryta, for inclacumab or for any other product candidates we may seek to develop in the future.

Applications for product candidates could fail to receive regulatory approval for many reasons, including, but not limited to:

- we may not be able to demonstrate to the satisfaction of regulatory authorities (including the EMA) that Oxbryta, inclacumab or any other product candidates we may develop are safe and effective for any proposed indications;
- the FDA or comparable foreign regulatory authorities may disagree with our plans or expectations regarding the pathways and endpoints for approval, including the availability of accelerated approval, or the design or implementation of our nonclinical studies or clinical trials;
- the populations studied in our clinical programs may not be sufficiently broad or representative to assure safety or demonstrate efficacy in the full population for which we seek approval;
- the FDA or comparable foreign regulatory authorities may require additional nonclinical studies or clinical trials beyond those we anticipate;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data and results from our nonclinical studies or clinical trials;
- the data and results collected from nonclinical studies or clinical trials of Oxbryta, inclacumab and any other product candidates that we may identify and pursue may not be sufficient to support the submission for regulatory approval;
- we may be unable to demonstrate to the FDA or comparable foreign regulatory authorities that a product candidate's risk-benefit ratio for its proposed indication is acceptable;
- the FDA or comparable foreign regulatory authorities may find deficiencies with or fail to approve the manufacturing processes, test procedures and specifications, or facilities of third-party manufacturers with which we contract and rely on for all clinical and commercial supplies of Oxbryta, inclacumab and any other product candidates (if any); and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may change in a manner that renders our development or manufacturing efforts insufficient for approval.

The lengthy regulatory review and approval process, as well as the inherent unpredictability of the results of nonclinical studies and clinical trials, and our reliance on third-party manufacturers for any product candidates, may result in our failure to obtain regulatory approval to market Oxbryta outside of the United States or to market inclacumab or other product candidates that we may pursue in the United States or elsewhere, which would significantly harm our business, prospects, financial condition and results of operations.

Expedited development and regulatory approval programs for Oxbryta, such as the accelerated approval under Subpart H, may not lead to a faster development or regulatory review or approval process, may not lead to any approval, and may lead to an approval that is later withdrawn.

The FDA approved Oxbryta through the accelerated approval process under Subpart H, and we plan to seek approval under the accelerated approval process under Subpart H for a sNDA to expand the current Oxbryta label to include treatment of SCD in children ages 4 to 11 years. While the FDA approved Oxbryta under Subpart H, we cannot be assured that our planned sNDA will benefit from or receive accelerated approval under Subpart H, or that any other product candidates that we may develop will qualify for or benefit from any such expedited programs in the United States, including under Subpart H, or in any foreign regulatory jurisdictions.

In June 2017, the EMA granted PRIME designation for Oxbryta for the treatment of SCD. The PRIME program is a regulatory mechanism that provides for early and proactive EMA support to medicine developers to help patients benefit as early as possible from innovative new products that have demonstrated the potential to significantly address an unmet medical need. We cannot be assured that Oxbryta or any other product candidates that we may develop will benefit from a PRIME program designation.

The FDA grants accelerated approval under Subpart H for new drugs that address serious or life-threatening illnesses and that provide meaningful therapeutic benefit to patients over existing treatments. Under Subpart H, the FDA may grant marketing approval for a new drug product on the basis of adequate and well-controlled clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity.

Drugs approved under Subpart H are required to be further evaluated in at least one post-marketing study to verify clinical benefit. To satisfy such requirement, we are conducting our TCD post-confirmatory study, the HOPE-KIDS 2 Study. We previously announced that the FDA agreed that TCD flow velocity would be an acceptable primary endpoint in a post-approval confirmatory study of Oxbryta to demonstrate stroke risk reduction for purposes of full approval by the FDA and that we had reached final agreement with the FDA on the design of the TCD post-confirmatory study.

We temporarily paused screening and enrollment on our HOPE-KIDS 2 Study due to the impact of the COVID-19 pandemic. Activities on our clinical trials have now resumed, with appropriate measures in place. Assessment of the long-term impact of COVID-19 on our clinical trials is ongoing and we may not be able to complete this study or any other successful post-marketing confirmatory study as required to maintain approval and achieve full approval, or data and results from our required post-marketing confirmatory program may not verify Oxbryta's clinical benefit to maintain approval and achieve full approval, in which case the product may be required to be withdrawn from market approval.

Access to any expedited program, including through the FDA (such as accelerated approval under Subpart H), may be withdrawn by the FDA or a foreign regulatory authority if it believes that the program is no longer supported by data from our clinical development, and accelerated approval under Subpart H may be withdrawn if, among other reasons, required post-marketing confirmatory studies are not completed or if the FDA determines the results of post-marketing confirmatory studies do not verify clinical benefit.

All of our programs other than Oxbryta are still in earlier development stages, so we remain very reliant on the potential success of Oxbryta in the clinic and in the marketplace. If we are unable to successfully commercialize Oxbryta for SCD or complete clinical development of Oxbryta, or experience delays in doing so, our business will be materially harmed.

To date, we have invested a majority of our efforts and financial resources in the nonclinical and clinical development of Oxbryta, including conducting nonclinical studies and clinical trials, submitting and obtaining approval for an NDA, and providing general and administrative support for these operations. Our other clinical product candidates are in the earlier stages of development, and our only clinical development program for Oxbryta is in SCD. Our future success is highly dependent on our ability to successfully continue to develop, obtain and maintain regulatory approval for, and commercialize Oxbryta inside and outside the United States for SCD.

We are evaluating Oxbryta in SCD patients in our ongoing HOPE-KIDS 1 Study, our HOPE-KIDS 2 Study (which is our post-approval confirmatory study), and other ongoing and planned clinical trials. In light of the COVID-19 pandemic, we temporarily delayed certain of our research and development activities, including temporarily pausing screening and enrollment in all GBT-sponsored clinical studies. Activities on our clinical trials have now resumed, with appropriate measures in place. Assessment of the long-term impact of COVID-19 on our clinical trials is ongoing.

All of our other programs are in earlier stages of research and development. As a result, even after in-licensing the inclacumab program, we are very dependent on Oxbryta for our business, prospects, financial condition and results of operations.

We are also very dependent on the data and results that we obtain over time from our clinical program for Oxbryta, including the HOPE-KIDS 2 Study. The primary endpoint of the HOPE-KIDS 2 Study relates to TCD measurement, and we have not previously conducted any Phase 3 clinical study of Oxbryta in SCD patients using this primary endpoint, nor do we believe this measure has been used as a primary endpoint for any registrational studies for any other SCD therapies.

As we continue our clinical development of Oxbryta, the additional data we generate could be different from, including less favorable in terms of efficacy and/or safety, than the data generated and discussed with the FDA to date. If this were to occur, it could significantly impact our continued development and commercialization of Oxbryta. In addition, depending on the results we obtain from our HOPE-KIDS 2 Study, which we intend to satisfy our post-approval confirmatory requirement under Subpart H, accelerated approval of Oxbryta under Subpart H may be withdrawn (which would also mean full approval would not be achieved, and could also mean that Oxbryta could be required to be removed from the market) if the required post-marketing confirmatory program is not completed or if the FDA determines the results do not verify clinical risk/benefit. If our planned submission of a sNDA to expand the current Oxbryta label to include treatment of SCD in children ages 4 to 11 years is approved and our HOPE-KIDS 2 Study also serves as the post-approval confirmatory study under Subpart H for any such pediatric approval, any accelerated approval of Oxbryta in this pediatric population, if any, may be withdrawn as well depending on the results we obtain from the HOPE-KIDS 2 Study. We do not have a special protocol assessment agreement in place with the FDA for our HOPE-KIDS 2 Study.

We cannot be certain that Oxbryta, inclacumab or any other product candidates that we seek to develop will be successful in nonclinical studies or clinical trials or receive and maintain any regulatory approvals. If we do not receive regulatory approval for, regulatory approval is withdrawn from, or we otherwise fail to successfully commercialize Oxbryta, inclacumab or any other product candidates, we are likely to need to spend significant additional time and resources to identify other product candidates, advance them through nonclinical and clinical development and apply for regulatory approvals, which would adversely affect our business, prospects, financial condition and results of operations.

The development of Oxbryta as a potential disease-modifying anti-sickling agent in SCD patients represents a novel therapeutic approach, and there is a risk that the outcomes of our clinical trials will not be favorable or otherwise support any further decision to seek or grant or maintain any regulatory approval.

We have concentrated our product research and development efforts on developing novel, mechanism-based therapeutics for the treatment of grievous blood-based disorders with significant unmet need, and our future success depends on the success of this therapeutic approach. The clinical trial requirements of the FDA and other comparable regulatory agencies and the criteria these regulators use to determine the safety and efficacy of any product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential product. To date, there are only four approved therapies for SCD, Oxbryta, crizanlizumab, hydroxyurea, and L-glutamine, and Oxbryta is the first approved therapy directed toward preventing the polymerization of hemoglobin molecules as a mechanism to reduce red blood cell sickling in SCD patients. As a result, the design and conduct of clinical trials for a therapeutic product candidate such as Oxbryta that targets this mechanism in SCD patients are subject to unknown risks, and we may experience setbacks with our ongoing or planned clinical trials of Oxbryta in SCD because of the limited clinical experience with its mechanism of action in these patients.

In particular, regulatory authorities in the United States and Europe have not issued definitive guidance as to how to measure and achieve efficacy in treatments for SCD. Based on our discussions with the FDA regarding

the design for the HOPE Study, we determined to measure change in hemoglobin levels as the primary endpoint in the Phase 3 HOPE Study. This primary endpoint has not been used previously in a registration study for any SCD treatment. As a result, regulators outside of the United States have not determined that such data would signify a clinically meaningful result in SCD patients or would support seeking or obtaining regulatory approval.

We did not achieve statistically significant results with respect to either potential key secondary endpoint in Part A of the HOPE Study (relating to episodes of VOCs and to the Patient Reported Outcome instrument developed by us), and we may not achieve key endpoints in other clinical trials, such as any post-marketing confirmatory studies. In addition, we may not achieve the same results with respect to the primary endpoint in Part A of the HOPE Study in other ongoing of future clinical trials, including our ongoing TCD post-confirmatory study, the HOPE-KIDS 2 Study. Any inability to design clinical trials with protocols and endpoints acceptable to applicable regulatory authorities, and to obtain and maintain regulatory approvals for Oxbryta, inclacumab and any other product candidates that we may pursue, would have an adverse impact on our business, prospects, financial condition and results of operations.

Results of earlier studies may not be predictive of future clinical trial results, and initial studies may not establish or maintain an adequate safety or efficacy profile for Oxbryta, inclacumab or other product candidates that we may pursue to justify proceeding to advanced clinical trials or an application for regulatory approval.

The results of nonclinical studies and clinical trials of Oxbryta, inclacumab and of any future product candidates that we may pursue may not be predictive of the results of later-stage clinical trials, and interim results of a clinical trial may not necessarily predict final results. For example, our nonclinical studies and clinical trials to date of Oxbryta in SCD have involved mostly one genotype of SCD, known as HbSS, and the results of these studies may not be replicated in other genotypes of SCD in clinical trials or in the general patient population. In addition, the results obtained in our development program for SCD patients aged 12 years and older, such as in our Phase 3 HOPE Study, may not be replicated in our ongoing studies in pediatric populations, including our HOPE-KIDS 1 Study and HOPE-KIDS 2 Study.

Products evaluated in post-marketing studies and product candidates in later stages of clinical trials may fail to demonstrate the desired safety and efficacy despite having progressed through nonclinical studies and earlier clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier studies, and we cannot be certain that we will not face similar setbacks. Since Oxbryta was approved under Subpart H requiring successful completion of a confirmatory clinical trial to obtain full FDA approval, if the results of our confirmatory study fail to demonstrate efficacy and safety adequate to obtain full regulatory approval for Oxbryta and maintain its marketing approval in the United States, this would have a substantial impact on our business, prospects, financial condition and results of operations.

In addition, nonclinical and clinical data are often susceptible to various interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in nonclinical studies and clinical trials have nonetheless failed to obtain marketing approval, in part because of differing interpretations of data and results by regulatory authorities. For example, our HOPE-KIDS 1 Study and our ActIVe Phase 4 study designed to evaluate the effect of Oxbryta on exercise capacity, as measured by cardiopulmonary exercise testing (CPET) in patients 12 years of age and older with SCD, utilize an “open-label” trial design, and we may use open-label trial designs in the future. An open-label clinical trial is one in which both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. In many cases, open-label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels, as in the case of our HOPE-KIDS 1 Study. Open-label clinical trials may be subject to “patient bias,” where patients perceive their symptoms to have improved merely due to their awareness of receiving the treatment under investigation, or “investigator bias,” where those assessing and reviewing the physiological outcomes of the clinical trials are aware of the treatment administered to patients and may interpret

the information of a treated group more favorably given this knowledge. The results from an open-label trial may not be predictive of future clinical trial results with Oxbryta or any of our product candidates when studied in a controlled environment with a placebo or active control. In addition, data and results from later studies or programs may conflict with earlier findings for a variety of other reasons.

Our failure to demonstrate the required characteristics to support continued marketing of Oxbryta in the United States, full FDA approval, marketing approval for Oxbryta outside of the United States, or marketing approval for inclacumab or any other product candidate we may choose to develop, in any ongoing or future clinical trials would substantially harm our business, prospects, financial condition and results of operations.

Before we are able to obtain any marketing approval for Oxbryta outside of the United States, foreign regulatory authorities may impose additional requirements, the scope of which are not fully known at this time.

Before we can obtain any marketing approval for a drug candidate for any potential indication, we must successfully complete clinical trials. The FDA typically requires at least two pivotal, well-controlled Phase 3 clinical trials as a condition to the submission of an NDA and does not usually consider a single Phase 3 clinical trial to be adequate to support product approval. The FDA will typically only consider relying on one pivotal trial if, in addition, other well-controlled studies of the drug exist (for example, for other dosage forms or in other populations) or if the pivotal trial is a multi-center trial that provides highly reliable and statistically strong evidence of an important clinical benefit, and a confirmatory study would have been difficult to conduct on ethical grounds.

The FDA approved Oxbryta for the treatment of SCD under the accelerated approval pathway under Subpart H, and approval under this accelerated pathway means that we are required to conduct at least one post-marketing confirmatory study sufficient to verify Oxbryta's clinical benefit, which we intend to satisfy through our HOPE-KIDS 2 Study. With respect to Europe, the EMA accepted for review our Marketing Authorization Application, or MAA, seeking full marketing authorization of Oxbryta to treat hemolytic anemia in SCD patients ages 12 years and older. The MAA is undergoing standard review by the EMA, and it includes data from our Phase 3 HOPE Study and our Phase 2 HOPE-KIDS 1 Study, both of which enrolled patients at clinical sites in Europe.

Foreign authorities may not consider the results of our ongoing, planned or potential future clinical trials of Oxbryta to be sufficient to obtain or maintain any regulatory and/or pricing or reimbursement approvals outside of the United States. For example, in the EU the EMA may not approve the MAA we have submitted which is under standard review for the potential approval of Oxbryta to treat hemolytic anemia in SCD patients ages 12 years and older. Any post-marketing confirmatory studies, if required, would result in increased costs and potential delays in the clinical development and marketing approval process outside the United States, which may require us to expend more resources than are available to us. In addition, it is possible that the FDA and the comparable foreign authorities may have divergent opinions on the elements necessary for a successful NDA or other application for marketing authorization, as applicable, which may cause us to alter our development, regulatory and/or commercialization strategies.

We may encounter substantial delays in conducting or completing our clinical trials, which in turn will result in additional costs and may ultimately prevent successful or timely completion of the clinical development and commercialization of Oxbryta, inclacumab or any other product candidates we may identify and pursue.

Before obtaining marketing approval from regulatory authorities for the sale of any our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates in humans. In addition, because the FDA approved Oxbryta under the accelerated approval pathway under Subpart H, we must conduct at least one post-marketing confirmatory study to verify clinical risk/benefit, which we intend to satisfy through our HOPE-KIDS 2 Study. Clinical testing is expensive, time-consuming and uncertain

as to outcome, and we cannot guarantee that any of our current or future clinical trials for Oxbryta or any other product candidates we may pursue will be conducted as planned or completed on schedule, if at all. For example, in light of the COVID-19 pandemic, we temporarily paused all site activation, screening and enrollment activities for our HOPE-KIDS 2 Study (other than, where feasible, contracting and other administrative study start-up activities). Activities on our clinical trials have now resumed, with measures in place that we believe are appropriate. Assessment of the long-term impact of COVID-19 on our clinical trials is ongoing, and it is unknown whether we will be required to pause or delay such activities again in the future. A failure of one or more clinical trials can occur at any stage of testing. Events that may prevent successful or timely completion of clinical development include:

- delays or failures in reaching a consensus with regulatory agencies on study design, including clinical endpoints sufficient to support an approval decision;
- delays or failures to receive approval for conduct of clinical studies in one or more geographies, which could result in delays in enrollment and availability of data and results;
- delays or failures in reaching agreement on acceptable terms with a sufficient number of prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- delays in obtaining required Institutional Review Board, or IRB, or ethics committee approval for each clinical trial site;
- delays in recruiting a sufficient number of suitable patients to participate in our clinical trials;
- imposition of a clinical hold by any regulatory authority, including if imposed due to safety concerns after an inspection of our clinical trial operations or study sites;
- failure by our CROs, clinical sites, participating clinicians or patients, other third parties or us to adhere to clinical trial, regulatory or legal requirements;
- failure to perform in accordance with the FDA's good clinical practices, or GCPs, or applicable regulatory requirements in other countries;
- delays in the testing, validation, manufacturing and delivery of sufficient quantities of Oxbryta or our product candidates or study related devices to the clinical sites and patients;
- delays in having patients enroll or complete participation in a study in accordance with applicable protocols or protocol amendments or return for post-treatment follow-up;
- reduction in the number of participating clinical trial sites or patients, including by dropping out of a trial;
- failure to address in an adequate or timely manner any patient safety concerns that arise during the course of a trial;
- unanticipated costs or increases in costs of clinical trials of Oxbryta or our product candidates;
- the occurrence of serious adverse events or other safety concerns associated with Oxbryta or our product candidates; or
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols or obtaining additional IRB or other approvals to conduct or complete clinical studies of Oxbryta or our product candidates.

We could also encounter delays if a clinical trial is suspended or terminated for any reason (which could occur as a result of termination by us, by the IRBs or ethics committees of the institutions in which such trials are being conducted, by an independent Safety Review Board for such trial, or by the FDA or other regulatory

authorities). A clinical trial can be suspended or terminated for a wide variety of reasons, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by us, or the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, or failure to demonstrate a benefit from using Oxbryta or a drug candidate. In addition, if we make manufacturing or formulation changes to Oxbryta or our product candidates, we may need to conduct additional studies to bridge the development program from the data and results for the previous version to the modified version.

Clinical trial delays could shorten any periods during which we may have the exclusive right to commercialize a drug or product candidate or allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize Oxbryta and our product candidates. In addition, any delays in completing our clinical trials will increase our costs, slow down our drug development and approval process or jeopardize our ability to maintain our current FDA approval of Oxbryta (or to achieve full FDA approval or any product approvals outside of the United States), and jeopardize our ability to continue or commence product sales and generate revenues. Any of these occurrences may significantly harm our business, prospects, financial condition and results of operations.

Difficulty in enrolling patients or maintaining compliance with dosing or other requirements in our clinical trials could delay or prevent clinical trials of Oxbryta or our product candidates, which in turn could delay or prevent our ability to obtain or maintain the regulatory approvals necessary to commercialize Oxbryta and our product candidates.

Identifying and qualifying patients to participate in our ongoing and planned clinical trials of Oxbryta, inclacumab, and any other product candidates that we may develop are critical to our success. Our clinical development efforts are initially focused on rare chronic blood diseases. For example, according to estimates by the Centers for Disease Control and Prevention, the prevalence of SCD, for which Oxbryta is indicated, is approximately 100,000 individuals in the United States. Accordingly, there are limited patient pools from which to draw for clinical trials in our target indications. We may not be able to identify, recruit, and enroll a sufficient number of subjects to complete our clinical trials of Oxbryta because of the perceived risks and benefits of Oxbryta, the availability of competing therapies and clinical trials, the proximity and availability of clinical trial sites for prospective subjects and the subject referral practices of physicians, among other factors.

Further, if subjects in our clinical trials fail to comply with our dosing regimens or other requirements in our clinical trials, we may not be able to generate clinical data acceptable to the FDA or comparable regulatory authorities in our trials. For example, successful conduct of our HOPE-KIDS 2 Study (our post-approval confirmatory study) will require consistency in TCD measurements, which is why we are providing specific training and equipment to participating clinical trial sites in such clinical trial. Failure to achieve consistent high-quality readings could result in data that are difficult to interpret or that delay or confound the results. If clinical sites or patients are unwilling or unable to participate in, complete or comply with the protocols for our studies for any reason, the timeline for recruiting subjects, conducting studies and obtaining regulatory approval of potential products may be delayed.

If we experience difficulties or delays in enrollment or are otherwise unable to successfully complete any clinical trial of Oxbryta, or any other product candidates we may pursue, our costs are likely to increase, and our ability to obtain and maintain regulatory approval (or achieve full regulatory approval of Oxbryta) and generate product revenue from Oxbryta and any of these product candidates will be impaired. Any of these occurrences would harm our business, prospects, financial condition and results of operations.

If serious adverse events or unacceptable side effects are identified during the development of Oxbryta or our product candidates, we may need to delay, limit or terminate our clinical development activities.

Clinical trials by their nature utilize only a small sample of the potential patient population. For example, our Phase 3 HOPE Study in SCD patients represents only a very small fraction of all patients with SCD. Side

effects of Oxbryta, inclacumab or any other product candidates that we may develop may be uncovered only in later stages of clinical trials, or only in trials involving different patient populations (such as pediatric patients), or only during post-approval studies, such as our HOPE-KIDS 2 Study (our TCD confirmatory study), or the safety reporting required for approved products. Many approved drugs and product candidates that initially showed promise in early stage testing have later been found to cause side effects that prevented their further development. Moreover, a nonclinical toxicology study with Oxbryta in non-humans and clinical trials involving other hemoglobin modifiers (other than Oxbryta) have shown a decrease in oxygen delivery to tissue when a significant percentage of hemoglobin is modified. Hemoglobin modifiers, by increasing HbS's affinity for oxygen, can cause a shift in oxygen levels, potentially resulting in tissue hypoxia. To date, clinical studies of Oxbryta have not shown evidence of tissue hypoxia. However, if Oxbryta or any other product candidates that we may develop are associated with tissue hypoxia or any other undesirable side effects or unexpected undesirable characteristics in clinical trials or nonclinical studies, we may need to abandon their development or limit their development to more narrow uses or subpopulations, which could adversely affect our business, prospects, financial condition and results of operations. In addition, with respect to Oxbryta, such a result may also significantly impact or require us to terminate our commercialization of Oxbryta.

Although the FDA and the European Commission have each granted orphan drug designation for Oxbryta for the potential treatment of SCD, we may not receive orphan drug designation for inclacumab or any other product candidates for which we may submit new applications for orphan drug designation, and any orphan drug designations that we have received or may receive in the future may not confer marketing exclusivity or other expected commercial benefits.

Our business strategy focuses on the development of product candidates for the treatment of rare, chronic blood disorders that may be eligible for FDA or EU orphan drug designation. Regulatory authorities in some jurisdictions, including the United States and the EU, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States. In the EU, the Committee for Orphan Medicinal Products of the EMA recommends orphan drug designation to promote the development of medical products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the EU and for which no satisfactory method of diagnosis, prevention, or treatment is authorized (or in other very limited circumstances). In 2015 and 2016, respectively, the FDA and the European Commission (acting on a positive recommendation by the EMA) each granted orphan drug designation for Oxbryta for the treatment of patients with SCD.

Generally, if a drug with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for the same drug for the same indication for that time period. The applicable period is seven years in the United States and 10 years in the EU. The EU exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

Although the FDA and the EMA have each granted orphan drug designation to Oxbryta for the treatment of SCD, we may apply for orphan drug designation for Oxbryta in other jurisdictions or for other indications, or for inclacumab or other product candidates we may develop and pursue in the future. Applicable regulatory authorities may not grant us these additional designations. In addition, the exclusivity granted under any orphan drug designations that we have received from the FDA and the EMA, or may receive from any other regulatory authorities (if any), may not effectively protect Oxbryta or any other product candidate we pursue from competition because different drugs can be approved for the same condition. For example, in the United States,

even after an orphan drug is approved, the FDA can subsequently approve another drug for the same condition if the FDA concludes that the later drug is clinically superior, or the FDA can approve a competitor application for the same drug for a different indication than the orphan drug designation. In addition, legislators or regulators may reevaluate and elect to modify orphan drug exclusivity laws or regulations in ways that could materially impact existing or future orphan drug designations. We do not know if, when, or how such authorities may change their orphan drug regulations and policies in the future, and it is uncertain how any changes may affect our business. Any inability to secure or maintain orphan drug designation or the exclusivity benefits of this designation would have an adverse impact on our ability to develop and commercialize our product candidates. In addition, even if any orphan drug designations we receive are maintained, we may be unable to realize significant commercial benefits from these regulatory exclusivities for Oxbryta or any other product candidate we pursue.

Risks Related to Our Reliance on Third Parties

We rely, and will continue to rely, on third parties to conduct some of our nonclinical studies and all of our clinical trials and also to perform other tasks for us. If these third parties perform in an unsatisfactory manner, it may harm our business.

We have relied upon and plan to continue to rely upon third-party CROs, including our CROs for our clinical trials of Oxbryta, to monitor and manage data for some of our ongoing nonclinical studies and for all of our clinical programs. We rely on these parties for execution of these nonclinical studies and clinical trials, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies and trials are conducted in accordance with the applicable protocol, legal, regulatory, and scientific standards and our reliance on the CROs does not relieve us of our regulatory responsibilities. We and our CROs and other vendors are required to comply with all applicable cGMPs, GCPs, and current good laboratory practices, or GLPs, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area, or EEA, and comparable foreign regulatory authorities. Regulatory authorities enforce these regulations through periodic inspections of study sponsors, principal investigators, study sites, manufacturing facilities, nonclinical testing facilities and other contractors. If we or any of our CROs or other vendors fail to comply with applicable regulations, the data generated in our nonclinical studies and clinical trials may be deemed unreliable and the applicable regulatory authorities may suspend regulatory approval or require us to repeat or to perform additional nonclinical and clinical studies before approving our marketing applications, which would delay the regulatory review and approval process, perhaps significantly.

In addition, the execution of nonclinical studies and clinical trials, the subsequent compilation and analysis of the data and results produced, and the supply of product for our trials and commercialization, requires coordination among various parties. In order for these functions to be carried out effectively and efficiently, it is imperative that these parties communicate and coordinate with one another. These third parties may terminate their agreements with us upon short notice for our uncured material breach, or under certain other circumstances. If any of our relationships with our third-party CROs or other key vendors (including manufacturing and testing facilities) terminates, we may not be able to enter into arrangements with alternative CROs or other key vendors on a timely basis or at all, or do so on commercially reasonable terms. In addition, our CROs and other key vendors are not our employees, and except for remedies available to us under our agreements with them, we cannot control whether they devote sufficient time and resources to our programs. Furthermore, these third party CROs or other key vendors may also have relationships with other entities, some of which may be our competitors. If CROs or other key vendors do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the data and results they obtain or the product they supply is compromised for any reason (including failure to adhere to our protocols, or regulatory requirements), our development activities may be extended, delayed, or terminated and we may not be able to seek, obtain or maintain regulatory approval for or successfully commercialize Oxbryta or any of our product candidates. Switching or adding CROs or any other key vendors involves additional cost, time and

management resources and focus. In addition, our CROs or other key vendors may also generate higher costs than anticipated.

In addition, in connection with any NDA or MMA for our product candidates, pre-approval inspections by a regulatory agency of our facilities and/or those of third parties involved in the drug development program may occur, including at clinical trial sites, CMOs or other third parties on which we are very reliant. Significant negative results from pre-approval inspections, if any, could materially delay potential approval of the drug candidate. Accordingly, our dependence on third-party CROs, other key vendors and other third parties may subject us to challenges, delays and costs that have a material adverse impact on our business, prospects, financial condition and results of operations.

We rely entirely on third parties for the manufacturing of Oxbryta, inclacumab and for any other product candidates we may pursue for nonclinical studies and clinical trials, and we expect to continue to do so for the commercialization of Oxbryta in the United States and for any other product commercialization we may conduct. Our business could be harmed if any of those third parties fail to provide us with sufficient quantities of drug product, or fail to do so at acceptable quality or quantity levels or prices.

We do not currently have, nor do we plan to acquire, the infrastructure or capability internally to manufacture drug supplies for our ongoing commercialization of Oxbryta and for any clinical trials we are conducting or may conduct for Oxbryta, inclacumab or any other future product candidates, and we do not presently expect that we will establish or acquire the resources necessary to manufacture any of our product candidates on a commercial scale. We rely, and expect to continue to rely, wholly on third-party manufacturers to produce our product candidates for our clinical trials, as well as for commercial manufacture or any required post-marketing studies of Oxbryta, and we expect to do the same with respect to any other product candidates, if any, that receives marketing approval. If any manufacturer with whom we contract fails to perform its obligations, we may be forced to manufacture the materials ourselves, for which do not currently have or anticipate developing the requisite capabilities or resources, or enter into an agreement with one or more different manufacturers, which we may not be able to do on reasonable terms and timelines, if at all. Although we generally do not begin a clinical trial unless we believe we have a sufficient supply of a product candidate to complete the trial, any significant delay or discontinuity in the supply of a product candidate, or the raw material components thereof, for an ongoing clinical trial due to the need to replace a third-party manufacturer could considerably delay the clinical development and potential regulatory approval of our product candidates, which could harm our business and results of operations. We expect to rely on multiple third parties for the manufacture of commercial supplies of Oxbryta as well as for inclacumab or any other product candidates, if approved.

We may be unable to establish or maintain any agreements with third-party manufacturers for Oxbryta, inclacumab or any other product candidates, or to do so on acceptable terms. Even if we are able to establish or maintain agreements with third-party manufacturers for Oxbryta, inclacumab or any other product candidates, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach or termination of the manufacturing agreement by the third party or by us, including at a time that is costly or inconvenient for us;
- the inability of the third party to satisfy our ordering requirements as to quality, quantity and/or price, including, without limitation, potential impact on supply chain due to the impact of public health risks, such as the COVID-19 pandemic;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the unwillingness of the third party to extend or renew terms with us when desired.

Our reliance on third-party manufacturers in connection with inclacumab entails additional potential risks, in connection with the transfer of technology from Roche to our third-party manufacturer for inclacumab, and the

requirement for approval by the FDA of any Investigational New Drug application, or IND, from the new site, which may not be successful. In addition, because of our lack of experience manufacturing a biologic product, we will have greater reliance on the expertise and experience of our third-party manufacturer for inclacumab.

Furthermore, all of our contract manufacturers are engaged with other companies to supply and/or manufacture materials or products for such companies, which exposes our manufacturers to regulatory and market risks for the production of such third-party materials and products. As a result, failure to meet the regulatory requirements for the production of those materials and products may affect the regulatory assessment or clearance of our contract manufacturers' facilities generally, and industry consolidation, pricing or other market factors may cause our contract manufacturers to scale back, terminate or refuse to renew desired arrangements for our materials. Any of these factors could negatively impact our ability to commercialize Oxbryta or develop, obtain additional regulatory approval for or further market, as applicable, Oxbryta or our product candidates, if approved.

Oxbryta, inclacumab and any future product candidates that we may identify and pursue may compete with other product candidates and marketed drugs for access to manufacturing facilities. Any performance failure on the part of our existing or future manufacturers could delay or impair clinical development, marketing approval or commercialization. Although we believe we have adequate supplies to commercialize Oxbryta and conduct our ongoing clinical trials, if we are unable to enter into relationships with additional contract manufacturers, or our current or future contract manufacturers cannot perform as agreed, we may experience delays and incur additional costs in our continued commercialization and clinical development activities. Our current and anticipated future dependence upon others for the manufacturing of Oxbryta, our product candidates and any other marketed drugs may adversely affect our future profit margins and our ability to commercialize Oxbryta or any other product candidates that receive marketing approval on a timely and competitive basis.

If the contract manufacturing facilities on which we rely do not continue to meet regulatory requirements or are unable to meet our supply demands, our business will be harmed.

All entities involved in the preparation of therapeutics for clinical trials or commercial sale, including our existing contract manufacturers for Oxbryta and for our product candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical trials must be manufactured in accordance with cGMPs, or similar regulatory requirements outside the United States. These regulations govern manufacturing processes and procedures, including recordkeeping, and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of contaminants or to inadvertent changes in the properties or stability of Oxbryta or our product candidates. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, suspension of production, seizures or voluntary recalls of product candidates or marketed drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect clinical or commercial supplies of Oxbryta, inclacumab or any of our future product candidates.

Among other requirements, we or our contract manufacturers must supply all necessary documentation in support of an NDA or MAA seeking approval of a product candidate on a timely basis and must adhere to GLP and cGMP regulations enforced by the FDA and other regulatory agencies through their facilities inspection programs. The facilities and quality systems of some or all of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval for Oxbryta. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of Oxbryta, inclacumab or any of our future product candidates or the associated quality systems. Although we oversee the contract manufacturers, we cannot control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with these complex regulatory requirements. If these manufacturers, facilities, records or systems do not pass pre-approval

inspections and reviews, additional regulatory approval of Oxbryta or regulatory approval of inclacumab or any of our other future product candidates may never be granted or may be substantially delayed.

In addition, at any time following approval of a product for sale, the regulatory authorities also may audit the manufacturing facilities of our third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that could be costly or time consuming for us or a third party to implement, and that may include the temporary or permanent suspension of a clinical study or commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business.

Additionally, if supply from one approved manufacturer is interrupted, an alternative manufacturer would need to be qualified through a supplement to an NDA, MAA variation or equivalent foreign regulatory filing, which would result in further delay, uncertainty and costs. If this occurs, our commercial distribution or clinical trials could be delayed significantly as we establish alternative supply sources. In some cases, the technical skills required to manufacture our products or product candidates may be proprietary to the original manufacturer and we may have contractual restrictions or other challenges in seeking to transfer such skills to a back-up or alternate supplier. In addition to verifying that any new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations, we would also need to verify, such as through a manufacturing comparability study, that any new manufacturing process will produce our product or product candidate according to the specifications previously submitted to or approved by the FDA or another regulatory authority. The delays and costs associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates or commercialize our products in a timely manner or within budget. In addition, changes in manufacturers often involve changes in manufacturing procedures and processes, which, in the case of the manufacturers that supply our product candidates, could require that we conduct bridging studies between our prior clinical supply used in our clinical trials and that of any new manufacturer. We may be unsuccessful in demonstrating the comparability of clinical supplies, which could require the conduct of additional clinical trials and result in the suspension of or delays in our commercialization activities and clinical development plans. Any of these factors could cause us to incur higher costs and could cause the delay or termination of clinical trials, regulatory submissions, required approvals, or commercialization of Oxbryta or our product candidates. Furthermore, if our suppliers fail to meet contractual requirements and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials may be delayed or we could lose potential revenue.

Our reliance on third parties requires us to share our trade secrets and confidential information, which increases the possibility that a competitor will discover them or that our critical information will be misappropriated or disclosed.

Because we rely on third parties to manufacture Oxbryta and to conduct other aspects of our clinical development activities, as well as for inclacumab and any other product candidates we may pursue, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, other forms of agreement with any collaborators, CROs, manufacturers and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets and confidential information may become known by our competitors, may inadvertently be incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor’s discovery of our trade secrets or confidential information, or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

Our agreements typically restrict the ability of certain collaborators, CROs, manufacturers, other key vendors and consultants to publish data, although many of our contracts provide for the right to publish data in specified circumstances. A significant breach of these publication provisions could impair our competitive position. In addition, we conduct joint research and development programs that may require us to share trade secrets and other confidential information. Despite our efforts to protect our trade secrets and confidential information, our competitors may discover them, either through breach of agreements relating to these programs, independent development or publication of information where we do not have proprietary or otherwise protected rights at the time of publication. A competitor's discovery of our trade secrets or confidential information would impair our competitive position and have an adverse impact on our business.

Risks Related to Our Intellectual Property

If we or our licensors are unable to obtain and maintain sufficient intellectual property protection for Oxbryta or our product candidates, or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize product candidates similar or identical to ours, and our ability to successfully commercialize Oxbryta, inclacumab and other product candidates that we may pursue may be impaired. Changes in patent policy and rules could impair our ability to protect our products and increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

As is the case with other biopharmaceutical companies, our success depends in large part on our ability to obtain and maintain protection of the intellectual property, particularly patents, that we may exclusively license or own solely and jointly with others in the United States and other countries with respect to Oxbryta and our product candidates and technology, including inclacumab. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to Oxbryta and our product candidates.

Obtaining and enforcing biopharmaceutical patents is costly, time consuming, uncertain and complex, and we or our licensors may not be able to file and prosecute all necessary or desirable patent applications, or maintain, enforce and license any patents that may issue from such patent applications, at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. We may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the rights to patents licensed to third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. If our current or future licensors, licensees or collaboration partners fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our licensors, licensees or collaboration partners are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal, technological and factual questions and has in recent years been the subject of much litigation. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States, or vice versa. Further, we may not be aware of all third-party intellectual property rights potentially relating to Oxbryta or our product candidates. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing or, in some cases, not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are and will remain highly uncertain. The patent examination process may require us or our licensors, licensees or collaboration partners to narrow the scope of the claims of our or our licensors', licensees' or collaboration partners' pending and future patent applications, which may limit the scope of patent protection that may be obtained. Our pending and future patent applications may not result in patents being issued that protect Oxbryta, inclacumab or any future product candidates, in

whole or in part, or which effectively prevent others from commercializing competitive product candidates. Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our patents by developing similar or alternative product candidates in a non-infringing manner, or by successfully seeking to narrow or invalidate our patents or render them unenforceable. Our and our licensors', licensees' or collaboration partners' patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications, and then only to the extent the issued claims cover the technology.

We cannot assure you that all of the potentially relevant prior art relating to our patents and patent applications has been found. If such prior art exists, it can invalidate a patent or prevent a patent from issuing from a pending patent application. Moreover, we may be subject to a third-party preissuance submission of prior art to the United States Patent and Trademark Office, or USPTO, or become involved in opposition, derivation, reexamination, *inter partes* review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize Oxbryta or our product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize drugs without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize Oxbryta, inclacumab or any future product candidates.

In addition, the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical product candidates, or limit the duration of the patent protection of Oxbryta or our product candidates. 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 patent portfolio may not provide us with sufficient rights to exclude others from commercializing drugs similar or identical to ours.

The United States has enacted patent reform legislation from time to time and the United States Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would diminish the value of our patents and patent applications or narrow the scope of our patent protection, or weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

Assuming the other requirements for patentability are met, in the United States prior to March 15, 2013, the first to make the claimed invention is entitled to the patent, while outside the United States, the first-to-file a patent application is entitled to the patent. After March 2013, under the Leahy-Smith America Invents Act, or AIA, enacted in 2011, the United States has moved to a first-to-file system similar to other countries' systems. The AIA also includes a number of significant changes that affect the way patent applications are prosecuted, and may also affect patent litigation. The effects of these changes are currently unclear as the USPTO must still implement various regulations, the courts have yet to address certain of these provisions and the applicability of the AIA and new regulations remain to be issued. Accordingly, it is not clear what, if any, impact the AIA will have on the operation of our business. However, the AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of patents that may issue from such patent applications, all of which could have a material adverse effect on our business and

financial condition. Any further changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents and patent applications or narrow the scope of our potential patent protection.

Our products and product candidates may be eligible for other forms of exclusivity (e.g., data exclusivity) for varying periods in varying jurisdictions. For example, we expect inclacumab, if approved, would be eligible for regulatory exclusivity (e.g., data exclusivity for biologics and orphan drug exclusivity) in various jurisdictions such as the U.S. and Europe, which exclusivities may extend beyond patent expiry in the case of inclacumab. Both the United States and the EU provide pathways for biologics competitors to seek approval for biosimilar products at the end of the relevant exclusivity period or, in some circumstances, before such period expires (for example, if a biosimilar applicant obtains approval for one or more of the indications approved for the innovator product by extrapolating clinical data from one indication to support approval for other indications). As a result, the available forms of exclusivity may not provide us with sufficient protections to exclude others from commercializing drugs similar or identical to ours.

We may become subject to claims alleging infringement of third parties' patents or proprietary rights and/or claims seeking to invalidate our patents, which would be costly, time consuming and, if successfully asserted against us, delay or prevent the development and commercialization of Oxbryta, inclacumab or any future product candidates that we may develop.

We cannot assure that Oxbryta, inclacumab or any future product candidates that we may develop will not infringe existing or future third-party patents. Because patent applications can take many years to issue and may be confidential for 18 months or more after filing, there may be applications now pending of which we are unaware and which may later result in issued patents that we may infringe by commercializing Oxbryta or any future product candidates that we may develop. We may additionally be unaware of one or more issued patents that would be infringed by the manufacture, sale or use of Oxbryta, inclacumab or any of our other product candidates.

We may in the future become party to, or be threatened with, adversarial proceedings or litigation against us regarding third party intellectual property rights with respect to Oxbryta, inclacumab or any other of our future product candidates, that would cause us to incur substantial expenses and, if successful against us, could cause us to pay substantial damages, including treble damages and attorneys' fees if we are found to be willfully infringing a third party's patents. We may also be required to indemnify parties with whom we have contractual relationships against such claims. If a patent infringement suit were brought against us, we could be forced to stop or delay research, development, manufacturing or sales of the product or product candidate that is the subject of the suit. As a result of patent infringement claims, or to avoid potential claims, we may choose to seek, or be required to seek, a license from the third party to continue developing, manufacturing and marketing Oxbryta and our product candidates and would most likely be required to pay license fees or royalties or both, that could be significant. These licenses may not be available on acceptable terms, or at all. Even if we were able to obtain a license, the rights may be nonexclusive, which would give our competitors access to the same intellectual property licensed to us. Ultimately, we could be prevented from commercializing a product, or forced to redesign it, or to cease some aspect of our business operations if, as a result of actual or threatened patent infringement claims, we are unable to enter into licenses on acceptable terms. Even if we are successful in defending against such claims, such litigation can be expensive, uncertain, and time consuming to litigate, and would divert management's attention from our core business. Any of these events could harm our business significantly.

In addition to infringement claims against us, if third parties prepare and file patent applications in the United States that also claim technology similar or identical to ours, we may have to participate in interference or derivation proceedings in the USPTO to determine which party is entitled to a patent on the disputed invention. We may also become involved in similar opposition proceedings in the European Patent Office or similar offices in other jurisdictions regarding our intellectual property rights with respect to Oxbryta and our product candidates and technology.

We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful.

Competitors or other parties may infringe our patents or other intellectual property. Although we are not currently involved in any intellectual property litigation, if we were to initiate legal proceedings against a third party to enforce a patent covering Oxbryta or one of our product candidates, the defendant could counterclaim that the patent covering Oxbryta or our product candidate is invalid and/or unenforceable. In addition, there is an abbreviated regulatory pathway, under the Biologics Price Competition and Innovation Act of 2009, for the regulatory approval of biosimilar or interchangeable biologic products, which could create a litigation pathway for a third party to challenge patents covering inclacumab. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are multiple potential grounds for a validity challenge or an unenforceability assertion. The outcome following legal assertions of invalidity and unenforceability is often highly unpredictable.

Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms.

In addition, our defense of litigation, interference or derivation proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our business and operations including our ability to commercialize Oxbryta, raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties, or enter into development partnerships that would help us bring Oxbryta and our product candidates to domestic and foreign markets.

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

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

We may be subject to claims that former employees, collaborators or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. For example, inventorship disputes may arise from conflicting obligations of third parties involved in developing our product candidates or as a result of questions regarding co-ownership of potential joint inventions. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership or we may enter into agreements to clarify the scope of our rights in such intellectual property. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business and operations including our ability to raise the funds necessary to commercialize Oxbryta, continue our clinical trials, continue our research programs, license necessary technology from third parties, or enter into development partnerships that would help us bring our product candidates to market. 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 jointly own patents and patent applications with third parties. Our ability to exploit or enforce these patent rights, or to prevent the third party from granting licenses to others with respect to these patent rights, may be limited in some circumstances.

We jointly own certain patents and patent applications with third parties. In the absence of an agreement with each co-owner of jointly owned patent rights, we will be subject to default rules pertaining to joint ownership. Some countries require the consent of all joint owners to exploit, license or assign jointly owned patents, and if we are unable to obtain that consent from the joint owners, we may be unable to exploit the invention or to license or assign our rights under these patents and patent applications in those countries. For example, we have exclusively licensed from the Regents of the University of California, or Regents, worldwide patent rights covering Oxbryta and certain Oxbryta analogs, some of which patent rights we jointly own with the Regents. Additionally, in the United States, each co-owner may be required to be joined as a party to any claim or action we may wish to bring to enforce these patent rights, which may limit our ability to pursue third party infringement claims.

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 employees' former employers 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.

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

We seek to protect our confidential proprietary information, in part, by confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and collaborators. These agreements are designed to protect our proprietary information. However, we cannot be certain that such agreements have been entered into with all relevant parties, and we cannot be certain 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. For example, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. We also seek to preserve the integrity and confidentiality of our confidential proprietary information by maintaining physical security of our premises and physical and electronic security of our information technology systems, but it is possible that these security measures could be breached. Enforcing a claim that a third party obtained illegally and is using trade secrets or confidential know-how is expensive, time consuming and unpredictable. The enforceability of confidentiality agreements may vary from jurisdiction to jurisdiction. If any of our confidential proprietary information were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position. 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.

Failure to obtain or maintain trade secrets or confidential know-how trade protection could adversely affect our competitive position. Moreover, our competitors may independently develop substantially equivalent proprietary information and may even apply for patent protection in respect of the same. If successful in obtaining such patent protection, our competitors could limit our use of our trade secrets or confidential know-how.

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 employ outside firms and rely on them to pay many of these fees. The USPTO and various non- U.S. governmental patent agencies require compliance with a number of complex procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other 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, 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, with 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 our product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries worldwide, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and may also export infringing products to territories where we have patent protection but patent enforcement is not strong. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights throughout the world. 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, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

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

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological complexity and legal complexity. Therefore, obtaining and enforcing biopharmaceutical patents is costly, time-consuming and inherently uncertain. In addition, the AIA has been recently enacted in the United States, resulting in significant changes to the U.S. patent system.

An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned to a “first-to-file” system for deciding which party should be granted a patent when two or more patent applications

are filed by different parties claiming the same invention. A third party that files a patent application in the USPTO after that date but before us could, therefore, be awarded a patent covering an invention of ours even if we had made the invention before it was made by the third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application, but circumstances could prevent us from promptly filing patent applications on our inventions.

Among some of the other changes introduced by the AIA are changes that limit where a patentee may file a patent infringement suit and provide opportunities for third parties to challenge any issued patent in the USPTO. This applies to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. The AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

The USPTO recently has developed regulations and procedures to govern administration of the AIA, and many of the substantive changes to patent law associated with the AIA, and, in particular, the first to file provisions, only became effective on March 16, 2013. Accordingly, the courts have yet to address many of these provisions and it is not clear what, if any, impact the AIA will have on the operation of our business. The AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our or our licensors' or collaboration partners' patent applications and the enforcement or defense of our or our licensors' or collaboration partners' issued patents, all of which could have an adverse effect on our business and financial condition.

Additionally, the U.S. Supreme Court has ruled on several patent cases in recent years narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this has also contributed to uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. Similarly, the complexity and uncertainty of European patent laws has also increased in recent years. In addition, the European patent system is relatively stringent in the type of amendments that are allowed during prosecution. These changes could limit our ability to obtain new patents in the future that may be important for our business.

Risks Related to Our Business and Industry

Pandemics such as the one caused by the novel strain of coronavirus, SARS-CoV-2, which causes COVID-19, as well as similar outbreaks and other public health crises, could adversely impact our business, including our commercialization activities, clinical trials and preclinical studies.

Pandemics, similar outbreaks and other public health crises could adversely impact our business. For example, the outbreak of the novel coronavirus, SARS-CoV-2, which causes coronavirus disease 2019 (COVID-19), has evolved into a global pandemic that has significantly impacted people and entities throughout the world. As a result of the COVID-19 pandemic, we have experienced and may continue to experience disruptions that could materially impact our business. The extent to which this pandemic or other health crises, or changes in laws and regulations such as shelter-in-place orders, impact our business and operating results will depend on future developments that are highly uncertain and cannot be accurately predicted, including new information that may emerge concerning COVID-19 and the actions taken to contain COVID-19 or treat its impact, among others.

As a result of the COVID-19 pandemic, various aspects of our business operations have been, and could continue to be, disrupted. In response to the pandemic, we implemented a work from home policy, with our administrative and certain other employees continuing their work outside of our offices, and restricted on-site staff to only a limited number of employees who have critical needs to be in the facility. The increase in working remotely could increase our cyber security risk, create data accessibility concerns, and make us more susceptible to communication disruptions, any of which could adversely impact our business operations or delay necessary interactions with local and federal regulators, ethics committees, manufacturing sites and clinical trial sites. In addition, as a result of shelter-in-place orders or other mandated travel restrictions, staff conducting on-site research and development may have limited access to our laboratory space, and these core activities may be significantly limited or curtailed, possibly for an extended period of time.

The COVID-19 pandemic has also reduced the ability to engage with the medical and investor communities, including due to the cancellation or reformatting of conferences scheduled throughout the year. For example, in light of the COVID-19 pandemic, we temporarily suspended our field team from most in-person interactions, including visits to physician offices, clinics and hospitals as well as in-person meetings with payors. These and other measures may significantly impact our ability to commercialize Oxbryta, such as by impacting new patient enrollments.

In addition, our ongoing and planned clinical trials have been and will likely continue to be affected by the COVID-19 pandemic. For example, in light of the COVID-19 pandemic, we temporarily paused screening and enrollment in all GBT-sponsored clinical studies (other than, where feasible, certain contracting and other administrative study start-up activities). Activities on our clinical trials have now resumed, with measures in place that we believe are appropriate. Assessment of the long-term impact of COVID-19 on our clinical trials is ongoing, and it is unknown whether we will be required to pause or delay such activities again in the future. Any prolongation or de-prioritization of our clinical trials or delay in regulatory review resulting from such disruptions could materially affect the development and study of Oxbryta or our product candidates. Study procedures (particularly any procedures that may be deemed non-essential), site initiation, participant recruitment and enrollment, participant dosing, shipment of our study compound, distribution of clinical trial materials, study monitoring, site inspections and data analysis may be delayed or paused due to changes in hospital or research institution policies, federal, state or local regulations, prioritization of hospital and other medical resources toward pandemic efforts, or other reasons related to the pandemic. If COVID-19 continues to spread, some participants and clinical investigators may not be able to comply with clinical trial protocols and we may experience increased patient study withdrawals or protocol deviations. For example, this may occur if quarantines or other travel limitations (whether voluntary or required) may impede participant movement, affect access to study sites, or interrupt healthcare services for a prolonged period of time. As a result, we may be unable to conduct our clinical trials.

Furthermore, the COVID-19 pandemic has resulted in, and could continue to cause, interruptions or delays in the operations of the FDA and other domestic or foreign regulatory agencies, which could impact the conduct of our clinical trials, the ability to seek agency input on our regulatory strategies and potential filings or interactions with regulatory agencies that oversee our research, development and promotional activities. For example, the COVID-19 pandemic has led the FDA to place some foreign and domestic inspections on hold. Should the FDA determine that an inspection is necessary for approval of a marketing application and an inspection cannot be completed during the review cycle due to restrictions on travel, FDA has stated that it generally intends to issue a complete response letter. Additionally, if there is inadequate information to make a determination on the acceptability of a facility, FDA may defer action on the application until an inspection can be completed. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may also experience delays in their regulatory activities. The extent and impact of such any such disruptions or delays are currently unpredictable.

Our and our vendors' and collaborators' research, preclinical development, and manufacturing operations also may be adversely impacted by the COVID-19 pandemic. We currently utilize third parties to, among other

things, supply and manufacture raw materials, components, and Oxbryta and our product candidates, to ship Oxbryta and our product candidates and manufacturing materials, and to perform certain testing relating to Oxbryta and our product candidates, including clinical studies and stability testing. If we, or any third parties in our supply chain for materials which are used in either the manufacture of Oxbryta or our product candidates or the conduct of our research and development, are adversely impacted by restrictions resulting from the coronavirus outbreak, our supply chain may be disrupted and our ability to manufacture and ship Oxbryta and our product candidates for commercial and research and development activities may be limited. In particular, the FDA has granted Emergency Use Authorization to certain vaccines for COVID-19, and more are likely to be authorized in the future. The resultant demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, may make it more difficult to obtain materials or manufacturing slots for the supply needed to support the commercialization of Oxbryta or the development of our product candidates.

In addition, the trading prices for our common stock and other biopharmaceutical companies have been highly volatile as a result of the COVID-19 pandemic. As a result, we may face difficulties raising capital through equity or debt financings, or such financing transactions may be on unfavorable terms. While the potential economic impact brought by and the duration of the pandemic may be difficult to assess or predict, it has already caused, and is likely to result in further, significant disruption of global financial markets, which may reduce our ability to access capital either at all or on favorable terms. Furthermore, a recession, depression or other sustained adverse market event resulting from the spread of COVID-19 could materially and adversely affect our business and the value of our common stock.

The ultimate impact of the COVID-19 pandemic, or any other health epidemic, is highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts on our business, our commercialization activities, our clinical and preclinical programs, our clinical, preclinical, research, manufacturing, and regulatory activities, healthcare systems or the global economy as a whole. However, these effects could have a material adverse impact on our operations, and we will continue to monitor the situation closely.

Our future success depends on our ability to retain key employees, consultants and advisors and to attract, retain and motivate qualified personnel.

We are highly dependent on the management, commercial, research and development, clinical, financial and business development expertise of our executive officers, as well as the other members of our team. Although we have employment offer letters with each of our executive officers, each of them may terminate their employment with us at any time. We do not maintain “key person” insurance for any of our executives or employees.

Recruiting and retaining qualified scientific, medical, clinical, technical operations personnel and sales and marketing personnel will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval for and commercialize our product candidates. Competition to hire qualified personnel in our industry and geographic market is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. The COVID-19 pandemic, as well as similar outbreaks or other significant business disruptions, may make such efforts more challenging. Furthermore, to the extent we hire personnel from competitors, we may be subject to allegations that they have been improperly solicited or that they have divulged proprietary or other confidential information, or that their former employers own their research output. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist

us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

We have recently implemented sales, marketing and distribution capabilities and expect to expand our product development capabilities, and, as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

With our recent establishment of infrastructure required for commercialization of Oxbryta and our current and planned product development activities, we have experienced significant and rapid growth in the number of our employees and the scope of our operations, particularly in the areas of sales, marketing and distribution, regulatory affairs, research and drug development. To manage this and future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources, we may not be able to effectively manage the expansion of our operations or recruit, train and retain a sufficient number of qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage our recent or future growth could delay the execution of our business plans or disrupt our operations.

If we are not successful in discovering, developing, acquiring or commercializing additional product candidates, our ability to expand our business and achieve our strategic objectives could be impaired.

Although a substantial amount of our effort will focus on the continued commercialization, clinical testing and seeking of additional regulatory approval of Oxbryta, a key element of our strategy is to pursue, develop and commercialize a portfolio of products utilizing proprietary discovery and development technology. We are seeking to do so through our internal research programs and may also selectively pursue commercially synergistic in-licensing or acquisition of additional assets, such as inclacumab. With the exception of Oxbryta, all of our other potential product candidates remain in the earlier development stages. Research programs to identify product candidates require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for many reasons, including the following:

- the research methodology used may not be successful in identifying potential product candidates;
- competitors may develop alternatives that render our product candidates obsolete or less attractive;
- product candidates we develop may nevertheless be covered by third parties' patents or other exclusive rights;
- the market for a product candidate may change during our program so that such a product may become unreasonable to continue to develop;
- a product candidate may on further study be shown to have harmful side effects, lack of potential efficacy or other characteristics that indicate it is unlikely to meet applicable regulatory criteria or remain reasonable to continue to develop;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and
- a product candidate may not be accepted as safe and effective by patients, the medical community or third-party payors, if applicable.

If we fail to develop and successfully commercialize inclacumab or any other product candidates, our business and future prospects may be harmed and our business will be more vulnerable to any problems that we encounter in developing and commercializing Oxbryta.

If successful product liability claims are brought against us, we may incur substantial liability and costs. If the use of Oxbryta or our product candidates harms patients, or is perceived to harm patients even when such harm is unrelated to Oxbryta or our product candidates, our regulatory approvals could be revoked or otherwise negatively impacted and we could be subject to costly and damaging product liability claims.

The commercialization of Oxbryta, the use of Oxbryta and our product candidates, including inclacumab, in clinical trials and the sale of any other products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. There is a risk that Oxbryta or our product candidates may induce adverse events. The risk of product liability claims may be increased now that Oxbryta is approved and being sold in the United States. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- impairment of our business reputation;
- withdrawal of clinical trial participants;
- costs due to related litigation;
- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- increased warnings on product labels or additional restrictions imposed by regulatory authorities;
- the recall of Oxbryta or our product candidates;
- the inability to commercialize Oxbryta or our product candidates; and
- decreased demand for Oxbryta or our product candidates, if approved for commercial sale.

We carry product liability insurance in amounts that we believe are sufficient in light of our current commercial activities and clinical programs, but we may not be able to obtain and maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. On occasion, large judgments have been awarded in class action lawsuits based on drugs or medical treatments that had unanticipated adverse effects. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business.

During the course of treatment, patients may suffer adverse events, including death, for reasons that may or may not be related to our products or product candidates. Such events can be time-consuming to address, could subject us to costly litigation, require us to pay substantial amounts of money to injured patients, can delay, negatively impact or end our opportunity to receive or maintain regulatory approval to market our products or product candidates, if approved, can require us to suspend or abandon our commercialization efforts of any approved product candidates, or can impair our ability to raise funds to pursue our development or commercialization efforts. Investigations of these events may interrupt our sales efforts, delay our regulatory approval process in other countries, or impact and limit the type of regulatory approvals our product candidates receive or maintain. As a result of these factors, a product liability claim, even if successfully defended, could have a material adverse effect on our business, financial condition or results of operations.

We may choose to 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 ultimately be more profitable or for which there is a greater likelihood of success.

Because we have limited resources, we may forego or delay the pursuit of opportunities with programs or product candidates or for indications that later prove to have greater commercial potential than those we do pursue. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs for product candidates, including inclacumab, may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic collaboration, licensing or other partnering arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate, or 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 partnering arrangement.

Any collaboration, distribution or other arrangements that we might enter into in the future may not be successful, which could adversely affect our operations and financial condition.

We may seek collaboration, distribution or other arrangements with pharmaceutical or biotechnology companies for the development or commercialization of Oxbryta, inclacumab and potential future product candidates. For example, we have entered into an License and Collaboration Agreement with Syros Pharmaceuticals, Inc., to discover, develop and commercialize novel therapies for SCD and beta thalassemia, as well as an exclusive agreement with Biopharma-Middle East and Africa, or Biopharma-MEA, to distribute Oxbryta in the GCC region. We may enter into additional collaboration, distribution or other arrangements on a selective basis depending on the merits of retaining commercialization rights for ourselves as compared to entering into selective arrangements with leading pharmaceutical or biotechnology companies for our products or product candidates, both in the United States and internationally. To the extent that we decide to enter into such arrangements, we will face significant competition in seeking appropriate partners. Whether we reach a definitive agreement for any collaboration, distribution or other arrangement will depend, among other things, upon our assessment of the partner's resources and expertise, the terms and conditions of the proposed arrangement and the proposed partner's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or comparable foreign regulatory authorities, the potential market for a product or a product candidate, the costs and complexities of manufacturing and delivering a product or product candidate to patients, the potential of competing products, any uncertainty with respect to our ownership of technology, which can occur if there is a challenge to our ownership without regard to the merits of the challenge and industry and market conditions generally. Moreover, these arrangements are complex and time consuming to negotiate, document and implement, and we may not be successful in our efforts to establish and implement additional collaborations or other alternative arrangements should we so chose to enter into such arrangements. The terms of any collaborations or other arrangements that we may establish may not be favorable to us.

Any collaboration, distribution or other arrangement that we enter into may not be successful and may increase our potential liabilities. The success of our arrangements will depend heavily on the efforts and activities of us and our partners, who generally have significant discretion in determining the efforts and resources that they will apply to these collaborations. Disagreements between parties to an arrangement regarding research, development and commercialization matters can lead to delays in the development process or commercializing the applicable product or product candidate and, in some cases, costly and time-consuming disputes or termination of the arrangement. These disagreements can be difficult to resolve successfully, and any such termination or expiration would adversely affect us financially and could harm our business reputation. In addition, we are reliant on our partners' compliance with applicable laws and regulations in the region in which they operate, such as in the GCC region with respect to our arrangement with Biopharma-MEA. A partner's failure to comply with applicable law could result in liability for us, and negatively impact our operations and business reputation. Many of such arrangements in the pharmaceutical and biotechnology industries do not result in successful outcomes, for a wide variety of reasons.

Our current and anticipated international operations may expose us to business, regulatory, political, operational, financial, pricing and reimbursement and economic risks associated with doing business outside of the United States.

Our business strategy currently incorporates international expansion as we evaluate data from our Phase 3 HOPE Study, plan to conduct additional studies inside and outside the United States, and plan to seek to obtain regulatory approval to commercialize Oxbryta in additional patient populations inside the United States as well as in patient populations outside the United States. Doing business internationally involves a number of risks, including but not limited to:

- restrictions and obligations imposed by privacy regulations, such as provisions under the GDPR, applicable to the collection and use of personal health data in the European Union;
- multiple, conflicting, and changing laws and regulations such as tax laws, export and import restrictions, employment laws, regulatory requirements, and any requirements to obtain other governmental approvals, permits, and licenses;
- failure by us to obtain and maintain regulatory approvals for the sale or use of our products in various countries;
- additional potentially relevant third-party patent rights;
- complexities and difficulties in obtaining protection for and enforcing our intellectual property;
- difficulties in staffing and managing our current and potential foreign operations;
- complexities associated with managing multiple payor reimbursement regimes, government payors, or patient self-pay systems;
- limits in our ability to penetrate international markets;
- financial risks, such as longer payment cycles, difficulty collecting accounts receivable, the impact of local and regional financial crises on demand and payment for our products, and exposure to foreign currency exchange rate fluctuations;
- natural disasters, political and economic instability, including wars, terrorism, and political unrest, outbreak of disease, boycotts, curtailment of trade, and other business restrictions;
- certain expenses including, among others, expenses for travel, translation, and insurance; and
- regulatory and compliance risks that relate to maintaining accurate information and control over sales and activities that may fall within the purview of the FCPA, its books and records provisions, or its anti-bribery provisions.

Any such factors may impose additional responsibilities, obligations or liability in relation to our current and planned activities outside the United States, and we may be required to put in place additional mechanisms and make additional expenditures to ensure compliance with existing and new requirements, which could significantly harm our future international expansion and operations and, consequently, our results of operations.

We are subject to certain U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions, and other trade laws and regulations (collectively, "Trade Laws"). We can face serious consequences for violations.

Among other matters, Trade Laws prohibit companies and their employees, agents, clinical research organizations, legal counsel, accountants, consultants, contractors, and other partners from authorizing, promising, offering, providing, soliciting, or receiving directly or indirectly, corrupt or improper payments or anything else of value to or from recipients in the public or private sector. Violations of Trade Laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax

reassessments, breach of contract and fraud litigation, reputational harm, and other consequences. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We also expect our activities outside the United States to increase over time. We engage third parties for clinical trials and/or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals, have entered into an exclusive agreement with Biopharma-MEA to distribute Oxbryta in the GCC region, and expect to contract with additional third parties with respect to the distribution and commercialization of Oxbryta and our other product candidates in territories outside the United States, if approved for marketing in any such territories. We can be held liable for the corrupt or other illegal activities of our personnel, agents, or partners, even if we do not explicitly authorize or have prior knowledge of such activities.

Misconduct or other improper activities of our employees, agents, contractors or collaborators could adversely affect our reputation and our business, prospects, operating results and financial condition.

We cannot ensure that our compliance controls, policies, and procedures will in every instance protect us from acts committed by our employees, agents, contractors or collaborators that would violate the law or regulations of the jurisdictions in which we operate, including FDA, healthcare, employment, foreign corrupt practices, environmental, competition, and patient privacy regulations. Misconduct by our employees, agents, contractors, or collaborators could include intentional or unintentional failures to:

- comply with EMA or FDA regulations or similar regulations of comparable foreign regulatory authorities;
- provide accurate information to the FDA or EMA or comparable foreign regulatory authorities;
- comply with cGMP regulations and manufacturing standards that we have established and comply with applicable healthcare fraud and abuse regulations in the jurisdictions in which we operate;
- report financial information or data accurately; or
- disclose unauthorized activities to us.

In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Misconduct could also involve the improper use of, including trading on, information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation.

Additionally, our business activities may be subject to the FCPA and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate. The FCPA generally prohibits offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to a non-U.S. government official in order to influence official action, or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. Our business is heavily regulated and, therefore, involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, the health care providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these prescribers and purchasers are subject to regulation under the FCPA.

There is no certainty that all of our employees, agents, contractors, or collaborators, or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these requirements. We have adopted a code of conduct, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may be ineffective 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 comply with these requirements. 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.

Our internal computer systems, or those of our third-party vendors, may fail or suffer security breaches, which could result in a material disruption of our business and operations.

Despite the implementation of security measures, our internal computer systems and those of our third-party vendors are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures, and the prevalent use of mobile devices that access confidential information increases the risk of data security breaches. With respect to our data and information technology infrastructure, we continue to invest in the protection of such infrastructure, but there can be no assurance that our efforts will prevent service interruptions or identify breaches in our systems.

If any such event were to occur and cause interruptions in our operations, it could adversely affect our business and operations or result in the loss of critical or sensitive information, which could result in financial, legal, business or reputational harm to us. For example, the loss of data from completed or ongoing clinical trials or nonclinical studies for Oxbryta or any of our product candidates could harm our commercialization activities, result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of our product candidates could be delayed. In addition, our liability insurance may not be sufficient in type or amount to cover us against claims related to security breaches, cyber-attacks and other related breaches. As a result, any such cyber-attacks or breaches could have a material adverse effect on our business.

Risks Related to Our Equity Securities

The market price of our common stock has been and may continue to be highly volatile.

The market price of our common stock has experienced volatility since our initial public offering in August 2015 and is likely to continue to be volatile. Our stock price could be subject to wide fluctuations in response to a variety of factors, including the following:

- failure to successfully develop and commercialize Oxbryta, inclacumab or any other product candidates, including results relating to our commercialization of Oxbryta in the United States;
- adverse results or delays in, or the halting of, our nonclinical studies or clinical trials, especially in our ongoing or future clinical program for Oxbryta for the treatment of SCD;
- reports of adverse events from our commercialization or clinical trials of Oxbryta, or from clinical trials of any other product candidates that we may develop;
- any delay in the review of, or potential action with respect to, our previous or planned filing of any IND, NDA or MAA for Oxbryta, inclacumab or for any other product candidates that we may develop and any adverse development or perceived adverse development with respect to the FDA’s or any other regulatory agency’s review of such filing;
- adverse regulatory decisions affecting Oxbryta, inclacumab or any other product candidates we may develop, including any delay in or denial of potential approval in accordance with our plans and expectations;
- inability to obtain additional funding;
- failure to prosecute, maintain or enforce our intellectual property rights;

- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- changes in laws or regulations applicable to Oxbryta or future products;
- inability to obtain adequate product supply for Oxbryta or our product candidates or the inability to do so at acceptable prices;
- introduction of new products, services or technologies by our competitors;
- failure to enter into or perform under strategic collaborations;
- failure to meet or exceed any financial projections that we or the investment community may provide;
- the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;
- additions or departures of key scientific or management personnel;
- significant lawsuits, including patent or stockholder litigation;
- changes in the market valuations of similar companies;
- sales of our common stock by us or our stockholders in the future;
- trading volume of our common stock; and
- the other risks described in this “Risk Factors” section.

In addition, companies trading in the stock market in general, and the NASDAQ Stock Market, or NASDAQ, in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors, including the effects of the COVID-19 pandemic on the global economy, may negatively affect the market price of our common stock, regardless of our actual operating performance. For example, negative publicity regarding drug pricing and price increases by pharmaceutical companies has negatively impacted, and may continue to negatively impact, the markets for biotechnology and pharmaceutical stocks. In the past, following periods of volatility in the market, securities class-action litigation has often been instituted against companies. Such litigation, if instituted against us, could result in substantial costs and diversion of management’s attention and resources, which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or our guidance.

Our quarterly and annual operating results may fluctuate significantly in the future, which makes it difficult for us to predict our future operating results. Our operating results may fluctuate due to a variety of factors, many of which are outside of our control and may be difficult to predict, including the following:

- our ability to successfully commercialize Oxbryta or any of our product candidates, if approved, and the timing and costs of our commercialization activities;
- the timing and cost of, and level of investment in, research and development activities relating to Oxbryta and our product candidates, which may change from time to time;
- the timing and success or failure of clinical trials for Oxbryta and our product candidates or competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners;

- our ability to obtain and maintain full regulatory approval for Oxbryta in the United States (including potential pediatric approval) and to obtain regulatory approval of Oxbryta outside of the United States (including potential European approval) as well as regulatory approval for our product candidates, and the timing and scope of any such approvals we may receive;
- the cost of manufacturing Oxbryta and our product candidates, which may vary depending on the quantity of production and the terms of our agreements with manufacturers;
- our ability to attract, hire, train and retain qualified personnel;
- expenditures that we will or may incur to acquire or develop additional product candidates and technologies;
- the level of demand for Oxbryta and our product candidates, if approved, which may vary significantly;
- future accounting pronouncements or changes in our accounting policies;
- the risk/benefit profile, cost and reimbursement policies with respect to Oxbryta and our products candidates, if approved, and existing and potential future drugs that compete with Oxbryta and our product candidates;
- whether Oxbryta or any of our product candidates are subject to any compliance-related challenges or sanctions, or any intellectual-property related challenges; and
- the changing and volatile U.S., European and global economic environments, including economic volatility as a result of the COVID-19 pandemic.

The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated financial guidance we may provide.

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

We will need additional capital in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders. In August 2020, we filed a registration statement on Form S-3 pursuant to which we may issue up to $200.0 million in shares of common stock in sales deemed to be “at-the-market offerings” as defined by the Securities Act of 1933, as amended, and an unlimited amount of shares of our common stock, preferred stock, debt securities, warrants and/or units. Any sale or issuance of securities pursuant to this registration statement or otherwise may result in dilution to our stockholders and may cause the market price of our stock to decline. Furthermore, new investors purchasing securities that we may issue and sell in the future could obtain rights superior to the rights of our existing stockholders.

We are also authorized to grant stock options and other equity-based awards to our employees, directors and consultants pursuant to our Amended and Restated 2015 Stock Option and Incentive Plan, or 2015 Plan. The

number of shares available for future grant under the 2015 Plan will automatically increase each year by up to 4% of all shares of our capital stock outstanding as of December 31 of the prior calendar year, subject to the ability of our board of directors or compensation committee to take action to reduce the size of the increase in any given year. In addition, in January 2017 our board of directors approved our 2017 Inducement Equity Plan, and thereafter amended and restated the plan as the Amended and Restated 2017 Inducement Plan, or the 2017 Inducement Plan. The 2017 Inducement Plan enables us and our subsidiaries to grant non-qualified stock options and other equity-based awards to induce employees who are not currently employed by us or our subsidiaries to accept employment with us or our subsidiaries. As of December 31, 2020, there were 1,277,475 shares reserved under the 2017 Inducement Plan (subject to adjustment for reorganization, recapitalization, stock dividend, stock split, or similar changes in our capital stock) for issuance to new employees entering into employment with us. In addition, we have reserved shares of common stock for issuance pursuant to our Amended and Restated 2015 Employee Stock Purchase Plan, or 2015 ESPP, which number of shares will automatically increase each year on January 1, from January 1, 2016 to January 1, 2025, by the lesser of 3,000,000 shares of common stock, (ii) 1% of all shares of our capital stock outstanding as of December 31 of the prior calendar year, or (iii) such lesser number of shares as determined by the administrator of our 2015 ESPP. Currently, we plan to register the increased number of shares available for issuance under the 2015 Plan and the 2015 ESPP each year. If our board of directors elects to increase the number of shares available for future grant under the 2015 Plan, the 2017 Inducement Plan or the 2015 ESPP, our stockholders may experience additional dilution, and our stock price may fall.

A significant portion of our total outstanding shares may be sold into the market in the near future, which could cause the market price of our common stock to drop significantly.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. A significant portion of our outstanding shares of common stock are held by a small number of stockholders, including our directors, officers and significant stockholders. Sales by our stockholders of a substantial number of shares, or the expectation that such sales may occur, could significantly reduce the market price of our common stock.

We have also registered or intend to register all shares of our common stock subject to options or other equity awards issued or reserved for future issuance under our equity incentive plans. As a result, these shares will be available for sale in the public market subject to vesting arrangements and exercise of options, and restrictions under applicable securities laws. In addition, our directors, executive officers and certain affiliates have established or may in the future establish programmed selling plans under Rule 10b5-1 of the Exchange Act for the purpose of effecting sales of our common stock. If any of these events cause a large number of our shares to be sold in the public market, the sales could reduce the trading price of our common stock and impede our ability to raise future capital.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

Our executive officers, directors, five percent stockholders and their affiliates beneficially owned approximately 60% of our outstanding common stock as of December 31, 2020, based on the latest publicly available information.

These stockholders have the ability to influence us through their ownership positions. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders, acting together, may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may believe are in your best interest as one of our stockholders.

We have broad discretion in the use of our capital resources consisting of cash and cash equivalents and short and long-term marketable securities, and may invest or spend our capital resources in ways with which you do not agree or in ways that ultimately may not increase the value of your investment.

We have broad discretion over the use of our capital resources consisting of cash and cash equivalents and short and long-term marketable securities. You may not agree with our decisions, and our use of our capital resources may not yield any returns to our stockholders. We expect to use our existing capital resources to continue the commercialization and clinical development of Oxbryta for the treatment of SCD, including in our Phase 2a HOPE-KIDS 1 Study, our Phase 3 HOPE-KIDS 2 Study, our other research and development activities including other clinical and nonclinical studies, including for inclacumab, and for working capital and general corporate purposes. Our failure to apply our capital resources effectively could compromise our ability to pursue our growth strategy and we might not be able to yield a significant return, if any, on our investment of these resources. Our stockholders will not have the opportunity to influence our decisions on how to use our capital resources.

Provisions in our restated certificate of incorporation and amended and restated bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders or remove our current management.

Our restated certificate of incorporation, amended and restated bylaws and Delaware law contain provisions that may have the effect of delaying or preventing a change in control of us or changes in our management. Our restated certificate of incorporation and amended and restated bylaws include provisions that:

- authorize “blank check” preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;
- create a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our board of directors, the chairperson of our board of directors, our chief executive officer or our president;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- provide that our directors may be removed only for cause;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- specify that no stockholder is permitted to cumulate votes at any election of directors;
- expressly authorize our board of directors to modify, alter or repeal our amended and restated bylaws; and
- require supermajority votes of the holders of our common stock to amend specified provisions of our amended and restated certificate of incorporation and amended and restated bylaws.

These provisions, alone or together, could delay or prevent hostile takeovers and changes in control or changes in our management.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us.

Any provision of our restated certificate of incorporation or amended and restated bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

Our future ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.

We have incurred substantial losses during our history and do not expect to become profitable in the near future and we may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire. Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards, or NOLs, and other pre-change tax attributes (such as research tax credits) to offset its post-change income or taxes may be limited. We experienced an ownership change as a result of our initial public offering and an ownership change as a result of some of our follow-on offerings; however we do not believe that these ownership changes will significantly limit our ability to use these pre-change NOL carryforwards. We may experience subsequent shifts in our stock ownership, including as a result of our future follow-on offering, some of which are outside of our control. As a result, if we earn net taxable income, our ability to use our pre-change NOL carryforwards to offset U.S. federal taxable income may become subject to limitations, which could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. On June 29, 2020, California enacted legislation AB 85 limiting our ability to use our state NOLs and imposing a cap on the amount of business incentives tax credits (R&D credit) for taxable years 2020, 2021, and 2022. In addition, pursuant to the Tax Cuts and Jobs Act of 2017 (as modified by the Coronavirus Aid, Relief, and Economic Security Act of 2020), we may not use net operating loss carry-forwards arising in taxable years beginning after December 31, 2017 to reduce our taxable income in any year beginning after December 31, 2020 by more than 80% and we may not carry back any net operating losses arising in taxable years ending after December 31, 2020 to prior years. These new rules apply regardless of the occurrence of an "ownership change."

We do not currently intend to pay dividends on our common stock, and, consequently, our stockholders' ability to achieve a return on their investment will depend on appreciation in the price of our common stock.

We do not currently intend to pay any cash dividends on our common stock for the foreseeable future. We currently intend to invest our future earnings, if any, to fund our growth. Therefore, you are not likely to receive any dividends on your common stock for the foreseeable future. Since we do not intend to pay dividends, your ability to receive a return on your investment will depend on any future appreciation in the market value of our common stock. There is no guarantee that our common stock will appreciate or even maintain the price at which our holders have purchased it.

General Risk Factors

Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

Our ability to invest in and expand our business and meet our financial obligations, to attract and retain third-party contractors and collaboration partners and to raise additional capital depends on our operating and financial performance, which, in turn, is subject to numerous factors, including the prevailing economic and political conditions and financial, business and other factors beyond our control, such as the rate of unemployment (particularly as a result of the COVID-19 pandemic), the number of uninsured persons in the United States, the results of presidential elections, other political influences and inflationary pressures. For

example, an overall decrease in or loss of insurance coverage among individuals in the United States as a result of unemployment, underemployment or the potential repeal of certain provisions of the ACA, may decrease the demand for healthcare services and pharmaceuticals. Additionally, the availability of healthcare services and resources is currently constrained due to the COVID-19 pandemic. If fewer patients are seeking medical care because they do not have insurance coverage or are unable to obtain medical care for their conditions due to resource constraints on the healthcare system, we may experience difficulties in the commercialization of Oxbryta and any eventual commercialization of our product candidates, and our business, results of operations, financial condition and cash flows could be adversely affected.

In addition, certain events have caused, and may cause or contribute to global financial crises, which have triggered and may in the future lead to extreme volatility and disruptions in the capital and credit markets. For example, in January 2020, the U.K. formally exited from the EU (such event commonly known as Brexit). Brexit has and could continue to adversely affect European and/or worldwide economic and market conditions and could continue to contribute to instability in the global financial markets and create uncertainty surrounding our business, including affecting our existing relationships with third parties that conduct some of our nonclinical studies and clinical trials and our ability to enter into new relationships with vendors and other third-party contractors, which could have an adverse effect on our business, financial results and operations. The measures could also adversely affect our ability to raise additional capital, potentially disrupt the markets in which we currently conduct and plan to conduct operations and the tax jurisdictions in which we operate and adversely change tax benefits or liabilities in these or other jurisdictions. In addition, changes in, and legal uncertainty with regard to, national and international laws and regulations may present difficulties for our clinical and regulatory strategy.

A severe or prolonged economic downturn, including as a result of the COVID-19 pandemic, could result in a variety of risks to our business, including reduced ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our relationships with our contractors and potential collaboration partners. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the COVID-19 pandemic, current economic climate and financial market conditions could adversely impact our business.

We incur significant costs, and expend significant time and effort, to comply with the rules applicable to us as a public company, including Section 404 of the Sarbanes-Oxley Act of 2002. If we fail to comply with these rules, including maintaining proper and effective systems of disclosure controls and internal controls over financial reporting, the accuracy and timeliness of our financial reporting may be adversely affected, and we could be subject to sanctions or other penalties that would harm our business.

As a public company, we are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, or Exchange Act, Section 404, or Section 404, of the Sarbanes-Oxley Act of 2002, or Sarbanes-Oxley, and the rules and regulations of NASDAQ. The Exchange Act requires us to file accurate and timely quarterly, annual and current reports with the SEC. Section 404 generally requires our management and independent registered public accounting firm to report on the effectiveness of our internal control over financial reporting and requires us to include an opinion from our independent registered public accounting firm on the effectiveness of our internal control over financial reporting. We are also subject to significant corporate governance and executive compensation-related provisions of the Dodd-Frank Wall Street Reform and Consumer Protection Act, or Dodd-Frank, including the “say on pay” rules adopted by the SEC under Dodd-Frank. We incur significant legal, accounting and other expenses, and expend significant time and effort by management and other personnel, to comply with the rules applicable to us as a public company.

We carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and our Chief Financial Officer, of the effectiveness of our internal control over financial reporting for the purpose of providing the reports required by Section 404. Based on our assessment and using the Committee of Sponsoring Organizations of the Treadway Commission, or COSO, criteria, our

management, Chief Executive Officer and Chief Financial Officer, have concluded that, as of December 31, 2020, our internal control over financial reporting was effective. As required under Section 404 of Sarbanes-Oxley, our independent registered public accounting firm has tested the design and operating effectiveness of our controls over financial reporting and has provided the required attestation report with respect to our internal control over financial reporting. During the course of our or their subsequent review and testing, however, material weaknesses or significant deficiencies may be identified and we may be unable to remediate them before we must provide the required reports. If material weaknesses or significant deficiencies in our internal control over financial reporting are identified in the future, we may not detect or remediate errors on a timely basis and our consolidated financial statements may be materially misstated. We or our independent registered public accounting firm may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall. In addition, any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from NASDAQ or other adverse consequences that would materially harm our business.

Moreover, stockholder activism, the current political environment, and increased levels of government scrutiny and regulatory reform may lead to substantial new regulations and disclosure obligations for public companies, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate. Our management and other personnel will need to devote a substantial amount of time to any new compliance initiatives. In addition, any new rules and regulations will increase our legal and financial compliance costs and will make some activities more time consuming and costly. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain our current levels of such coverage. New laws and regulations as well as changes to existing laws and regulations affecting public companies, including the provisions of Sarbanes-Oxley and rules adopted by the SEC and by NASDAQ, would likely result in increased costs to us as we respond to their requirements.

We or the third parties upon whom we depend may be adversely affected by earthquakes, outbreaks of disease (such as the COVID-19 pandemic) or other natural disasters, and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Earthquakes, outbreaks of disease (such as the COVID-19 pandemic) or other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects. As a result of the COVID-19 pandemic, we have been prevented from using all or a significant portion of our headquarters, and future events (including pandemics, earthquakes, power outages or natural disasters) may prevent us in the future from using all or a significant portion of our facilities. In addition, damage to or restrictions on the use of critical infrastructure, such as the manufacturing facilities of our third-party contract manufacturers or other facilities critical to our research and development activities, may render it difficult or, in certain cases, impossible for us to continue certain aspects of our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and are unlikely to 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, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third

parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

We may be subject to adverse legislative or regulatory tax changes that could negatively impact our financial condition.

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect our stockholders or us. In recent years, many such changes have been made and changes are likely to continue to occur in the future. For example, in December 2017, Congress passed the Tax Cuts and Jobs Act, which made broad and complex changes to the tax laws. We cannot predict whether, when, in what form, or with what effective dates, tax laws, regulations and rulings may be enacted, promulgated or decided, which could result in an increase in our, or our stockholders', tax liability or require changes in the manner in which we operate in order to minimize increases in our tax liability.

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

The trading market for our common stock depends, in part, on the research and reports that securities or industry analysts publish about us or our business. Securities and industry analysts may not publish an adequate amount of research on our company, which may negatively impact the trading price for our stock. In addition, if one or more of the analysts who cover us downgrade our stock or publish inaccurate or unfavorable research about our business, our stock price would likely decline or increase in volatility. Further, if our operating results fail to meet the forecasts of analysts, 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.

Item 1B. ***Unresolved Staff Comments***

None.

Item 2. ***Properties***

Our headquarters, where we have office and research and development laboratory space, is located in South San Francisco, California, where we lease 164,150 square feet of space pursuant to a noncancelable operating lease, or Lease.

We believe that our existing facilities are sufficient for our current needs and for the foreseeable future.

Item 3. ***Legal Proceedings***

As of the date of this annual report on Form 10-K, we are not party to any material legal proceedings. In the future, we may become subject to legal proceedings and claims 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 began trading on The NASDAQ Global Select Market on August 12, 2015 and trades under the symbol "GBT". Prior to such time, there was no public market for our common stock.

Recent Sales of Unregistered Securities

During the year ended December 31, 2020, we did not issue or sell any unregistered securities not previously disclosed in a Quarterly Report on Form 10-Q or in a Current Report on Form 8-K.

Issuer Purchases of Equity Securities

We did not repurchase any securities during the quarter ended December 31, 2020.

Holders of Common Stock

As of February 18, 2021, there were 6 holders of record of 62,156,860 outstanding shares of our common stock. We believe that the number of beneficial owners of our common stock at that date was substantially greater.

Securities Authorized for Issuance under Equity Compensation Plans

Information about our equity compensation plans is incorporated by reference to Item 12 of Part III of this Annual Report.

Dividend Policy

We have never declared or paid any cash dividends. We currently expect to retain all future earnings, if any, for use in the operation and expansion of our business, and therefore do not anticipate paying any cash dividends in the foreseeable future.

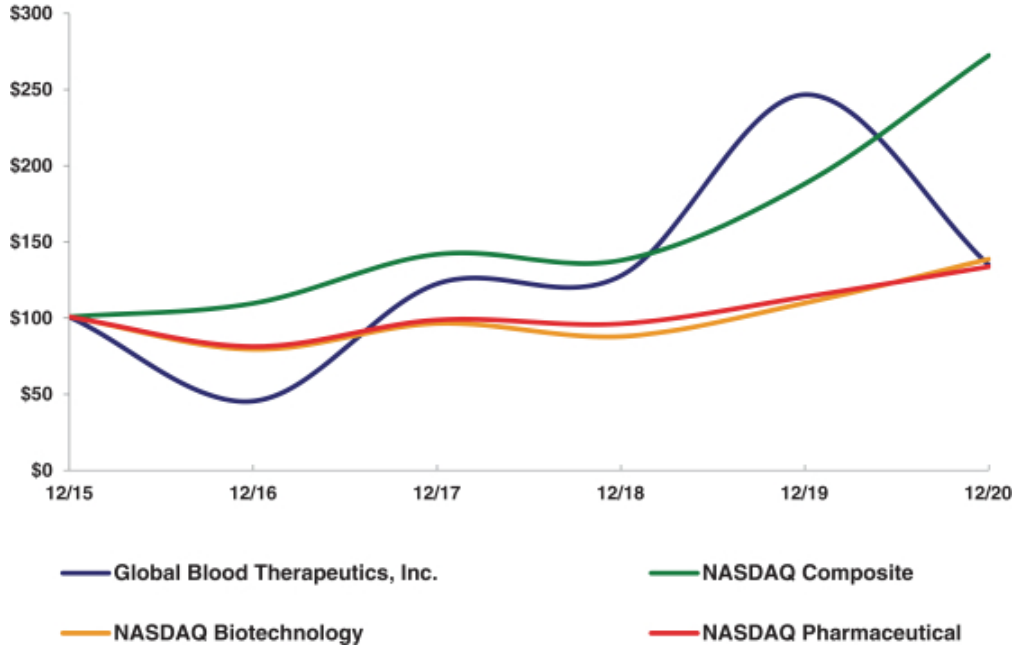
Performance Graph

The following is not deemed "filed" with the Securities and Exchange Commission and is not to be incorporated by reference into any filing we make under the Securities Act of 1933, as amended, whether made before or after the date hereof and irrespective of any general incorporation by reference language in such filing.

The graph below matches Global Blood Therapeutics, Inc.'s cumulative 52-Month total shareholder return on common stock with the cumulative total returns of the NASDAQ Composite index, the NASDAQ

Biotechnology index, and the NASDAQ Pharmaceutical index. The graph tracks the performance of a $100 investment in our common stock and in each index (with the reinvestment of all dividends) from December 31, 2015 to December 31, 2020.

COMPARISON OF 5 YEAR CUMULATIVE TOTAL RETURN*
Among Global Blood Therapeutics, Inc., the NASDAQ Composite Index,
the NASDAQ Biotechnology Index and the NASDAQ Pharmaceutical Index



* $100 invested on 12/31/15 in stock or index, including reinvestment of dividends. Fiscal year ending December 31.

	12/31/15	12/31/16	12/31/17	12/31/18	12/31/19	12/31/20
Global Blood Therapeutics, Inc.	**100.00**	**44.70**	**121.71**	**126.97**	**245.87**	**133.96**
NASDAQ Composite	**100.00**	**108.87**	**141.13**	**137.12**	**187.44**	**271.64**
NASDAQ Biotechnology	**100.00**	**78.65**	**95.67**	**87.19**	**109.08**	**137.90**
NASDAQ Pharmaceutical	**100.00**	**80.51**	**97.95**	**95.46**	**113.09**	**132.91**

The stock price performance included in this graph is not necessarily indicative of future stock price performance.

Item 6. *Selected Financial Data*

The information set forth below for the three years ended December 31, 2020 is not necessarily indicative of results of future operations, and should be read in conjunction with Item 7, Management's Discussion and Analysis of Financial Condition and Results of Operations and the Consolidated Financial Statements and related notes thereto included in Item 8 of this Annual Report on Form 10-K to fully understand factors that may affect the comparability of the information presented below (in thousands, except for share and per share data):

	Years Ended December 31,		
	2020	2019	2018
Summary of Operations Data:			
Product sales, net	$ 123,803	$ 2,108	$ —
Costs and operating expenses			
Cost of sales	1,986	48	—
Research and development	155,122	174,556	131,307
Selling, general and administrative	210,851	117,088	51,435
Gain on lease modification [1]	(984)	(8,301)	—
Total costs and operating expenses	366,975	283,391	182,742
Loss from operations	(243,172)	(281,283)	(182,742)
Interest income	5,834	15,591	8,964
Interest expenses	(9,809)	(894)	(346)
Other expenses, net	(406)	(180)	(69)
Net loss	$ (247,553)	$ (266,766)	$ (174,193)
Basic and diluted net loss per common share	$ (4.04)	$ (4.57)	$ (3.41)
Weighted-average number of shares used in computing basic and diluted net loss per common share	61,334,037	58,321,612	51,150,728

(1) During the year ended December 31, 2020 and 2019, we recorded a gain on lease modification related to our prior premises located in South San Francisco, California.

	As of December 31,		
(in thousands)	2020	2019	2018
Selected Consolidated Balance Sheet Data:			
Cash and cash equivalents and marketable securities	$ 560,892	$ 694,999	$ 591,815
Working capital	553,131	556,544	452,007
Total assets	724,002	796,099	617,643
Long-term debt	148,815	73,559	—
Accumulated deficit	(986,469)	(738,916)	(472,150)
Total stockholders' equity	416,157	578,694	572,799

Item 7. ***Management's Discussion and Analysis of Financial Condition and Results of Operations***

You should read the following discussion and analysis of our financial condition and results of operations together with the section of this annual report entitled "Selected Financial Data" and our consolidated financial statements and related notes included elsewhere in this annual report. This discussion and other parts of this annual report contain forward-looking statements that involve risk and uncertainties, such as statements of our plans, objectives, expectations, and intentions. In this annual report, words such as "may," "will," "expect," "anticipate," "estimate," "intend," and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements, as described elsewhere herein. As a result of many factors, including those factors set forth in the "Risk Factors" section of this annual report, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a biopharmaceutical company dedicated to the discovery, development and delivery of life-changing treatments that provide hope to underserved patient communities. Founded in 2011, our goal is to transform the treatment and care of sickle cell disease, or SCD, a lifelong, devastating inherited blood disorder that is marked by red blood cell, or RBC, destruction and occluded blood flow and hypoxia, which leads to anemia, stroke, multi-organ failure, severe pain crises, and shortened patient life span. Our mission is driven by the historical lack of understanding, investment and attention given to SCD. Although the fundamental cause of SCD has been understood for decades, therapeutic innovation and access to care has significantly lagged compared to many other rare diseases. For example, there are approximately three times more individuals in the U.S. living with SCD than cystic fibrosis, or CF. However, since the enactment of the Orphan Drug Act passed in 1983, only four drugs have been approved for SCD compared to 15 drugs approved for CF. As a result of the lack of treatment options, patients with SCD suffer serious morbidity and premature mortality.

In November 2019, the U.S. Food and Drug Administration, or FDA, granted accelerated approval for our first medicine, Oxbryta® (voxelotor) tablets for the treatment of SCD in adults and children 12 years of age and older. Oxbryta, an oral therapy taken once daily, is the first FDA-approved treatment that directly inhibits sickle hemoglobin, or HbS, polymerization, the root cause of SCD.

By early December 2019, we began to make Oxbryta available to patients through our specialty pharmacy partner network. In addition, we established GBT Source Solutions®, a comprehensive program for patients who are prescribed Oxbryta that provides a wide range of practical, educational and financial support customized to each patient's needs. In addition, we have focused on securing reimbursement and expanding patient access. By the end of September 2020, one quarter ahead of our goal, we secured broad Oxbryta reimbursement coverage for 90% of lives covered by payers either through published policies or verified patient adjudication. We also secured fee-for-service Medicaid coverage in 44 states, including all 17 priority states where most SCD patients live.

We have a number of ongoing clinical trials of Oxbryta. The Phase 2a HOPE-KIDS 1 Study, an open-label, single- and multiple-dose trial, is evaluating the safety, tolerability, pharmacokinetics and exploratory treatment effect of Oxbryta in pediatric patients aged 4 to 17 years with SCD. The Phase 3 HOPE-KIDS 2 Study, a post-approval confirmatory study we initiated in December 2019 as a condition of the accelerated approval of Oxbryta in the United States, uses transcranial Doppler, or TCD, flow velocity to seek to demonstrate a decrease in stroke risk in children 2 to 15 years of age. The ActIVe Phase 4 study, a pilot, open-label, single-arm study, aims to evaluate the effect of Oxbryta on exercise capacity, as measured by cardiopulmonary exercise testing (CPET) in patients 12 years of age and older with SCD. We also expect to conduct additional clinical studies of Oxbryta, including to seek to expand the potential approved product label into younger pediatric populations as well as to study further the efficacy and safety profile of Oxbryta for SCD patients.

In January 2021, the European Medicines Agency, or EMA, accepted for review our Marketing Authorization Application, or MAA, seeking full marketing authorization of Oxbryta to treat hemolytic anemia

(which is low hemoglobin due to red blood cell destruction) in SCD patients ages 12 years and older, and the MAA is undergoing standard review by the EMA. In addition, we plan to submit by mid-2021 a supplemental New Drug Application, or sNDA, to expand the current Oxbryta label to include treatment of SCD in children ages 4 to 11 years, under the FDA's accelerated approval pathway. Thereafter, we also plan to submit a New Drug Application, or NDA, for a new age-appropriate formulation for this patient population. To provide early access prior to potentially receiving additional marketing approval, we have established an expanded access protocol for eligible SCD patients in the United States and an early access program for eligible SCD patients for outside the United States. In addition, we have entered into an exclusive agreement with Biopharma-Middle East and Africa, or Biopharma-MEA, to distribute Oxbryta in the six countries that make up the GCC region (Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, and the United Arab Emirates), where the U.S. approval of Oxbryta can be referenced to allow for access to the medicine while health authorities conduct their reviews.

Beyond Oxbryta, we are engaged in other research and development activities, including working on new targets to potentially develop next generation of treatments for SCD, including inclacumab, a P-selectin inhibitor, which is a clinically validated target in SCD, known to reduce the incidence of vaso-occlusive crises, or VOCs, and our next generation hemoglobin polymerization inhibitor, GBT021601, or GBT601.

As part of our efforts to build our pipeline, we regularly evaluate opportunities to in-license, acquire or invest in new business, technology or assets or engage in related discussions with other business entities.

We licensed inclacumab from F. Hoffmann-La Roche Ltd. and Hoffmann-La Roche Inc. (together, "Roche") under the License Agreement we entered into in August 2018, or Roche Agreement. Prior to licensing inclacumab to us, Roche conducted clinical studies that enrolled more than 700 non-SCD patients and demonstrated an encouraging pharmacokinetic, safety, and tolerability profile for inclacumab. We expect to be able to leverage the safety data from Roche's prior clinical studies, as we proceed with our development of inclacumab as a potential treatment to reduce the frequency of VOCs in patients with SCD and to reduce the hospital VOC readmission rate for patients that require inpatient treatment for an initial VOC episode. We expect to initiate two pivotal clinical trials by the end of the first half of 2021. One study will be a chronic prevention study with an endpoint of the reduction in VOCs over a 48-week treatment period, and the other study will focus on hospital readmissions with an endpoint of the reduction of the rate of readmission to hospitals for VOC within 90 days following an initial hospitalization for VOC.

While still in early stages, we have an ongoing collaboration with Syros Pharmaceuticals, Inc., or Syros, which we entered into with a License and Collaboration Agreement, or Syros Agreement, in December 2019, to discover, develop and commercialize novel therapies for SCD and beta thalassemia. We are currently exploring orally available, small molecule drugs designed to upregulate fetal hemoglobin. Under the Syros Agreement, we have an option to obtain an exclusive worldwide license to develop, manufacture and commercialize any compounds or products resulting from the collaboration, subject to Syros' option to co-promote the first product in the United States.

In March 2020, the Centers for Disease Control and Prevention, or CDC, declared a global pandemic related to SARS-CoV-2, the virus that causes coronavirus disease 2019, or COVID-19, and the pandemic has impacted our business, including our commercialization of Oxbryta and our research and development activities. For example, we implemented a temporary work from home policy; temporarily suspended our field team from most in-person interactions, including visits to physician offices, clinics and hospitals as well as in-person meetings with payors; and temporarily delayed or paused certain research and development activities, including screening and enrollment in all clinical studies sponsored by us. As we continue to monitor and work toward resumption of all trial activities, we are continuing with administrative trial-start up activities (such as contracting and IRB/EC approvals). Notably, the COVID-19 pandemic has not significantly impacted our supply of Oxbryta. We continue to believe we have an adequate supply of Oxbryta to sustain estimated patient need through 2021, and we are continuing to produce Oxbryta tablets.

We have seen a significant decrease in weekly new patient prescriptions for Oxbryta from a peak in early March, and we expect the rate of new patient prescriptions may remain lower depending on the course of the pandemic. While we intend to resume normal operations as soon as practicable, we do not know for certain the extent or duration of these and other disruptions or the long-term impact on our business. Since mid-March 2020, when we made the decision to suspend in-person visits to health professionals our field teams, we have been engaging with healthcare professionals, or HCPs, and payors through increased use of digital and internet-based education and outreach, as well as limited face-to-face engagements in some settings following appropriate COVID-19 protocols.

We are not profitable and have incurred losses and negative cash flows from operations each year since our inception. We have financed our operations primarily through sale of equity securities and debt financing. In December 2018, we completed a follow-on offering and issued 3,409,090 shares of common stock at a price of $41.54 per share with proceeds of $141.1 million net of underwriting costs and commissions and offering expenses. In addition, in January 2019, we sold an additional 511,363 shares of our common stock directly to the underwriters when they exercised their over-allotment option at the price of $41.54 per share for proceeds of $21.2 million net of underwriting costs and commissions. In June 2019, we completed a follow-on offering and issued 3,375,527 shares of common stock at a price of $57.12 per share with proceeds of $192.4 million net of underwriting costs and commissions and offering expenses. In addition, in July 2019, we sold an additional 100,000 shares of our common stock directly to the underwriters when they exercised their over-allotment option at the price of $57.12 per share for proceeds of $5.7 million net of underwriting costs and commissions. In December 2019, we entered into a $150.0 million term loan agreement and drew down proceeds of $72.5 million net of debt issuance costs. We drew down the remaining $74.8 million net of debt issuance costs in November 2020.

Our net losses were $247.6 million for the year ended December 31, 2020, $266.8 million for the year ended December 31, 2019 and $174.2 million for the year ended December 31, 2018. As of December 31, 2020, we had an accumulated deficit of $986.5 million. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs and from selling, general and administrative costs associated with our operations. We had $494.8 million in cash and cash equivalents and $66.1 million in marketable securities as of December 31, 2020.

Critical Accounting Polices and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with United States generally accepted accounting principles, or U.S. GAAP. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the reported expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value 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 that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management's judgments and estimates.

Revenue Recognition

Pursuant to Accounting Standards Codification, Topic 606, *Revenue from Contracts with Customers*, or ASC 606, we recognize revenue upon transfer of control of promised products or services to customers in an amount that reflects the consideration we expect to receive in exchange for those products or services.

To determine revenue recognition for arrangements that we determine are within the scope of ASC 606, we perform the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy a performance obligation. We only apply the five-step model to contracts when it is probable that we will collect substantially all of the consideration we are entitled to in exchange for the goods or services we transfer to the customer.

Product sales, net

Our product sales consist of U.S. sales of Oxbryta, which we began shipping to customers in December 2019. Prior to December 2019, we had no product sales. We sell Oxbryta to a limited number of specialty pharmacies and a specialty distributor, or collectively, Customers. These agreements with our Customers provide for transfer of title to the product at the time the product has been delivered to the Customers. The Customers subsequently dispense our product directly to a patient or resell our product to hospitals and certain pharmacies.

We recognize revenue on product sales when the Customers obtain control of our product, which occurs at a point in time, typically upon delivery to our Customers. It is at that point that we have a right to payment and that our Customers obtain title and the risks and rewards of ownership. Shipping and handling activities are considered to be fulfillment activities rather than a separate performance obligation. Payment terms are typically 30-60 days following delivery to our Customers. Because payment is expected shortly after delivery, we do not adjust the amount of consideration expected to be received for the effects of a significant financing component.

We consider the effects of items that can decrease the transaction price such as variable consideration and consideration payable to Customers or payer. Amounts related to such items are estimated at contract inception and updated at the end of each reporting period as additional information becomes available. The amount of variable consideration may be constrained and is included in the transaction price only to the extent it is probable that a significant reversal of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is resolved. Revenue from product sales is recorded after considering the impact of the following variable consideration amounts along with the constraint at the time of revenue recognition:

Rebates: We are subject to government mandated rebates for Medicaid Drug Rebate Program, Medicare Part D Prescription Drug Benefit Program, and other government health care programs in the United States. Rebate amounts are based upon contractual agreements or legal requirements with public sector benefit providers. We use the expected-value method for estimating these rebates based on statutory discount rates and expected utilization. The expected utilization of rebates is estimated based on third party data from the specialty pharmacies and specialty distributor. Estimates for these rebates are adjusted quarterly to reflect the most recent information. We record an accrued liability for unpaid rebates related to products for which control has been transferred to Customers.

Prompt payment discounts: We provide discounts to our Customers if they pay for our products within a defined period of time after title transfers, which terms are explicitly stated in the contract. We use the most-likely-amount method for estimating prompt payment discounts. We expect that our Customers will earn prompt payment discounts. As a result, we deduct the full amount of those discounts from total product sales when revenues are recognized and record these discounts as a reduction of accounts receivable.

Co-payment assistance: We provide co-payment assistance to patients who have commercial insurance and meet certain eligibility requirements. We use the expected-value method for estimating co-payment assistance based on estimates of program redemption using data provided by third-party administrators. Estimates for the co-payment assistance are adjusted quarterly to reflect actual experience. We record an accrued liability for unredeemed co-payment assistance related to products for which control has been transferred to Customers.

Medicare Part D Coverage Gap: The Medicare Part D coverage gap is a federal program to subsidize the costs of prescription drugs for Medicare beneficiaries in the United States, which mandates manufacturers to

fund a portion of the Medicare Part D insurance coverage gap for prescription drugs sold to eligible patients. Funding of the coverage gap is generally invoiced and paid in arrears. We estimate the impact of the Medicare Part D coverage gap using the expected-value method based on an amount expected to be incurred for the current quarter's activity, plus an accrual balance for known prior quarters. Estimates for the impact of the Medicare Part D coverage gap are adjusted quarterly to reflect actual experience. We record an accrued liability for unpaid reserves related to the Medicare Part D coverage gap.

Product returns: Consistent with industry practice, we offer limited product return rights and generally allow for the return of product that is damaged or defective, or within a few months prior to and up to a few months after the product expiration date. We consider several factors in the estimation of potential product returns, including expiration dates of the product shipped, the limited product return rights, third-party data in monitoring channel inventory levels, shelf life of the product, prescription trends, and other relevant factors. We expect product returns to be immaterial. Other than these limited returns, we do not provide any product warranties.

Chargebacks: Chargebacks are discounts that occur when contracted parties purchase directly from a specialty distributor. Contracted parties, which currently consist primarily of Public Health Service Institutions and federal government entities purchasing via the Federal Supply Schedule, generally purchase the product at a discounted price. The specialty distributor, in turn, charges back the difference between the price initially paid by the specialty distributor and the discounted price paid to the specialty distributor by the contracted parties to us. The reserves for chargeback are based on known sales to contracted parties. We establish the reserves for chargebacks in the same period that the related revenue is recognized, resulting in a reduction of product revenue and receivables.

Distributor fees: Our specialty distributor provides distribution services to us for a fee, based on a contractually determined fixed percentage of sales. We estimate these distributor fees and record such estimates in the same period the related revenue is recognized, resulting in a reduction of product revenue. We record an accrued liability for unpaid distributor fees.

Each of the above items is variable consideration, which we record at the time of revenue recognition, and require significant estimates, judgement and information obtained from external sources. If management's estimates differ from actual results, we will record adjustments that would affect product sales in the period of adjustment.

The following table summarizes activity with respect to our sales allowances and accruals for the year ended December 31, 2020 and 2019 (in thousands):

	Rebates, co-payment assistance, Medicare Part D coverage gap, product returns and distributor fees	Prompt payment discounts and chargebacks	Total
Balances at December 31, 2018	$ —	$ —	$ —
Provision related to current period sales	529	113	642
Credit or payments made during the period	—	—	—
Balances at December 31, 2019	**$ 529**	**$ 113**	**$ 642**
Provision related to current period sales	13,697	4,351	18,048
Credit or payments made during the period	(7,821)	(3,713)	(11,534)
Balance at December 31, 2020	**$ 6,405**	**$ 751**	**$ 7,156**

Other revenue recognition considerations

Oxbryta is our only product. The only performance obligation included in our contracts is the delivery of Oxbryta to our Customers. Therefore, no allocation of transaction price among performance obligations is necessary. Consequently, the transaction price determined after considering the impacts of variable consideration is recognized at the time control is transferred to our Customers, which is upon delivery of Oxbryta to our Customers.

Because all sales of Oxbryta are in the United States and because our Customers are each a large distributor with similar variable consideration impacts, we provide revenue numbers on a total basis without further disaggregation. Additionally, we do not have any contract assets or liabilities, other than accounts receivable, related to our sales of Oxbryta.

Accruals of Research and Development and Manufacturing Costs

We record accruals for estimated costs of research, nonclinical and clinical studies and manufacturing development. These costs are a significant component of our research and development expenses. A substantial portion of our ongoing research and development activities are conducted by third-party service providers, including contract research organizations and contract manufacturing organizations. We also accrue for estimated costs of manufacturing activities for inventories. These costs are a significant component of the cost of our inventory.

We accrue the costs incurred under our agreements with these third parties based on actual work completed in accordance with agreements established with these third parties. We determine the accruals for research and development through discussions with internal personnel and external service providers as to the progress or stage of completion of the clinical studies and the agreed-upon fee to be paid for such services.

The accrual for contract manufacturing activities is based on an estimate of manufacturing activities completed to date, contractual rates, and amounts invoiced and paid to date at the end of each reporting period. We determine the percentage of manufacturing activities completed to date based on discussions with the contract manufacturing organizations, oversight of the manufacturing activities and anticipated timeline.

As actual costs become known, we adjust our accruals. We have not experienced any material deviations between accrued costs and actual costs. However, actual clinical and manufacturing services performed, number of subjects enrolled, and the rate of subject enrollment may vary from our estimates, resulting in adjustments to research and development costs or inventories in future periods. Changes in these estimates that result in material changes to our accruals could materially affect our results of operations or amounts of inventories capitalized.

Results of Operations

Comparison of the years ended December 31, 2020 and 2019

(in thousands, except percentages)	Year Ended December 31, 2020	2019	Change 2020/2019 $	%
Product sales, net	$ 123,803	$ 2,108	$121,695	5,773%
Costs and operating expenses:				
Cost of sales	1,986	48	1,938	*
Research and development	155,122	174,556	(19,434)	(11)
Selling, general and administrative	210,851	117,088	93,763	80
Gain on lease modification	(984)	(8,301)	7,317	88
Total costs and operating expenses	366,975	283,391	83,584	29
Loss from operations	(243,172)	(281,283)	38,111	(14)
Interest income	5,834	15,591	(9,757)	(63)
Interest expenses	(9,809)	(894)	(8,915)	(997)
Other expenses, net	(406)	(180)	(226)	126
Net loss	$(247,553)	$(266,766)	$ (19,213)	(7)%

* Change is not meaningful

Product sales, net

Product sales consist of sales of Oxbryta, which was approved by the FDA in late November 2019. We commenced shipments of Oxbryta and fully launched with a deployed sales force in early December 2019.

Cost of sales

Cost of sales of $2.0 million and $48,000 for the year ended December 31, 2020 and 2019, respectively, is related to certain costs incurred after FDA approval related to the cost of Oxbryta sold. Prior to receiving FDA approval for Oxbryta in November 2019, we recorded all costs incurred in the manufacture of Oxbryta as research and development expense. We expect to sell inventory previously expensed to research and development throughout 2021, and, accordingly we expect our costs of product sales of Oxbryta to increase as a percentage of net sales in future periods as we produce and sell inventory that reflects the full cost of manufacturing the product.

Research and development

Research and development expenses consist primarily of costs incurred for the development of Oxbryta and product candidates, which include:

- employee-related expenses, which include salaries, benefits and stock-based compensation;
- expenses incurred under agreements with consultants, third-party research and manufacturing organizations, and investigative clinical trial sites that conduct research and development activities on our behalf;
- the costs related to production of clinical supplies, including fees paid to contract manufacturers;
- laboratory and vendor expenses related to the execution of nonclinical studies and clinical trials;
- payments upon achievement of certain clinical development and regulatory milestones in relation with license agreement; and

- facilities and other allocated expenses, which include expenses for rent and maintenance of facilities, depreciation and amortization expense and other supplies.

We expense all research and development costs in the periods in which they are incurred. Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and clinical sites. Nonrefundable advance payments for goods or services to be received in future periods for use in research and development activities are deferred and capitalized. The capitalized amounts are then expensed as the related goods are delivered and the services are performed.

The largest component of our total operating expenses is our investment in research and development activities, including the clinical development of Oxbryta. We allocate research and development salaries, benefits, stock-based compensation and indirect costs to Oxbryta, inclacumab and other product candidates that we may pursue on a program-specific basis.

We expect our research and development expenses will increase in future periods as we continue to invest in research and development activities related to developing Oxbryta and product candidates, and as programs advance into later stages of development and we begin to conduct larger clinical trials. The process of conducting the necessary clinical research to obtain regulatory approval is costly and time-consuming, and research and development is highly uncertain. As a result, we are unable to determine the duration and completion costs of our research and development projects or when and to what extent we will generate revenue from the commercialization and sale of any of our product candidates.

The following table summarizes our research and development expenses incurred during the respective periods (in thousands, except percentages):

	Years Ended December 31,		Change 2020/2019	
	2020	2019	$	%
Costs incurred by development program:				
Oxbryta for the treatment of SCD	$ 83,945	$ 117,827	$(33,882)	(29)%
Other preclinical programs	45,360	47,015	(1,655)	(4)
Inclacumab for the treatment of SCD	25,817	9,472	16,345	173
Oxbryta for the treatment of hypoxemic pulmonary disorders	—	242	(242)	*
Total research and development expenses	$ 155,122	$ 174,556	$(19,434)	(11)%

* Change is not meaningful

Research and development expenses decreased by $19.4 million, or 11%, to $155.1 million for the year ended December 31, 2020 from $174.6 million for the year ended December 31, 2019. The decrease was primarily due to a $33.9 million decrease in external costs for Oxbryta related to manufacturing costs and medical affairs costs that were previously expensed to research and development prior to approval by the FDA and a $1.7 million decrease in other preclinical programs. The decrease was partially offset by a $16.3 million increase in external costs associated with inclacumab driven by the manufacturing activities. Stock-based compensation expense related to research and development was $18.1 million for the year ended December 31, 2020 and $19.1 million for the year ended December 31, 2019. The increase was primarily due to hiring additional personnel and stock price appreciation.

Selling, general and administrative expenses

Selling, general and administrative expenses consist primarily of costs incurred in our executive, commercial, finance, corporate development, human resource, information technology, legal, compliance and other general and administrative functions, which include:

- employee-related expenses, which include salaries, benefits and stock-based compensation;
- fees to third-party vendors providing customer support services;
- expenses incurred under agreements with consultants; and
- facilities and other allocated expenses, which include expenses for rent and maintenance of facilities, depreciation and amortization expense and other supplies.

We expense all selling, general and administrative costs in the periods in which they are incurred. We expect our general and administrative expenses to continue to grow as we progress through this early stage of the commercialization of Oxbryta.

General and administrative expenses increased by $93.8 million, or 80%, to $210.9 million for the year ended December 31, 2020 from $117.1 million for the year ended December 31, 2019. The increase was primarily due to an increase of $32.9 million in salary and benefit costs due to a greater number of employees, a $26.9 million increase in stock-based compensation expense as a result of our hiring additional personnel and stock price appreciation, a $26.0 million increase in professional and consulting services due to the growth of our operations and the commercialization of Oxbryta, and an $8.0 million increase in other general and administrative expense due to the growth of our operations, such as higher rent expenses resulting from our move into the new facility. Selling, general and administrative related stock-based compensation expense was $53.4 million and $26.5 million for the year ended December 31, 2020 and 2019, respectively.

Gain on lease modification

Gain on lease modification of $1.0 million and $8.3 million for the year ended December 31, 2020 and 2019, respectively, was related to the lease amendment of our previous premises located in South San Francisco, California for 67,185 square feet of space in October 2019.

Interest income

Interest income was $5.8 million in 2020 compared to interest income of $15.6 million in 2019. The $9.8 million decrease was primarily due to decrease in interest income from our investment balances.

Interest expenses

Interest expense was $9.8 million in 2020 compared to interest expense of $0.9 million in 2019. The $8.9 million increase was primarily due to higher interest expense related to our Term Loan entered in December 2019.

Income Taxes

As of December 31, 2020, we had federal net operating loss carryforwards of approximately $829.1 million to offset future federal taxable income, with $209.9 million available through 2037 and $619.2 million available indefinitely. We also had state net operating loss carryforwards of approximately $587.1 million that may offset future state taxable income, through 2040. Current federal and state tax laws include substantial restrictions on the utilization of net operating losses and tax credits in the event of an ownership change. Even if the carryforwards are available, they may be subject to annual limitations, lack of future taxable income, or future

ownership changes that could result in the expiration of the carryforwards before they are utilized. At December 31, 2020, we recorded a 100% valuation allowance against our deferred tax assets of approximately $325.7 million, as at that time our management believed it was uncertain that they would be fully realized. If we determine in the future that we will be able to realize all or a portion of our net operating loss carryforwards, an adjustment to our net operating loss carryforwards would increase net income in the period in which we make such a determination.

For the years ended December 31, 2019 and 2018

The comparison of the fiscal years ended December 31, 2019 and 2018 can be found in our annual report on Form 10-K for the fiscal year ended December 31, 2019 located within Part II, Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations, which is incorporated herein by reference.

Liquidity and Capital Resources

We are not profitable and have incurred losses and negative cash flows from operations each year since our inception. We have financed our operations primarily through sale of equity securities. As of December 31, 2020, we had $494.8 million in cash and cash equivalents and $66.1 million in marketable securities. On December 17, 2019, we entered into the Loan Agreement, or Term Loan, with funds managed by Pharmakon Advisors LP, which are BioPharma Credit PLC, as collateral agent, Biopharma Credit Investments V (Master) LP, as a lender, and BPCR Limited Partnership, as a lender, and collectively, the Lenders, for a senior secured credit facility consisting of an initial tranche of $75.0 million and the option to draw an additional $75.0 million until December 31, 2020. The first tranche, in the amount of $75.0 million, was funded in connection with the closing date of the Term Loan in December 2019, and the second tranche, in the amount of $75.0 million, was funded in November 2020.

On August 5, 2020, we filed a shelf registration statement on Form S-3, or Shelf Registration Statement, with the SEC relating to the registration of our common stock, preferred stock, debt securities, warrants and units or any combination thereof. Concurrently with the filing of the Shelf Registration Statement, we entered into a Sales Agreement with SVB Leerink LLC, or Sales Agent, to provide for the offering, issuance and sale by us of up to an aggregate of $200.0 million of our common stock from time to time in "at-the-market" offerings under the Shelf Registration Statement, or Sales Agreement. We have agreed to pay to the Sales Agent cash commissions of up to 3.0% of the gross proceeds from sales of common stock pursuant to the Sales Agreement. We have not issued any shares or received any proceeds pursuant to the Sales Agreement through December 31, 2020.

Our primary use of cash is to fund operations. Cash used to fund operations is impacted by the timing of when we pay these expenses, as reflected in the change in our outstanding accounts payable and accrued expenses.

We believe that our existing capital resources will be sufficient to fund our planned operations for at least the next twelve months. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. We believe we may continue to require additional financing to commercialize Oxbryta, advance Oxbryta through clinical development, to acquire and develop other product candidates and to fund operations for the foreseeable future. We may continue to seek funds through equity or debt financings, collaborative or other arrangements with corporate sources, or through other sources of financing. Adequate additional funding may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed could have a negative impact on our financial condition and our ability to pursue our business strategies. Our future funding requirements will depend on many factors, including:

- our ability to successfully commercialize Oxbryta, inclacumab and any other product candidates we may identify and develop in any territories;

- the manufacturing, selling, and marketing costs associated with the commercialization of Oxbryta and the potential commercialization of inclacumab and any other product candidates we may identify and develop, including the cost and timing of establishing or maintaining our sales and marketing capabilities in any territory(ies);
- the amount and timing of sales and other revenues from Oxbryta, inclacumab and any other product candidates we may identify and develop, including the sales price and the availability of adequate third-party reimbursement;
- the time and cost necessary to conduct and complete multiple ongoing studies (including our HOPE-KIDS 1 Study, our Phase 3 HOPE-KIDS 2 Study, and other studies;
- the time and cost necessary to conduct and complete any additional clinical studies required to pursue additional regulatory approvals for Oxbryta for SCD, including our Phase 3 HOPE-KIDS 2 Study (which is intended as our required confirmatory study to move from our current Subpart H approval to a full approval of Oxbryta) and any studies to support potential label expansions into younger SCD pediatric populations, or any other post-marketing studies for Oxbryta for SCD;
- the progress, data and results of clinical trials of Oxbryta and product candidates;
- the progress, timing, scope and costs of our nonclinical studies, our clinical trials and other related activities, including our ability to enroll subjects in a timely manner for our ongoing and future clinical trials of Oxbryta, inclacumab or any other product candidate that we may identify and develop;
- the costs of obtaining clinical and commercial supplies of Oxbryta, inclacumab and any other product candidates we may identify and develop;
- our ability to advance our development programs, including for Oxbryta, inclacumab and any other potential product candidate programs we may identify and pursue, the timing and scope of these development activities, and the availability of approval for any of our other product candidates;
- our ability to successfully obtain any additional regulatory approvals from any regulatory authorities, and the scope of any such regulatory approvals, to market and sell Oxbryta, inclacumab and any other product candidates we may identify and develop in any territory(ies);
- the cash requirements of any future acquisitions or discovery of product candidates;
- the time and cost necessary to respond to technological and market developments;
- the extent to which we may acquire or in-license other product candidates and technologies, and the costs and timing associated with any such acquisitions or in-licenses;
- our ability to attract, hire, and retain qualified personnel; and
- the costs of maintaining, expanding, and protecting our intellectual property portfolio.

Further, our operating plan may change, and we may need additional funds to meet operational needs and capital requirements for commercialization, clinical trials and other research and development expenditures. We currently have no credit facility or committed sources of capital. Because of the numerous risks and uncertainties associated with the development and commercialization of Oxbryta and product candidates and ongoing developments in connection with the COVID-19 pandemic, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated commercialization, clinical trials and research and development activities.

The following table summarizes our cash flows for the periods indicated:

	Year Ended December 31,		
(in thousands)	2020	2019	2018
Cash used in operating activities	$ (211,862)	$ (194,417)	$ (135,375)
Cash provided by (used in) investing activities	317,312	(76,861)	(184,157)
Cash provided by financing activities	87,120	298,158	397,906
Net increase in cash, cash equivalents and restricted cash	$ 192,570	$ 26,880	$ 78,374

Cash flows from operating activities

Net cash used in operating activities for the year ended December 31, 2020 was $211.9 million, consisting of a net loss of $247.6 million, which was partially offset by non-cash charges of $71.5 million for stock-based compensation and $12.5 million for net depreciation and amortization expense. The change in our net operating assets and liabilities was due primarily to an increase of $36.8 million in inventories to support our current and anticipated Oxbryta commercial sales, an increase in accounts receivable of $14.9 million due to higher Oxbryta commercial sales, a decrease of $10.1 million in accrued liabilities primarily due to the payout of the accrued $20.0 million upfront payment to Syros in January 2020 and timing of manufacturing activities offset by higher sales and allowance accrual due to higher Oxbryta commercial sales, an increase of $8.4 million in accounts payable due to timing of payments, and an increase of $6.4 million in accrued compensation related to higher number of employees.

Net cash used in operating activities was $194.4 million for the year ended December 31, 2019, consisting of a net loss of $266.8 million, which was partially offset by non-cash charges of $45.7 million for stock-based compensation, $8.3 million for gain on lease modification and $7.9 million for depreciation and amortization expense. The change in our net operating assets and liabilities was due primarily to an increase of $24.7 million of accrued liabilities primarily related to higher research and development activities and higher professional and consulting services due to the growth of our operations, an increase of $7.5 million of accrued compensation related to a higher number of employees, an increase of $4.5 million of accounts payable due to timing of payments, an increase of $2.6 million of accounts receivables as we commercially launched Oxbryta in December 2019, an increase of $3.1 million of prepaid expenses primarily due to advance payment made in connection with our inclacumab program and to support our commercialization of Oxbryta, and an increase of $1.3 million in inventories as we began capitalizing Oxbryta as inventory upon receipt of FDA approval in November 2019 and commercially launched Oxbryta in December 2019.

Net cash used in operating activities was $135.4 million for the year ended December 31, 2018, consisting of a net loss of $174.2 million, which was partially offset by non-cash charges of $30.1 million for stock-based compensation and $4.0 million for depreciation and amortization expense. The change in our net operating assets and liabilities was due primarily to an increase of $2.5 million of prepaid expenses due to advance payments made in connection with our Phase 3 HOPE Study and our Phase 2a HOPE-KIDS 1 Study, an increase of $8.0 million of accrued liabilities related to higher research and development activities and higher professional and consulting services due to the growth of our operations, an increase of $1.5 million of accrued compensation related to a higher headcount and a decrease of $1.3 million of accounts payable due to timing of payments. The remainder of changes in operating assets and liabilities are primarily related to continuous growth of our operations.

Cash flows from investing activities

Cash provided by investing activities for the year ended December 31, 2020 was $317.3 million, consisting of maturities of marketable securities of $384.0 million, which are partially offset by purchases of marketable securities of $57.9 million and purchases of property and equipment of $8.8 million.

Net cash used in investing activities for the year ended December 31, 2019 was $76.9 million, primarily consisting of the purchase of marketable securities of $434.9 million, and purchase of property and equipment for our office and laboratory facility of $3.5 million, which are partially offset by maturities of marketable securities of $361.5 million.

Net cash used in investing activities for the year ended December 31, 2018 was $184.2 million, primarily consisting of the purchase of marketable securities of $361.4 million, and purchase of property and equipment for our office and laboratory facility of $4.8 million, which are partially offset by maturities of marketable securities of $182.0 million.

Cash flows from financing activities

Cash provided by financing activities for the year ended December 31, 2020 was $87.1 million. The cash provided by financing activities in 2020 was primarily from net proceeds of $74.8 million from the second tranche of the Term Loan that we entered in 2019 and $17.6 million from the issuance of common stock to participants in the Employee Stock Purchase Plan, or ESPP, and exercise of stock options, which were partially offset by $5.3 million of taxes paid related to net share settlement of equity awards.

Cash provided by financing activities was $298.2 million for the year ended December 31, 2019. The cash provided by financing activities in 2019 was primarily from net proceeds of $219.4 million from the issuance of common stock in connection with our follow-on offerings completed in 2019, net proceeds of $72.5 million from the debt financing completed in 2019, and to a lesser extent, proceeds of $13.9 million from the issuance of common stock to participants in the ESPP and exercise of stock options, which are partially offset by $7.6 million of taxes paid related to net shares settlement of equity awards.

Cash provided by financing activities was $397.9 million for the year ended December 31, 2018. The cash provided by financing activities in 2018 was primarily from net proceeds of $396.5 million from the issuance of common stock in connection with our follow-on offerings completed in January 2018, March 2018 and December 2018, and to a lesser extent, proceeds of $7.7 million from the issuance of common stock to participants in the ESPP and exercise of stock options, which are partially offset by $6.3 million of taxes paid related to net shares settlement of equity awards.

Off-Balance Sheet Arrangements

As of December 31, 2020, we had no off-balance sheet arrangements as defined in Item 303(a)(4) of Regulation S-K as promulgated by the Securities and Exchange Commission, or SEC.

Contractual Obligations and Other Commitments

In December 2019, we entered into the Term Loan for a senior secured credit facility consisting of an initial term loan of $75.0 million, with an option to draw an additional $75.0 million until December 31, 2020. The first tranche of $75.0 million was funded in December 2019 and the second tranche of the $75.0 million was funded in November 2020. The Term Loan carries a 72-month term and provides for interest only payments for the first 39 months, followed by consecutive equal quarterly payments. The Term Loan bears interest at a floating per annum interest rate equal to 7.00% plus the greater of: (a) LIBOR rate or (b) 2%. Interest on amounts outstanding are payable quarterly in arrears. We are obligated to pay an additional fee to the Lenders determined by

multiplying the principal amount being paid or prepaid multiplied by 2% when such payments are made. The obligations under the Term Loan are secured by a first priority security interest in and a lien on substantially all of our assets, subject to certain exceptions.

The following table summarizes our contractual obligations under our loan agreement and the operating leases as of December 31, 2020 (in thousands):

		Payments Due by Period				
	Total	2021	2022	2023	2024	Thereafter
Term Loan	$ 201,938	$ 13,500	$ 13,500	$ 62,813	$ 58,313	$ 53,812
Operating lease obligations	$ 123,470	$ 11,841	$ 12,222	$ 12,584	$ 12,948	$ 73,875
Total contractual obligations	$ 325,408	$ 25,341	$ 25,722	$ 75,397	$ 71,261	$ 127,687

We have excluded from the above table $24.4 million in contractual obligations related to uncertain tax positions as we cannot make a reasonably reliable estimate of the period of cash settlement.

In December 2019, we entered into the Syros Agreement to discover, develop and commercialize novel therapies for SCD and beta thalassemia. Under the agreement, Syros will use its leading gene control platform to identify therapeutic targets and discover drugs that potentially induce fetal hemoglobin, and we have an option to obtain an exclusive worldwide license to develop, manufacture and commercialize any compounds or products resulting from the agreement, subject to Syros' option to co-promote the first product in the United States. If we exercise the option, we will be responsible for all development, manufacture, regulatory activities and commercialization of the compound or product. Syros and we will be responsible for our own costs incurred to conduct research activities, except that we will fund up to $40.0 million in preclinical research for at least three years. Unless earlier terminated or extended, the research program under the agreement will end on the third anniversary of the agreement.

Under the terms of the Syros Agreement, we paid Syros an upfront payment of $20.0 million in January 2020, and, if we exercise our option under the agreement, we may be obligated to pay Syros up to $315.0 million in option exercise, development, regulatory, commercialization and sales-based milestones per product candidate and product resulting from the agreement. We will also be obligated to pay Syros, subject to certain reductions, tiered mid- to high-single digit royalties as percentages of calendar year net sales on any product resulting from the agreement. As of December 31, 2019, we have recognized the $20.0 million upfront payment in our research and development costs for year ended December 31, 2019. No milestone payments were recognized for the year ended December 31, 2020. We have recognized $8.6 million of research reimbursement to Syros in our research and development cost for the year ended December 31, 2020.

In August 2018, we entered into the Roche Agreement pursuant to which Roche granted us an exclusive and sublicensable worldwide license under certain patent rights and know-how to develop and commercialize inclacumab for all indications and uses, except diagnostic use. Roche retained a non-exclusive, worldwide, perpetual, royalty-free license to inclacumab solely for any diagnostic use. As of December 31, 2019, we have paid Roche an upfront payment of $2.0 million. We are obligated to make contingent payments to Roche totaling approximately $125.5 million in milestone payments for the SCD indication, including up to $40.5 million based on achievement of certain clinical development and regulatory milestones for inclacumab in the SCD indication, and up to $85.0 million based on achievement of certain thresholds for annual net sales of inclacumab. As of December 31, 2020, we have paid Roche a clinical development milestone payment of $2.0 million. We are also obligated to make contingent payments to Roche up to an additional $6.4 million in milestone payments, which are owed to a third party, based on achievement of such clinical development and regulatory milestones for inclacumab. In addition, we are obligated to make contingent payments to Roche up to $19.25 million in milestone payments based on achievement of certain clinical development and regulatory milestones for inclacumab for any indication other than the SCD indication.

Recent Accounting Pronouncements

In December 2019, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, No. 2019-12, *Income Taxes (Topic 740), Simplifying the Accounting for Income Taxes*. The new guidance eliminates certain exceptions related to the approach for intraperiod tax allocation, the methodology for calculating income taxes in an interim period, and the recognition of deferred tax liabilities for outside basis differences. It also clarifies and simplifies other aspects of the accounting for income taxes. ASU 2019-12 is effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2020 and the applicable amendments will be applied on a prospective basis. We do not expect the adoption of this new standard will have a material impact on our consolidated financial statements.

Accounting Pronouncements Adopted

In August 2018, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, No. 2018-15, *Intangibles—Goodwill and Other—Internal-Use Software (Subtopic 350-40), Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract*, or ASU 2018-15. ASU No. 2018-15 requires a customer that is a party to a cloud computing service contract to follow the internal-use software guidance in Subtopic 350-40 to determine which implementation costs to capitalize and which costs to expense. The amendments in this update are effective for annual reporting periods beginning after December 15, 2019, and interim periods within those fiscal years. The amendments in this update should be applied either retrospectively or prospectively to all implementation costs incurred after the date of adoption. We adopted ASU No. 2018-15 in the first quarter of 2020 and applied the guidance prospectively to the implementation costs incurred in our implementations of various cloud computing arrangements that are service contracts. The adoption of this new standard did not have a material impact on our consolidated financial statements.

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement (Topic 820)*. The new standard modifies the disclosure requirements on fair value measurements in Topic 820, Fair Value Measurement, including removals of, modification to, and additional disclosure requirements from Topic 820. The amendment of ASU No. 2018-13 removes disclosure requirements from Topic 820 in the areas of (1) the amount of and reasons for transfers between Level 1 and Level 2 of the fair value hierarchy, (2) the policy for timing of transfers between levels, and (3) the valuation processes for Level 3 fair value measurements. The amendments in this update are effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019. Except for certain amendments related to Level 3 fair value measurements, all the other amendments should be applied retrospectively to all periods presented upon their effective date. We adopted ASU No. 2018-13 in the first quarter of 2020 and applied the guidance retrospectively. The adoption of this new standard did not have a material impact on our consolidated financial statements.

In June 2016, the FASB issued ASU No. 2016-13, *Measurement of Credit Losses on Financial Instruments (Topic 326)*, which amends the guidance on the impairment of financial instruments. The new standard adds to U.S. GAAP an impairment model that is based on expected losses rather than incurred losses, which is known as the current expected credit loss, or CECL model. The CECL model applies to most debt instruments (other than those measured at fair value), trade and other receivables, financial guarantee contracts, and loan commitments. Available-for-sale debt securities are scoped out of this guidance. Our investment portfolio primarily consists of available-for-sale debt securities carried at fair value. Our accounts receivable are not long term in nature and we do not expect to write off accounts receivable. The amendments in this update are effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019. We adopted ASU No. 2016-13 in the first quarter of 2020 and applied the guidance prospectively. The adoption of this new standard did not have a material impact on our consolidated financial statements.

Item 7A. ***Quantitative and Qualitative Disclosures about Market Risk***

Interest Rate Sensitivity

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities. We have invested primarily in money market funds, negotiable certificates of deposit, U.S. treasury notes, federal agency notes and corporate debt securities. The fair value of our investments, including those included in cash and cash equivalents and marketable securities, was $552.3 million as of December 31, 2020 and $644.2 million as of December 31, 2019.

Our investment policy is to limit credit exposure through diversification and investment in highly rated securities. We, along with our investment advisors, actively review current investment ratings, company specific events, and general economic conditions in managing our investments.

We performed a sensitivity analysis to determine the impact a change in interest rates would have on the value of our investment portfolio. Based on our investment positions as of December 31, 2020, a hypothetical 100 basis point increase in interest rate would result in a $0.2 million decline in the fair market value of our portfolio. Such losses would only be realized if we sold the investments prior to maturity.

We are also exposed to interest rate risk with respect to the senior secured credit facility that we entered into in December 2019, or Term Loan, that bears variable interest based on LIBOR. The outstanding principal balance of the Term Loan was $150.0 million as of December 31, 2020. We currently do not use interest rate derivative instruments to manage our exposure to interest rate fluctuations. We monitor our market interest rate risk exposures from the Term Loan using a sensitivity analysis. Our sensitivity analysis estimates the exposure to the Term Loan assuming a hypothetical 100 basis points change in interest rates on our $150.0 million of unhedged variable rate debt. A hypothetical 100 basis point change in interest rates would result in changes in the annual interest expenses recognized from the Term Loan of between $0.3 million and $1.5 million per year over the term of the debt.

These analyses do not consider the effect of any change in overall economic activity that could impact interest rates. Further, in the event of an increase in interest rates of significant magnitude, we may take actions to further mitigate our exposure to the change. However, due to the uncertainty of the specific actions that would be taken and their possible effects, these analyses assume no changes in our financial structure.

Item 8. ***Financial Statements and Supplementary Data***

GLOBAL BLOOD THERAPEUTICS, INC.
INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Years Ended December 31, 2020 and 2019

Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors
Global Blood Therapeutics, Inc.:

Opinions on the Consolidated Financial Statements and Internal Control Over Financial Reporting

We have audited the accompanying consolidated balance sheets of Global Blood Therapeutics, Inc. and subsidiaries (the Company) as of December 31, 2020 and 2019, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for each of the years in the three-year period ended December 31, 2020, and the related notes (collectively, the consolidated financial statements). We also have audited the Company's internal control over financial reporting as of December 31, 2020, based on criteria established in *Internal Control – Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2020 and 2019, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2020, in conformity with U.S. generally accepted accounting principles. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2020 based on criteria established in *Internal Control – Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission.

Change in Accounting Principle

As discussed in Note 2 to the consolidated financial statements, the Company has changed its method of accounting for leases as of January 1, 2019 due to the adoption of FASB Accounting Standards Update 2016-02, *Leases (Topic 842)*.

Basis for Opinions

The Company's management is responsible for these consolidated financial statements, 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 Annual Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the Company's consolidated financial statements and an opinion on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (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 audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audit of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated 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 consolidated financial statements. Our audit also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

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.

Critical Audit Matters

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

Assessment of the estimated manufacturing activities completed to date

As discussed in Note 5 to the consolidated financial statements, the Company has accrued manufacturing costs of $9,125 thousand as of December 31, 2020. As discussed in Note 2 to the consolidated financial statements, this accrual is based on an estimate of manufacturing activities completed to date by contract manufacturing organizations, contractual rates, and amounts invoiced and paid as of the end of each reporting period.

We identified the assessment of estimated manufacturing activities completed to date as a critical audit matter. The percentage of manufacturing activities completed to date is a subjective estimate based on the Company's discussions with the contract manufacturing organizations, oversight of the manufacturing activities and the anticipated timeline. Evaluating this estimate required a higher degree of auditor judgment and changes to this estimate could have had a significant impact on the amount of accrued manufacturing costs recorded by the Company.

The following are the primary procedures we performed to address this critical audit matter. We evaluated the design and tested the operating effectiveness of certain internal controls related to accrued manufacturing costs. This included a control related to the estimation of the percentage of manufacturing activities completed to date. We selected certain accrued manufacturing costs and assessed the Company's estimate of the percentage of manufacturing activities completed to date by: (1) inquiring with Company personnel responsible for overseeing the contract manufacturing activities to understand progress of the manufacturing activities; (2) inspecting correspondence received from contract manufacturing organizations, if any, and comparing the reported information to the Company's estimate; and (3) inspecting executed change orders and original contract terms, including the timeline and budget, and comparing them to the Company's estimated percentage of manufacturing activities completed to date.

Accrual for Medicaid rebates

As discussed in Note 2 to the consolidated financial statements, the Company recognizes revenue upon transfer of control of products to customers in an amount that reflects the consideration expected to be

received in exchange for those products, including the effects of items that can decrease the transaction price, such as variable consideration. Variable consideration includes, among other items, government mandated rebates for the Medicaid Drug Rebate Program and other government health care programs. The Company estimates these rebates based on statutory discount rates and expected utilization. The expected utilization of rebates is estimated based on third party data from the specialty pharmacies and specialty distributor. As discussed in Note 5 to the consolidated financial statements, the Company had accrued sales deductions of $6,405 thousand as of December 31, 2020, which includes amounts related to Medicaid rebates.

We identified the evaluation of the Medicaid rebates accrual as a critical audit matter as it requires subjective auditor judgment. Specifically, subjective auditor judgment was required to evaluate the underlying assumption of expected utilization of rebates by program participants based on the payer mix of the Company's gross sales.

The following are the primary procedures we performed to address this critical audit matter. We evaluated the design and tested the operating effectiveness of certain internal controls related to the accrual for Medicaid rebates. This included controls related to the development of the expected utilization assumption. We tested the Medicaid rebate accrual estimate using a combination of Company internal data, externally sourced data, historical actual information and statutory rebate rates, and compared the result to the Company's estimate. We evaluated the Company's ability to accurately estimate the accrual for Medicaid rebates by comparing historical accruals to the amounts actually invoiced and paid for the same period. We evaluated the relevance and reliability of external information used in management's estimates by comparing source data to the data used in the Company's estimation model. We involved government pricing professionals with specialized skills and knowledge, who assisted in the evaluation of management's method and models for consistency with government pricing regulations.

/s/ KPMG LLP

We have served as the Company's auditor since 2014.

San Francisco, California
February 24, 2021

GLOBAL BLOOD THERAPEUTICS, INC.

Consolidated Balance Sheets

(In thousands, except share and per share amounts)

	December 31, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 494,766	$ 302,237
Short-term marketable securities	66,126	307,732
Accounts receivable, net	17,500	2,637
Inventories	40,223	1,277
Prepaid expenses	12,599	9,422
Other assets, current	949	4,692
Total current assets	632,163	627,997
Property and equipment, net	37,882	27,113
Long-term marketable securities	—	85,030
Operating lease right-of-use assets	50,722	52,775
Restricted cash	2,436	2,395
Other assets, noncurrent	799	789
Total assets	$ 724,002	$ 796,099
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 19,078	$ 10,621
Accrued liabilities	31,133	41,358
Accrued compensation	23,985	17,578
Other liabilities, current	4,836	1,896
Total current liabilities	79,032	71,453
Long-term debt	148,815	73,559
Operating lease liabilities, noncurrent	79,176	72,359
Other liabilities, noncurrent	822	34
Total liabilities	307,845	217,405
Commitments and contingencies (Note 8)		
Stockholders' equity:		
Preferred stock, $0.001 par value, 5,000,000 shares authorized at December 31, 2020 and 2019, respectively, and none issued and outstanding as of December 31, 2020 and 2019	—	—
Common stock, $0.001 par value, 150,000,000 shares authorized at December 31, 2020 and 2019, respectively; 61,898,090 and 60,644,380 shares issued and outstanding at December 31, 2020 and 2019, respectively	62	61
Additional paid-in capital	1,402,262	1,316,795
Accumulated other comprehensive income	302	754
Accumulated deficit	(986,469)	(738,916)
Total stockholders' equity	416,157	578,694
Total liabilities and stockholders' equity	$ 724,002	$ 796,099

See accompanying notes.

GLOBAL BLOOD THERAPEUTICS, INC.

Consolidated Statements of Operations and Comprehensive Loss

(In thousands, except share and per share amounts)

	Year Ended December 31,		
	2020	2019	2018
Product sales, net	$ 123,803	$ 2,108	$ —
Costs and operating expenses:			
Cost of sales	1,986	48	—
Research and development	155,122	174,556	131,307
Selling, general and administrative	210,851	117,088	51,435
Gain on lease modification	(984)	(8,301)	—
Total costs and operating expenses	366,975	283,391	182,742
Loss from operations	(243,172)	(281,283)	(182,742)
Other income (expense):			
Interest income	5,834	15,591	8,964
Interest expenses	(9,809)	(894)	(346)
Other expenses, net	(406)	(180)	(69)
Total other income (expense), net	(4,381)	14,517	8,549
Net loss	(247,553)	(266,766)	(174,193)
Other comprehensive loss:			
Net unrealized gain (loss) on marketable securities, net of tax	(452)	802	288
Comprehensive loss	$ (248,005)	$ (265,964)	$ (173,905)
Basic and diluted net loss per common share	$ (4.04)	$ (4.57)	$ (3.41)
Weighted-average number of shares used in computing basic and diluted net loss per common share	61,334,037	58,321,612	51,150,728

See accompanying notes.

GLOBAL BLOOD THERAPEUTICS, INC.

Consolidated Statements of Stockholders' Equity

(In thousands, except share amounts)

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2017	46,131,723	$ 46	$ 617,051	$ (336)	$ (297,957)	$ 318,804
Issuance of common stock upon equity offerings, net of issuance costs	8,403,826	8	396,026	—	—	396,034
Issuance of common stock upon exercise of stock options	596,434	1	6,021	—	—	6,022
Issuance of common stock upon vesting of restricted share units, net of shares withheld for employee taxes	255,039	1	(6,253)	—	—	(6,252)
Issuance of common stock pursuant to ESPP purchases	61,031	—	1,647	—	—	1,647
Vesting of restricted stock purchases	192,246	—	369	—	—	369
Stock-based compensation expense	—	—	30,080	—	—	30,080
Net unrealized gain (loss) on marketable securities	—	—	—	288	—	288
Net loss	—	—	—	—	(174,193)	(174,193)
Balance at December 31, 2018	55,640,299	$ 56	$1,044,941	$ (48)	$ (472,150)	$ 572,799
Issuance of common stock upon equity offerings, net of issuance costs	3,986,890	4	219,667	—	—	219,671
Issuance of common stock upon exercise of stock options	538,503	1	11,635	—	—	11,636
Issuance of common stock upon vesting of restricted share units, net of shares withheld for employee taxes	368,357	—	(7,617)	—	—	(7,617)
Issuance of common stock pursuant to ESPP purchases	63,280	—	2,361	—	—	2,361
Vesting of restricted stock purchases	47,051	—	157	—	—	157
Stock-based compensation expense	—	—	45,651	—	—	45,651
Net unrealized gain (loss) on marketable securities	—	—	—	802	—	802
Net loss	—	—	—	—	(266,766)	(266,766)
Balance at December 31, 2019	60,644,380	$ 61	$1,316,795	$ 754	$ (738,916)	$ 578,694
Issuance of common stock upon exercise of stock options	525,788	—	13,328	—	—	13,328
Issuance of common stock upon vesting of restricted share units, net of shares withheld for employee taxes	629,857	1	(5,288)	—	—	(5,287)
Issuance of common stock pursuant to ESPP purchases	98,065	—	4,137	—	—	4,137
Stock-based compensation expense	—	—	73,290	—	—	73,290
Net unrealized gain (loss) on marketable securities	—	—	—	(452)	—	(452)
Net loss	—	—	—	—	(247,553)	(247,553)
Balance at December 31, 2020	61,898,090	$ 62	$1,402,262	$ 302	$ (986,469)	$ 416,157

See accompanying notes.

GLOBAL BLOOD THERAPEUTICS, INC.

Consolidated Statements of Cash Flows
(In thousands)

	Year Ended December 31,		
	2020	2019	2018
CASH FLOWS FROM OPERATING ACTIVITIES:			
Net loss	$(247,553)	$(266,766)	$(174,193)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	8,323	8,605	4,607
Amortization (accretion) of premium (discount) on marketable securities	119	(2,057)	(661)
Non-cash interest expense	1,523	43	—
Amortization of operating lease right-of-use assets,	2,500	1,327	—
Stock-based compensation	71,477	45,651	30,080
Gain on lease modification	(984)	(8,301)	—
Loss from disposal of fixed assets, net	—	—	45
Changes in operating assets and liabilities:			
Accounts receivables	(14,863)	(2,637)	—
Inventories	(36,779)	(1,277)	—
Prepaid expenses	(702)	(3,085)	(2,500)
Other assets, current	(23)	(2,112)	(1,278)
Accounts payable	8,374	4,499	(1,285)
Accrued liabilities	(10,089)	24,706	8,031
Accrued compensation	6,407	7,543	1,457
Other liabilities, current	(587)	(1,482)	742
Operating lease liabilities	173	893	—
Other liabilities, noncurrent	822	33	(420)
Net cash used in operating activities	(211,862)	(194,417)	(135,375)
CASH FLOWS FROM INVESTING ACTIVITIES:			
Purchases of property and equipment	(8,754)	(3,460)	(4,824)
Proceeds from sale of property and equipment	—	45	75
Purchases of marketable securities	(57,936)	(434,919)	(361,405)
Maturities of marketable securities	384,002	361,473	181,997
Net cash provided by (used in) investing activities	317,312	(76,861)	(184,157)
CASH FLOWS FROM FINANCING ACTIVITIES:			
Proceeds from issuance of common stock, net of issuance costs	—	219,443	396,501
Proceeds from issuance of long-term debt, net of debt issuance costs	74,799	72,475	—
Proceeds from issuance of common stock in settlement of employee stock purchase plan and exercise of stock options	17,608	13,857	7,657
Taxes paid related to net share settlement of equity awards	(5,287)	(7,617)	(6,252)
Net cash provided by financing activities	87,120	298,158	397,906
Net increase in cash, cash equivalents and restricted cash	192,570	26,880	78,374
Cash, cash equivalents and restricted cash at beginning of period	304,632	277,752	199,378
Cash, cash equivalents and restricted cash at end of period	$ 497,202	$ 304,632	$ 277,752
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:			
Cash paid for interest	$ 6,283	$ —	$ —
SUPPLEMENTAL DISCLOSURES OF NON-CASH FINANCING INFORMATION:			
Accrued issuance costs	$ (59)	$ 85	$ 467
Leasehold improvements paid for by landlord	$ 10,709	$ 17,231	$ —
Accrued purchase of property and equipment	$ 6	$ 78	$ 48

	Year Ended December 31,		
	2020	2019	2018
RECONCILIATION OF CASH, CASH EQUIVALENTS, AND RESTRICTED CASH TO THE CONSOLIDATED BALANCE SHEETS			
Cash, cash equivalents	$ 494,766	$ 302,237	$ 275,357
Restricted cash	2,436	2,395	2,395
Total cash and cash equivalents and restricted cash	$ 497,202	$ 304,632	$ 277,752

See accompanying notes.

GLOBAL BLOOD THERAPEUTICS, INC.
Notes to Consolidated Financial Statements

1. Organization and Basis of Presentation

Global Blood Therapeutics, Inc., or the Company, we, us, or our, was incorporated in Delaware in February 2011 and commenced operations in May 2012. We are a biopharmaceutical company dedicated to the discovery, development and delivery of life-changing treatments that provide hope to underserved patient communities. In late November 2019, we received U.S. Food and Drug Administration, or FDA, accelerated approval for our first medicine, Oxbryta® (voxelotor) tablets for the treatment of sickle cell disease, or SCD, in adults and children 12 years of age and older. In early December 2019, we began to make Oxbryta available to patients through our specialty pharmacy partner network. Our principal operations are based in South San Francisco, California, and we operate in one segment.

Need for Additional Capital

In the course of our development activities, we have sustained operating losses and we expect such losses to continue over the next several years. Our ultimate success depends on the outcome of our commercialization of Oxbryta and research and development activities. Since inception through December 31, 2020, we have incurred cumulative net losses of $986.5 million. We expect to incur additional losses for the foreseeable future to commercialize Oxbryta and conduct product research and development, and expect to potentially raise additional capital to fully implement our business plan. If needed, we intend to raise such capital through borrowings, the issuance of additional equity, and potentially through strategic alliances with partner companies or other transactions. However, if such financing is not available at adequate levels, we will need to re-evaluate our operating plans. We believe that our existing cash and cash equivalents and marketable securities will be sufficient to fund our cash requirements for at least twelve months subsequent to the issuance of these financial statements.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America, or U.S. GAAP.

Use of Estimates

The preparation of the accompanying consolidated financial statements in accordance with U.S. GAAP requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, and the reported amounts of variable consideration and costs and expenses during the reporting period. We base our estimates and assumptions on historical experience when available and on various factors that we believe to be reasonable under the circumstances. We evaluate our estimates and assumptions on an ongoing basis. Our actual results could differ from these estimates under different assumptions or conditions.

Principles of Consolidation

The accompanying consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries. All significant intercompany transactions and balances have been eliminated upon consolidation.

Segment Reporting

We have determined that we operate in a single segment based upon the way the business is organized for making operating decisions and assessing performance. We have only one operating segment related to the development of pharmaceutical products. All property and equipment is maintained in the United States.

Cash and Cash Equivalents

We consider all highly liquid investments with original maturities of three months or less at the time of purchase to be cash equivalents. Cash equivalents, which consist primarily of amounts invested in money market accounts, are stated at fair value.

Investments in Marketable Securities

We invest in marketable securities, primarily money market funds, corporate debt securities, government securities, government agency securities, and certificates of deposits. We classify our marketable securities as available-for-sale securities and report them at fair value in cash equivalents or marketable securities on the consolidated balance sheets with related unrealized gains and losses included within accumulated other comprehensive income (loss) on the consolidated balance sheet. The amortized cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity, which is included in interest income on the consolidated statements of operations and comprehensive loss. Realized gains and losses and declines in value judged to be other-than-temporary, if any, on available-for-sale securities are included in interest and other income (loss). The cost of securities sold is based on the specific identification method. Interest and dividends on securities classified as available-for-sale are included in interest income.

We regularly review all of our investments for other-than-temporary declines in estimated fair value. Our review includes the consideration of the cause of the impairment, including the creditworthiness of the security issuers, the number of securities in an unrealized loss position, the severity and duration of the unrealized losses, whether we have the intent to sell the securities and whether it is more likely than not that we will be required to sell the securities before the recovery of their amortized cost basis. When we determine that the decline in estimated fair value of an investment is below the amortized cost basis and the decline is other than temporary, we reduce the carrying value of the security and record a loss for the amount of such decline.

Fair Value Measurement

The carrying amounts of certain financial instruments, including cash and cash equivalents, accounts receivable, accounts payable and accrued liabilities approximate fair value due to their relatively short maturities.

Concentration of Risk

Credit Risk

We invest in a variety of financial instruments and, by our Board approved investment policy, limit the amount of credit exposure with any one issuer, industry or geographic area for investments other than instruments backed by the U.S. federal government.

Major Customers

We have entered into distribution agreements with certain limited specialty pharmacies and a specialty distributor. For the year ended December 31, 2020, our two largest customers represented approximately 92% of our product revenue and approximately 88% of our accounts receivable balance at December 31, 2020.

Major Suppliers

We do not currently have any of our own manufacturing facilities, and therefore depend on an outsourced manufacturing strategy for the production of Oxbryta for commercial use and for the production of our product candidates for clinical trials. We have contracts in place with one third-party manufacturer that is approved for the commercial production of Oxbryta and two third-party suppliers that are approved for Oxbryta's active pharmaceutical ingredient. Although there are potential sources of supply other than our existing manufacturers and suppliers, any new supplier would be required to qualify under applicable regulatory requirements.

Accounts Receivables, net

Accounts receivables are recorded net of estimates of variable consideration for which reserves are established and which result from discounts and chargebacks that are offered within contracts between us and a limited number of specialty pharmacies and a specialty distributor in the United States. These reserves are classified as reductions of accounts receivable.

We estimate the allowance for doubtful accounts using current expected credit loss model, or CECL model. Under the CECL model, the allowance for doubtful accounts reflects the net amount expected to be collected from the account receivables. We evaluate the collectability of these cash flow based on the asset's amortized cost, the risk of loss even when that risk is remote, losses over an asset's contractual life, and other relevant information available to us. Accounts receivable balances are written off against the allowance when it is probable that the receivable will not be collected. Given the nature and history of our accounts receivable, we determined that an allowance for doubtful accounts was not required at December 31, 2020.

Inventories

Inventories are stated at the lower of cost or estimated net realizable value, on a first-in, first out, or FIFO, basis. We use actual costs to determine our cost basis for inventories. Inventories consist of raw materials, work-in-process, and finished goods.

We began capitalizing costs as inventory when the product candidate received regulatory approval. Prior to regulatory approval, we recorded inventory costs related to product candidates as research and development expenses.

We periodically assess the recoverability of our inventory and reduce the carrying value of the inventory when items are determined to be obsolete, defective or in excess of forecasted sales requirements. Inventory write-downs for excess, defective and obsolete inventory are recorded as a cost of sales. There have been no write-downs of our inventories for the periods presented.

Property and Equipment, Net

Property and equipment are stated at cost, less accumulated depreciation and amortization. Depreciation is provided using the straight-line method over the estimated useful lives of the assets, which is three years for computer equipment and five years for laboratory equipment. Leasehold improvements are amortized over the shorter of the lease term or the estimated useful life of the improvements. Depreciation and amortization begins at the time the asset is placed in service. Maintenance and repairs are charged as expense in the statements of operations and comprehensive loss as incurred. Upon sale or retirement of assets, the cost and related accumulated depreciation and amortization are removed from the consolidated balance sheet and any resulting gain or loss is reflected in operations.

Impairment of Long-Lived Assets

We evaluate our long-lived assets, including property and equipment, for impairment whenever events or changes in circumstances indicate that the carrying value of these assets 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 the asset is expected to generate over its remaining life. 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. There have been no impairments of our long-lived assets for the periods presented.

Restricted Cash

Restricted cash consists of cash deposits held by our financial institution as collateral for our letter of credit under our facility lease.

Accruals of Research and Development and Manufacturing Costs

We record accruals for estimated costs of research, nonclinical and clinical studies and manufacturing development. These costs are a significant component of our research and development expenses. A substantial portion of our ongoing research and development activities are conducted by third-party service providers, including contract research organizations and contract manufacturing organizations. We also accrue for estimated costs of manufacturing activities for inventories. These costs are a significant component of the cost of our inventory.

We accrue the costs incurred under our agreements with these third parties based on actual work completed in accordance with agreements established with these third parties. We determine the accruals for research and development costs through discussions with internal personnel and external service providers as to the progress or stage of completion of the clinical studies and the agreed-upon fee to be paid for such services.

The accrual for contract manufacturing activities is based on an estimate of manufacturing activities completed to date, contractual rates, and amounts invoiced and paid to date at the end of each reporting period. We determine the percentage of manufacturing activities completed to date based on discussions with the contract manufacturing organizations, oversight of the manufacturing activities and anticipated timeline.

As actual costs become known, we adjust our accruals. We have not experienced any material deviations between accrued costs and actual costs. However, actual clinical and manufacturing services performed, number of subjects enrolled, and the rate of subject enrollment may vary from our estimates, resulting in adjustments to research and development costs or inventories in future periods. Changes in these estimates that result in material changes to our accruals of research and development and manufacturing costs could materially affect our results of operations or amounts of inventories capitalized.

Revenue Recognition

Pursuant to Accounting Standards Codification, Topic 606, *Revenue from Contracts with Customers*, or ASC 606, we recognize revenue upon transfer of control of promised products or services to customers in an amount that reflects the consideration we expect to receive in exchange for those products or services.

To determine revenue recognition for arrangements that we determine are within the scope of ASC 606, we perform the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy a performance obligation. We only apply the five-step model to contracts when it is probable that we will collect substantially all of the consideration we are entitled to in exchange for the goods or services we transfer to the customer.

Product sales, net

Our product sales consist of U.S. sales of Oxbryta, which we began shipping to customers in December 2019. Prior to December 2019, we had no product sales. We sell Oxbryta to a limited number of specialty pharmacies and a specialty distributor, or collectively, Customers. These agreements with our Customers provide for transfer of title to the product at the time the product has been delivered to the Customers. The Customers subsequently dispense our products directly to a patient or resell our products to hospitals and certain pharmacies.

We recognize revenue on product sales when the Customers obtain control of our product, which occurs at a point in time, typically upon delivery to our Customers. It is at that point that we have a right to payment and that our Customers obtain title and the risks and rewards of ownership. Shipping and handling activities are considered to be fulfillment activities rather than a separate performance obligation. Payment terms are typically 30-60 days following delivery to our Customers. Because payment is expected shortly after delivery, we do not adjust the amount of consideration expected to be received for the effects of a significant financing component.

We consider the effects of items that can decrease the transaction price, such as variable consideration and consideration payable to Customers or payer. Amounts related to such items are estimated at contract inception and updated at the end of each reporting period as additional information becomes available. The amount of variable consideration may be constrained and is included in the transaction price only to the extent it is probable that a significant reversal of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is resolved. Revenue from product sales is recorded after considering the impact of the following variable consideration amounts along with the constraint at the time of revenue recognition:

Rebates: We are subject to government mandated rebates for Medicaid Drug Rebate Program, Medicare Part D Prescription Drug Benefit Program, and other government health care programs in the United States. Rebate amounts are based upon contractual agreements or legal requirements with public sector benefit providers. We use the expected-value method for estimating these rebates based on statutory discount rates and expected utilization. The expected utilization of rebates is estimated based on third party data from the specialty pharmacies and specialty distributor. Estimates for these rebates are adjusted quarterly to reflect the most recent information. We record an accrued liability for unpaid rebates related to products for which control has been transferred to Customers.

Prompt payment discounts: We provide discounts to our Customers if they pay for our products within a defined period of time after title transfers, which terms are explicitly stated in the contract. We use the most-likely-amount method for estimating prompt payment discounts. We expect that our Customers will earn prompt payment discounts. As a result, we deduct the full amount of those discounts from total product sales when revenues are recognized and record these discounts as a reduction of accounts receivable.

Co-payment assistance: We provide co-payment assistance to patients who have commercial insurance and meet certain eligibility requirements. We use the expected-value method for estimating co-payment assistance based on estimates of program redemption using data provided by third-party administrators. Estimates for the co-payment assistance are adjusted quarterly to reflect actual experience. We record an accrued liability for unredeemed co-payment assistance related to products for which control has been transferred to Customers.

Medicare Part D Coverage Gap: The Medicare Part D coverage gap is a federal program to subsidize the costs of prescription drugs for Medicare beneficiaries in the United States, which mandates manufacturers to fund a portion of the Medicare Part D insurance coverage gap for prescription drugs sold to eligible patients. Funding of the coverage gap is generally invoiced and paid in arrears. We estimate the impact of the Medicare Part D coverage gap using the expected-value method based on an amount expected to be incurred for the current quarter’s activity, plus an accrual balance for known prior quarters. Estimates for the impact of the Medicare Part D coverage gap are adjusted quarterly to reflect actual experience. We record an accrued liability for unpaid reserves related to the Medicare Part D coverage gap.

Product returns: Consistent with industry practice, we offer limited product return rights and generally allow for the return of product that is damaged or defective, or within a few months prior to and up to a few months after the product expiration date. We consider several factors in the estimation of potential product returns, including expiration dates of the product shipped, the limited product return rights, third-party data in monitoring channel inventory levels, shelf life of the product, prescription trends, and other relevant factors. We expect product returns to be immaterial. Other than these limited returns, we do not provide any product warranties.

Chargebacks: Chargebacks are discounts that occur when contracted parties purchase directly from a specialty distributor. Contracted parties, which currently consist primarily of Public Health Service Institutions and federal government entities purchasing via the Federal Supply Schedule, generally purchase the product at a discounted price. The specialty distributor, in turn, charge back the difference between the price initially paid by the specialty distributor and the discounted price paid to the specialty distributor by the contracted parties to us. The reserves for chargeback are based on known sales to contracted parties. We establish the reserves for

chargebacks in the same period that the related revenue is recognized, resulting in a reduction of product revenue and receivables.

Distributor fees: Our specialty distributor provides distribution services to us for a fee, based on a contractually determined fixed percentage of sales. We estimate these distributor fees and record such estimates in the same period the related revenue is recognized, resulting in a reduction of product revenue. We record an accrued liability for unpaid distributor fees.

Other revenue recognition considerations

Oxbryta is our only product. The only performance obligation included in our contracts is the delivery of Oxbryta to our Customers. Therefore, no allocation of transaction price amongst performance obligations is necessary. Consequently, the transaction price determined after considering the impacts of variable consideration is recognized at the time control is transferred to our Customers, which is upon delivery of Oxbryta to our Customers.

Because all sales of Oxbryta are in the United States and because our Customers are each a large distributor with similar variable consideration impacts, we provide revenue numbers on a total basis without further disaggregation. Additionally, we do not have any contract assets or liabilities, other than accounts receivable, related to our sales of Oxbryta.

Cost of Sales

Cost of sales consists primarily of direct and indirect costs related to the manufacturing of Oxbryta products sold, including third-party manufacturing costs, packaging services, freight, storage costs, allocation of overhead costs of employees involved with production, and Oxbryta net sales-based royalties payable to the Regents of the University of California. Costs incurred prior to FDA approval of Oxbryta in November 2019 have been recorded as research and development expense in our consolidated statement of operations and comprehensive loss.

Leases

Pursuant to Accounting Standards Codification, Topic 842, *Leases*, or ASC 842, adopted on January 1, 2019, we determine if an arrangement is or contains a lease at inception by assessing whether the arrangement contains an identified asset and whether we have the right to control the identified asset. Right-of-use, or ROU, assets represent our right to use an underlying asset for the lease term and lease liabilities represent our 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 received and initial direct costs incurred, as applicable.

As most of our leases do not provide an implicit rate, we use our incremental borrowing rate based on the information available at the commencement date in determining the present value of future payments. We consider our credit risk, term of the lease, and total lease payments and adjust for the impact of collateral, as necessary, when calculating our incremental borrowing rates. The lease terms may include options to extend or terminate the lease when it is reasonably certain that we will exercise any such options. Lease cost for our operating leases is recognized on a straight-line basis over the lease term.

We have elected to not separate lease and non-lease components for any leases within its existing classes of assets and, as a result, account for any lease and non-lease components as a single lease component. We have also elected to not recognize any leases within its existing classes of assets with a term of 12 months or less.

ROU assets and operating lease liabilities are remeasured upon certain modifications to leases using the present value of remaining lease payments and estimated incremental borrowing rate upon lease modification.

Leases (Topic 840) Prior to the Adoption of Topic 842

We enter into lease agreements for our office and laboratory facilities. These leases are classified as operating leases. Rent expense is recognized on a straight-line basis over the noncancelable term of the lease and, accordingly, we record the difference between cash rent payments and the recognition of rent expense as a deferred rent liability, which is included within other liabilities on the consolidated balance sheet. Incentives granted under our facilities leases, including rent holiday and allowances to fund leasehold improvements, are deferred and are recognized as adjustments to rental expense on a straight-line basis over the noncancelable term of the lease.

Comprehensive Income (Loss)

Comprehensive income (loss) is defined as a change in equity of a business enterprise during a period, resulting from transactions from non-owner sources. Our comprehensive income (loss) is comprised of net loss and changes in unrealized gains and losses on our marketable securities.

Research and Development

Research and development costs are expensed as incurred and consist of salaries and benefits, stock-based compensation expense, lab supplies and facility costs, as well as fees paid to other nonemployees and entities that conduct certain research and development activities on our behalf. Amounts incurred in connection with license agreements are also included in research and development expense. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are capitalized and then expensed as the related goods are delivered or the services are performed.

Long-term Debt

Long-term debt consists of our loan agreement, or Term Loan, with funds managed by Pharmakon Advisors LP, which are BioPharma Credit PLC, as collateral agent and a lender, and Biopharma Credit Investments V (Master) LP, as a lender, and collectively, the Lenders. We accounted for the Term Loan as a debt financing arrangement. Interest expense is accrued using the effective interest rate method over the estimated period the debt will be repaid. Debt issuance costs have been recorded as a debt discount in our consolidated balance sheets and are being amortized and recorded as interest expense throughout the life of the Term Loan using the effective interest rate method. We consider whether there are any embedded features in our debt instruments that require bifurcation and separate accounting as derivative financial instruments pursuant to Accounting Standards Codification, or ASC, Topic 815, *Derivatives and Hedging*. There are no embedded features identified from our Term Loan that require bifurcation and separating accounting.

Stock-Based Compensation

We measure and recognize stock-based compensation expense, including employee and non-employee equity awards, based on fair value at the grant date. We use the Black-Scholes-Merton option-pricing model to calculate fair value. Stock-based compensation expense recognized in the consolidated statements of operations is based on stock awards ultimately vested, taking into consideration actual forfeitures.

Income Taxes

We use the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on the differences between the financial reporting and the tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. We must then assess the likelihood that the resulting deferred tax assets will be realized. A valuation allowance is provided when it is more likely than not that some portion or all of a deferred tax asset will not be realized. Due to our lack of earnings history, the net deferred tax assets have been fully offset by a valuation allowance.

We recognize benefits of uncertain tax positions if it is more likely than not that such positions will be sustained upon examination based solely on their technical merits, as the largest amount of benefit that is more likely than not to be realized upon the ultimate settlement. It is our policy to include penalties and interest expense related to income taxes as a component of other expense and interest expense, respectively, as necessary. To date, there have been no interest or penalties incurred in relation to the unrecognized tax benefits.

Net Loss per Share

Basic net loss per share is calculated by dividing the net loss by the weighted average number of shares of common stock outstanding during the period, without consideration of common stock equivalents. Diluted net loss per share is the same as basic net loss per share, since the effects of potentially dilutive securities are antidilutive given our net loss.

Recent Accounting Pronouncements

In December 2019, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, No. 2019-12, *Income Taxes (Topic 740), Simplifying the Accounting for Income Taxes*. The new guidance eliminates certain exceptions related to the approach for intraperiod tax allocation, the methodology for calculating income taxes in an interim period, and the recognition of deferred tax liabilities for outside basis differences. It also clarifies and simplifies other aspects of the accounting for income taxes. ASU 2019-12 is effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2020 and the applicable amendments will be applied on a prospective basis. We do not expect the adoption of this new standard to have a material impact on our consolidated financial statements.

Accounting Pronouncements Adopted

In August 2018, FASB, issued ASU No. 2018-15, *Intangibles—Goodwill and Other—Internal-Use Software (Subtopic 350-40), Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract*, or ASU 2018-15. ASU No. 2018-15 requires a customer that is a party to a cloud computing service contract to follow the internal-use software guidance in Subtopic 350-40 to determine which implementation costs to capitalize and which costs to expense. The amendments in this update are effective for annual reporting periods beginning after December 15, 2019, and interim periods within those fiscal years. The amendments in this update should be applied either retrospectively or prospectively to all implementation costs incurred after the date of adoption. We adopted ASU No. 2018-15 in the first quarter of 2020 and applied the guidance prospectively to the implementation costs incurred in our implementations of various cloud computing arrangements that are service contracts. The adoption of this new standard did not have a material impact on our consolidated financial statements.

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement (Topic 820)*. The new standard modifies the disclosure requirements on fair value measurements in Topic 820, Fair Value Measurement, including removals of, modification to, and additional disclosure requirements from Topic 820. The amendment of ASU No. 2018-13 removes disclosure requirements from Topic 820 in the areas of (1) the amount of and reasons for transfers between Level 1 and Level 2 of the fair value hierarchy, (2) the policy for timing of transfers between levels, and (3) the valuation processes for Level 3 fair value measurements. The amendments in this update are effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019. Except for certain amendments related to Level 3 fair value measurements, all the other amendments should be applied retrospectively to all periods presented upon their effective date. We adopted ASU No. 2018-13 in the first quarter of 2020 and applied the guidance retrospectively. The adoption of this new standard did not have a material impact on our consolidated financial statements.

In June 2016, the FASB issued ASU No. 2016-13, *Measurement of Credit Losses on Financial Instruments (Topic 326)*, which amends the guidance on the impairment of financial instruments. The new standard adds to

U.S. GAAP an impairment model that is based on expected losses rather than incurred losses, which is known as the current expected credit loss, or CECL model. The CECL model applies to most debt instruments (other than those measured at fair value), trade and other receivables, financial guarantee contracts, and loan commitments. Available-for-sale debt securities are scoped out of this guidance. Our investment portfolio primarily consists of available-for-sale debt securities carried at fair value. Our accounts receivable are not long term in nature and we do not expect to write off accounts receivable. The amendments in this update are effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019. We adopted ASU No. 2016-13 in the first quarter of 2020 and applied the guidance prospectively. The adoption of this new standard did not have a material impact on our consolidated financial statements.

3. Fair Value Measurements

Fair value accounting is applied for all financial assets and liabilities that are recognized or disclosed at fair value in the consolidated financial statements on a recurring basis (at least annually). Our financial instruments consist of cash and cash equivalents, marketable securities, accounts receivables, accounts payable and accrued liabilities. Cash and cash equivalents and marketable securities reported at their respective fair values on our consolidated balance sheets. The remaining financial instruments are reported on our consolidated balance sheets at cost that approximate current fair values due to their relatively short maturities.

Assets and liabilities recorded at fair value on a recurring basis in the consolidated balance sheets are categorized based upon the level of judgment associated with the inputs used to measure their fair values. Fair value is defined as the exchange price that would be received for an asset or an exit price that would be paid to transfer a liability in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. The authoritative guidance on fair value measurements establishes a three-tier fair value hierarchy for disclosure of fair value measurements as follows:

Level 1—Inputs are unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date;

Level 2—Inputs are observable, unadjusted quoted prices in active markets for similar assets or liabilities, unadjusted quoted prices for identical or similar assets or liabilities in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the related assets or liabilities; and

Level 3—Unobservable inputs that are significant to the measurement of the fair value of the assets or liabilities that are supported by little or no market data.

The following table summarizes our financial assets measured at fair value on a recurring basis (in thousands):

	December 31, 2020			
	Total	Level 1	Level 2	Level 3
Financial Assets:				
Money market funds	$486,174	$486,174	$ —	$ —
Corporate debt securities	29,804	—	29,804	—
U.S. government agency securities	15,943	—	15,943	—
Certificates of deposits	243	—	243	—
U.S. government securities	20,136	—	20,136	—
Total financial assets	$552,300	$486,174	$66,126	$ —

	December 31, 2019			
	Total	Level 1	Level 2	Level 3
Financial Assets:				
Money market funds	$250,535	$250,535	$ —	$ —
Corporate debt securities	152,149	—	152,149	—
U.S. government agency securities	95,032	—	95,032	—
Certificates of deposits	6,282	—	6,282	—
U.S. government securities	140,244	—	140,244	—
Total financial assets	$644,242	$250,535	$393,707	$ —

We estimate the fair values of our investments in corporate debt securities, government and government related securities and certificates of deposits by taking into consideration valuations obtained from third-party pricing services. The fair value of our marketable securities classified within Level 2 is based upon observable inputs that may include benchmark yields, reported trades, broker/dealer quotes, issuer spreads, two-sided markets, benchmark securities, bids, offers and reference data including market research publications. At December 31, 2020, the weighted average remaining contractual maturities of our Level 2 investments was less than one year and all of these investments are rated A-1/P-1/F1 or A/A2, or higher by Moody's and S&P.

4. Available-for-Sale Securities

Estimated fair values of available-for-sale securities are generally based on prices obtained from commercial pricing services. The following table is a summary of available-for-sale securities recorded in cash and cash equivalents, or marketable securities in our Consolidated Balance Sheets (in thousands):

	December 31, 2020				December 31, 2019			
	Amortized Cost	Unrealized Gains	Unrealized (Losses)	Estimated Fair Value	Amortized Cost	Unrealized Gains	Unrealized (Losses)	Estimated Fair Value
Financial Assets:								
Money market funds	$486,174	$ —	$ —	$486,174	$250,535	$ —	$ —	$250,535
Corporate debt securities	29,641	163	—	29,804	151,773	384	(8)	152,149
U.S. government agency securities	15,906	37	—	15,943	94,963	73	(4)	95,032
Certificates of deposits	241	2	—	243	6,239	43	—	6,282
U.S. government securities	20,036	100	—	20,136	139,978	266	—	140,244
Total	$551,998	$ 302	$ —	$552,300	$643,488	$ 766	$ (12)	$644,242

The following table summarizes the classification of the available-for-sale securities on our consolidated balance sheets (in thousands):

	December 31, 2020	December 31, 2019
Cash and cash equivalents	$ 486,174	$ 251,480
Short-term marketable securities	66,126	307,732
Long-term marketable securities	—	85,030
Total	$ 552,300	$ 644,242

5. Balance Sheet Components

Property and Equipment

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

	December 31,	
	2020	2019
Laboratory equipment	$11,922	$ 8,314
Computer equipment	3,023	2,224
Leasehold improvements	32,281	13,785
Construction-in-progress	517	19,289
Total property and equipment	47,743	43,612
Less: accumulated depreciation and amortization	(9,861)	(16,499)
Property and equipment, net	$37,882	$ 27,113

Depreciation expense was $8.3 million for the year ended December 31, 2020, $8.6 million for the year ended December 31, 2019 and $4.7 million for the year ended December 31, 2018. Refer to Note 8—Commitments and Contingencies for details on acceleration of depreciation expenses recognized during the years ended December 31, 2020 and 2019.

Accrued Liabilities

Accrued liabilities consist of the following (in thousands):

	December 31,	
	2020	2019
Accrued research and development costs	$10,677	$ 26,480
Accrued manufacturing costs	9,125	9,466
Accrued professional and consulting services	4,107	4,564
Accrued sales deductions	6,405	529
Other	819	319
Total accrued liabilities	$31,133	$ 41,358

Other liabilities, current

Other liabilities consist of the following (in thousands):

	December 31,	
	2020	2019
Operating lease liabilities, current	$4,836	$ 1,866
Other payable	—	30
Total other liabilities, current	$4,836	$ 1,896

6. Inventories

We began capitalizing inventories in November 2019 once the FDA approved Oxbryta. Inventories consist of the following (in thousands):

	December 31,	
	2020	2019
Raw materials	$11,273	$ 700
Work-in-process	26,994	525
Finished goods	1,956	52
Total inventories	$40,223	$1,277

For the year ended December 31, 2020, we have capitalized $1.8 million of share-based compensation expense to our inventories. See Note 10 - Share-based Compensation for details on share-based compensation expenses recognized during the year ended December 31, 2020.

7. Long-term Debt

Term Loan

On December 17, 2019, we entered into the Loan Agreement, or Term Loan, with funds managed by Pharmakon Advisors LP, which are BioPharma Credit PLC, as collateral agent, Biopharma Credit Investments V (Master) LP, as a lender, and BPCR Limited Partnership, as a lender, and collectively, the Lenders, for a senior secured credit facility consisting of an initial tranche of $75.0 million and the option to draw an additional $75.0 million until December 31, 2020. The first tranche, in the amount of $75.0 million, was funded in connection with the closing date of the Term Loan in December 2019, and the second tranche of the Term Loan, in the amount of $75.0 million was funded in November 2020.

The Term Loan carries a 72-month term. The Term Loan bears interest at a floating per annum interest rate equal to 7.00% plus the greater of (a) the 3-month LIBOR rate and (b) 2%. In the event we default, the interest rate would be 3% above the rate that is otherwise applicable thereto. Interest on amounts outstanding are payable quarterly in arrears. The Term Loan repayment schedule provides for interest only payments for the first 39 months, followed by consecutive equal quarterly payments of principal and interest commencing in March 2023 and continuing through the maturity of December 2025.

We have the option to prepay all or a portion of the borrowed amounts under the Term Loan. If we exercise this option, we must pay a prepayment fee between 1% and 3% of the principal amount being prepaid depending on the timing of the prepayment, or Prepayment Fee. If the prepayment occurs before December 2022, we must also pay an amount equal to the sum of all interest that would have accrued and been payable from date of prepayment through December 2022, or Make Whole Amount. We are obligated to pay an additional fee to the Lenders determined by multiplying the principal amount being paid or prepaid multiplied by 2%, or Paydown Fee, when such payments are made.

In the event of default or change in control, all unpaid principal and all accrued and unpaid interest amounts (if any) become immediately due and payable, at which point, we will be subject to the Prepayment Fee, the Make Whole Amount (if any) and the Paydown Fee. Events of default include, but are not limited to, a payment default, a material adverse change, and insolvency. The obligations under the Term Loan are secured by a first priority security interest in and a lien on substantially all of our assets, subject to certain exceptions.

Debt issuance costs paid directly to the Lenders of $1.1 million and the other debt issuance costs of $0.5 million were treated as discounts on the Term Loan. These debt discounts along with the Paydown Fee are being amortized or accreted to interest expenses throughout the life of the Term Loan using the effective interest rate method. As of December 31, 2020, there were unamortized issuance costs and debt discounts of $1.3 million, which were recorded as a direct deduction from the Term Loan on the consolidated balance sheet. In addition, we paid the Lenders $1.1 million for the option to draw the additional $75.0 million, which was capitalized as a deferred asset and amortized on a straight-line basis through December 31, 2020. Any remaining unamortized amount is reclassed to debt discount at the time of closing of the second tranche of the Term Loan. We closed the second tranche of the Term Loan in November 2020 and $0.2 million of the unamortized deferred asset related to the option to draw the second tranche was reclassed as the discount on the notes payable.

Future payments of principal and interest on the Term Loan as of December 31, 2020 (in thousands):

2021	13,500
2022	13,500
2023	62,813
2024	58,313
2025	53,812
Total minimum payments	201,938
Less amount representing interest	(48,938)
Less amount representing Paydown Fee	(3,000)
Long-term debt, gross	150,000
Discount on notes payable	(1,596)
Accretion of Paydown Fee	411
Long-term debt	$148,815

8. Commitments and Contingencies

Leases

We have operating leases for our headquarters, where we have office and research and development laboratory facilities, and equipment. Our leases have remaining lease terms of 1 to 10 years. Most of these leases require monthly lease payments that may be subject to annual increases throughout the lease term. Certain of these leases include renewal options at our election, with renewal terms that can extend the lease term from 1 to 10 years. These optional periods have not been considered in the determination of the right-of-use assets, or ROU assets, or lease liabilities associated with these leases as we did not consider it reasonably certain that we would exercise the options.

Lease costs included in operating expense in the consolidated statement of operations and comprehensive loss in relation to these operating leases were $12.4 million and $7.8 million for the year ended December 31, 2020 and 2019, respectively. Included in these lease costs were variable lease costs, which were not included within the measurement of our operating ROU assets and operating lease liabilities in the amount of $2.6 million and $2.5 million for the year ended December 31, 2020 and 2019, respectively. The variable lease cost is comprised primarily of our cost in certain research and development arrangements that contain embedded equipment, and our proportionate share of operating expenses, property taxes, and insurance in relation with our

facility lease. These costs are classified as operating lease expense due to our election to not separate lease and non-lease components.

Supplemental information related to leases for the period reported is as follows (in thousands, except weighted-average remaining lease term and weighted-average discount rate):

	For the year ended December 31,	
	2020	2019
ROU assets obtained in exchange for new operating lease upon adoption of ASC 842	$ —	$ 14,177
Adjustment to ROU assets as a result of the lease modification for the Prior Premises	(106)	(13,802)
ROU assets obtained for new operating lease liabilities	205	53,727
Operating lease liabilities arising from obtaining ROU assets	205	25,929
Cash paid for amounts included in the measurement of lease liabilities	7,696	4,481
Weighted-average remaining lease term of operating leases (in years)	9.2	10.1
Weighted-average discount rate of operating leases	8.66%	8.66%

The majority of our lease costs are driven by our operating lease for our headquarters in South San Francisco, where we have office and research and development laboratory facilities.

In March 2017, we entered into a noncancelable operating lease, or Original Lease, for approximately 67,185 square feet of space in South San Francisco, California, or Prior Premises.

In August 2018, we entered into an amendment to the Original Lease, or Lease Amendment, to relocate the leased premises from the Prior Premises to a to-be-constructed building consisting of approximately 164,150 rentable square feet of space, or Substitute Premises, when the Substitute Premises are ready for occupancy, or Substitute Premises Payment Commencement Date. The Lease Amendment has a contractual term, or Substitute Premises Term, of 10 years from the Substitute Premises Payment Commencement Date. The Lease Amendment grants us an option to extend the Lease Amendment for an additional 10-year period. Future minimum rental payments under the Lease Amendment during the 10-year term are $121.5 million in the aggregate. Under the Lease Amendment, we are obligated to pay to the landlord certain costs, including taxes and operating expenses. The Lease Amendment also provides a tenant inducement allowance of up to $27.9 million, of which $4.1 million, if utilized, would be repaid to the landlord in the form of additional monthly rent with interest applied. As of December 31, 2020 and 2019, we have capitalized $32.3 million and $19.0 million, respectively, of costs within property and equipment, net for construction of leasehold improvements at the Substitute Premises, which were mostly acquired with the tenant inducement provided under the Lease Amendment.

On October 1, 2019, we determined that the Lease Amendment for the Substitute Premises had commenced as we had the right to control the Substitute Premises, which was deemed to be a lease modification. We determined the Lease Amendment consisted of two separate contracts under ASC 842. One contract was related to a new ROU asset for the Substitute Premises, which was to be accounted for as a new lease, and the other was related to the modification of the lease term of the Prior Premises.

With the commencement of the Lease Amendment, the lease term for the Original Lease was reduced, with the modified lease term expiring on June 1, 2020. We determined that the reduction of the lease term would be accounted for as a lease modification to the Prior Lease. On October 1, 2019, we remeasured the present value of future lease payments during the modified lease term to be $2.9 million, using an incremental borrowing rate of approximately 8.78%. We recognized the amount of remeasurement of the lease liability as an adjustment to the

ROU asset, reducing the carrying amount of the ROU asset to zero, and recognized a gain on lease modification of $8.3 million for the year ended December 31, 2019. An additional gain on lease modification of $1.0 million was recognized for the year ended December 31, 2020 to write off the remaining lease liability related to the Original Lease when we vacated the building. As of December 31, 2020, and 2019, the unamortized operating lease liability associated with the Prior Premises was $nil and $1.8 million, respectively.

On October 1, 2019, or Substitute Premises Commencement Date, we measured the present value of future lease payments that included the expected utilization of tenant inducements, using an incremental borrowing rate of approximately 8.66%. We recorded a ROU asset and a lease liability for $53.7 million associated with the Substitute Premises. During the years ended December 31, 2020 and 2019, the landlord paid approximately $10.7 million and $17.2 million, respectively, out of tenant inducement allowances for construction of leasehold improvements at the Substitute Premises, which was recognized as an increase in the operating lease liability. The balances of the ROU asset were approximately $50.6 million and $52.8 million as of December 31, 2020 and 2019, respectively. The balances for the operating lease liability were approximately $83.8 million and $72.4 million as of December 31, 2020, and 2019, respectively.

After relocating to the Substitute Premise, we surrendered and delivered the Prior Premises to the landlord in May 2020, upon which time we had no further obligations with respect to the Prior Premises other than with respect to the Initial Allowance, which we will repay to the landlord in the form of additional monthly rent with interest applied over the term of the Original Lease. Upon signing of the Lease Amendment, we re-evaluated the remaining useful life of the leasehold improvements at the Prior Premises and started to amortize the leasehold improvements over the remaining period of expected use, resulting in an acceleration of depreciation expenses for approximately $3.8 million and $7.0 million for the years ended December 31, 2020 and 2019, respectively.

As of December 31, 2020, the maturities of our operating lease liabilities under Topic 842 were as follows (in thousands):

Year ending December 31,	Amount
2021	11,841
2022	12,222
2023	12,584
2024	12,948
2025	13,368
Thereafter	60,507
Total lease payments	123,470
Less: Imputed interest	(39,458)
Present value of operating lease liabilities	$ 84,012

Rent expense was $9.8 million for the year ended December 31, 2020, $5.2 million for the year ended December 31, 2019, and $3.6 million for the year ended December 31, 2018. The operating leases require us to share in prorated operating expenses and property taxes based upon actual amounts incurred; those amounts are not fixed for future periods and, therefore, are not included in the future commitments listed above.

Indemnifications

We indemnify each of our directors and officers for certain events or occurrences, subject to certain limits, while the director or the officer is or was serving at our request in such capacity, as permitted under Delaware law and in accordance with its certificate of incorporation and bylaws. The term of the indemnification period lasts as long as a director or an officer may be subject to any proceeding arising out of acts or omissions of such director in such capacity. The maximum amount of potential future indemnification is unlimited; however, we currently hold director and officer liability insurance. This insurance allows the transfer of risk associated with

our exposure and may enable us to recover a portion of any future amounts paid. We believe that the fair value of these indemnification obligations is minimal. Accordingly, we have not recognized any liabilities relating to these obligations for any period presented.

Contingencies

In the ordinary course of business, we may be subject to legal claims and regulatory actions that could have a material adverse effect on our business or financial position. We assess our potential liability in such situations by analyzing potential outcomes, assuming various litigation, regulatory and settlement strategies. If we determine a loss is probable and its amount can be reasonably estimated, we accrue an amount equal to the estimated loss.

No losses and no provision for a loss contingency have been recorded to date.

Contingent Payments

In December 2019, we entered into an agreement, the Syros Agreement, with Syros Pharmaceuticals, Inc., or Syros, to discover, develop and commercialize novel therapies for SCD and beta thalassemia. Under the agreement, Syros will use its leading gene control platform to identify therapeutic targets and discover drugs that potentially induce fetal hemoglobin, and we have an option to obtain an exclusive worldwide license to develop, manufacture and commercialize any compounds or products resulting from the agreement, subject to Syros' option to co-promote the first product in the United States. If we exercise the option, we will be responsible for all development, manufacture, regulatory activities and commercialization of the compound or product. Syros and we will be responsible for our own costs incurred to conduct research activities, except that we will fund up to $40.0 million in preclinical research for at least three years. Unless earlier terminated or extended, the research program under the agreement will end on the third anniversary of the agreement.

Under the terms of the Syros Agreement, we paid Syros an upfront payment of $20.0 million in January 2020, and, if we exercise our option under the agreement, we may be obligated to pay Syros up to $315.0 million in option exercise, development, regulatory, commercialization and sales-based milestones per product candidate and product resulting from the agreement. We will also be obligated to pay Syros, subject to certain reductions, tiered mid- to high-single digit royalties as percentages of calendar year net sales on any product resulting from the agreement. As of December 31, 2019, we have recognized the $20.0 million upfront payment in our research and development costs for year ended December 31, 2019. No milestone payments were recognized for the year ended December 31, 2020. We have recognized $8.6 million of research reimbursement to Syros in our research and development cost for the year ended December 31, 2020.

In August 2018, we entered into the License Agreement, or Roche Agreement, with F. Hoffmann-La Roche Ltd. and Hoffmann-La Roche Inc. (together, "Roche"), pursuant to which Roche granted us an exclusive and sublicensable worldwide license under certain patent rights and know-how to develop and commercialize inclacumab for all indications and uses, except diagnostic use. Roche retained a non-exclusive, worldwide, perpetual, royalty-free license to inclacumab solely for any diagnostic use. As of December 31, 2019, we have paid Roche an upfront payment of $2.0 million, which was recognized in our research and development costs for year ended December 31, 2018. We are obligated to make contingent payments to Roche totaling approximately $125.5 million in milestone payments for the SCD indication, including up to $40.5 million based on achievement of certain clinical development and regulatory milestones for inclacumab in the SCD indication, and up to $85.0 million based on achievement of certain thresholds for annual net sales of inclacumab. As of December 31, 2020, we have recognized a $2.0 million clinical development milestone payment in our research and development costs for the year ended December 31, 2020. We are also obligated to make contingent payments to Roche up to an additional $6.4 million in milestone payments, which are owed to a third party, based on achievement of such clinical development and regulatory milestones for inclacumab. We are also obligated to make contingent payments to Roche up to $19.25 million in milestone payments based on

achievement of certain clinical development and regulatory milestones for inclacumab for any indication other than the SCD indication.

9. Stockholders' Equity

Follow-on Offerings

In June 2019, we completed a follow-on offering and issued 3,375,527 shares of common stock at a price of $57.12 per share for proceeds of $192.4 million net of underwriting costs and commissions and offering expenses. In addition, in July 2019, we sold an additional 100,000 shares of our common stock directly to the underwriters when they exercised their over-allotment option at the price of $57.12 per share for proceeds of $5.7 million net of underwriting costs and commissions.

In December 2018, we completed a follow-on offering and issued 3,409,090 shares of common stock at a price of $41.54 per share for proceeds of $141.1 million net of underwriting costs and commissions and offering expenses. In addition, in January 2019, we sold an additional 511,363 shares of our common stock directly to the underwriters when they exercised their over-allotment option at the price of $41.54 per share for proceeds of $21.2 million net of underwriting costs and commissions.

Common Stock Reserved for Issuance

We have reserved sufficient shares of common stock for issuance upon the exercise of stock options, vesting of restricted stock units and restricted shares subject to future vesting. Common stockholders are entitled to dividends if and when declared by the board of directors, subject to the prior rights of any preferred stockholders. As of December 31, 2020, no common stock dividends had been declared by the board of directors.

We have reserved shares of common stock for future issuance as follows:

	December 31,	
	2020	2019
Restricted stock units	2,625,056	1,848,772
Options issued and outstanding	3,327,330	3,573,860
Shares available for future grant under the 2015 Plan and 2017 Inducement Equity Plan	6,018,567	4,478,656
Employee stock purchase plan	254,590	252,655
Total	12,225,543	10,153,943

10. Share-based Compensation

Amended and Restated 2017 Inducement Equity Plan

In January 2017, we adopted the 2017 Inducement Equity Plan and amended the plan in December 2019 with the Amended and Restated 2017 Inducement Plan, or the 2017 Inducement Plan. Under the 2017 Inducement Plan, shares of our common stock are reserved for the issuance of non-qualified stock options and other equity-based awards to induce highly-qualified prospective officers and employees who are not currently employed by us or our subsidiaries to become employed with our company. Awards granted
under the 2017 Inducement Plan expire no later than 10 years from the date of grant. For non-statutory stock options, the option price shall not be less than 100% of the fair market value on the day of grant. Options granted generally vest over four years and vest at a rate of 25% upon the first anniversary of the issuance date and 1/16th per quarter over the following three years thereafter. Restricted stock units granted generally vest at a rate of 25% upon the first anniversary of the issuance date and 1/8th per half year over the following three years thereafter. The number of shares initially reserved for grant is subject to adjustment for reorganization, recapitalization, stock dividend, stock split, or similar changes in our capital stock. As of December 31, 2020, there were 1,277,475 shares reserved for the future issuance of equity awards under the 2017 Inducement Plan.

2015 Stock Option and Incentive Plan

In July 2015, we adopted the 2015 Stock Option and Incentive Plan, or 2015 Plan. Under the 2015 Plan, shares of our common stock are reserved for the issuance of stock options, restricted stock, and other equity-based awards to employees, non-employee directors, and consultants under terms and provisions established by the Board of Directors and approved by our stockholders at inception. Awards granted under the 2015 Plan expire no later than 10 years from the date of grant. For incentive stock options and non-statutory stock options, the option price shall not be less than 100% of the fair market value on the day of grant. If at the time we grant an option and the optionee directly or by attribution owns stock possessing more than 10% of the total combined voting power of all our classes of stock, the option price is required to be at least 110% of the fair market value on the day of grant. Options granted typically vest over a 4-year period but may be granted with different vesting terms. Restricted stock units granted generally vest at a rate of $1/8^{th}$ per half year over the 4-year period. As of December 31, 2020, there were 4,741,092 shares reserved for the future issuance of equity awards under the 2015 Plan.

2012 Stock Option and Grant Plan

In 2012, we adopted the 2012 Stock Option and Grant Plan, or 2012 Plan, under which our Board of Directors was authorized to grant incentive stock options to employees, including officers and members of the Board of Directors who are also employees of ours, and non-statutory stock options (options that do not qualify as incentive options) and/or our restricted stock and other equity-based awards to our employees, officers, directors, or consultants. Awards granted under the 2012 Plan expire no later than 10 years from the date of grant. Upon adoption of the 2015 Plan, no new awards or grants are permitted under the 2012 Plan.

Stock Option Activity

The following table summarizes activity under our stock option plans, including the 2017 Inducement Plan, 2015 Plan and the 2012 Plan and related information (in thousands, except share and per share amounts and term):

	Number of Options	Weighted-Average Exercise Price	Weighted-Average remaining contractual term (years)	Aggregate Intrinsic Value
Outstanding—December 31, 2019	3,573,860	$ 36.24	7.55	
Options granted	719,561	65.36		
Options exercised	(525,788)	25.35		
Options canceled	(440,303)	52.78		
Outstanding—December 31, 2020	3,327,330	$ 42.07	7.02	$ 29,720
Vested and exercisable—December 31, 2020	2,151,326	$ 34.77	6.33	$ 28,616

The aggregate intrinsic value was calculated as the difference between the exercise price of the options and the fair value of our common stock as of December 31, 2020. The total intrinsic value of options exercised was $23.0 million for the year ended December 31, 2020, $23.5 million for the year ended December 31, 2019, and $23.4 million for the year ended December 31, 2018. The weighted-average estimated fair value of stock options granted was $40.76 for the year ended December 31, 2020, $32.30 for the year ended December 31, 2019, and $33.58 for the year ended December 31, 2018.

Stock Options Granted to Employees with Service-based Vesting Valuation Assumptions

The fair values of stock options granted to employees were calculated using the following assumptions:

	Year Ended December 31,		
	2020	2019	2018
Expected term (in years)	5.1-6.1	5.3-6.1	5.3-6.1
Volatility	69.6%-71.8%	69.8%-72.2%	68.7%-71.8%
Risk-free interest rate	0.3%-1.8%	1.4%-2.6%	2.6%-3.0%
Dividend yield	—	—	—

In determining the fair value of the options granted, we used the Black-Scholes-Merton option-pricing model and assumptions discussed below.

Expected Term—Our expected term represents the period that the options granted are expected to be outstanding and is determined using the simplified method (based on the mid-point between the vesting date and the end of the contractual term). We have limited historical information to develop reasonable expectations about future exercise patterns and post-vesting employment termination behavior for our stock option grants.

Expected Volatility—We use peer company price volatility as well as the historical volatility of our own common stock to estimate expected stock price volatility due to the limited trading history for our common stock since our IPO in August 2015. When selecting comparable publicly traded biopharmaceutical companies on which we have based our expected stock price volatility, we selected companies with comparable characteristics to us, including enterprise value, risk profiles, position within the industry, and with historical share price information sufficient to meet the expected life of the stock-based awards. The historical volatility data was computed using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of the stock-based awards. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available.

Risk-Free Interest Rate—The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of option.

Expected Dividend—We have never paid dividends on our common stock and have no plans to pay dividends on our common stock. Therefore, we used an expected dividend yield of zero.

Restricted Stock Units

In January 2017, the Compensation Committee of our Board of Directors approved the commencement of granting restricted stock units, or RSUs, to our employees. RSUs are share awards that entitle the holder to receive freely tradable shares of our common stock upon the completion of a specific period of continued service. RSUs are generally subject to forfeiture if employment terminates prior to the release of vesting restrictions. RSUs granted are valued at the market price of our common stock on the date of grant. We recognize noncash compensation expense for the fair value of RSUs on a straight-line basis over the requisite service period of these awards.

The following table summarizes activity of RSUs granted to employees with service-based vesting under the 2017 Inducement Plan and 2015 Plan and related information (in thousands, except share, per share amounts and vesting period):

	Number of RSUs	Weighted-Average Grant Date Fair Value	Weighted-Average Remaining Vesting Period (years)	Aggregate Intrinsic Value
Non-vested units—December 31, 2019	1,848,772	$ 49.19	1.54	$146,959
RSUs granted	1,577,047	64.28		
RSUs vested	(710,403)	50.84		
RSUs forfeited	(505,060)	56.30		
Non-vested units—December 31, 2020	2,210,356	$ 57.80	1.45	$ 95,731

Market-Condition Awards Granted to Employees

2017 Market-Condition RSU Awards

On August 11, 2017, our Board of Directors approved awards up to an aggregate of 365,250 RSUs to certain of our senior management team under the 2015 Plan, the vesting of which was contingent upon a combination of continued employment and achieving certain market capitalization milestones, which we refer to as the 2017 Market-Condition RSU Awards. The 2017 Market-Condition RSU Awards would not vest until the achievement of their respective market capitalization milestones, which were required to occur on or before December 31, 2019. The grant date fair value of the 2017 Market-Condition RSU Awards was estimated using a Monte Carlo simulation model. The derived service periods, which are the estimated periods of time that would be required to satisfy the market conditions, are also determined at the grant date. We record expense on a straight-line basis over the applicable derived service periods. In 2019, 156,000 shares and 3,250 shares of 2017 Market-Condition RSU Awards were vested and were forfeited, respectively. There were no non-vested 2017 Market-Condition RSU Awards as of December 31, 2020 and 2019.

We recognized $36,500 and $3.1 million in stock-based compensation expense related to the 2017 Market-Condition RSU Awards for the year ended December 31, 2019 and December 31, 2018, respectively. No expenses recorded related to the 2017 Market-Condition RSU Awards for the year ended December 31, 2020.

2020 Market-Condition RSU Awards

The Compensation Committee of our Board of Directors granted, effective June 1, 2020, awards of up to an aggregate of 414,700 RSUs to certain of our senior management, including our executive officers, under the 2015 Plan, the vesting of which is contingent upon the achievement of three escalating stock price targets, which we refer to as the 2020 Market-Condition RSU Awards. Upon the achievement of the respective stock price targets, 50% of the RSUs allotted to that tranche will vest, while the remaining 50% will vest on the first anniversary of the date the stock price target was achieved, subject to the employee's continued employment or other service relationship with us through such vesting date. Under the terms of the awards, if the stock price targets are not achieved for all or some of the tranches on or before June 30, 2024, the unvested awards will be automatically terminated and forfeited. The compensation cost for the RSUs with a market condition is not reversed when the market condition is not satisfied. The target prices and vesting tranches are set forth in the table below:

Stock Price Targets	Number of Units Allotted
$109.20	82,940
$145.60	145,145
$182.00	186,615

The grant date fair value of the 2020 Market-Condition RSU Awards was estimated using a Monte Carlo simulation model, which includes variables such as the expected volatility of the Company's share price and interest rates to generate potential future outcomes. We recognize the related compensation expense on a straight-line basis over the applicable derived service periods, which are the estimated periods of time that would be required to satisfy the market conditions.

The following table summarizes activity of the 2020 Market-Condition RSU Awards under the 2015 Plan and related information (in thousands, except share, per share amounts and vesting period):

	Number of Units	Weighted-Average Grant Date Fair Value	Weighted-Average Remaining Vesting Period (years)	Aggregate Intrinsic Value
Non-vested market-condition awards — December 31, 2019	—	$ —	—	
Granted	421,000	49.95		
Vested	—	—		
Forfeited	(6,300)	49.95		
Non-vested market-condition awards — December 31, 2020	414,700	$ 49.95	1.21	$ 17,961

The following table summarizes the assumptions used to estimate the fair value of the market-condition awards as of the grant date:

Valuation date stock price	$68.67
Volatility	68.1%
Risk-free interest rate	0.26%
Dividend yield	—

At December 31, 2020, total unrecognized compensation expense related to non-vested market-condition awards was $13.0 million, which is expected to be recognized over their respective remaining derived service periods. The weighted average derived service period is 1.21 years. For the year ended December 31, 2020, we recognized $7.7 million in stock-based compensation expense related to the 2020 Market-Condition RSU Awards.

Employee Stock Purchase Plan

In July 2015, we adopted the 2015 Employee Stock Purchase Plan, or 2015 ESPP. Under the 2015 ESPP, our employees may purchase common stock through payroll deductions at a price equal to 85% of the lower of the fair market value of the stock at the beginning of the offering period or at the end of each applicable purchase period. The 2015 ESPP provided for offering periods of six months in duration. As approved by the Compensation Committee of the Board of Directors in December 2017, the 2015 ESPP provides for offering periods of two years in duration with purchase periods occurring every six months during an offering period. The purchase periods end on either January 31 or July 31. Contributions under the 2015 ESPP are limited to a maximum of 15% of an employee's eligible compensation. ESPP purchases are settled with common stock from the ESPP's previously authorized and available pool of shares. The 2015 ESPP was amended and restated in March 2020. The amended 2015 ESPP moves the timing of the purchase periods end on either February 28 (or February 29, if applicable) or August 31. Once each of the existing offering period ends, the next offering period immediately following will be a one-time transitional offering period, starting with one 7-month purchase period followed by three 6-month purchase periods. After this one-time transition offering period, all following offering periods will remain for two years with four equal six-month purchase periods. During the year ended December 31, 2020, 98,065 shares were issued under the ESPP for $4.1 million.

The fair values of the rights granted under the 2015 ESPP were calculated using the following assumptions:

	Year Ended December 31, 2020	Year Ended December 31, 2019
Expected term (in years)	0.5 – 2.1	0.5 – 2.0
Volatility	47.0-77.0%	46.5-75.4%
Risk-free interest rate	0.1-1.5%	1.7-2.6%
Dividend yield	—%	—%

Stock-Based Compensation Expense

Total stock-based compensation recognized by functions was as follows (in thousands):

	Year Ended December 31,		
	2020	2019	2018
Research and development	$ 18,061	$ 19,140	$ 12,747
Selling, general and administrative	53,416	26,511	17,333
Total stock-based compensation expense	$ 71,477	$ 45,651	$ 30,080

Unrecognized Stock-Based Compensation Expense and Weighted-Average Remaining Amortization Period

As of December 31, 2020, the unrecognized stock-based compensation cost, and the estimated weighted-average amortization period, using the straight-line attribution method, was as follows (in thousands, except amortization period):

	Unrecognized Compensation Cost	Weighted-average remaining amortization period (years)
Stock Options	$ 38,440	2.3
Restricted stock units	110,837	2.7
Market-Condition restricted stock units	12,989	1.2
ESPP	3,743	0.7
Total unrecognized stock-based compensation expense	$ 166,009	2.5

11. Defined Contribution Plan

In 2013, we began to sponsor a 401(k) retirement plan, in which substantially all of our full-time employees are eligible to participate. Eligible participants may contribute a percentage of their annual compensation to this plan, subject to statutory limitations. We made contributions to the Plan for eligible participants, and recorded contribution expenses of $2.1 million for the year ended December 31, 2020, $1.4 million for the year ended December 31, 2019, and $0.8 million for the year ended December 31, 2018.

12. Income Taxes

The components of the loss before income taxes were as follows (in thousands):

	Year Ended December 31,		
	2020	2019	2018
Loss before provision for income taxes:			
United States	$(247,327)	$(266,595)	$(174,190)
International	(226)	(167)	—
	$(247,553)	**$(266,762)**	**$(174,190)**

No provision for income taxes was recorded for the years ended December 31, 2020, December 31, 2019, and December 31, 2018. We have incurred net operating losses for all the periods presented. We have not reflected any benefit of such net operating loss (NOL) carryforwards in the accompanying consolidated financial statements. We have established a full valuation allowance against the related deferred tax assets due to the uncertainty surrounding the realization of such assets.

The effective tax rate of the provision for income taxes differs from the federal statutory rate as follows:

	Year Ended December 31,		
	2020	2019	2018
Federal statutory income tax rate	21.0%	21.0%	21.0%
State taxes	7.4	9.7	1.3
Federal and state tax credits	4.3	4.9	7.1
Change in valuation allowance	(32.4)	(37.2)	(33.3)
Foreign rate differential	—	—	1.7
Officer compensation limitation	(0.8)	(1.0)	(0.7)
Stock based compensation/Non-deductible changes in fair value	0.6	1.7	2.9
Liquidation of foreign entities	—	0.9	—
Other	(0.1)	—	—
Provision for Taxes	0.0%	0.0%	0.0%

The components of the deferred tax assets and liabilities are as follows (in thousands):

	December 31,	
	2020	2019
Deferred tax assets:		
Net operating loss carryforwards	$ 216,092	$ 157,685
Tax credits	76,684	62,862
Operating lease liability	23,147	16,177
Accruals and reserves	6,503	3,996
Stock based compensation	14,981	11,166
Intangibles	8,507	8,243
Other	904	408
Gross deferred tax assets	346,818	260,537
Valuation allowance	(325,710)	(245,000)
Net deferred tax assets	21,108	15,537
Operating lease – ROU asset	(13,975)	(14,971)
Property and equipment	(7,050)	(352)
Other	(83)	(214)
Gross deferred tax liabilities	(21,108)	(15,537)
Net deferred tax assets	$ —	$ —

Realization of the deferred tax assets is dependent upon future taxable income, if any, the amount and timing of which are uncertain. We have established a valuation allowance to offset deferred tax assets as of December 31, 2020 and 2019 due to the uncertainty of realizing future tax benefits from our net operating loss carryforwards and other deferred tax assets. The valuation allowance increased approximately $80.7 million and $99.2 million during the years ended December 31, 2020, and 2019, respectively. The increase in the valuation allowance is mainly related to the increase in net operating loss carryforwards and the increase in tax credits generated during the respective taxable years.

As of December 31, 2020, we had federal net operating loss carryforwards of approximately $829.1 million to offset future federal taxable income, with $209.9 million available through 2037 and $619.2 million available indefinitely. We also had state net operating loss carryforwards of approximately $587.1 million that may offset future state taxable income through 2040. Current federal and state tax laws include substantial restrictions on the utilization of net operating losses and tax credits in the event of an ownership change. Even if the carryforwards are available, they may be subject to annual limitations, lack of future taxable income, or future ownership changes that could result in the expiration of the carryforwards before they are utilized. At December 31, 2020, we recorded a 100% valuation allowance against our deferred tax assets of approximately $325.7 million, as at that time our management believed it was uncertain that they would be fully realized. If we determine in the future that we will be able to realize all or a portion of our net operating loss carryforwards, an adjustment to valuation allowance would increase net income in the period in which we make such a determination.

In general, if we experience a greater than 50 percentage point aggregate change in ownership over a three-year period (a Section 382 ownership change), utilization of our pre-change NOL carryforwards are subject to an annual limitation under Section 382 of the Internal Revenue Code (California has similar laws). The annual limitation generally is determined by multiplying the value of our stock at the time of such ownership change (subject to certain adjustments) by the applicable long-term tax-exempt rate. Such limitations may result in expiration of a portion of the NOL carryforwards that were generated prior to 2018 before utilization. We have not utilized any NOL carryovers through December 31, 2020.

No liability related to uncertain tax positions is recorded on the consolidated financial statements. All uncertain tax positions are currently recorded as a reduction to our deferred tax asset. It is our policy to include penalties and interest expense related to income taxes as a component of other expense and interest expense, respectively, as necessary.

A reconciliation of the beginning and ending amount of unrecognized tax benefits is as follows (in thousands):

	December 31,	
	2020	2019
Balance at beginning of year	$ 21,598	$ 16,232
Additions based on tax positions related to current year	3,346	5,366
Decreased for prior period positions	(498)	—
Unrecognized tax benefit—December 31	$ 24,446	$ 21,598

We do not expect that our uncertain tax positions will materially change in the next twelve months. The reversal of the uncertain tax benefits will not impact our effective tax rate as we continue to maintain a full valuation allowance against our deferred tax assets.

We file federal, state and foreign income tax returns in the United States and in multiple foreign jurisdictions. We are not currently under examination by income tax authorities in federal, state or other jurisdictions. All tax returns will remain open for examination by the federal and state authorities for three and four years, respectively, from the date of utilization of any net operating loss or credits.

13. Net Loss per Share

Basic net loss per share is computed by dividing net loss by the weighted-average number of common shares outstanding for the period. Since we were in a loss position for all periods presented, diluted net loss per share is the same as basic net loss per share for all periods as the inclusion of all potential common shares outstanding would have been anti-dilutive.

The following securities were not included in the diluted net loss per share calculations because their effect was anti-dilutive:

	December 31,		
	2020	2019	2018
Options to purchase common stock	3,327,330	3,573,860	3,243,551
Restricted shares subject to future vesting	—	—	47,051
Restricted stock units	2,625,056	1,848,772	975,419
Total	5,952,386	5,422,632	4,266,021

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Selected Quarterly Financial Information (unaudited)

The following table provides the selected consolidated quarterly financial data for 2020 and 2019:

	Quarter Ended							
(in thousands, except per share amounts)	**December 31, 2020**	**September 30, 2020**	**June 30, 2020**	**March 31, 2020**	**December 31, 2019**	**September 30, 2019**	**June 30, 2019**	**March 31, 2019**
Product sales, net	$ 41,295	$ 36,889	$ 31,501	$ 14,118	$ 2,108	$ —	$ —	$ —
Loss from operations	$ (59,373)	$ (58,311)	$ (52,036)	$ (73,452)	$ (99,214)	$ (68,742)	$ (60,804)	$ (52,523)
Net loss	$ (61,806)	$ (59,881)	$ (52,840)	$ (73,026)	$ (95,975)	$ (64,547)	$ (57,321)	$ (48,923)
Basic and diluted net loss per common share	$ (1.00)	$ (0.97)	$ (0.86)	$ (1.20)	$ (1.59)	$ (1.07)	$ (1.01)	$ (0.87)

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

Our management carried out an evaluation, with the participation of our Chief Executive Officer and our Chief Financial Officer, of 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 the end of the period covered by this Annual Report on Form 10-K. In connection with that evaluation, our Chief Executive Officer and our Chief Financial Officer concluded that our disclosure controls and procedures were effective. Disclosure controls and procedures means controls and procedures designed to ensure that information required to be disclosed by us in the reports that we file or submit is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms. These disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports that we file or submit is accumulated and communicated to management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosure.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rule 13a-15(f) and 15d-15(f) under the Securities Exchange Act of 1934, as amended). Our management, including our Chief Executive Officer and our Chief Financial Officer assessed the effectiveness of our internal control over financial reporting using the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO, in Internal Control—2013 Integrated Framework. Based on that assessment, our management concluded that our internal control over financial reporting was effective as of December 31, 2020. The effectiveness of our internal control over financial reporting as of December 31, 2020 has been audited by KPMG LLP, an independent registered public accounting firm, as stated in its report which is included in Item 8 of this Annual Report on Form 10-K.

Changes in Internal Control over Financial Reporting

There have been no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the quarter ended December 31, 2020 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Inherent Limitations on Effectiveness of Controls

Internal control over financial reporting may not prevent or detect all errors and all fraud. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Also, projections of any evaluation of effectiveness of internal control 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. Accordingly, our disclosure controls and procedures are designed to provide reasonable, not absolute, assurance that the objectives of our disclosure control system are met.

Item 9B. ***Other Information***

None.

PART III

Item 10. ***Directors, Executive Officers and Corporate Governance***

Except as set forth below, the information required by this item is incorporated by reference from our definitive Proxy Statement to be filed with the SEC in connection with our 2021 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2020.

We have adopted a Code of Business Conduct and Ethics that applies to all of our directors, officers and employees, including our principal executive officer and principal financial officer. The Code of Business Conduct and Ethics is posted on our website at https://www.ir.gbt.com.

We intend to satisfy the disclosure requirement under Item 5.05 of Form 8-K regarding an amendment to, or waiver from, a provision of this Code of Business Conduct and Ethics by posting such information on our website, at the address and location specified above and, to the extent required by the listing standards of The NASDAQ Stock Market, by filing a Current Report on Form 8-K with the SEC, disclosing such information.

Item 11. ***Executive Compensation***

The information required by this item is incorporated by reference from our definitive Proxy Statement to be filed with the SEC in connection with our 2021 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2020.

Item 12. ***Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters***

The information required by this item is incorporated by reference from our definitive Proxy Statement to be filed with the SEC in connection with our 2021 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2020.

Item 13. ***Certain Relationships and Related Transactions and Director Independence***

The information required by this item is incorporated by reference from our definitive Proxy Statement to be filed with the SEC in connection with our 2021 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2020.

Item 14. ***Principal Accounting Fees and Services***

The information required by this item is incorporated by reference from our definitive Proxy Statement to be filed with the SEC in connection with our 2021 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2020.

PART IV

Item 15. ***Exhibits and Financial Statement Schedules***

(a) The following documents are filed as part of this report:

(1) CONSOLIDATED FINANCIAL STATEMENTS

The consolidated financial statements filed as part of this Annual Report on Form 10-K are listed in the "Index to Consolidated Financial Statements" under Part II, Item 8 of this Annual Report on Form 10-K.

(2) CONSOLIDATED FINANCIAL STATEMENT SCHEDULES

Consolidated financial statement schedules have been omitted in this Annual Report on Form 10-K because they are not applicable, not required under the instructions, or the information requested is set forth in the consolidated financial statements or related notes thereto.

(3) EXHIBITS

The exhibits listed in the accompanying Exhibit Index are filed as part of, or incorporated by reference into, this Annual Report on Form 10-K.

Item 16. ***Form 10-K Summary***

None.

Exhibit Index

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
3.1	Restated Certificate of Incorporation.	S-1/A	7/31/2015	3.2	
3.2	Amended and Restated Bylaws.	S-1/A	7/31/2015	3.4	
4.1	Specimen Common Stock Certificate.	S-1/A	7/31/2015	4.1	
4.2	Description of Securities	10-K	2/26/2020	4.2	
10.1#	2012 Stock Option and Grant Plan and forms of award agreements thereunder	S-1	7/8/2015	10.1	
10.2#	Amended and Restated 2015 Stock Option and Incentive Plan and forms of award agreements thereunder	—	—	—	X
10.3#	Employment Offer Letter Agreement by and between the Registrant and Ted W. Love, M.D., dated May 19, 2014	S-1	7/8/2015	10.3	
10.4#	Employment Offer Letter Agreement by and between the Registrant and Jeffrey Farrow, dated February 19, 2016	8-K	4/4/2016	10.1	
10.5	Form of Indemnification Agreement by and between the Registrant and each of its directors and officers	S-1/A	7/31/2015	10.8	
10.6#	Amended and Restated 2015 Employee Stock Purchase Plan	10-Q	5/6/2020	10.5	
10.7#	Amended and Restated Cash Incentive Bonus Plan	—	—	—	X
10.8#	Amended and Restated 2017 Inducement Equity Plan and forms of award agreements thereunder	—	—	—	X
10.9#	Employment Offer Letter by and between the Registrant and Patricia Suvari, dated October 7, 2016	10-K	3/13/2017	10.17	
10.10	Lease by and between the Registrant and HCP Oyster Point III LLC, dated March 17, 2017	8-K	3/22/2017	10.1	
10.11	Sales Agreement by and between the Registrant and SVB Leerink LLC, dated August 5, 2020	S-3ASR	8/5/2020	1.2	
10.12#	Amended and Restated Severance and Change in Control Policy	—	—	—	X
10.13#	Employment Offer Letter by and between the Registrant and David Johnson, dated February 21, 2018	10-Q	5/7/2018	10.4	
10.14+	License Agreement by and between the Registrant and F. Hoffmann-La Roche Ltd. and Hoffmann-La Roche Inc., dated August 22, 2018	10-Q/A	3/29/2019	10.1	
10.15	First Amendment to Lease by and between the Registrant and HCP Oyster Point III LLC, dated August 29, 2018	8-K	8/30/2018	10.1	

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
10.16#	Non-Employee Director Compensation Policy	—	—	—	X
10.17#	Employment Offer Letter by and between the Registrant and Brian Cathers, Ph.D., dated January 21, 2019	10-K	2/27/2019	10.19	
10.18#	Employment Offer Letter by and between the Registrant and Eric Fink, dated June 17, 2019	10-Q	8/7/2019	10.1	
10.19#	Employment Offer Letter by and between the Registrant and Jung Choi, dated March 16, 2015	10-Q	5/10/2019	10.1	
10.20+	License and Collaboration Agreement by and between the Registrant and Syros Pharmaceuticals, Inc., dated December 17, 2019	10-K	2/26/2020	10.20	
10.21+	Loan Agreement by and among the Registrant, BioPharma Credit PLC, and Biopharma Credit Investments V (Master) LP, dated December 17, 2019	10-K	2/26/2020	10.21	
21.1	Subsidiaries of the Registrant	—	—	—	X
23.1	Consent of KPMG LLP, Independent Registered Public Accounting Firm	—	—	—	X
24.1	Power of Attorney (included on signature page to this Annual Report)	—	—	—	X
31.1	Certification of Principal Executive Officer required by Rule 13a-14(a) and Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	—	—	—	X
31.2	Certification of Principal Financial Officer required by Rule 13a-14(a) and Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	—	—	—	X
32.1*	Certification of Principal Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	—	—	—	X
32.2*	Certification of Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	—	—	—	X
101.SCH	Inline XBRL Taxonomy Extension Schema Document	—	—	—	X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document	—	—	—	X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document.	—	—	—	X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document.	—	—	—	X

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document.	—	—	—	X
104	Cover Page Interactive Data File (formatted as inline XBRL with applicable taxonomy extension information contained in Exhibits 101.)	—	—	—	X

Represents management compensation plan, contract or arrangement.
+ Portions of this exhibit have been omitted as confidential information.
* The certifications attached as Exhibit 32.1 and 32.2 that accompany this Annual Report on Form 10-K are not deemed filed with the SEC and are not to be incorporated by reference into any filing of the registrant under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Form 10-K, irrespective of any general incorporation language contained in such filing.

SIGNATURES

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

GLOBAL BLOOD THERAPEUTICS, INC.

By: /s/ Ted W. Love
Ted W. Love, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

Date: February 24, 2021

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Ted W. Love, M.D. and Jeffrey Farrow, and each of them, his true and lawful attorneys-in-fact, with full power of substitution, for him in any and all capacities, to sign any and all 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, hereby ratifying and confirming all that said attorneys-in-fact or any of them or their substitute or substitutes may lawfully do or cause to be done by virtue thereof.

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 in the capacities and on the dates indicated:

Signature	Title	Date
/s/ Ted W. Love Ted W. Love, M.D.	President, Chief Executive Officer and Director *(Principal Executive Officer)*	February 24, 2021
/s/ Jeffrey Farrow Jeffrey Farrow	Chief Financial Officer *(Principal Financial Officer and Principal Accounting Officer)*	February 24, 2021
/s/ Willie L. Brown, Jr. Willie L. Brown, Jr	Director	February 24, 2021
/s/ Scott W. Morrison Scott W. Morrison	Director	February 24, 2021
/s/ Deval L. Patrick Deval L. Patrick	Director	February 24, 2021
/s/ Mark L. Perry Mark L. Perry	Director	February 24, 2021
/s/ Glenn F. Pierce Glenn F. Pierce, M.D., Ph.D.	Director	February 24, 2021
/s/ Philip A. Pizzo Philip A. Pizzo, M.D.	Director	February 24, 2021
/s/ Dawn Svoronos Dawn Svoronos	Director	February 24, 2021
/s/ Wendy Yarno Wendy Yarno	Director	February 24, 2021

Exhibit 10.2

GLOBAL BLOOD THERAPEUTICS, INC.

AMENDED AND RESTATED 2015 STOCK OPTION AND INCENTIVE PLAN

SECTION 1. GENERAL PURPOSE OF THE PLAN; DEFINITIONS

The name of the plan is the Global Blood Therapeutics, Inc. Amended and Restated 2015 Stock Option and Incentive Plan (the "Plan"). The purpose of the Plan is to encourage and enable the officers, employees, Non-Employee Directors and other key persons (including Consultants) of Global Blood Therapeutics, Inc., a Delaware corporation (the "Company"), and its Subsidiaries upon whose judgment, initiative and efforts the Company largely depends for the successful conduct of its business to acquire a proprietary interest in the Company. It is anticipated that providing such persons with a direct stake in the Company's welfare will assure a closer identification of their interests with those of the Company and its stockholders, thereby stimulating their efforts on the Company's behalf and strengthening their desire to remain with the Company.

The following terms shall be defined as set forth below:

"*Act*" means the Securities Act of 1933, as amended, and the rules and regulations thereunder.

"*Administrator*" means either the Board or the compensation committee of the Board or a similar committee performing the functions of the compensation committee and which is comprised of not less than two Non-Employee Directors who are independent.

"*Award*" or "*Awards,*" except where referring to a particular category of grant under the Plan, shall include Incentive Stock Options, Non-Qualified Stock Options, Stock Appreciation Rights, Restricted Stock Units, Restricted Stock Awards, Unrestricted Stock Awards, Cash-Based Awards, Performance Share Awards and Dividend Equivalent Rights.

"*Award Certificate*" means a written or electronic document setting forth the terms and provisions applicable to an Award granted under the Plan. Each Award Certificate is subject to the terms and conditions of the Plan.

"*Board*" means the Board of Directors of the Company.

"*Cash-Based Award*" means an Award entitling the recipient to receive a cash-denominated payment.

"*Code*" means the Internal Revenue Code of 1986, as amended, and any successor Code, and related rules, regulations and interpretations.

"*Consultant*" means any natural person that provides bona fide services to the Company, and such services are not in connection with the offer or sale of securities in a capital-raising transaction and do not directly or indirectly promote or maintain a market for the Company's securities.

"*Covered Employee*" means an employee who is a "Covered Employee" within the meaning of Section 162(m) of the Code.

"*Dividend Equivalent Right*" means an Award entitling the grantee to receive credits based on cash dividends that would have been paid on the shares of Stock specified in the Dividend Equivalent Right (or other award to which it relates) if such shares had been issued to and held by the grantee.

"*Effective Date*" means the date on which the Plan becomes effective as set forth in Section 21.

"*Exchange Act*" means the Securities Exchange Act of 1934, as amended, and the rules and regulations thereunder.

"*Fair Market Value*" of the Stock on any given date means the fair market value of the Stock determined in good faith by the Administrator; provided, however, that if the Stock is admitted to quotation on the NASDAQ Capital Market, the NASDAQ Global Market, the NASDAQ Global Select Market, the New York Stock Exchange or another national securities exchange, the determination shall be made by reference to the closing price of the Stock as quoted on the applicable exchange. If there is no closing price for such date, the determination shall be made by reference to the last date preceding such date for which there is a closing price; provided further, however, that if the date for which Fair Market Value is determined is the first day when trading prices for the Stock are reported on a national securities exchange, the Fair Market Value shall be the "Price to the Public" (or equivalent) set forth on the cover page for the final prospectus relating to the Company's Initial Public Offering.

"*Incentive Stock Option*" means any Stock Option designated and qualified as an "incentive stock option" as defined in Section 422 of the Code.

"*Initial Public Offering*" means the consummation of the first underwritten, firm commitment public offering pursuant to an effective registration statement under the Act covering the offer and sale by the Company of its equity securities, or such other event as a result of or following which the Stock shall be publicly held.

"*Non-Employee Director*" means a member of the Board who is not also an employee of the Company or any Subsidiary.

"*Non-Qualified Stock Option*" means any Stock Option that is not an Incentive Stock Option.

"*Option*" or "*Stock Option*" means any option to purchase shares of Stock granted pursuant to Section 5.

"*Performance-Based Award*" means any Restricted Stock Award, Restricted Stock Units, Performance Share Award or Cash-Based Award granted to a Covered Employee that is intended to qualify as "performance-based compensation" under Section 162(m) of the Code and the regulations promulgated thereunder.

"*Performance Criteria*" means the criteria that the Administrator selects for purposes of establishing the Performance Goal or Performance Goals for an individual for a Performance Cycle. The Performance Criteria (which shall be applicable to the organizational level specified by the Administrator, including, but not limited to, the Company or a unit, division, group, or Subsidiary of the Company) that will be used to establish Performance Goals are limited to the following: achievement of specified research and development, publication, clinical and/or regulatory milestones, total shareholder return, earnings before interest, taxes, depreciation and amortization, net income (loss) (either before or after interest, taxes, depreciation and/or amortization), changes in the market price of the Stock, economic value-added, funds from operations or similar measure, sales or revenue, acquisitions or strategic transactions, operating income (loss), cash flow (including, but not limited to, operating cash flow and free cash flow), return on capital, assets, equity, or investment, return on sales, gross or net profit levels, productivity, expense, margins, operating efficiency, customer satisfaction, working capital, earnings (loss) per share of Stock, sales or market shares and number of customers, any of which may be measured either in absolute terms or as compared to any incremental increase or as compared to results of a peer group.

"*Performance Cycle*" means one or more periods of time, which may be of varying and overlapping durations, as the Administrator may select, over which the attainment of one or more Performance Criteria will be measured for the purpose of determining a grantee's right to and the payment of a Restricted Stock Award, Restricted Stock Units, Performance Share Award or Cash-Based Award, the vesting and/or payment of which is subject to the attainment of one or more Performance Goals. Each such period shall not be less than 12 months.

"*Performance Goals*" means, for a Performance Cycle, the specific goals established in writing by the Administrator for a Performance Cycle based upon the Performance Criteria.

"*Performance Share Award*" means an Award entitling the recipient to acquire shares of Stock upon the attainment of specified performance goals.

"*Restricted Shares*" means the shares of Stock underlying a Restricted Stock Award that remain subject to a risk of forfeiture or the Company's right of repurchase.

"*Restricted Stock Award*" means an Award of Restricted Shares subject to such restrictions and conditions as the Administrator may determine at the time of grant.

"*Restricted Stock Units*" means an Award of stock units subject to such restrictions and conditions as the Administrator may determine at the time of grant.

"*Sale Event*" shall mean (i) the sale of all or substantially all of the assets of the Company on a consolidated basis to an unrelated person or entity, (ii) a merger, reorganization or consolidation pursuant to which the holders of the Company's outstanding voting power and outstanding stock immediately prior to such transaction do not own a majority of the outstanding voting power and outstanding stock or other equity interests of the resulting or successor entity (or its ultimate parent, if applicable) immediately upon completion of such transaction, (iii) the

sale of all of the Stock of the Company to an unrelated person, entity or group thereof acting in concert, or (iv) any other transaction in which the owners of the Company's outstanding voting power immediately prior to such transaction do not own at least a majority of the outstanding voting power of the Company or any successor entity immediately upon completion of the transaction other than as a result of the acquisition of securities directly from the Company.

"*Sale Price*" means the value as determined by the Administrator of the consideration payable, or otherwise to be received by stockholders, per share of Stock pursuant to a Sale Event.

"*Section 409A*" means Section 409A of the Code and the regulations and other guidance promulgated thereunder.

"*Stock*" means the Common Stock, par value $0.001 per share, of the Company, subject to adjustments pursuant to Section 3.

"*Stock Appreciation Right*" means an Award entitling the recipient to receive shares of Stock having a value equal to the excess of the Fair Market Value of the Stock on the date of exercise over the exercise price of the Stock Appreciation Right multiplied by the number of shares of Stock with respect to which the Stock Appreciation Right shall have been exercised.

"*Subsidiary*" means any corporation or other entity (other than the Company) in which the Company has at least a 50 percent interest, either directly or indirectly.

"*Ten Percent Owner*" means an employee who owns or is deemed to own (by reason of the attribution rules of Section 424(d) of the Code) more than 10 percent of the combined voting power of all classes of stock of the Company or any parent or subsidiary corporation.

"*Unrestricted Stock Award*" means an Award of shares of Stock free of any restrictions.

SECTION 2. ADMINISTRATION OF PLAN; ADMINISTRATOR AUTHORITY TO SELECT GRANTEES AND DETERMINE AWARDS

(a) Administration of Plan. The Plan shall be administered by the Administrator.

(b) Powers of Administrator. The Administrator shall have the power and authority to grant Awards consistent with the terms of the Plan, including the power and authority:

(i) to select the individuals to whom Awards may from time to time be granted;

(ii) to determine the time or times of grant, and the extent, if any, of Incentive Stock Options, Non-Qualified Stock Options, Stock Appreciation Rights, Restricted Stock Awards, Restricted Stock Units, Unrestricted Stock Awards, Cash-Based Awards, Performance Share Awards and Dividend Equivalent Rights, or any combination of the foregoing, granted to any one or more grantees;

(iii) to determine the number of shares of Stock to be covered by any Award;

(iv) to determine and modify from time to time the terms and conditions, including restrictions, not inconsistent with the terms of the Plan, of any Award, which terms and conditions may differ among individual Awards and grantees, and to approve the forms of Award Certificates;

(v) to accelerate at any time the exercisability or vesting of all or any portion of any Award; provided, that the Administrator generally shall not exercise such discretion to accelerate Awards subject to Sections 7 and 8 except in the event of the grantee's death, disability or retirement, or a change in control of the Company (including a Sale Event);

(vi) subject to the provisions of Section 5(c), to extend at any time the period in which Stock Options may be exercised; and

(vii) at any time to adopt, alter and repeal such rules, guidelines and practices for administration of the Plan and for its own acts and proceedings as it shall deem advisable; to interpret the terms and provisions of the Plan and any Award (including related written instruments); to make all determinations it deems advisable for the administration of the Plan; to decide all disputes arising in connection with the Plan; and to otherwise supervise the administration of the Plan.

All decisions and interpretations of the Administrator shall be binding on all persons, including the Company and Plan grantees.

(c) Delegation of Authority to Grant Awards. Subject to applicable law, the Administrator, in its discretion, may delegate to the Chief Executive Officer of the Company or a committee comprised of the Chief Executive Officer of the Company and one or more other officer of the Company all or part of the Administrator's authority and duties with respect to the granting of Awards to individuals who are not subject to the reporting and other provisions of Section 16 of the Exchange Act. Any such delegation by the Administrator shall include a limitation as to the amount of Awards that may be granted during the period of the delegation and shall contain guidelines as to the determination of the exercise price and the vesting criteria. The Administrator may revoke or amend the terms of a delegation at any time but such action shall not invalidate any prior actions of the Administrator's delegate or delegates that were consistent with the terms of the Plan.

(d) Award Certificate. Awards under the Plan shall be evidenced by Award Certificates that set forth the terms, conditions and limitations for each Award which may include, without limitation, the term of an Award and the provisions applicable in the event employment or service terminates.

(e) Indemnification. Neither the Board nor the Administrator, nor any member of either or any delegate thereof, shall be liable for any act, omission, interpretation, construction or determination made in good faith in connection with the Plan, and the members of the Board and the Administrator (and any delegate thereof) shall be entitled in all cases to indemnification and reimbursement by the Company in respect of any claim, loss, damage or expense (including, without limitation, reasonable attorneys' fees) arising or resulting therefrom to the fullest extent permitted by law and/or under the Company's certificate of incorporation or bylaws or any directors' and officers' liability insurance coverage which may be in effect from time to time and/or any indemnification agreement between such individual and the Company.

(f) Foreign Award Recipients. Notwithstanding any provision of the Plan to the contrary, in order to comply with the laws in other countries in which the Company and its Subsidiaries operate or have employees or other individuals eligible for Awards, the Administrator, in its sole discretion, shall have the power and authority to: (i) determine which Subsidiaries shall be covered by the Plan; (ii) determine which individuals outside the United States are eligible to participate in the Plan; (iii) modify the terms and conditions of any Award granted to individuals outside the United States to comply with applicable foreign laws; (iv) establish subplans and modify exercise procedures and other terms and procedures, to the extent the Administrator determines such actions to be necessary or advisable (and such subplans and/or modifications shall be attached to this Plan as appendices); provided, however, that no such subplans and/or modifications shall increase the share limitations contained in Section 3(a) hereof; and (v) take any action, before or after an Award is made, that the Administrator determines to be necessary or advisable to obtain approval or comply with any local governmental regulatory exemptions or approvals. Notwithstanding the foregoing, the Administrator may not take any actions hereunder, and no Awards shall be granted, that would violate the Exchange Act or any other applicable United States securities law, the Code, or any other applicable United States governing statute or law.

SECTION 3. STOCK ISSUABLE UNDER THE PLAN; MERGERS; SUBSTITUTION

(a) Stock Issuable. The maximum number of shares of Stock reserved and available for issuance under the Plan shall be 1,430,000 shares (the "Initial Limit"), subject to adjustment as provided in Section 3(c), plus on January 1, 2016 and each January 1 thereafter, the number of shares of Stock reserved and available for issuance under the Plan shall be cumulatively increased by four percent (4%) of the number of shares of Stock issued and outstanding on the immediately preceding December 31 or such lesser number of shares of Stock as determined by the Administrator (the "Annual Increase"). Subject to such overall limitation, the maximum aggregate number of shares of Stock that may be issued in the form of Incentive Stock Options shall not exceed the Initial Limit cumulatively increased on January 1, 2016 and on each January 1 thereafter by the lesser of the Annual Increase for such year or 2,857,000 shares of Stock, subject in all cases to adjustment as provided in Section 3(c). The shares of Stock underlying any Awards under the Plan and under the Company's 2012 Stock Option and Grant Plan, as amended, that are forfeited, canceled, held back upon exercise of an Option or settlement of an Award to cover the exercise price or tax withholding, reacquired by the Company prior to vesting, satisfied without the issuance of Stock or otherwise terminated (other than by exercise) shall be added back to the shares of Stock available for issuance under the Plan. In the event the Company repurchases shares of Stock on the open market, such shares shall not be added to the shares of Stock available for issuance under the Plan. Subject to such overall limitations, shares of Stock may be issued up to such maximum number pursuant to any type or types of Award; provided, however, that Stock Options or Stock Appreciation Rights with respect to no more than 1,750,000 shares of Stock may be granted to any one individual grantee during any one calendar year period. The shares available for issuance under the Plan may be authorized but unissued shares of Stock or shares of Stock reacquired by the Company.

(b) [Reserved].

(c) Changes in Stock. Subject to Section 3(d) hereof, if, as a result of any reorganization, recapitalization, reclassification, stock dividend, stock split, reverse stock split or other similar change in the Company's capital stock, the outstanding shares of Stock are increased or decreased or are exchanged for a different number or kind of shares or other securities of the Company, or additional shares or new or different shares or other securities of the Company or other non-cash assets are distributed with respect to such shares of Stock or other securities, or, if, as a result of any merger or consolidation, sale of all or substantially all of the assets of the Company, the outstanding shares of Stock are converted into or exchanged for securities of the Company or any successor entity (or a parent or subsidiary thereof), the Administrator shall make an appropriate or proportionate adjustment in (i) the maximum number of shares reserved for issuance under the Plan, including the maximum number of shares that may be issued in the form of Incentive Stock Options, (ii) the number of Stock Options or Stock Appreciation Rights that can be granted to any one individual grantee and the maximum number of shares that may be granted under a Performance-Based Award, (iii) the number and kind of shares or other securities subject to any then outstanding Awards under the Plan, (iv) the repurchase price, if any, per share subject to each outstanding Restricted Stock Award, and (v) the exercise price for each share subject to any then outstanding Stock Options and Stock Appreciation Rights under the Plan, without changing the aggregate exercise price (i.e., the exercise price multiplied by the number of Stock Options and Stock Appreciation Rights) as to which such Stock Options and Stock Appreciation Rights remain exercisable. The Administrator shall also make equitable or proportionate adjustments in the number of shares subject to outstanding Awards and the exercise price and the terms of outstanding Awards to take into consideration cash dividends paid other than in the ordinary course or any other extraordinary corporate event. The adjustment by the Administrator shall be final, binding and conclusive. No fractional shares of Stock shall be issued under the Plan resulting from any such adjustment, but the Administrator in its discretion may make a cash payment in lieu of fractional shares.

(d) Mergers and Other Transactions. Except as the Administrator may otherwise specify with respect to particular Awards in the applicable Award Certificate, in the case of and subject to the consummation of a Sale Event, the parties thereto may cause the assumption or continuation of Awards theretofore granted by the successor entity, or the substitution of such Awards with new Awards of the successor entity or parent thereof, with appropriate adjustment as to the number and kind of shares and, if appropriate, the per share exercise prices, as such parties shall agree. To the extent the parties to such Sale Event do not provide for the assumption, continuation or substitution of Awards, the Plan and all outstanding Awards hereunder will terminate upon the effective time of the Sale Event. Notwithstanding the foregoing, the Administrator may, in its discretion or to the extent provided in the relevant Award Certificate, cause certain Awards to become vested and/or exercisable immediately prior to such Sale Event. In the event of such termination, (i) the Company shall have the right, but not the obligation, to make or provide for a cash payment to the grantees holding Options and Stock Appreciation Rights, in exchange for the cancellation thereof, in an amount equal to the difference between (A) the Sale Price multiplied by the number of shares of Stock subject to outstanding Options and Stock Appreciation Rights (to the extent then exercisable after taking into account any acceleration thereunder at prices not in excess of the Sale Price) and (B) the aggregate exercise price of all such outstanding Options and Stock Appreciation Rights; or (ii)

each grantee shall be permitted, within a specified period of time prior to the consummation of the Sale Event as determined by the Administrator, to exercise all outstanding Options and Stock Appreciation Rights (to the extent then exercisable) held by such grantee, including those that will become exercisable upon the consummation of the Sale Event (provided that such exercise shall be subject to the consummation of the Sale Event). The Company shall also have the right, but not the obligation, to make or provide a cash payment to the grantees holding other Awards, in exchange for cancellation thereof an amount equal to the Sale Price multiplied by the number of shares subject to such Awards, to be paid at the time of the Sale Event or upon the later vesting of such Awards.

Notwithstanding anything to the contrary herein, in the event a grantee's service relationship is terminated by the Company or any successor without Cause within one year following the consummation of a Sale Event, any Awards assumed or substituted in a Sale Event which are subject to vesting conditions, the lapse or achievement of any conditions and/or a right of repurchase in favor of the Company or a successor entity, shall accelerate in full, and any Awards accelerated in such manner with conditions and restrictions relating to the attainment of performance goals will be deemed achieved at one hundred percent (100%) of target levels. As used in this subsection (d) only, "Cause" shall mean dismissal as a result of (i) any material breach by the grantee of any agreement between the grantee and the Company; (ii) the conviction of, indictment for or plea of nolo contendere by the grantee to a felony or a crime involving moral turpitude; or (iii) any material misconduct or willful and deliberate non-performance (other than by reason of disability) by the grantee of the grantee's duties to the Company.

SECTION 4. ELIGIBILITY

Grantees under the Plan will be such full or part-time officers and other employees, Non-Employee Directors and other key persons (including Consultants) of the Company and its Subsidiaries as are selected from time to time by the Administrator in its sole discretion.

SECTION 5. STOCK OPTIONS

(a) Award of Stock Options. The Administrator may grant Stock Options under the Plan. Any Stock Option granted under the Plan shall be in such form as the Administrator may from time to time approve.

Stock Options granted under the Plan may be either Incentive Stock Options or Non-Qualified Stock Options. Incentive Stock Options may be granted only to employees of the Company or any Subsidiary that is a "subsidiary corporation" within the meaning of Section 424(f) of the Code. To the extent that any Option does not qualify as an Incentive Stock Option, it shall be deemed a Non-Qualified Stock Option.

Stock Options granted pursuant to this Section 5 shall be subject to the following terms and conditions and shall contain such additional terms and conditions, not inconsistent with the terms of the Plan, as the Administrator shall deem desirable. If the Administrator so determines, Stock Options may be granted in lieu of cash compensation at the optionee's election, subject to such terms and conditions as the Administrator may establish.

(b) Exercise Price. The exercise price per share for the Stock covered by a Stock Option granted pursuant to this Section 5 shall be determined by the Administrator at the time of grant but shall not be less than one hundred percent (100%) of the Fair Market Value on the date of grant. In the case of an Incentive Stock Option that is granted to a Ten Percent Owner, the option price of such Incentive Stock Option shall be not less than one hundred ten percent (110%) of the Fair Market Value on the grant date.

(c) Option Term. The term of each Stock Option shall be fixed by the Administrator, but no Stock Option shall be exercisable more than ten years after the date the Stock Option is granted. In the case of an Incentive Stock Option that is granted to a Ten Percent Owner, the term of such Stock Option shall be no more than five years from the date of grant.

(d) Exercisability; Rights of a Stockholder. Stock Options shall become exercisable at such time or times, whether or not in installments, as shall be determined by the Administrator at or after the grant date. The Administrator may at any time accelerate the exercisability of all or any portion of any Stock Option. An optionee shall have the rights of a stockholder only as to shares acquired upon the exercise of a Stock Option and not as to unexercised Stock Options.

(e) Method of Exercise. Stock Options may be exercised in whole or in part, by giving written or electronic notice of exercise to the Company, specifying the number of shares to be purchased. Payment of the purchase price may be made by one or more of the following methods except to the extent otherwise provided in the Option Award Certificate:

(i) In cash, by certified or bank check or other instrument acceptable to the Administrator;

(ii) Through the delivery (or attestation to the ownership following such procedures as the Company may prescribe) of shares of Stock that are not then subject to restrictions under any Company plan. Such surrendered shares shall be valued at Fair Market Value on the exercise date;

(iii) By the optionee delivering to the Company a properly executed exercise notice together with irrevocable instructions to a broker to promptly deliver to the Company cash or a check payable and acceptable to the Company for the purchase price; provided that in the event the optionee chooses to pay the purchase price as so provided, the optionee and the broker shall comply with such procedures and enter into such agreements of indemnity and other agreements as the Administrator shall prescribe as a condition of such payment procedure; or

(iv) With respect to Stock Options that are not Incentive Stock Options, by a “net exercise” arrangement pursuant to which the Company will reduce the number of shares of Stock issuable upon exercise by the largest whole number of shares with a Fair Market Value that does not exceed the aggregate exercise price.

Payment instruments will be received subject to collection. The transfer to the optionee on the records of the Company or of the transfer agent of the shares of Stock to be purchased pursuant to the exercise of a Stock Option will be contingent upon receipt from the optionee (or a purchaser acting in his stead in accordance with the provisions of the Stock Option) by the Company of the full purchase price for such shares and the fulfillment of any other requirements

contained in the Option Award Certificate or applicable provisions of laws (including the satisfaction of any withholding taxes that the Company is obligated to withhold with respect to the optionee). In the event an optionee chooses to pay the purchase price by previously-owned shares of Stock through the attestation method, the number of shares of Stock transferred to the optionee upon the exercise of the Stock Option shall be net of the number of attested shares. In the event that the Company establishes, for itself or using the services of a third party, an automated system for the exercise of Stock Options, such as a system using an internet website or interactive voice response, then the paperless exercise of Stock Options may be permitted through the use of such an automated system.

(f) Annual Limit on Incentive Stock Options. To the extent required for "incentive stock option" treatment under Section 422 of the Code, the aggregate Fair Market Value (determined as of the time of grant) of the shares of Stock with respect to which Incentive Stock Options granted under this Plan and any other plan of the Company or its parent and subsidiary corporations become exercisable for the first time by an optionee during any calendar year shall not exceed $100,000. To the extent that any Stock Option exceeds this limit, it shall constitute a Non-Qualified Stock Option.

SECTION 6. STOCK APPRECIATION RIGHTS

(a) Award of Stock Appreciation Rights. The Administrator may grant Stock Appreciation Rights under the Plan. A Stock Appreciation Right is an Award entitling the recipient to receive shares of Stock having a value equal to the excess of the Fair Market Value of a share of Stock on the date of exercise over the exercise price of the Stock Appreciation Right multiplied by the number of shares of Stock with respect to which the Stock Appreciation Right shall have been exercised.

(b) Exercise Price of Stock Appreciation Rights. The exercise price of a Stock Appreciation Right shall not be less than one hundred percent (100%) of the Fair Market Value of the Stock on the date of grant.

(c) Grant and Exercise of Stock Appreciation Rights. Stock Appreciation Rights may be granted by the Administrator independently of any Stock Option granted pursuant to Section 5 of the Plan.

(d) Terms and Conditions of Stock Appreciation Rights. Stock Appreciation Rights shall be subject to such terms and conditions as shall be determined from time to time by the Administrator. The term of a Stock Appreciation Right may not exceed ten years.

SECTION 7. RESTRICTED STOCK AWARDS

(a) Nature of Restricted Stock Awards. The Administrator may grant Restricted Stock Awards under the Plan. A Restricted Stock Award is any Award of Restricted Shares subject to such restrictions and conditions as the Administrator may determine at the time of grant. Conditions may be based on continuing employment (or other service relationship) and/or achievement of pre-established performance goals and objectives. The terms and conditions of each such Award Certificate shall be determined by the Administrator, and such terms and conditions may differ among individual Awards and grantees.

(b) Rights as a Stockholder. Upon the grant of the Restricted Stock Award and payment of any applicable purchase price, a grantee shall have the rights of a stockholder with respect to the voting of the Restricted Shares and receipt of dividends; provided that if the lapse of restrictions with respect to the Restricted Stock Award is tied to the attainment of performance goals, any dividends paid by the Company during the performance period shall accrue and shall not be paid to the grantee until and to the extent the performance goals are met with respect to the Restricted Stock Award. Unless the Administrator shall otherwise determine, (i) uncertificated Restricted Shares shall be accompanied by a notation on the records of the Company or the transfer agent to the effect that they are subject to forfeiture until such Restricted Shares are vested as provided in Section 7(d) below, and (ii) certificated Restricted Shares shall remain in the possession of the Company until such Restricted Shares are vested as provided in Section 7(d) below, and the grantee shall be required, as a condition of the grant, to deliver to the Company such instruments of transfer as the Administrator may prescribe.

(c) Restrictions. Restricted Shares may not be sold, assigned, transferred, pledged or otherwise encumbered or disposed of except as specifically provided herein or in the Restricted Stock Award Certificate. Except as may otherwise be provided by the Administrator either in the Award Certificate or, subject to Section 18 below, in writing after the Award is issued, if a grantee's employment (or other service relationship) with the Company and its Subsidiaries terminates for any reason, any Restricted Shares that have not vested at the time of termination shall automatically and without any requirement of notice to such grantee from or other action by or on behalf of, the Company be deemed to have been reacquired by the Company at its original purchase price (if any) from such grantee or such grantee's legal representative simultaneously with such termination of employment (or other service relationship), and thereafter shall cease to represent any ownership of the Company by the grantee or rights of the grantee as a stockholder. Following such deemed reacquisition of Restricted Shares that are represented by physical certificates, a grantee shall surrender such certificates to the Company upon request without consideration.

(d) Vesting of Restricted Shares. The Administrator at the time of grant shall specify the date or dates and/or the attainment of pre-established performance goals, objectives and other conditions on which the non-transferability of the Restricted Shares and the Company's right of repurchase or forfeiture shall lapse. Subsequent to such date or dates and/or the attainment of such pre-established performance goals, objectives and other conditions, the shares on which all restrictions have lapsed shall no longer be Restricted Shares and shall be deemed "vested."

SECTION 8. RESTRICTED STOCK UNITS

(a) Nature of Restricted Stock Units. The Administrator may grant Restricted Stock Units under the Plan. A Restricted Stock Unit is an Award of stock units that may be settled in shares of Stock upon the satisfaction of such restrictions and conditions at the time of grant. Conditions may be based on continuing employment (or other service relationship) and/or achievement of pre-established performance goals and objectives. The terms and conditions of each such Award Certificate shall be determined by the Administrator, and such terms and conditions may differ among individual Awards and grantees. Except in the case of Restricted Stock Units with a deferred settlement date that complies with Section 409A, at the end of the vesting period, the Restricted Stock Units, to the extent vested, shall be settled in the form of shares of Stock. Restricted Stock Units with deferred settlement dates are subject to Section 409A and shall contain such additional terms and conditions as the Administrator shall determine in its sole discretion in order to comply with the requirements of Section 409A.

(b) Election to Receive Restricted Stock Units in Lieu of Compensation. The Administrator may, in its sole discretion, permit a grantee to elect to receive a portion of future cash compensation otherwise due to such grantee in the form of an award of Restricted Stock Units. Any such election shall be made in writing and shall be delivered to the Company no later than the date specified by the Administrator and in accordance with Section 409A and such other rules and procedures established by the Administrator. Any such future cash compensation that the grantee elects to defer shall be converted to a fixed number of Restricted Stock Units based on the Fair Market Value of Stock on the date the compensation would otherwise have been paid to the grantee if such payment had not been deferred as provided herein. The Administrator shall have the sole right to determine whether and under what circumstances to permit such elections and to impose such limitations and other terms and conditions thereon as the Administrator deems appropriate. Any Restricted Stock Units that are elected to be received in lieu of cash compensation shall be fully vested, unless otherwise provided in the Award Certificate.

(c) Rights as a Stockholder. A grantee shall have the rights as a stockholder only as to shares of Stock acquired by the grantee upon settlement of Restricted Stock Units; provided, however, that the grantee may be credited with Dividend Equivalent Rights with respect to the stock units underlying his Restricted Stock Units, subject to the provisions of Section 13 and such terms and conditions as the Administrator may determine.

(d) Termination. Except as may otherwise be provided by the Administrator either in the Award Certificate or, subject to Section 18 below, in writing after the Award is issued, a grantee's right in all Restricted Stock Units that have not vested shall automatically terminate upon the grantee's termination of employment (or cessation of service relationship) with the Company and its Subsidiaries for any reason.

SECTION 9. UNRESTRICTED STOCK AWARDS

Grant or Sale of Unrestricted Stock. The Administrator may grant (or sell at par value or such higher purchase price determined by the Administrator) an Unrestricted Stock Award under the Plan. An Unrestricted Stock Award is an Award pursuant to which the grantee may receive shares of Stock free of any restrictions under the Plan. Unrestricted Stock Awards may be granted in respect of past services or other valid consideration, or in lieu of cash compensation due to such grantee.

SECTION 10. CASH-BASED AWARDS

Grant of Cash-Based Awards. The Administrator may grant Cash-Based Awards under the Plan. A Cash-Based Award is an Award that entitles the grantee to a payment in cash upon the attainment of specified Performance Goals. The Administrator shall determine the maximum duration of the Cash-Based Award, the amount of cash to which the Cash-Based Award pertains, the conditions upon which the Cash-Based Award shall become vested or payable, and such other provisions as the Administrator shall determine. Each Cash-Based Award shall specify a cash-denominated payment amount, formula or payment ranges as determined by the Administrator. Payment, if any, with respect to a Cash-Based Award shall be made in accordance with the terms of the Award and may be made in cash.

SECTION 11. PERFORMANCE SHARE AWARDS

(a) Nature of Performance Share Awards. The Administrator may grant Performance Share Awards under the Plan. A Performance Share Award is an Award entitling the grantee to receive shares of Stock upon the attainment of performance goals. The Administrator shall determine whether and to whom Performance Share Awards shall be granted, the performance goals, the periods during which performance is to be measured, which may not be less than one year except in the case of a Sale Event, and such other limitations and conditions as the Administrator shall determine.

(b) Rights as a Stockholder. A grantee receiving a Performance Share Award shall have the rights of a stockholder only as to shares of Stock actually received by the grantee under the Plan and not with respect to shares subject to the Award but not actually received by the grantee. A grantee shall be entitled to receive shares of Stock under a Performance Share Award only upon satisfaction of all conditions specified in the Performance Share Award Certificate (or in a performance plan adopted by the Administrator).

(c) Termination. Except as may otherwise be provided by the Administrator either in the Award agreement or, subject to Section 18 below, in writing after the Award is issued, a grantee's rights in all Performance Share Awards shall automatically terminate upon the grantee's termination of employment (or cessation of service relationship) with the Company and its Subsidiaries for any reason.

SECTION 12. PERFORMANCE-BASED AWARDS TO COVERED EMPLOYEES

(a) Performance-Based Awards. The Administrator may grant one or more Performance-Based Awards in the form of a Restricted Stock Award, Restricted Stock Units, Performance Share Awards or Cash-Based Award payable upon the attainment of Performance Goals that are established by the Administrator and relate to one or more of the Performance Criteria, in each case on a specified date or dates or over any period or periods determined by the Administrator. The Administrator shall define in an objective fashion the manner of calculating the Performance Criteria it selects to use for any Performance Cycle. Depending on the Performance Criteria used to establish such Performance Goals, the Performance Goals may be expressed in terms of overall Company performance or the performance of a division, business unit, or an individual. The Administrator, in its discretion, may adjust or modify the calculation of Performance Goals for such Performance Cycle in order to prevent the dilution or enlargement of the rights of an individual (i) in the event of, or in anticipation of, any unusual or extraordinary corporate item, transaction, event or development, (ii) in recognition of , or in anticipation of, any other unusual or nonrecurring events affecting the Company or the financial statements of the Company or (iii) in response to, or in anticipation of, changes in applicable laws, regulations, accounting principles or business conditions; provided, however, that the Administrator may not exercise such discretion in a manner that would increase the Performance-Based Award granted to a Covered Employee. Each Performance-Based Award shall comply with the provisions set forth below.

(b) Grant of Performance-Based Awards. With respect to each Performance-Based Award granted to a Covered Employee (or any other eligible individual that the Administrator determines is reasonably likely to become a Covered Employee), the Administrator shall select, within the first 90 days of a Performance Cycle (or, if shorter, within the maximum period allowed under Section 162(m) of the Code) the Performance Criteria for such grant, and the Performance Goals with respect to each Performance Criterion (including a threshold level of performance below which no amount will become payable with respect to such Award). Each Performance-Based Award will specify the amount payable, or the formula for determining the amount payable, upon achievement of the various applicable performance targets. The Performance Criteria established by the Administrator may be (but need not be) different for each Performance Cycle and different Performance Goals may be applicable to Performance-Based Awards to different Covered Employees.

(c) Payment of Performance-Based Awards. Following the completion of a Performance Cycle, the Administrator shall meet to review and certify in writing whether, and to what extent, the Performance Goals for the Performance Cycle have been achieved and, if so, to also calculate and certify in writing the amount of the Performance-Based Awards earned for the Performance Cycle. The Administrator shall then determine the actual size of each Covered Employee's Performance-Based Award, and, in doing so, may reduce or eliminate the amount of the Performance-Based Award for a Covered Employee if, in its sole judgment, such reduction or elimination is appropriate.

(d) Maximum Award Payable. The maximum Performance-Based Award payable to any one Covered Employee under the Plan for a Performance Cycle is 1,750,000 shares of Stock (subject to adjustment as provided in Section 3(c) hereof) or $2,000,000 in the case of a Performance-Based Award that is a Cash-Based Award.

SECTION 13. DIVIDEND EQUIVALENT RIGHTS

(a) Dividend Equivalent Rights. The Administrator may grant Dividend Equivalent Rights under the Plan. A Dividend Equivalent Right is an Award entitling the grantee to receive credits based on cash dividends that would have been paid on the shares of Stock specified in the Dividend Equivalent Right (or other Award to which it relates) if such shares had been issued to the grantee. A Dividend Equivalent Right may be granted hereunder to any grantee as a component of an award of Restricted Stock Units, Restricted Stock Award or Performance Share Award or as a freestanding award. The terms and conditions of Dividend Equivalent Rights shall be specified in the Award Certificate. Dividend equivalents credited to the holder of a Dividend Equivalent Right may be paid currently or may be deemed to be reinvested in additional shares of Stock, which may thereafter accrue additional equivalents. Any such reinvestment shall be at Fair Market Value on the date of reinvestment or such other price as may then apply under a dividend reinvestment plan sponsored by the Company, if any. Dividend Equivalent Rights may be settled in cash or shares of Stock or a combination thereof, in a single installment or installments. A Dividend Equivalent Right granted as a component of an Award of Restricted Stock Units, a Restricted Stock Award with performance vesting or a Performance Share Award shall provide that such Dividend Equivalent Right shall be settled only upon settlement or payment of, or lapse of restrictions on, such other Award, and that such Dividend Equivalent Right shall expire or be forfeited or annulled under the same conditions as such other Award.

(b) Termination. Except as may otherwise be provided by the Administrator either in the Award Certificate or, subject to Section 18 below, in writing after the Award is issued, a grantee's rights in all Dividend Equivalent Rights or equivalent interest granted as a component of any award of Restricted Stock Units, Restricted Stock Award or Performance Share Award that has not yet vested shall automatically terminate upon the grantee's termination of employment (or cessation of service relationship) with the Company and its Subsidiaries for any reason.

SECTION 14. TRANSFERABILITY OF AWARDS

(a) Transferability. Except as provided in Section 14(b) below, during a grantee's lifetime, his or her Awards shall be exercisable only by the grantee, or by the grantee's legal representative or guardian in the event of the grantee's incapacity. No Awards shall be sold, assigned, transferred or otherwise encumbered or disposed of by a grantee other than by will or by the laws of descent and distribution or pursuant to a domestic relations order. No Awards shall be subject, in whole or in part, to attachment, execution, or levy of any kind, and any purported transfer in violation hereof shall be null and void.

(b) Administrator Action. Notwithstanding Section 14(a), the Administrator, in its discretion, may provide either in the Award Certificate regarding a given Award or by subsequent written approval that the grantee (who is an employee or director) may transfer his or her Non-Qualified Options to his or her immediate family members, to trusts for the benefit of such family members, or to partnerships in which such family members are the only partners, provided that the transferee agrees in writing with the Company to be bound by all of the terms and conditions of this Plan and the applicable Award. In no event may an Award be transferred by a grantee for value.

(c) Family Member. For purposes of Section 14(b), "family member" shall mean a grantee's child, stepchild, grandchild, parent, stepparent, grandparent, spouse, former spouse, sibling, niece, nephew, mother-in-law, father-in-law, son-in-law, daughter-in-law, brother-in-law, or sister-in-law, including adoptive relationships, any person sharing the grantee's household (other than a tenant of the grantee), a trust in which these persons (or the grantee) have more than fifty percent (50%) of the beneficial interest, a foundation in which these persons (or the grantee) control the management of assets, and any other entity in which these persons (or the grantee) own more than fifty percent (50%) of the voting interests.

(d) Designation of Beneficiary. To the extent permitted by the Administrator, each grantee to whom an Award has been made under the Plan may designate a beneficiary or beneficiaries to exercise any Award or receive any payment under any Award payable on or after the grantee's death. Any such designation shall be on a form provided for that purpose by the Administrator and shall not be effective until received by the Administrator. If no beneficiary has been designated by a deceased grantee, or if the designated beneficiaries have predeceased the grantee, the beneficiary shall be the grantee's estate.

SECTION 15. TAX WITHHOLDING

(a) Payment by Grantee. Each grantee shall, no later than the date as of which the value of an Award or of any Stock or other amounts received thereunder first becomes includable in the gross income of the grantee for Federal income tax purposes, pay to the Company, or make arrangements satisfactory to the Administrator regarding payment of, any Federal, state, or local taxes of any kind required by law to be withheld by the Company with respect to such income. The Company and its Subsidiaries shall, to the extent permitted by law, have the right to deduct any such taxes from any payment of any kind otherwise due to the grantee. The Company's obligation to deliver evidence of book entry (or stock certificates) to any grantee is subject to and conditioned on tax withholding obligations being satisfied by the grantee.

(b) Payment in Stock. Subject to approval by the Administrator, a grantee may elect to have the Company's minimum required tax withholding obligation satisfied, in whole or in part, by authorizing the Company to withhold from shares of Stock to be issued pursuant to any Award a number of shares with an aggregate Fair Market Value (as of the date the withholding is effected) that would satisfy the withholding amount due. For purposes of share withholding, the Fair Market Value of withheld shares shall be determined in the same manner as the value of Stock includible in income of the Participants.

SECTION 16. SECTION 409A AWARDS

To the extent that any Award is determined to constitute "nonqualified deferred compensation" within the meaning of Section 409A (a "409A Award"), the Award shall be subject to such additional rules and requirements as specified by the Administrator from time to time in order to comply with Section 409A. In this regard, if any amount under a 409A Award is payable upon a "separation from service" (within the meaning of Section 409A) to a grantee who is then considered a "specified employee" (within the meaning of Section 409A), then no such payment shall be made prior to the date that is the earlier of (i) six months and one day after the grantee's separation from service, or (ii) the grantee's death, but only to the extent such delay is necessary to prevent such payment from being subject to interest, penalties and/or additional tax imposed pursuant to Section 409A. Further, the settlement of any such Award may not be accelerated except to the extent permitted by Section 409A.

SECTION 17. TERMINATION OF EMPLOYMENT, TRANSFER, LEAVE OF ABSENCE, ETC.

(a) Termination of Employment. If the grantee's employer ceases to be a Subsidiary, the grantee shall be deemed to have terminated employment for purposes of the Plan.

(b) For purposes of the Plan, the following events shall not be deemed a termination of employment:

(i) a transfer to the employment of the Company from a Subsidiary or from the Company to a Subsidiary, or from one Subsidiary to another; or

(ii) an approved leave of absence for military service or sickness, or for any other purpose approved by the Company, if the employee's right to re-employment is guaranteed either by a statute or by contract or under the policy pursuant to which the leave of absence was granted or if the Administrator otherwise so provides in writing.

SECTION 18. AMENDMENTS AND TERMINATION

The Board may, at any time, amend or discontinue the Plan and the Administrator may, at any time, amend or cancel any outstanding Award for the purpose of satisfying changes in law or for any other lawful purpose, but no such action shall adversely affect rights under any outstanding Award without the holder's consent. Except as provided in Section 3(c) or 3(d), without prior stockholder approval, in no event may the Administrator exercise its discretion to reduce the exercise price of outstanding Stock Options or Stock Appreciation Rights or effect repricing through cancellation and re-grants or cancellation of Stock Options or Stock Appreciation Rights in exchange for cash. To the extent required under the rules of any securities exchange or market system on which the Stock is listed, to the extent determined by the Administrator to be required by the Code to ensure that Incentive Stock Options granted under the Plan are qualified under Section 422 of the Code, or to ensure that compensation earned under Awards qualifies as performance-based compensation under Section 162(m) of the Code, Plan amendments shall be subject to approval by the Company stockholders entitled to vote at a meeting of stockholders. Nothing in this Section 18 shall limit the Administrator's authority to take any action permitted pursuant to Section 3(c) or 3(d).

SECTION 19. STATUS OF PLAN

With respect to the portion of any Award that has not been exercised and any payments in cash, Stock or other consideration not received by a grantee, a grantee shall have no rights greater than those of a general creditor of the Company unless the Administrator shall otherwise expressly determine in connection with any Award or Awards. In its sole discretion, the Administrator may authorize the creation of trusts or other arrangements to meet the Company's obligations to deliver Stock or make payments with respect to Awards hereunder, provided that the existence of such trusts or other arrangements is consistent with the foregoing sentence.

SECTION 20. GENERAL PROVISIONS

(a) No Distribution. The Administrator may require each person acquiring Stock pursuant to an Award to represent to and agree with the Company in writing that such person is acquiring the shares without a view to distribution thereof.

(b) Delivery of Stock Certificates. Stock certificates to grantees under this Plan shall be deemed delivered for all purposes when the Company or a stock transfer agent of the Company shall have mailed such certificates in the United States mail, addressed to the grantee, at the grantee's last known address on file with the Company. Uncertificated Stock shall be deemed delivered for all purposes when the Company or a Stock transfer agent of the Company shall have given to the grantee by electronic mail (with proof of receipt) or by United States mail, addressed to the grantee, at the grantee's last known address on file with the Company, notice of issuance and recorded the issuance in its records (which may include electronic "book

entry" records). Notwithstanding anything herein to the contrary, the Company shall not be required to issue or deliver any certificates evidencing shares of Stock pursuant to the exercise of any Award, unless and until the Administrator has determined, with advice of counsel (to the extent the Administrator deems such advice necessary or advisable), that the issuance and delivery of such certificates is in compliance with all applicable laws, regulations of governmental authorities and, if applicable, the requirements of any exchange on which the shares of Stock are listed, quoted or traded. All Stock certificates delivered pursuant to the Plan shall be subject to any stop-transfer orders and other restrictions as the Administrator deems necessary or advisable to comply with federal, state or foreign jurisdiction, securities or other laws, rules and quotation system on which the Stock is listed, quoted or traded. The Administrator may place legends on any Stock certificate to reference restrictions applicable to the Stock. In addition to the terms and conditions provided herein, the Administrator may require that an individual make such reasonable covenants, agreements, and representations as the Administrator, in its discretion, deems necessary or advisable in order to comply with any such laws, regulations, or requirements. The Administrator shall have the right to require any individual to comply with any timing or other restrictions with respect to the settlement or exercise of any Award, including a window-period limitation, as may be imposed in the discretion of the Administrator.

(c) Stockholder Rights. Until Stock is deemed delivered in accordance with Section 20(b), no right to vote or receive dividends or any other rights of a stockholder will exist with respect to shares of Stock to be issued in connection with an Award, notwithstanding the exercise of a Stock Option or any other action by the grantee with respect to an Award.

(d) Other Compensation Arrangements; No Employment Rights. Nothing contained in this Plan shall prevent the Board from adopting other or additional compensation arrangements, including trusts, and such arrangements may be either generally applicable or applicable only in specific cases. The adoption of this Plan and the grant of Awards do not confer upon any employee any right to continued employment with the Company or any Subsidiary.

(e) Trading Policy Restrictions. Option exercises and other Awards under the Plan shall be subject to the Company's insider trading policies and procedures, as in effect from time to time.

(f) Clawback Policy. Awards under the Plan shall be subject to the Company's clawback policy, as in effect from time to time.

SECTION 21. EFFECTIVE DATE OF PLAN

This Plan shall become effective immediately prior to the Company's Initial Public Offering, following stockholder approval of the Plan in accordance with applicable state law, the Company's bylaws and certificate of incorporation, and applicable stock exchange rules or pursuant to written consent. No grants of Stock Options and other Awards may be made hereunder after the tenth anniversary of the Effective Date and no grants of Incentive Stock Options may be made hereunder after the tenth anniversary of the date the Plan is approved by the Board.

SECTION 22. GOVERNING LAW

This Plan and all Awards and actions taken thereunder shall be governed by, and construed in accordance with, the laws of the State of Delaware, applied without regard to conflict of law principles.

Approved by the Board of Directors: July 23, 2015

Approved by the Stockholders: July 27, 2015

Amended: January 9, 2020

INCENTIVE STOCK OPTION AGREEMENT
UNDER THE GLOBAL BLOOD THERAPEUTICS, INC.
2015 STOCK OPTION AND INCENTIVE PLAN

Name of Optionee: _____

No. of Option Shares: _____

Option Exercise Price per Share: $ _____[1]

Grant Date: _____

Vesting Commencement Date: _____[2]

Expiration Date: _____

Pursuant to the Global Blood Therapeutics, Inc. 2015 Stock Option and Incentive Plan as amended through the date hereof (the "Plan"), Global Blood Therapeutics, Inc., a Delaware corporation (the "Company"), hereby grants to the Optionee named above an option (the "Stock Option") to purchase on or prior to the Expiration Date specified above all or part of the number of shares of Common Stock, par value $0.001 per share (the "Stock"), of the Company specified above at the Option Exercise Price per Share specified above subject to the terms and conditions set forth herein and in the Plan.

SECTION 23. Exercisability Schedule. No portion of this Stock Option may be exercised until such portion shall have become exercisable. Except as set forth below, and subject to the discretion of the Administrator (as defined in Section 2 of the Plan) to accelerate the exercisability schedule hereunder, this Stock Option shall be exercisable as follows: _____, so long as Optionee remains an employee or other service provider (including a consultant) of the Company or a Subsidiary on such dates.[3] Once exercisable, this Stock Option shall continue to be exercisable at any time or times prior to the close of business on the Expiration Date, subject to the provisions hereof and of the Plan.

SECTION 24. Manner of Exercise.

(a) The Optionee may exercise this Stock Option only in the following manner: from time to time on or prior to the Expiration Date of this Stock Option, the Optionee may give written notice to the Administrator of his or her election to purchase some or all of the Option Shares purchasable at the time of such notice. This notice shall specify the number of Option Shares to be purchased.

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1 Note to Form: FMV on Grant Date (110% of FMV if a 10% owner)
2 Note to Form: Up to 10 years (5 if a 10% owner)
3 Note to Form: Maximum of $100,000 per year to qualify as an incentive stock option.

Payment of the purchase price for the Option Shares may be made by one or more of the following methods: (i) in cash, by certified or bank check or other instrument acceptable to the Administrator; (ii) through the delivery (or attestation to the ownership) of shares of Stock that have been purchased by the Optionee on the open market or that are beneficially owned by the Optionee and are not then subject to any restrictions under any Company plan and that otherwise satisfy any holding periods as may be required by the Administrator; or (iii) by the Optionee delivering to the Company a properly executed exercise notice together with irrevocable instructions to a broker to promptly deliver to the Company cash or a check payable and acceptable to the Company to pay the option purchase price, provided that in the event the Optionee chooses to pay the option purchase price as so provided, the Optionee and the broker shall comply with such procedures and enter into such agreements of indemnity and other agreements as the Administrator shall prescribe as a condition of such payment procedure; or (iv) a combination of (i), (ii) and (iii) above. Payment instruments will be received subject to collection.

The transfer to the Optionee on the records of the Company or of the transfer agent of the Option Shares will be contingent upon (i) the Company's receipt from the Optionee of the full purchase price for the Option Shares, as set forth above, (ii) the fulfillment of any other requirements contained herein or in the Plan or in any other agreement or provision of laws, and (iii) the receipt by the Company of any agreement, statement or other evidence that the Company may require to satisfy itself that the issuance of Stock to be purchased pursuant to the exercise of Stock Options under the Plan and any subsequent resale of the shares of Stock will be in compliance with applicable laws and regulations. In the event the Optionee chooses to pay the purchase price by previously-owned shares of Stock through the attestation method, the number of shares of Stock transferred to the Optionee upon the exercise of the Stock Option shall be net of the Shares attested to.

(b) The shares of Stock purchased upon exercise of this Stock Option shall be transferred to the Optionee on the records of the Company or of the transfer agent upon compliance to the satisfaction of the Administrator with all requirements under applicable laws or regulations in connection with such transfer and with the requirements hereof and of the Plan. The determination of the Administrator as to such compliance shall be final and binding on the Optionee. The Optionee shall not be deemed to be the holder of, or to have any of the rights of a holder with respect to, any shares of Stock subject to this Stock Option unless and until this Stock Option shall have been exercised pursuant to the terms hereof, the Company or the transfer agent shall have transferred the shares to the Optionee, and the Optionee's name shall have been entered as the stockholder of record on the books of the Company. Thereupon, the Optionee shall have full voting, dividend and other ownership rights with respect to such shares of Stock.

(c) The minimum number of shares with respect to which this Stock Option may be exercised at any one time shall be 100 shares, unless the number of shares with respect to which this Stock Option is being exercised is the total number of shares subject to exercise under this Stock Option at the time.

(d) Notwithstanding any other provision hereof or of the Plan, no portion of this Stock Option shall be exercisable after the Expiration Date hereof.

SECTION 25. Termination of Employment or Service Relationship. If the Optionee's employment by or other service relationship with the Company or a Subsidiary (as defined in the Plan) is terminated, the period within which to exercise the Stock Option may be subject to earlier termination as set forth below.

(a) Termination Due to Death. If the Optionee's employment or other service relationship terminates by reason of the Optionee's death, any portion of this Stock Option outstanding on such date, to the extent exercisable on the date of death, may thereafter be exercised by the Optionee's legal representative or legatee for a period of 12 months from the date of death or until the Expiration Date, if earlier.

(b) Termination Due to Disability. If the Optionee's employment or other service relationship terminates by reason of the Optionee's disability (as determined by the Administrator), any portion of this Stock Option outstanding on such date, to the extent exercisable on the date of such termination of employment, may thereafter be exercised by the Optionee for a period of 12 months from the date of disability or until the Expiration Date, if earlier.

(c) Termination for Cause. If the Optionee's employment or other service relationship terminates for Cause, any portion of this Stock Option outstanding on such date shall terminate immediately and be of no further force and effect. For purposes hereof, "Cause" shall mean, unless otherwise provided in an employment agreement between the Company and the Optionee, a determination by the Administrator that the Optionee shall be dismissed as a result of (i) any material breach by the Optionee of any agreement between the Optionee and the Company; (ii) the conviction of, indictment for or plea of nolo contendere by the Optionee to a felony or a crime involving moral turpitude; or (iii) any material misconduct or willful and deliberate non-performance (other than by reason of disability) by the Optionee of the Optionee's duties to the Company.

(d) Other Termination. If the Optionee's employment or other service relationship terminates for any reason other than the Optionee's death, the Optionee's disability, or Cause, and unless otherwise determined by the Administrator, any portion of this Stock Option outstanding on such date may be exercised, to the extent exercisable on the date of termination, for a period of six months from the date of termination or until the Expiration Date, if earlier.

Any portion of this Stock Option that is not exercisable on the date of termination shall terminate and be of no further force or effect on the date that is three months following the date of termination, or the Expiration Date if earlier; provided that if the Administrator determines to accelerate the exercisability of any such portion of the Stock Option during such period, such Stock Option shall remain exercisable for the applicable period set forth in this Section 3. The Administrator's determination of the reason for termination of the Optionee's employment or other service relationship shall be conclusive and binding on the Optionee and his or her representatives or legatees.

SECTION 26. Incorporation of Plan. Notwithstanding anything herein to the contrary, this Stock Option shall be subject to and governed by all the terms and conditions of the Plan, including the powers of the Administrator set forth in Section 2(b) of the Plan. Capitalized terms in this Agreement shall have the meaning specified in the Plan, unless a different meaning is specified herein.

SECTION 27. Transferability. This Agreement is personal to the Optionee, is non-assignable and is not transferable in any manner, by operation of law or otherwise, other than by will or the laws of descent and distribution. This Stock Option is exercisable, during the Optionee's lifetime, only by the Optionee, and thereafter, only by the Optionee's legal representative or legatee.

SECTION 28. Status of the Stock Option. This Stock Option is intended to qualify as an "incentive stock option" under Section 422 of the Internal Revenue Code of 1986, as amended (the "Code"), but the Company does not represent or warrant that this Stock Option qualifies as such. The Optionee should consult with his or her own tax advisors regarding the tax effects of this Stock Option and the requirements necessary to obtain favorable income tax treatment under Section 422 of the Code, including, but not limited to, holding period requirements. To the extent any portion of this Stock Option does not so qualify as an "incentive stock option," such portion shall be deemed to be a non-qualified stock option. If the Optionee intends to dispose or does dispose (whether by sale, gift, transfer or otherwise) of any Option Shares within the one-year period beginning on the date after the transfer of such shares to him or her, or within the two-year period beginning on the day after the grant of this Stock Option, he or she will so notify the Company within 30 days after such disposition.

SECTION 29. Tax Withholding. The Optionee shall, not later than the date as of which the exercise of this Stock Option becomes a taxable event for Federal income tax purposes, pay to the Company or make arrangements satisfactory to the Administrator for payment of any Federal, state, and local taxes required by law to be withheld on account of such taxable event. The Company shall have the authority to cause the minimum required tax withholding obligation to be satisfied, in whole or in part, by withholding from shares of Stock to be issued to the Optionee a number of shares of Stock with an aggregate Fair Market Value that would satisfy the minimum withholding amount due.

SECTION 30. No Obligation to Continue Employment. Neither the Company nor any Subsidiary is obligated by or as a result of the Plan or this Agreement to continue the Optionee in employment and neither the Plan nor this Agreement shall interfere in any way with the right of the Company or any Subsidiary to terminate the employment of the Optionee at any time.

SECTION 31. Integration. This Agreement constitutes the entire agreement between the parties with respect to this Stock Option and supersedes all prior agreements and discussions between the parties concerning such subject matter.

SECTION 32. Data Privacy Consent. In order to administer the Plan and this Agreement and to implement or structure future equity grants, the Company, its subsidiaries and affiliates and certain agents thereof (together, the "Relevant Companies") may process any and all personal or professional data, including but not limited to Social Security or other identification number, home address and telephone number, date of birth and other information that is necessary or desirable for the administration of the Plan and/or this Agreement (the "Relevant

Information"). By entering into this Agreement, the Optionee (i) authorizes the Company to collect, process, register and transfer to the Relevant Companies all Relevant Information; (ii) waives any privacy rights the Optionee may have with respect to the Relevant Information; (iii) authorizes the Relevant Companies to store and transmit such information in electronic form; and (iv) authorizes the transfer of the Relevant Information to any jurisdiction in which the Relevant Companies consider appropriate. The Optionee shall have access to, and the right to change, the Relevant Information. Relevant Information will only be used in accordance with applicable law.

SECTION 33. Notices. Notices hereunder shall be mailed or delivered to the Company at its principal place of business and shall be mailed or delivered to the Optionee at the address on file with the Company or, in either case, at such other address as one party may subsequently furnish to the other party in writing.

GLOBAL BLOOD THERAPEUTICS, INC.

By: _____
Name:
Title:

The foregoing Agreement is hereby accepted and the terms and conditions thereof hereby agreed to by the undersigned. Electronic acceptance of this Agreement pursuant to the Company's instructions to the Optionee (including through an online acceptance process) is acceptable.

Dated: _____

_____
Optionee's Signature

Optionee's name and address:

_____

_____

_____

NON-QUALIFIED STOCK OPTION AGREEMENT
FOR COMPANY EMPLOYEES
UNDER GLOBAL BLOOD THERAPEUTICS, INC.
2015 STOCK OPTION AND INCENTIVE PLAN

Name of Optionee:	_____
No. of Option Shares:	_____
Option Exercise Price per Share:	$ _____[4]
Grant Date:	_____
Vesting Commencement Date:	_____
Expiration Date:	_____[5]

Pursuant to the Global Blood Therapeutics, Inc. 2015 Stock Option and Incentive Plan as amended through the date hereof (the "Plan"), Global Blood Therapeutics, Inc., a Delaware corporation (the "Company"), hereby grants to the Optionee named above an option (the "Stock Option") to purchase on or prior to the Expiration Date specified above all or part of the number of shares of Common Stock, par value $0.001 per share (the "Stock") of the Company specified above at the Option Exercise Price per Share specified above subject to the terms and conditions set forth herein and in the Plan. This Stock Option is not intended to be an "incentive stock option" under Section 422 of the Internal Revenue Code of 1986, as amended.

SECTION 34. Exercisability Schedule. No portion of this Stock Option may be exercised until such portion shall have become exercisable. Except as set forth below, and subject to the discretion of the Administrator (as defined in Section 2 of the Plan) to accelerate the exercisability schedule hereunder, this Stock Option shall be exercisable as follows: _____, so long as Optionee remains an employee or other service provider (including a consultant) of the Company or a Subsidiary on such dates. Once exercisable, this Stock Option shall continue to be exercisable at any time or times prior to the close of business on the Expiration Date, subject to the provisions hereof and of the Plan.

SECTION 35. Manner of Exercise.

(a) The Optionee may exercise this Stock Option only in the following manner: from time to time on or prior to the Expiration Date of this Stock Option, the Optionee may give written notice to the Administrator of his or her election to purchase some or all of the Option Shares purchasable at the time of such notice. This notice shall specify the number of Option Shares to be purchased.

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4 Note to Form: FMV on Grant Date

5 Note to Form: No more than 10 years

Payment of the purchase price for the Option Shares may be made by one or more of the following methods: (i) in cash, by certified or bank check or other instrument acceptable to the Administrator; (ii) through the delivery (or attestation to the ownership) of shares of Stock that have been purchased by the Optionee on the open market or that are beneficially owned by the Optionee and are not then subject to any restrictions under any Company plan and that otherwise satisfy any holding periods as may be required by the Administrator; (iii) by the Optionee delivering to the Company a properly executed exercise notice together with irrevocable instructions to a broker to promptly deliver to the Company cash or a check payable and acceptable to the Company to pay the option purchase price, provided that in the event the Optionee chooses to pay the option purchase price as so provided, the Optionee and the broker shall comply with such procedures and enter into such agreements of indemnity and other agreements as the Administrator shall prescribe as a condition of such payment procedure; (iv) by a "net exercise" arrangement pursuant to which the Company will reduce the number of shares of Stock issuable upon exercise by the largest whole number of shares with a Fair Market Value that does not exceed the aggregate exercise price; or (v) a combination of (i), (ii), (iii) and (iv) above. Payment instruments will be received subject to collection.

The transfer to the Optionee on the records of the Company or of the transfer agent of the Option Shares will be contingent upon (i) the Company's receipt from the Optionee of the full purchase price for the Option Shares, as set forth above, (ii) the fulfillment of any other requirements contained herein or in the Plan or in any other agreement or provision of laws, and (iii) the receipt by the Company of any agreement, statement or other evidence that the Company may require to satisfy itself that the issuance of Stock to be purchased pursuant to the exercise of Stock Options under the Plan and any subsequent resale of the shares of Stock will be in compliance with applicable laws and regulations. In the event the Optionee chooses to pay the purchase price by previously-owned shares of Stock through the attestation method, the number of shares of Stock transferred to the Optionee upon the exercise of the Stock Option shall be net of the Shares attested to.

(b) The shares of Stock purchased upon exercise of this Stock Option shall be transferred to the Optionee on the records of the Company or of the transfer agent upon compliance to the satisfaction of the Administrator with all requirements under applicable laws or regulations in connection with such transfer and with the requirements hereof and of the Plan. The determination of the Administrator as to such compliance shall be final and binding on the Optionee. The Optionee shall not be deemed to be the holder of, or to have any of the rights of a holder with respect to, any shares of Stock subject to this Stock Option unless and until this Stock Option shall have been exercised pursuant to the terms hereof, the Company or the transfer agent shall have transferred the shares to the Optionee, and the Optionee's name shall have been entered as the stockholder of record on the books of the Company. Thereupon, the Optionee shall have full voting, dividend and other ownership rights with respect to such shares of Stock.

(c) The minimum number of shares with respect to which this Stock Option may be exercised at any one time shall be 100 shares, unless the number of shares with respect to which this Stock Option is being exercised is the total number of shares subject to exercise under this Stock Option at the time.

(d) Notwithstanding any other provision hereof or of the Plan, no portion of this Stock Option shall be exercisable after the Expiration Date hereof.

SECTION 36. Termination of Employment or Service Relationship. If the Optionee's employment by or other service relationship with the Company or a Subsidiary (as defined in the Plan) is terminated, the period within which to exercise the Stock Option may be subject to earlier termination as set forth below.

(a) Termination Due to Death. If the Optionee's employment or other service relationship terminates by reason of the Optionee's death, any portion of this Stock Option outstanding on such date, to the extent exercisable on the date of death, may thereafter be exercised by the Optionee's legal representative or legatee for a period of 12 months from the date of death or until the Expiration Date, if earlier.

(b) Termination Due to Disability. If the Optionee's employment or other service relationship terminates by reason of the Optionee's disability (as determined by the Administrator), any portion of this Stock Option outstanding on such date, to the extent exercisable on the date of such termination of employment, may thereafter be exercised by the Optionee for a period of 12 months from the date of disability or until the Expiration Date, if earlier.

(c) Termination for Cause. If the Optionee's employment or other service relationship terminates for Cause, any portion of this Stock Option outstanding on such date shall terminate immediately and be of no further force and effect. For purposes hereof, "Cause" shall mean, unless otherwise provided in an employment agreement between the Company and the Optionee, a determination by the Administrator that the Optionee shall be dismissed as a result of (i) any material breach by the Optionee of any agreement between the Optionee and the Company; (ii) the conviction of, indictment for or plea of nolo contendere by the Optionee to a felony or a crime involving moral turpitude; or (iii) any material misconduct or willful and deliberate non-performance (other than by reason of disability) by the Optionee of the Optionee's duties to the Company.

(d) Other Termination. If the Optionee's employment or other service relationship terminates for any reason other than the Optionee's death, the Optionee's disability or Cause, and unless otherwise determined by the Administrator, any portion of this Stock Option outstanding on such date may be exercised, to the extent exercisable on the date of termination, for a period of six months from the date of termination or until the Expiration Date, if earlier.

Any portion of this Stock Option that is not exercisable on the date of termination shall terminate and be of no further force or effect on the date that is three months following the date of termination, or the Expiration Date if earlier; provided that if the Administrator determines to accelerate the exercisability of any such portion of the Stock Option during such period, such Stock Option shall remain exercisable for the applicable period set forth in this Section 3. The Administrator's determination of the reason for termination of the Optionee's employment or other service relationship shall be conclusive and binding on the Optionee and his or her representatives or legatees.

SECTION 37. Incorporation of Plan. Notwithstanding anything herein to the contrary, this Stock Option shall be subject to and governed by all the terms and conditions of the Plan, including the powers of the Administrator set forth in Section 2(b) of the Plan. Capitalized terms in this Agreement shall have the meaning specified in the Plan, unless a different meaning is specified herein.

SECTION 38. Transferability. This Agreement is personal to the Optionee, is non-assignable and is not transferable in any manner, by operation of law or otherwise, other than by will or the laws of descent and distribution. This Stock Option is exercisable, during the Optionee's lifetime, only by the Optionee, and thereafter, only by the Optionee's legal representative or legatee.

SECTION 39. Tax Withholding. The Optionee shall, not later than the date as of which the exercise of this Stock Option becomes a taxable event for Federal income tax purposes, pay to the Company or make arrangements satisfactory to the Administrator for payment of any Federal, state, and local taxes required by law to be withheld on account of such taxable event. The Company shall have the authority to cause the minimum required tax withholding obligation to be satisfied, in whole or in part, by withholding from shares of Stock to be issued to the Optionee a number of shares of Stock with an aggregate Fair Market Value that would satisfy the minimum withholding amount due.

SECTION 40. No Obligation to Continue Employment. Neither the Company nor any Subsidiary is obligated by or as a result of the Plan or this Agreement to continue the Optionee in employment and neither the Plan nor this Agreement shall interfere in any way with the right of the Company or any Subsidiary to terminate the employment of the Optionee at any time.

SECTION 41. Integration. This Agreement constitutes the entire agreement between the parties with respect to this Stock Option and supersedes all prior agreements and discussions between the parties concerning such subject matter.

SECTION 42. Data Privacy Consent. In order to administer the Plan and this Agreement and to implement or structure future equity grants, the Company, its subsidiaries and affiliates and certain agents thereof (together, the "Relevant Companies") may process any and all personal or professional data, including but not limited to Social Security or other identification number, home address and telephone number, date of birth and other information that is necessary or desirable for the administration of the Plan and/or this Agreement (the "Relevant Information"). By entering into this Agreement, the Optionee (i) authorizes the Company to collect, process, register and transfer to the Relevant Companies all Relevant Information; (ii) waives any privacy rights the Optionee may have with respect to the Relevant Information; (iii) authorizes the Relevant Companies to store and transmit such information in electronic form; and (iv) authorizes the transfer of the Relevant Information to any jurisdiction in which the Relevant Companies consider appropriate. The Optionee shall have access to, and the right to change, the Relevant Information. Relevant Information will only be used in accordance with applicable law.

SECTION 43. Notices. Notices hereunder shall be mailed or delivered to the Company at its principal place of business and shall be mailed or delivered to the Optionee at the address on file with the Company or, in either case, at such other address as one party may subsequently furnish to the other party in writing.

GLOBAL BLOOD THERAPEUTICS, INC.

By: _____
Name:
Title:

The foregoing Agreement is hereby accepted and the terms and conditions thereof hereby agreed to by the undersigned. Electronic acceptance of this Agreement pursuant to the Company's instructions to the Optionee (including through an online acceptance process) is acceptable.

Dated: _____

_____
Optionee's Signature

Optionee's name and address:

_____

_____

_____

NON-QUALIFIED STOCK OPTION AGREEMENT
FOR NON-EMPLOYEE DIRECTORS
UNDER GLOBAL BLOOD THERAPEUTICS, INC.
2015 STOCK OPTION AND INCENTIVE PLAN

Name of Optionee: _____

No. of Option Shares: _____

Option Exercise Price per Share: $ _____ [6]

Grant Date: _____

Vesting Commencement Date: _____

Expiration Date: _____ [7]

Pursuant to the Global Blood Therapeutics, Inc. 2015 Stock Option and Incentive Plan as amended through the date hereof (the "Plan"), Global Blood Therapeutics, Inc., a Delaware corporation (the "Company"), hereby grants to the Optionee named above, who is a Director of the Company but is not an employee of the Company, an option (the "Stock Option") to purchase on or prior to the Expiration Date specified above all or part of the number of shares of Common Stock, par value $0.001 per share (the "Stock"), of the Company specified above at the Option Exercise Price per Share specified above subject to the terms and conditions set forth herein and in the Plan. This Stock Option is not intended to be an "incentive stock option" under Section 422 of the Internal Revenue Code of 1986, as amended.

1. Exercisability Schedule. No portion of this Stock Option may be exercised until such portion shall have become exercisable. Except as set forth below, and subject to the discretion of the Administrator (as defined in Section 2 of the Plan) to accelerate the exercisability schedule hereunder, this Stock Option shall be exercisable as follows: 1/12th on each month following the grant date on the same day of the month as the grant date (and if there is no corresponding day, on the last day of the applicable month) for 11 months and the remaining 1/12th on the earlier of (i) the one-year anniversary of the grant date or (ii) the Company's next annual meeting of stockholders, so long as the Optionee remains in service as a member of the Board on such dates. Once exercisable, this Stock Option shall continue to be exercisable at any time or times prior to the close of business on the Expiration Date, subject to the provisions hereof and of the Plan.

2. Manner of Exercise.

(a) The Optionee may exercise this Stock Option only in the following manner: from time to time on or prior to the Expiration Date of this Stock Option, the Optionee may give written notice to the Administrator of his or her election to purchase some or all of the Option Shares purchasable at the time of such notice. This notice shall specify the number of Option Shares to be purchased.

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6 Note to Form: FMV on Grant Date

7 Note to Form: No more than 10 years

Payment of the purchase price for the Option Shares may be made by one or more of the following methods: (i) in cash, by certified or bank check or other instrument acceptable to the Administrator; (ii) through the delivery (or attestation to the ownership) of shares of Stock that have been purchased by the Optionee on the open market or that are beneficially owned by the Optionee and are not then subject to any restrictions under any Company plan and that otherwise satisfy any holding periods as may be required by the Administrator; (iii) by the Optionee delivering to the Company a properly executed exercise notice together with irrevocable instructions to a broker to promptly deliver to the Company cash or a check payable and acceptable to the Company to pay the option purchase price, provided that in the event the Optionee chooses to pay the option purchase price as so provided, the Optionee and the broker shall comply with such procedures and enter into such agreements of indemnity and other agreements as the Administrator shall prescribe as a condition of such payment procedure; (iv) by a "net exercise" arrangement pursuant to which the Company will reduce the number of shares of Stock issuable upon exercise by the largest whole number of shares with a Fair Market Value that does not exceed the aggregate exercise price; or (v) a combination of (i), (ii), (iii) and (iv) above. Payment instruments will be received subject to collection.

The transfer to the Optionee on the records of the Company or of the transfer agent of the Option Shares will be contingent upon (i) the Company's receipt from the Optionee of the full purchase price for the Option Shares, as set forth above, (ii) the fulfillment of any other requirements contained herein or in the Plan or in any other agreement or provision of laws, and (iii) the receipt by the Company of any agreement, statement or other evidence that the Company may require to satisfy itself that the issuance of Stock to be purchased pursuant to the exercise of Stock Options under the Plan and any subsequent resale of the shares of Stock will be in compliance with applicable laws and regulations. In the event the Optionee chooses to pay the purchase price by previously-owned shares of Stock through the attestation method, the number of shares of Stock transferred to the Optionee upon the exercise of the Stock Option shall be net of the Shares attested to.

(b) The shares of Stock purchased upon exercise of this Stock Option shall be transferred to the Optionee on the records of the Company or of the transfer agent upon compliance to the satisfaction of the Administrator with all requirements under applicable laws or regulations in connection with such transfer and with the requirements hereof and of the Plan. The determination of the Administrator as to such compliance shall be final and binding on the Optionee. The Optionee shall not be deemed to be the holder of, or to have any of the rights of a holder with respect to, any shares of Stock subject to this Stock Option unless and until this Stock Option shall have been exercised pursuant to the terms hereof, the Company or the transfer agent shall have transferred the shares to the Optionee, and the Optionee's name shall have been entered as the stockholder of record on the books of the Company. Thereupon, the Optionee shall have full voting, dividend and other ownership rights with respect to such shares of Stock.

(c) The minimum number of shares with respect to which this Stock Option may be exercised at any one time shall be 100 shares, unless the number of shares with respect to which this Stock Option is being exercised is the total number of shares subject to exercise under this Stock Option at the time.

(d) Notwithstanding any other provision hereof or of the Plan, no portion of this Stock Option shall be exercisable after the Expiration Date hereof.

2. Termination as Director. If the Optionee ceases to be a Director of the Company, the period within which to exercise the Stock Option may be subject to earlier termination as set forth below.

(a) Termination Due to Death. If the Optionee's service as a Director terminates by reason of the Optionee's death, any portion of this Stock Option outstanding on such date, to the extent exercisable on the date of death, may thereafter be exercised by the Optionee's legal representative or legatee for a period of 12 months from the date of death or until the Expiration Date, if earlier.

(b) Other Termination. If the Optionee ceases to be a Director for any reason other than the Optionee's death, any portion of this Stock Option outstanding on such date may be exercised, to the extent exercisable on the date the Optionee ceased to be a Director, for a period of six months from the date the Optionee ceased to be a Director or until the Expiration Date, if earlier.

Any portion of this Stock Option that is not exercisable on the date of termination shall terminate and be of no further force or effect on the date that is three months following the date of termination, or the Expiration Date if earlier; provided that if the Administrator determines to accelerate the exercisability of any such portion of the Stock Option during such period, such Stock Option shall remain exercisable for the applicable period set forth in this Section 3.

3. Incorporation of Plan. Notwithstanding anything herein to the contrary, this Stock Option shall be subject to and governed by all the terms and conditions of the Plan, including the powers of the Administrator set forth in Section 2(b) of the Plan. Capitalized terms in this Agreement shall have the meaning specified in the Plan, unless a different meaning is specified herein.

4. Transferability. This Agreement is personal to the Optionee, is non-assignable and is not transferable in any manner, by operation of law or otherwise, other than by will or the laws of descent and distribution. This Stock Option is exercisable, during the Optionee's lifetime, only by the Optionee, and thereafter, only by the Optionee's legal representative or legatee.

5. No Obligation to Continue as a Director. Neither the Plan nor this Stock Option confers upon the Optionee any rights with respect to continuance as a Director.

6. Integration. This Agreement constitutes the entire agreement between the parties with respect to this Stock Option and supersedes all prior agreements and discussions between the parties concerning such subject matter.

7. Data Privacy Consent. In order to administer the Plan and this Agreement and to implement or structure future equity grants, the Company, its subsidiaries and affiliates and certain agents thereof (together, the "Relevant Companies") may process any and all personal or professional data, including but not limited to Social Security or other identification number, home address and telephone number, date of birth and other information that is necessary or desirable for the administration of the Plan and/or this Agreement (the "Relevant Information"). By entering into this Agreement, the Grantee (i) authorizes the Company to collect, process, register and transfer to the Relevant Companies all Relevant Information; (ii) waives any privacy rights the Grantee may have with respect to the Relevant Information; (iii) authorizes the Relevant Companies to store and transmit such information in electronic form; and (iv) authorizes the transfer of the Relevant Information to any jurisdiction in which the Relevant Companies consider appropriate. The Grantee shall have access to, and the right to change, the Relevant Information. Relevant Information will only be used in accordance with applicable law.

8. Notices. Notices hereunder shall be mailed or delivered to the Company at its principal place of business and shall be mailed or delivered to the Optionee at the address on file with the Company or, in either case, at such other address as one party may subsequently furnish to the other party in writing.

GLOBAL BLOOD THERAPEUTICS, INC.

By: _____

Name:

Title:

The foregoing Agreement is hereby accepted and the terms and conditions thereof hereby agreed to by the undersigned. Electronic acceptance of this Agreement pursuant to the Company's instructions to the Grantee (including through an online acceptance process) is acceptable.

RESTRICTED STOCK UNIT AWARD AGREEMENT
FOR COMPANY EMPLOYEES
UNDER GLOBAL BLOOD THERAPEUTICS, INC.
2015 STOCK OPTION AND INCENTIVE PLAN

Name of Grantee: _____

No. of Restricted Stock Units: _____

Grant Date: _____

Vesting Commencement Date: _____

Pursuant to the Global Blood Therapeutics, Inc. 2015 Stock Option and Incentive Plan as amended through the date hereof (the "Plan"), Global Blood Therapeutics, Inc., a Delaware corporation (the "Company"), hereby grants an award of the number of Restricted Stock Units listed above (an "Award") to the Grantee named above. Each Restricted Stock Unit shall relate to one share of Common Stock, par value $0.001 per share (the "Stock") of the Company.

1. Restrictions on Transfer of Award. This Award may not be sold, transferred, pledged, assigned or otherwise encumbered or disposed of by the Grantee, and any shares of Stock issuable with respect to the Award may not be sold, transferred, pledged, assigned or otherwise encumbered or disposed of until (i) the Restricted Stock Units have vested as provided in Paragraph 2 of this Agreement and (ii) shares of Stock have been issued to the Grantee in accordance with the terms of the Plan and this Agreement.

2. Vesting of Restricted Stock Units. The restrictions and conditions of Paragraph 1 of this Agreement shall lapse as follows: _____ (each such date, a "Vesting Date"), so long as the Grantee remains an employee or other service provider (including a consultant) of the Company or a Subsidiary on such Dates. The Administrator may at any time accelerate the vesting schedule specified in this Paragraph 2.

3. Termination of Employment or Service Relationship. If the Grantee's employment by or other service relationship with the Company and its Subsidiaries terminates for any reason (including death or disability) prior to the satisfaction of the vesting conditions set forth in Paragraph 2 above, any Restricted Stock Units that have not vested as of such date shall automatically and without notice terminate and be forfeited unless the Administrator otherwise determines, in its sole discretion, within three months following the date of termination, to accelerate all or any portion of such unvested Restricted Stock Units, and neither the Grantee nor any of his or her successors, heirs, assigns, or personal representatives will thereafter have any further rights or interests in such unvested Restricted Stock Units.

4. Issuance of Shares of Stock. As soon as practicable following each Vesting Date (but in no event later than two and one-half months after the end of the year in which the Vesting Date occurs), the Company shall issue to the Grantee the number of shares of Stock equal to the aggregate number of Restricted Stock Units that have vested pursuant to Paragraph 2 of this Agreement on such date and the Grantee shall thereafter have all the rights of a stockholder of the Company with respect to such shares.

5. Incorporation of Plan. Notwithstanding anything herein to the contrary, this Agreement shall be subject to and governed by all the terms and conditions of the Plan, including the powers of the Administrator set forth in Section 2(b) of the Plan. Capitalized terms in this Agreement shall have the meaning specified in the Plan, unless a different meaning is specified herein.

6. Tax Withholding. The Grantee shall, not later than the date as of which the receipt of this Award becomes a taxable event for Federal income tax purposes, pay to the Company or make arrangements satisfactory to the Administrator for payment of any Federal, state, and local taxes required by law to be withheld on account of such taxable event. The Company may, in its sole discretion, satisfy all or any portion of such withholding obligations relating to this Award by any of the means or by a combination of such means described in this Paragraph 6, subject to the other terms set forth herein. Provided that the Grantee makes an advance election, in accordance with procedures established by the Company (including its applicable insider trading policies), prior to the date upon which any portion of the Award vests to satisfy withholding obligations, as to which means or combination of means permitted hereunder Grantee elects, the Company shall allow the Grantee to irrevocably elect any of the following means or a combination of such means to satisfy such withholding obligations through, as applicable, a mandatory arrangement at a brokerage firm designated by the Company that is a member of the Financial Industry Regulatory Authority (a "FINRA Dealer"): (i) withholding from a "same day sale" commitment with the FINRA Dealer whereby the Grantee irrevocably elects to sell a portion of the shares of Stock to be delivered in connection with the settlement of this Award to satisfy such withholding obligation and the Grantee also elects to sell the remaining shares of Stock, and whereby the FINRA Dealer irrevocably commits to forward the proceeds necessary to satisfy the withholding obligation directly to the Company and to forward the remaining cash proceeds to the Grantee; (ii) causing the Grantee to tender a cash payment; (iii) permitting the Grantee to enter into a "same day sale to cover commitment" with the FINRA Dealer whereby the Grantee irrevocably elects to sell a portion of the shares of Stock to be delivered in connection with the settlement of this Award to satisfy such withholding obligation and whereby the FINRA Dealer irrevocably commits to forward the proceeds necessary to satisfy the withholding obligation directly to the Company; or (iv) if authorized or required by the Compensation Committee of the Board, by withholding a number of shares of Stock with an aggregate Fair Market Value equal to such minimum tax withholding obligation. If the Grantee fails to make an election in advance as required by the Company's procedures, or if the Company's insider trading compliance officer determines that the Company's insider trading policies and procedures would prohibit or prevent the Grantee from making any such election, the Grantee shall be deemed to have elected the "same day sale to cover commitment" method under clause (iii) of this Paragraph 6 to satisfy Grantee's withholding obligations.

7. Section 409A of the Code. This Agreement shall be interpreted in such a manner that all provisions relating to the settlement of the Award are exempt from the requirements of Section 409A of the Code as "short-term deferrals" as described in Section 409A of the Code.

8. No Obligation to Continue Employment. Neither the Company nor any Subsidiary is obligated by or as a result of the Plan or this Agreement to continue the Grantee in employment and neither the Plan nor this Agreement shall interfere in any way with the right of the Company or any Subsidiary to terminate the employment of the Grantee at any time.

9. Integration. This Agreement constitutes the entire agreement between the parties with respect to this Award and supersedes all prior agreements and discussions between the parties concerning such subject matter.

10. Data Privacy Consent. In order to administer the Plan and this Agreement and to implement or structure future equity grants, the Company, its subsidiaries and affiliates and certain agents thereof (together, the "Relevant Companies") may process any and all personal or professional data, including but not limited to Social Security or other identification number, home address and telephone number, date of birth and other information that is necessary or desirable for the administration of the Plan and/or this Agreement (the "Relevant Information"). By entering into this Agreement, the Grantee (i) authorizes the Company to collect, process, register and transfer to the Relevant Companies all Relevant Information; (ii) waives any privacy rights the Grantee may have with respect to the Relevant Information; (iii) authorizes the Relevant Companies to store and transmit such information in electronic form; and (iv) authorizes the transfer of the Relevant Information to any jurisdiction in which the Relevant Companies consider appropriate. The Grantee shall have access to, and the right to change, the Relevant Information. Relevant Information will only be used in accordance with applicable law.

11. Notices. Notices hereunder shall be mailed or delivered to the Company at its principal place of business and shall be mailed or delivered to the Grantee at the address on file with the Company or, in either case, at such other address as one party may subsequently furnish to the other party in writing.

GLOBAL BLOOD THERAPEUTICS, INC.

By: _____
Name:
Title:

The foregoing Agreement is hereby accepted and the terms and conditions thereof hereby agreed to by the undersigned. Electronic acceptance of this Agreement pursuant to the Company's instructions to the Grantee (including through an online acceptance process) is acceptable.

Dated: _____

_____
Grantee's Signature

Grantee's name and address:

_____

_____

_____

RESTRICTED STOCK UNIT AWARD AGREEMENT
FOR NON-EMPLOYEE DIRECTORS
UNDER GLOBAL BLOOD THERAPEUTICS, INC.
2015 STOCK OPTION AND INCENTIVE PLAN

Name of Grantee: _____

No. of Restricted Stock Units: _____

Grant Date: _____

Vesting Commencement Date: _____

Pursuant to the Global Blood Therapeutics, Inc. 2015 Stock Option and Incentive Plan as amended through the date hereof (the "Plan"), Global Blood Therapeutics, Inc., a Delaware corporation (the "Company"), hereby grants an award of the number of Restricted Stock Units listed above (an "Award") to the Grantee named above. Each Restricted Stock Unit shall relate to one share of Common Stock, par value $0.001 per share (the "Stock") of the Company.

1. Restrictions on Transfer of Award. This Award may not be sold, transferred, pledged, assigned or otherwise encumbered or disposed of by the Grantee, and any shares of Stock issuable with respect to the Award may not be sold, transferred, pledged, assigned or otherwise encumbered or disposed of until (i) the Restricted Stock Units have vested as provided in Paragraph 2 of this Agreement and (ii) shares of Stock have been issued to the Grantee in accordance with the terms of the Plan and this Agreement.

2. Vesting of Restricted Stock Units. The restrictions and conditions of Paragraph 1 of this Agreement shall lapse as follows: 100% on the earlier of (i) the one-year anniversary of the grant date or (ii) the Company's next annual meeting of stockholders (each such date, a "Vesting Date"), so long as the Grantee remains in service as a member of the Board on such Dates. The Administrator may at any time accelerate the vesting schedule specified in this Paragraph 2.

3. Termination of Service. If the Grantee's service as a member of the Board terminates for any reason (including death or disability) prior to the satisfaction of the vesting conditions set forth in Paragraph 2 above, any Restricted Stock Units that have not vested as of such date shall automatically and without notice terminate and be forfeited, unless the Administrator otherwise determines, in its sole discretion, within three months following the date of termination, to accelerate all or any portion of such unvested Restricted Stock Units, and neither the Grantee nor any of his or her successors, heirs, assigns, or personal representatives will thereafter have any further rights or interests in such unvested Restricted Stock Units.

4. Issuance of Shares of Stock. As soon as practicable following each Vesting Date (but in no event later than two and one-half months after the end of the year in which the Vesting Date occurs), the Company shall issue to the Grantee the number of shares of Stock equal to the aggregate number of Restricted Stock Units that have vested pursuant to Paragraph 2 of this Agreement on such date and the Grantee shall thereafter have all the rights of a stockholder of the Company with respect to such shares.

5. Incorporation of Plan. Notwithstanding anything herein to the contrary, this Agreement shall be subject to and governed by all the terms and conditions of the Plan, including the powers of the Administrator set forth in Section 2(b) of the Plan. Capitalized terms in this Agreement shall have the meaning specified in the Plan, unless a different meaning is specified herein.

6. Section 409A of the Code. This Agreement shall be interpreted in such a manner that all provisions relating to the settlement of the Award are exempt from the requirements of Section 409A of the Code as "short-term deferrals" as described in Section 409A of the Code.

7. No Obligation to Continue as a Director. Neither the Plan nor this Award confers upon the Grantee any rights with respect to continuance as a Director and neither the Plan nor this Award shall interfere in any way with the right of the Company to terminate the service of the Grantee as a Director at any time.

8. Integration. This Agreement constitutes the entire agreement between the parties with respect to this Award and supersedes all prior agreements and discussions between the parties concerning such subject matter.

9. Data Privacy Consent. In order to administer the Plan and this Agreement and to implement or structure future equity grants, the Company, its subsidiaries and affiliates and certain agents thereof (together, the "Relevant Companies") may process any and all personal or professional data, including but not limited to Social Security or other identification number, home address and telephone number, date of birth and other information that is necessary or desirable for the administration of the Plan and/or this Agreement (the "Relevant Information"). By entering into this Agreement, the Grantee (i) authorizes the Company to collect, process, register and transfer to the Relevant Companies all Relevant Information; (ii) waives any privacy rights the Grantee may have with respect to the Relevant Information; (iii) authorizes the Relevant Companies to store and transmit such information in electronic form; and (iv) authorizes the transfer of the Relevant Information to any jurisdiction in which the Relevant Companies consider appropriate. The Grantee shall have access to, and the right to change, the Relevant Information. Relevant Information will only be used in accordance with applicable law.

10. Notices. Notices hereunder shall be mailed or delivered to the Company at its principal place of business and shall be mailed or delivered to the Grantee at the address on file with the Company or, in either case, at such other address as one party may subsequently furnish to the other party in writing.

GLOBAL BLOOD THERAPEUTICS, INC.

By: _____
Name:
Title:

The foregoing Agreement is hereby accepted and the terms and conditions thereof hereby agreed to by the undersigned. Electronic acceptance of this Agreement pursuant to the Company's instructions to the Grantee (including through an online acceptance process) is acceptable.

Dated: _____

_____
Grantee's Signature

Grantee's name and address:

_____

_____

_____

Exhibit 10.7

GLOBAL BLOOD THERAPEUTICS, INC.
AMENDED AND RESTATED CASH INCENTIVE BONUS PLAN

1. Purpose

This Amended and Restated Cash Incentive Bonus Plan (the "***Plan***") is intended to provide an annual incentive for superior work and to help motivate eligible employees of Global Blood Therapeutics, Inc. (the "***Company***") toward even higher achievement and business results, to further tie their goals and interests to those of the Company and its stockholders and to help enable the Company to attract and retain highly qualified employees. This Plan is intended to cover (i) eligible employees of the Company and (ii) eligible employees of the Company's wholly owned subsidiary Global Blood Therapeutics GmbH registered in Switzerland. For purposes of this Plan, the term "Company" is used herein to refer to either Global Blood Therapeutics, Inc. or Global Blood Therapeutics GmbH.

2. Participants

Except as provided in the remainder of this paragraph, each full-time and part-time employee of the Company who is employed for more than 30 hours a week and employed on the last day of the applicable Plan Year (except as specifically provided in Section 7) whose employment start date is before October 1st of the applicable Plan Year may participate in the Plan (each, a "***Participant***"). Temporary employees are not eligible to participate in the Plan, and sales employees who are eligible to participate in sales incentive compensation plans of the Company are not eligible to participate in the Plan.

3. Plan Year

The "Plan Year" is the calendar year.

4. Target Bonus Percentages

"Target Bonus Percentage" levels are the percentages of base salary that are generally expected to apply for bonuses under the Plan for any Plan Year at the position levels below. Target Bonus Percentage levels may vary from Plan Year to Plan Year and between positions. However, as a general guideline, the Target Bonus Percentage levels, which will typically be assigned to various categories of employees (and vary depending on responsibility level within each category), are as follows:

Position Level	Bonus Target	Weighting % (Corp./ Indiv.)
CEO	70%	100 / 0
EVP/C-Suite	50%	80 / 20
SVP (Section 16 or SMT)	45%	80 / 20
SVP	40%	60 / 40
VP	35%	60 / 40
Executive Director	32%	50 / 50

Senior Director / Sr. Principal Scientist	28%	50 / 50
Director / Principal Scientist	23%	40 / 60
Associate Director / Staff Scientist	20%	25 / 75
Sr. Manager / Sr. Scientist	18%	25 / 75
Manager / Scientist 2	15%	25 / 75
Associate Scientist / Scientist 1	12%	25 / 75
Analyst / Executive Assistant / Sr. Research Associate / Patient Navigator	12%	25 / 75
Sr. Administrative Assistant / Research Associate / Coordinator	10%	25 / 75
Support	10%	25 / 75

If a Participant moves to a higher Target Bonus Percentage level during the Plan Year, that Participant's Target Bonus Percentage will be reset at the higher level for the entire Plan Year. If a Participant moves to a lower Target Bonus Percentage level during the Plan Year, that Participant's Target Bonus Percentage will be reset at the lower level for the entire Plan Year. Target Bonus Percentage levels may be determined by the Compensation Committee of the Board of Directors of the Company (the "***Compensation Committee***"), in its sole discretion.

5. Administration

The Plan will be administered by the Compensation Committee, in its sole discretion, or, to the extent delegated by the Compensation Committee, a committee consisting of the Company's Chief Executive Officer and at least one other executive officer of the Company for Participants except (i) those at or above the level of Vice President who report directly to the Company's Chief Executive Officer or (ii) any "officers" as defined in Section 16 of the Securities Exchange Act of 1934, as amended, and Rule 16a-1 promulgated thereunder.

6. Bonus Determinations

(a) Corporate Performance Goals. A Participant may receive a bonus payment under the Plan based upon the attainment of one or more performance objectives that are established by the Compensation Committee and relate to financial and operational metrics with respect to the Company or any of its subsidiaries (the "***Corporate Performance Goals***").

(b) Calculation of Corporate Performance Goals. Corporate Performance Goals will be calculated in accordance with the Company's financial statements, generally accepted accounting principles, or under a methodology established by the Compensation Committee at the beginning of the Plan Year and that is consistently applied with respect to a Corporate Performance Goal in the relevant Plan Year.

(c) Target; Minimum; Maximum. Each Corporate Performance Goal shall have a "target" (100% attainment of the Corporate Performance Goal) and may also have a "minimum" hurdle and/or a "maximum" amount.

(d) Bonus Requirements. Except as otherwise set forth in this Section 6(d): (i) any bonuses paid to Participants under the Plan shall be based upon (A) objectively determinable

bonus formulas that tie such bonuses to one or more performance targets relating to the Corporate Performance Goals and/or (B) the Participant's contribution to the Company's success and his/her success in achieving his/her individual objectives for the Plan Year, (ii) bonus formulas for Participants shall be adopted for each Plan Year by the Compensation Committee (or its delegate, as applicable) and communicated to each Participant at the beginning of each Plan Year and (iii) no bonuses shall be paid to Participants unless and until the Compensation Committee (or its delegate, as applicable) makes a determination with respect to the attainment of the performance targets relating to the Corporate Performance Goals and/or individual objectives. If an employee who becomes a Participant during a Plan Year was not employed for the entire Plan Year, the Compensation Committee (or its delegate, if applicable) may prorate the bonus based on the number of days employed during the Plan Year. In addition, a Participant who is on a leave of absence during the Plan Year may be eligible for a prorated bonus amount provided that he or she has been actively employed by the Company during the Plan Year, has attained the applicable Corporate Performance Goals and/or individual objectives, as determined by the Compensation Committee, and is an active employee of the Company when bonuses are paid (except as specifically provided in Section 7). Notwithstanding the foregoing, the Compensation Committee may adjust bonuses payable under the Plan in its sole discretion.

(e) Individual Target Bonuses. The Compensation Committee (or its delegate, as applicable) shall establish a target bonus opportunity for each Participant for each Plan Year. For each Participant, the Compensation Committee (or its delegate, as applicable) shall have the authority to apportion the target award so that a portion of the target award shall be tied to attainment of Corporate Performance Goals and a portion of the target award shall be tied to attainment of individual performance objectives, in accordance with Section 4 above.

7. Termination of Employment; Death; Disability

No bonus will be paid to any employee whose employment is terminated prior to the date the bonus is actually paid by the Company, except if such termination is due to death or disability (as determined by Compensation Committee (or its delegate, as applicable)), unless otherwise specifically agreed by the Compensation Committee (or its delegate, as applicable).

If the Participant's employment with the Company terminates by reason of the Participant's disability or death during the Plan Year, the Participant or the Participant's legal representative, as applicable, will be paid a bonus in cash (if and to the extent earned) based upon actual base salary of the Participant from the beginning of the Plan Year through the date of disability, or death, as applicable. Any such bonus will be paid at the same time at which all other Participants receive their bonuses for the Plan Year, but in no event later than 2 ½ months following the end of the Plan Year in which the death or disability, as applicable, occurs.

8. Payment of Awards

Awards for any Plan Year will be paid in cash to a Participant or the Participant's legal representative, as applicable, no later than 2 ½ months following the end of applicable Plan Year. Benefits under the Plan are not transferable, and the Plan is unfunded.

9. Withholding of Taxes

Bonuses will be subject to income tax, if applicable, and employment tax withholding and contributions as required by applicable law.

10. Plan Amendments and Termination.

The Plan may be revised, modified, or terminated at any time in the sole discretion of the Compensation Committee or the Board.

Adopted: January 6, 2016
Amended and restated: January 7, 2020
Amended and restated: November 30, 2020, effective as of January 1, 2021

Exhibit 10.8

GLOBAL BLOOD THERAPEUTICS, INC.

AMENDED AND RESTATED 2017 INDUCEMENT EQUITY PLAN

SECTION 1. GENERAL PURPOSE OF THE PLAN; DEFINITIONS

The name of the plan is the Global Blood Therapeutics, Inc. Amended and Restated 2017 Inducement Equity Plan (the "Plan"). The purpose of the Plan is to enable Global Blood Therapeutics, Inc., a Delaware corporation (the "Company"), and its Subsidiaries to grant equity awards to induce highly-qualified prospective officers and employees who are not currently employed by the Company or its Subsidiaries to accept employment and to provide them with a proprietary interest in the Company. It is anticipated that providing such persons with a direct stake in the Company's welfare will assure a closer identification of their interests with those of the Company and its stockholders, thereby stimulating their efforts on the Company's behalf and strengthening their desire to remain with the Company. The Company intends that the Plan be reserved for persons to whom the Company may issue securities without stockholder approval as an inducement pursuant to Rule 5635(c)(4) of the Marketplace Rules of the NASDAQ Stock Market, Inc.

The following terms shall be defined as set forth below:

"*Administrator*" means either the Board or the compensation committee of the Board or a similar committee performing the functions of the compensation committee and which is comprised of not less than two Non-Employee Directors who are independent.

"*Award*" or "*Awards,*" except where referring to a particular category of grant under the Plan, shall include Stock Options, Stock Appreciation Rights, Restricted Stock Units, Restricted Stock Awards, Unrestricted Stock Awards and Dividend Equivalent Rights.

"*Award Certificate*" means a written or electronic document setting forth the terms and provisions applicable to an Award granted under the Plan. Each Award Certificate is subject to the terms and conditions of the Plan.

"*Board*" means the Board of Directors of the Company.

"*Code*" means the Internal Revenue Code of 1986, as amended, and any successor Code, and related rules, regulations and interpretations.

"*Dividend Equivalent Right*" means an Award entitling the grantee to receive credits based on cash dividends that would have been paid on the shares of Stock specified in the Dividend Equivalent Right (or other award to which it relates) if such shares had been issued to and held by the grantee.

"*Effective Date*" means the date on which the Plan is approved by the Board as set forth in Section 18.

"*Exchange Act*" means the Securities Exchange Act of 1934, as amended, and the rules and regulations thereunder.

"*Fair Market Value*" of the Stock on any given date means the fair market value of the Stock determined in good faith by the Administrator; provided, however, that if the Stock is admitted to quotation on the NASDAQ Capital Market, the NASDAQ Global Market, the NASDAQ Global Select Market, the New York Stock Exchange or another national securities exchange, the determination shall be made by reference to the closing price of the Stock as quoted on the applicable exchange. If there is no closing price for such date, the determination shall be made by reference to the last date preceding such date for which there is a closing price.

"*Non-Employee Director*" means a member of the Board who is not also an employee of the Company or any Subsidiary.

"*Option*" or "*Stock Option*" means any option to purchase shares of Stock granted pursuant to Section 5.

"*Restricted Shares*" means the shares of Stock underlying a Restricted Stock Award that remain subject to a risk of forfeiture or the Company's right of repurchase.

"*Restricted Stock Award*" means an Award of Restricted Shares subject to such restrictions and conditions as the Administrator may determine at the time of grant.

"*Restricted Stock Units*" means an Award of stock units subject to such restrictions and conditions as the Administrator may determine at the time of grant.

"*Sale Event*" shall mean (i) the sale of all or substantially all of the assets of the Company on a consolidated basis to an unrelated person or entity, (ii) a merger, reorganization or consolidation pursuant to which the holders of the Company's outstanding voting power and outstanding stock immediately prior to such transaction do not own a majority of the outstanding voting power and outstanding stock or other equity interests of the resulting or successor entity (or its ultimate parent, if applicable) immediately upon completion of such transaction, (iii) the sale of all of the Stock of the Company to an unrelated person, entity or group thereof acting in concert, or (iv) any other transaction in which the owners of the Company's outstanding voting power immediately prior to such transaction do not own at least a majority of the outstanding voting power of the Company or any successor entity immediately upon completion of the transaction other than as a result of the acquisition of securities directly from the Company.

"*Sale Price*" means the value as determined by the Administrator of the consideration payable, or otherwise to be received by stockholders, per share of Stock pursuant to a Sale Event.

"*Section 409A*" means Section 409A of the Code and the regulations and other guidance promulgated thereunder.

"*Stock*" means the Common Stock, par value $0.001 per share, of the Company, subject to adjustments pursuant to Section 3.

"*Stock Appreciation Right*" means an Award entitling the recipient to receive shares of Stock having a value equal to the excess of the Fair Market Value of the Stock on the date of exercise over the exercise price of the Stock Appreciation Right multiplied by the number of shares of Stock with respect to which the Stock Appreciation Right shall have been exercised.

"*Subsidiary*" means any corporation or other entity (other than the Company) in which the Company has at least a 50 percent interest, either directly or indirectly.

"*Unrestricted Stock Award*" means an Award of shares of Stock free of any restrictions.

SECTION 2. ADMINISTRATION OF PLAN; ADMINISTRATOR AUTHORITY TO SELECT GRANTEES AND DETERMINE AWARDS

(a) Administration of Plan. The Plan shall be administered by the Administrator.

(b) Powers of Administrator. The Administrator shall have the power and authority to grant Awards consistent with the terms of the Plan, including the power and authority:

(i) to select the individuals to whom Awards may from time to time be granted;

(ii) to determine the time or times of grant, and the extent, if any, of Stock Options, Stock Appreciation Rights, Restricted Stock Awards, Restricted Stock Units, Unrestricted Stock Awards and Dividend Equivalent Rights, or any combination of the foregoing, granted to any one or more grantees;

(iii) to determine the number of shares of Stock to be covered by any Award;

(iv) to determine and modify from time to time the terms and conditions, including restrictions, not inconsistent with the terms of the Plan, of any Award, which terms and conditions may differ among individual Awards and grantees, and to approve the forms of Award Certificates;

(v) to accelerate at any time the exercisability or vesting of all or any portion of any Award;

(vi) subject to the provisions of Section 5(c), to extend at any time the period in which Stock Options may be exercised; and

(vii) at any time to adopt, alter and repeal such rules, guidelines and practices for administration of the Plan and for its own acts and proceedings as it shall deem advisable; to interpret the terms and provisions of the Plan and any Award (including related written instruments); to make all determinations it deems advisable for the administration of the Plan; to decide all disputes arising in connection with the Plan; and to otherwise supervise the administration of the Plan.

All decisions and interpretations of the Administrator shall be binding on all persons, including the Company and Plan grantees.

(c) Award Certificate. Awards under the Plan shall be evidenced by Award Certificates that set forth the terms, conditions and limitations for each Award which may include, without limitation, the term of an Award and the provisions applicable in the event employment or service terminates.

(d) Indemnification. Neither the Board nor the Administrator, nor any member of either or any delegate thereof, shall be liable for any act, omission, interpretation, construction or determination made in good faith in connection with the Plan, and the members of the Board and the Administrator (and any delegate thereof) shall be entitled in all cases to indemnification and reimbursement by the Company in respect of any claim, loss, damage or expense (including, without limitation, reasonable attorneys' fees) arising or resulting therefrom to the fullest extent permitted by law and/or under the Company's certificate of incorporation or bylaws or any directors' and officers' liability insurance coverage which may be in effect from time to time and/or any indemnification agreement between such individual and the Company.

(e) Foreign Award Recipients. Notwithstanding any provision of the Plan to the contrary, in order to comply with the laws in other countries in which the Company and its Subsidiaries operate or have employees or other individuals eligible for Awards, the Administrator, in its sole discretion, shall have the power and authority to: (i) determine which Subsidiaries shall be covered by the Plan; (ii) determine which individuals outside the United States are eligible to participate in the Plan; (iii) modify the terms and conditions of any Award granted to individuals outside the United States to comply with applicable foreign laws; (iv) establish subplans and modify exercise procedures and other terms and procedures, to the extent the Administrator determines such actions to be necessary or advisable (and such subplans and/or modifications shall be attached to this Plan as appendices); provided, however, that no such subplans and/or modifications shall increase the share limitation contained in Section 3(a) hereof; and (v) take any action, before or after an Award is made, that the Administrator determines to be necessary or advisable to obtain approval or comply with any local governmental regulatory exemptions or approvals. Notwithstanding the foregoing, the Administrator may not take any actions hereunder, and no Awards shall be granted, that would violate the Exchange Act or any other applicable United States securities law, the Code, or any other applicable United States governing statute or law.

SECTION 3. STOCK ISSUABLE UNDER THE PLAN; MERGERS; SUBSTITUTION

(a) Stock Issuable. The maximum number of shares of Stock reserved and available for issuance under the Plan shall be 4,400,000 shares, subject to adjustment as provided in Section 3(c). For purposes of this limitation, the shares of Stock underlying any Awards under the Plan that are forfeited, canceled, held back upon exercise of an Option or settlement of an Award to cover the exercise price or tax withholding, reacquired by the Company prior to vesting, satisfied without the issuance of Stock or otherwise terminated (other than by exercise or settlement) shall be added back to the shares of Stock available for issuance under the Plan. In the event the Company repurchases shares of Stock on the open market, such shares shall not be added to the shares of Stock available for issuance under the Plan. Subject to such overall limitation, shares of Stock may be issued up to such maximum number pursuant to any type or types of Award. The shares available for issuance under the Plan may be authorized but unissued shares of Stock or shares of Stock reacquired by the Company.

(b) [Reserved].

(c) Changes in Stock. Subject to Section 3(d) hereof, if, as a result of any reorganization, recapitalization, reclassification, stock dividend, stock split, reverse stock split or other similar change in the Company's capital stock, the outstanding shares of Stock are increased or decreased or are exchanged for a different number or kind of shares or other securities of the Company, or additional shares or new or different shares or other securities of the Company or other non-cash assets are distributed with respect to such shares of Stock or other securities, or, if, as a result of any merger or consolidation, sale of all or substantially all of the assets of the Company, the outstanding shares of Stock are converted into or exchanged for securities of the Company or any successor entity (or a parent or subsidiary thereof), the Administrator shall make an appropriate or proportionate adjustment in (i) the maximum number of shares reserved for issuance under the Plan, (ii) the number and kind of shares or other securities subject to any then outstanding Awards under the Plan, (iii) the repurchase price, if any, per share subject to each outstanding Restricted Stock Award, and (iv) the exercise price for each share subject to any then outstanding Stock Options and Stock Appreciation Rights under the Plan, without changing the aggregate exercise price (i.e., the exercise price multiplied by the number of Stock Options and Stock Appreciation Rights) as to which such Stock Options and Stock Appreciation Rights remain exercisable. The Administrator shall also make equitable or proportionate adjustments in the number of shares subject to outstanding Awards and the exercise price and the terms of outstanding Awards to take into consideration cash dividends paid other than in the ordinary course or any other extraordinary corporate event. The adjustment by the Administrator shall be final, binding and conclusive. No fractional shares of Stock shall be issued under the Plan resulting from any such adjustment, but the Administrator in its discretion may make a cash payment in lieu of fractional shares.

(d) Mergers and Other Transactions. Except as the Administrator may otherwise specify with respect to particular Awards in the applicable Award Certificate, in the case of and subject to the consummation of a Sale Event, the parties thereto may cause the assumption or continuation of Awards theretofore granted by the successor entity, or the substitution of such Awards with new Awards of the successor entity or parent thereof, with appropriate adjustment as to the number and kind of shares and, if appropriate, the per share exercise prices, as such parties shall agree. To the extent the parties to such Sale Event do not provide for the assumption, continuation or substitution of Awards, the Plan and all outstanding Awards hereunder will terminate upon the effective time of the Sale Event. Notwithstanding the foregoing, the Administrator may, in its discretion or to the extent provided in the relevant Award Certificate, cause certain Awards to become vested and/or exercisable immediately prior to such Sale Event. In the event of such termination, (i) the Company shall have the right, but not the obligation, to make or provide for a cash payment to the grantees holding Options and Stock Appreciation Rights, in exchange for the cancellation thereof, in an amount equal to the difference between (A) the Sale Price multiplied by the number of shares of Stock subject to outstanding Options and Stock Appreciation Rights (to the extent then exercisable after taking into account any acceleration thereunder at prices not in excess of the Sale Price) and (B) the aggregate exercise price of all such outstanding Options and Stock Appreciation Rights; or (ii) each grantee shall be permitted, within a specified period of time prior to the consummation of the Sale Event as determined by the Administrator, to exercise all outstanding Options and Stock Appreciation Rights (to the extent then exercisable) held by such grantee, including those that

will become exercisable upon the consummation of the Sale Event (provided that such exercise shall be subject to the consummation of the Sale Event). The Company shall also have the right, but not the obligation, to make or provide a cash payment to the grantees holding other Awards, in exchange for cancellation thereof an amount equal to the Sale Price multiplied by the number of shares subject to such Awards, to be paid at the time of the Sale Event or upon the later vesting of such Awards.

Notwithstanding anything to the contrary herein, in the event a grantee's service relationship is terminated by the Company or any successor without Cause within one year following the consummation of a Sale Event, any Awards assumed or substituted in a Sale Event which are subject to vesting conditions, the lapse or achievement of any conditions and/or a right of repurchase in favor of the Company or a successor entity, shall accelerate in full, and any Awards accelerated in such manner with conditions and restrictions relating to the attainment of performance goals will be deemed achieved at one hundred percent (100%) of target levels. As used in this subsection (d) only, "Cause" shall mean dismissal as a result of (i) any material breach by the grantee of any agreement between the grantee and the Company; (ii) the conviction of, indictment for or plea of nolo contendere by the grantee to a felony or a crime involving moral turpitude; or (iii) any material misconduct or willful and deliberate non-performance (other than by reason of disability) by the grantee of the grantee's duties to the Company.

SECTION 4. ELIGIBILITY

Grantees under the Plan will be such full or part-time officers and other employees of the Company and its Subsidiaries to whom the Company may issue securities without stockholder approval in accordance with Rule 5635(c)(4) of the Marketplace Rules of the NASDAQ Stock Market, Inc., as selected from time to time by the Administrator in its sole discretion.

SECTION 5. STOCK OPTIONS

(a) Award of Stock Options. The Administrator may grant Stock Options under the Plan. Any Stock Option granted under the Plan shall be in such form as the Administrator may from time to time approve. All Stock Options granted under the Plan shall be non-qualified stock options.

Stock Options granted pursuant to this Section 5 shall be subject to the following terms and conditions and shall contain such additional terms and conditions, not inconsistent with the terms of the Plan, as the Administrator shall deem desirable.

(b) Exercise Price. The exercise price per share for the Stock covered by a Stock Option granted pursuant to this Section 5 shall be determined by the Administrator at the time of grant but shall not be less than one hundred percent (100%) of the Fair Market Value on the date of grant.

(c) Option Term. The term of each Stock Option shall be fixed by the Administrator, but no Stock Option shall be exercisable more than ten years after the date the Stock Option is granted.

(d) Exercisability; Rights of a Stockholder. Stock Options shall become exercisable at such time or times, whether or not in installments, as shall be determined by the Administrator at or after the grant date. The Administrator may at any time accelerate the exercisability of all or any portion of any Stock Option. An optionee shall have the rights of a stockholder only as to shares acquired upon the exercise of a Stock Option and not as to unexercised Stock Options.

(e) Method of Exercise. Stock Options may be exercised in whole or in part, by giving written or electronic notice of exercise to the Company, specifying the number of shares to be purchased. Payment of the purchase price may be made by one or more of the following methods except to the extent otherwise provided in the Option Award Certificate:

(i) In cash, by certified or bank check or other instrument acceptable to the Administrator;

(ii) Through the delivery (or attestation to the ownership following such procedures as the Company may prescribe) of shares of Stock that are not then subject to restrictions under any Company plan. Such surrendered shares shall be valued at Fair Market Value on the exercise date;

(iii) By the optionee delivering to the Company a properly executed exercise notice together with irrevocable instructions to a broker to promptly deliver to the Company cash or a check payable and acceptable to the Company for the purchase price; provided that in the event the optionee chooses to pay the purchase price as so provided, the optionee and the broker shall comply with such procedures and enter into such agreements of indemnity and other agreements as the Administrator shall prescribe as a condition of such payment procedure; or

(iv) By a “net exercise” arrangement pursuant to which the Company will reduce the number of shares of Stock issuable upon exercise by the largest whole number of shares with a Fair Market Value that does not exceed the aggregate exercise price.

Payment instruments will be received subject to collection. The transfer to the optionee on the records of the Company or of the transfer agent of the shares of Stock to be purchased pursuant to the exercise of a Stock Option will be contingent upon receipt from the optionee (or a purchaser acting in his stead in accordance with the provisions of the Stock Option) by the Company of the full purchase price for such shares and the fulfillment of any other requirements contained in the Option Award Certificate or applicable provisions of laws (including the satisfaction of any withholding taxes that the Company is obligated to withhold with respect to the optionee). In the event an optionee chooses to pay the purchase price by previously-owned shares of Stock through the attestation method, the number of shares of Stock transferred to the optionee upon the exercise of the Stock Option shall be net of the number of attested shares. In the event that the Company establishes, for itself or using the services of a third party, an automated system for the exercise of Stock Options, such as a system using an internet website or interactive voice response, then the paperless exercise of Stock Options may be permitted through the use of such an automated system.

SECTION 6. STOCK APPRECIATION RIGHTS

(a) Award of Stock Appreciation Rights. The Administrator may grant Stock Appreciation Rights under the Plan. A Stock Appreciation Right is an Award entitling the recipient to receive shares of Stock having a value equal to the excess of the Fair Market Value of a share of Stock on the date of exercise over the exercise price of the Stock Appreciation Right multiplied by the number of shares of Stock with respect to which the Stock Appreciation Right shall have been exercised.

(b) Exercise Price of Stock Appreciation Rights. The exercise price of a Stock Appreciation Right shall not be less than one hundred percent (100%) of the Fair Market Value of the Stock on the date of grant.

(c) Grant and Exercise of Stock Appreciation Rights. Stock Appreciation Rights may be granted by the Administrator independently of any Stock Option granted pursuant to Section 5 of the Plan.

(d) Terms and Conditions of Stock Appreciation Rights. Stock Appreciation Rights shall be subject to such terms and conditions as shall be determined from time to time by the Administrator. The term of a Stock Appreciation Right may not exceed ten years.

SECTION 7. RESTRICTED STOCK AWARDS

(a) Nature of Restricted Stock Awards. The Administrator may grant Restricted Stock Awards under the Plan. A Restricted Stock Award is any Award of Restricted Shares subject to such restrictions and conditions as the Administrator may determine at the time of grant. Conditions may be based on continuing employment (or other service relationship) and/or achievement of pre-established performance goals and objectives. The terms and conditions of each such Award Certificate shall be determined by the Administrator, and such terms and conditions may differ among individual Awards and grantees.

(b) Rights as a Stockholder. Upon the grant of the Restricted Stock Award and payment of any applicable purchase price, a grantee shall have the rights of a stockholder with respect to the voting of the Restricted Shares and receipt of dividends; provided that if the lapse of restrictions with respect to the Restricted Stock Award is tied to the attainment of performance goals, any dividends paid by the Company during the performance period shall accrue and shall not be paid to the grantee until and to the extent the performance goals are met with respect to the Restricted Stock Award. Unless the Administrator shall otherwise determine, (i) uncertificated Restricted Shares shall be accompanied by a notation on the records of the Company or the transfer agent to the effect that they are subject to forfeiture until such Restricted Shares are vested as provided in Section 7(d) below, and (ii) certificated Restricted Shares shall remain in the possession of the Company until such Restricted Shares are vested as provided in Section 7(d) below, and the grantee shall be required, as a condition of the grant, to deliver to the Company such instruments of transfer as the Administrator may prescribe.

(c) Restrictions. Restricted Shares may not be sold, assigned, transferred, pledged or otherwise encumbered or disposed of except as specifically provided herein or in the Restricted Stock Award Certificate. Except as may otherwise be provided by the Administrator either in the Award Certificate or, subject to Section 15 below, in writing after the Award is issued, if a grantee's employment (or other service relationship) with the Company and its Subsidiaries terminates for any reason, any Restricted Shares that have not vested at the time of termination shall automatically and without any requirement of notice to such grantee from or other action by or on behalf of, the Company be deemed to have been reacquired by the Company at its original purchase price (if any) from such grantee or such grantee's legal representative simultaneously with such termination of employment (or other service relationship), and thereafter shall cease to represent any ownership of the Company by the grantee or rights of the grantee as a stockholder. Following such deemed reacquisition of Restricted Shares that are represented by physical certificates, a grantee shall surrender such certificates to the Company upon request without consideration.

(d) Vesting of Restricted Shares. The Administrator at the time of grant shall specify the date or dates and/or the attainment of pre-established performance goals, objectives and other conditions on which the non-transferability of the Restricted Shares and the Company's right of repurchase or forfeiture shall lapse. Subsequent to such date or dates and/or the attainment of such pre-established performance goals, objectives and other conditions, the shares on which all restrictions have lapsed shall no longer be Restricted Shares and shall be deemed "vested."

SECTION 8. RESTRICTED STOCK UNITS

(a) Nature of Restricted Stock Units. The Administrator may grant Restricted Stock Units under the Plan. A Restricted Stock Unit is an Award of stock units that may be settled in shares of Stock upon the satisfaction of such restrictions and conditions at the time of grant. Conditions may be based on continuing employment (or other service relationship) and/or achievement of pre-established performance goals and objectives. The terms and conditions of each such Award Certificate shall be determined by the Administrator, and such terms and conditions may differ among individual Awards and grantees. Except in the case of Restricted Stock Units with a deferred settlement date that complies with Section 409A, at the end of the vesting period, the Restricted Stock Units, to the extent vested, shall be settled in the form of shares of Stock. Restricted Stock Units with deferred settlement dates are subject to Section 409A and shall contain such additional terms and conditions as the Administrator shall determine in its sole discretion in order to comply with the requirements of Section 409A.

(b) Rights as a Stockholder. A grantee shall have the rights as a stockholder only as to shares of Stock acquired by the grantee upon settlement of Restricted Stock Units; provided, however, that the grantee may be credited with Dividend Equivalent Rights with respect to the stock units underlying his Restricted Stock Units, subject to the provisions of Section 10 and such other terms and conditions as the Administrator may determine.

(c) Termination. Except as may otherwise be provided by the Administrator either in the Award Certificate or, subject to Section 13 below, in writing after the Award is issued, a grantee's right in all Restricted Stock Units that have not vested shall automatically terminate upon the grantee's termination of employment (or cessation of service relationship) with the Company and its Subsidiaries for any reason.

SECTION 9. UNRESTRICTED STOCK AWARDS

Grant or Sale of Unrestricted Stock. The Administrator may grant (or sell at par value or such higher purchase price determined by the Administrator) an Unrestricted Stock Award under the Plan. An Unrestricted Stock Award is an Award pursuant to which the grantee may receive shares of Stock free of any restrictions under the Plan. Unrestricted Stock Awards may be granted in respect of past services or other valid consideration, or in lieu of cash compensation due to such grantee.

SECTION 10. DIVIDEND EQUIVALENT RIGHTS

(a) Dividend Equivalent Rights. The Administrator may grant Dividend Equivalent Rights under the Plan. A Dividend Equivalent Right is an Award entitling the grantee to receive credits based on cash dividends that would have been paid on the shares of Stock specified in the Dividend Equivalent Right (or other Award to which it relates) if such shares had been issued to the grantee. A Dividend Equivalent Right may be granted hereunder to any grantee as a component of an award of Restricted Stock Units or Restricted Stock Award or as a freestanding award. The terms and conditions of Dividend Equivalent Rights shall be specified in the Award Certificate. Dividend equivalents credited to the holder of a Dividend Equivalent Right may be paid currently or may be deemed to be reinvested in additional shares of Stock, which may thereafter accrue additional equivalents. Any such reinvestment shall be at Fair Market Value on the date of reinvestment or such other price as may then apply under a dividend reinvestment plan sponsored by the Company, if any. Dividend Equivalent Rights may be settled in cash or shares of Stock or a combination thereof, in a single installment or installments. A Dividend Equivalent Right granted as a component of an Award of Restricted Stock Units or a Restricted Stock Award with performance vesting shall provide that such Dividend Equivalent Right shall be settled only upon settlement or payment of, or lapse of restrictions on, such other Award, and that such Dividend Equivalent Right shall expire or be forfeited or annulled under the same conditions as such other Award.

(b) Termination. Except as may otherwise be provided by the Administrator either in the Award Certificate or, subject to Section 15 below, in writing after the Award is issued, a grantee's rights in all Dividend Equivalent Rights or equivalent interest granted as a component of any award of Restricted Stock Units or Restricted Stock Award that has not yet vested shall automatically terminate upon the grantee's termination of employment (or cessation of service relationship) with the Company and its Subsidiaries for any reason.

SECTION 11. TRANSFERABILITY OF AWARDS

(a) Transferability. Except as provided in Section 11(b) below, during a grantee's lifetime, his or her Awards shall be exercisable only by the grantee, or by the grantee's legal representative or guardian in the event of the grantee's incapacity. No Awards shall be sold, assigned, transferred or otherwise encumbered or disposed of by a grantee other than by will or by the laws of descent and distribution or pursuant to a domestic relations order. No Awards shall be subject, in whole or in part, to attachment, execution, or levy of any kind, and any purported transfer in violation hereof shall be null and void.

(b) Administrator Action. Notwithstanding Section 11(a), the Administrator, in its discretion, may provide either in the Award Certificate regarding a given Award or by subsequent written approval that the grantee (who is an employee) may transfer his or her Stock Options to his or her immediate family members, to trusts for the benefit of such family members, or to partnerships in which such family members are the only partners, provided that the transferee agrees in writing with the Company to be bound by all of the terms and conditions of this Plan and the applicable Award. In no event may an Award be transferred by a grantee for value.

(c) Family Member. For purposes of Section 11(b), "family member" shall mean a grantee's child, stepchild, grandchild, parent, stepparent, grandparent, spouse, former spouse, sibling, niece, nephew, mother-in-law, father-in-law, son-in-law, daughter-in-law, brother-in-law, or sister-in-law, including adoptive relationships, any person sharing the grantee's household (other than a tenant of the grantee), a trust in which these persons (or the grantee) have more than fifty percent (50%) of the beneficial interest, a foundation in which these persons (or the grantee) control the management of assets, and any other entity in which these persons (or the grantee) own more than fifty percent (50%) of the voting interests.

(d) Designation of Beneficiary. To the extent permitted by the Administrator, each grantee to whom an Award has been made under the Plan may designate a beneficiary or beneficiaries to exercise any Award or receive any payment under any Award payable on or after the grantee's death. Any such designation shall be on a form provided for that purpose by the Administrator and shall not be effective until received by the Administrator. If no beneficiary has been designated by a deceased grantee, or if the designated beneficiaries have predeceased the grantee, the beneficiary shall be the grantee's estate.

SECTION 12. TAX WITHHOLDING

(a) Payment by Grantee. Each grantee shall, no later than the date as of which the value of an Award or of any Stock or other amounts received thereunder first becomes includable in the gross income of the grantee for Federal income tax purposes, pay to the Company, or make arrangements satisfactory to the Administrator regarding payment of, any Federal, state, or local taxes of any kind required by law to be withheld by the Company with respect to such income. The Company and its Subsidiaries shall, to the extent permitted by law, have the right to deduct any such taxes from any payment of any kind otherwise due to the grantee. The Company's obligation to deliver evidence of book entry (or stock certificates) to any grantee is subject to and conditioned on tax withholding obligations being satisfied by the grantee.

(b) Payment in Stock. Subject to approval by the Administrator, a grantee may elect to have the Company's minimum required tax withholding obligation satisfied, in whole or in part, by authorizing the Company to withhold from shares of Stock to be issued pursuant to any Award a number of shares with an aggregate Fair Market Value (as of the date the withholding is effected) that would satisfy the withholding amount due. For purposes of share withholding, the Fair Market Value of withheld shares shall be determined in the same manner as the value of Stock includible in income of the Participants. The Administrator may also require Awards to be subject to mandatory share withholding up to the required withholding amount. For purposes of share withholding, the Fair Market Value of withheld shares shall be determined in the same manner as the value of Stock includible in income of the Participants.

SECTION 13. SECTION 409A AWARDS

To the extent that any Award is determined to constitute "nonqualified deferred compensation" within the meaning of Section 409A (a "409A Award"), the Award shall be subject to such additional rules and requirements as specified by the Administrator from time to time in order to comply with Section 409A. In this regard, if any amount under a 409A Award is payable upon a "separation from service" (within the meaning of Section 409A) to a grantee who is then considered a "specified employee" (within the meaning of Section 409A), then no such payment shall be made prior to the date that is the earlier of (i) six months and one day after the grantee's separation from service, or (ii) the grantee's death, but only to the extent such delay is necessary to prevent such payment from being subject to interest, penalties and/or additional tax imposed pursuant to Section 409A. Further, the settlement of any such Award may not be accelerated except to the extent permitted by Section 409A.

SECTION 14. TERMINATION OF EMPLOYMENT, TRANSFER, LEAVE OF ABSENCE, ETC.

(a) Termination of Employment. If the grantee's employer ceases to be a Subsidiary, the grantee shall be deemed to have terminated employment for purposes of the Plan.

(b) For purposes of the Plan, the following events shall not be deemed a termination of employment:

(i) a transfer to the employment of the Company from a Subsidiary or from the Company to a Subsidiary, or from one Subsidiary to another; or

(ii) an approved leave of absence for military service or sickness, or for any other purpose approved by the Company, if the employee's right to re-employment is guaranteed either by a statute or by contract or under the policy pursuant to which the leave of absence was granted or if the Administrator otherwise so provides in writing.

SECTION 15. AMENDMENTS AND TERMINATION

The Board may, at any time, amend (including to increase the number of shares of Stock reserved and available for issuance hereunder) or discontinue the Plan and the Administrator may, at any time, amend or cancel any outstanding Award for the purpose of satisfying changes in law or for any other lawful purpose, but no such action shall adversely affect rights under any outstanding Award without the holder's consent. Except as provided in Section 3(c) or 3(d), without prior stockholder approval, in no event may the Administrator exercise its discretion to reduce the exercise price of outstanding Stock Options or Stock Appreciation Rights or effect repricing through cancellation and re-grants or cancellation of Stock Options or Stock Appreciation Rights in exchange for cash. Nothing in this Section 15 shall limit the Administrator's authority to take any action permitted pursuant to Section 3(c) or 3(d).

SECTION 16. STATUS OF PLAN

With respect to the portion of any Award that has not been settled or exercised and any payments in cash, Stock or other consideration not received by a grantee, a grantee shall have no rights greater than those of a general creditor of the Company unless the Administrator shall otherwise expressly determine in connection with any Award or Awards. In its sole discretion, the Administrator may authorize the creation of trusts or other arrangements to meet the Company's obligations to deliver Stock or make payments with respect to Awards hereunder, provided that the existence of such trusts or other arrangements is consistent with the foregoing sentence.

SECTION 17. GENERAL PROVISIONS

(a) No Distribution. The Administrator may require each person acquiring Stock pursuant to an Award to represent to and agree with the Company in writing that such person is acquiring the shares without a view to distribution thereof.

(b) Delivery of Stock Certificates. Stock certificates to grantees under this Plan shall be deemed delivered for all purposes when the Company or a stock transfer agent of the Company shall have mailed such certificates in the United States mail, addressed to the grantee, at the grantee's last known address on file with the Company. Uncertificated Stock shall be deemed delivered for all purposes when the Company or a Stock transfer agent of the Company shall have given to the grantee by electronic mail (with proof of receipt) or by United States mail, addressed to the grantee, at the grantee's last known address on file with the Company, notice of issuance and recorded the issuance in its records (which may include electronic "book entry" records). Notwithstanding anything herein to the contrary, the Company shall not be required to issue or deliver any certificates evidencing shares of Stock pursuant to the exercise of any Award, unless and until the Administrator has determined, with advice of counsel (to the extent the Administrator deems such advice necessary or advisable), that the issuance and delivery of such certificates is in compliance with all applicable laws, regulations of governmental authorities and, if applicable, the requirements of any exchange on which the shares of Stock are listed, quoted or traded. All Stock certificates delivered pursuant to the Plan shall be subject to any stop-transfer orders and other restrictions as the Administrator deems necessary or advisable to comply with federal, state or foreign jurisdiction, securities or other laws, rules and quotation system on which the Stock is listed, quoted or traded. The Administrator may place legends on any Stock certificate to reference restrictions applicable to the Stock. In addition to the terms and conditions provided herein, the Administrator may require that an individual make such reasonable covenants, agreements, and representations as the Administrator, in its discretion, deems necessary or advisable in order to comply with any such laws, regulations, or requirements. The Administrator shall have the right to require any individual to comply with any timing or other restrictions with respect to the settlement or exercise of any Award, including a window-period limitation, as may be imposed in the discretion of the Administrator.

(c) Stockholder Rights. Until Stock is deemed delivered in accordance with Section 17(b), no right to vote or receive dividends or any other rights of a stockholder will exist with respect to shares of Stock to be issued in connection with an Award, notwithstanding the exercise of a Stock Option or any other action by the grantee with respect to an Award.

(d) Other Compensation Arrangements; No Employment Rights. Nothing contained in this Plan shall prevent the Board from adopting other or additional compensation arrangements, including trusts, and such arrangements may be either generally applicable or applicable only in specific cases. The adoption of this Plan and the grant of Awards do not confer upon any employee any right to continued employment with the Company or any Subsidiary.

(e) Trading Policy Restrictions. Option exercises and other Awards under the Plan shall be subject to the Company's insider trading policies and procedures, as in effect from time to time.

(f) Clawback Policy. Awards under the Plan shall be subject to the Company's clawback policy, as in effect from time to time.

SECTION 18. EFFECTIVE DATE OF PLAN

This Plan shall become effective immediately upon the effective date as approved by the Board.

SECTION 19. GOVERNING LAW

This Plan and all Awards and actions taken thereunder shall be governed by, and construed in accordance with, the laws of the State of Delaware, applied without regard to conflict of law principles.

Approved by the Board of Directors: December 1, 2020

Effective Date: January 1, 2021

NON-QUALIFIED STOCK OPTION AGREEMENT
FOR COMPANY EMPLOYEES
UNDER GLOBAL BLOOD THERAPEUTICS, inc.
2017 INDUCEMENT EQUITY PLAN

Name of Optionee: _____

No. of Option Shares: _____

Option Exercise Price per Share: $_____[1]

Grant Date: _____

Vesting Commencement Date: _____

Expiration Date: _____[2]

Pursuant to the Global Blood Therapeutics, Inc. 2017 Inducement Equity Plan as amended through the date hereof (the "Plan"), Global Blood Therapeutics, Inc., a Delaware corporation (the "Company"), hereby grants to the Optionee named above an option (the "Stock Option") to purchase on or prior to the Expiration Date specified above all or part of the number of shares of Common Stock, par value $0.001 per share (the "Stock") of the Company specified above at the Option Exercise Price per Share specified above subject to the terms and conditions set forth herein and in the Plan. For the avoidance of doubt, this Stock Option is not issued under the Company's 2015 Stock Option and Incentive Plan, and does not reduce the share reserve under such equity plan. This Stock Option has been granted as an inducement pursuant to Rule 5635(c)(4) of the Marketplace Rules of the Nasdaq Stock Market, Inc. This Stock Option is not intended to be an "incentive stock option" under Section 422 of the Internal Revenue Code of 1986, as amended.

1. Exercisability Schedule. No portion of this Stock Option may be exercised until such portion shall have become exercisable. Except as set forth below, and subject to the discretion of the Administrator (as defined in Section 2 of the Plan) to accelerate the exercisability schedule hereunder, this Stock Option shall be exercisable as follows: _____, so long as Optionee remains an employee or other service provider (including a consultant) of the Company or a Subsidiary on such dates. Once exercisable, this Stock Option shall continue to be exercisable at any time or times prior to the close of business on the Expiration Date, subject to the provisions hereof and of the Plan.

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1 Note to Form: FMV on Grant Date

2 Note to Form: No more than 10 years

2. Manner of Exercise.

(a) The Optionee may exercise this Stock Option only in the following manner: from time to time on or prior to the Expiration Date of this Stock Option, the Optionee may give written notice to the Administrator of his or her election to purchase some or all of the Option Shares purchasable at the time of such notice. This notice shall specify the number of Option Shares to be purchased.

Payment of the purchase price for the Option Shares may be made by one or more of the following methods: (i) in cash, by certified or bank check or other instrument acceptable to the Administrator; (ii) through the delivery (or attestation to the ownership) of shares of Stock that have been purchased by the Optionee on the open market or that are beneficially owned by the Optionee and are not then subject to any restrictions under any Company plan and that otherwise satisfy any holding periods as may be required by the Administrator; (iii) by the Optionee delivering to the Company a properly executed exercise notice together with irrevocable instructions to a broker to promptly deliver to the Company cash or a check payable and acceptable to the Company to pay the option purchase price, provided that in the event the Optionee chooses to pay the option purchase price as so provided, the Optionee and the broker shall comply with such procedures and enter into such agreements of indemnity and other agreements as the Administrator shall prescribe as a condition of such payment procedure; (iv) by a “net exercise” arrangement pursuant to which the Company will reduce the number of shares of Stock issuable upon exercise by the largest whole number of shares with a Fair Market Value that does not exceed the aggregate exercise price; or (v) a combination of (i), (ii), (iii) and (iv) above. Payment instruments will be received subject to collection.

The transfer to the Optionee on the records of the Company or of the transfer agent of the Option Shares will be contingent upon (i) the Company’s receipt from the Optionee of the full purchase price for the Option Shares, as set forth above, (ii) the fulfillment of any other requirements contained herein or in the Plan or in any other agreement or provision of laws, and (iii) the receipt by the Company of any agreement, statement or other evidence that the Company may require to satisfy itself that the issuance of Stock to be purchased pursuant to the exercise of Stock Options under the Plan and any subsequent resale of the shares of Stock will be in compliance with applicable laws and regulations. In the event the Optionee chooses to pay the purchase price by previously-owned shares of Stock through the attestation method, the number of shares of Stock transferred to the Optionee upon the exercise of the Stock Option shall be net of the Shares attested to.

(b) The shares of Stock purchased upon exercise of this Stock Option shall be transferred to the Optionee on the records of the Company or of the transfer agent upon compliance to the satisfaction of the Administrator with all requirements under applicable laws or regulations in connection with such transfer and with the requirements hereof and of the Plan. The determination of the Administrator as to such compliance shall be final and binding on the Optionee. The Optionee shall not be deemed to be the holder of, or to have any of the rights of a holder with respect to, any shares of Stock subject to this Stock Option unless and until this Stock Option shall have been exercised pursuant to the terms hereof, the Company or the transfer agent shall have transferred the shares to the Optionee, and the Optionee’s name shall have been entered as the stockholder of record on the books of the Company. Thereupon, the Optionee shall have full voting, dividend and other ownership rights with respect to such shares of Stock.

(c) The minimum number of shares with respect to which this Stock Option may be exercised at any one time shall be 100 shares, unless the number of shares with respect to which this Stock Option is being exercised is the total number of shares subject to exercise under this Stock Option at the time.

(d) Notwithstanding any other provision hereof or of the Plan, no portion of this Stock Option shall be exercisable after the Expiration Date hereof.

3. Termination of Employment or Service Relationship. If the Optionee's employment by or other service relationship with the Company or a Subsidiary (as defined in the Plan) is terminated, the period within which to exercise the Stock Option may be subject to earlier termination as set forth below.

(a) Termination Due to Death. If the Optionee's employment or other service relationship terminates by reason of the Optionee's death, any portion of this Stock Option outstanding on such date, to the extent exercisable on the date of death, may thereafter be exercised by the Optionee's legal representative or legatee for a period of 12 months from the date of death or until the Expiration Date, if earlier.

(b) Termination Due to Disability. If the Optionee's employment or other service relationship terminates by reason of the Optionee's disability (as determined by the Administrator), any portion of this Stock Option outstanding on such date, to the extent exercisable on the date of such termination of employment, may thereafter be exercised by the Optionee for a period of 12 months from the date of disability or until the Expiration Date, if earlier.

(c) Termination for Cause. If the Optionee's employment or other service relationship terminates for Cause, any portion of this Stock Option outstanding on such date shall terminate immediately and be of no further force and effect. For purposes hereof, "Cause" shall mean, unless otherwise provided in an employment agreement between the Company and the Optionee, a determination by the Administrator that the Optionee shall be dismissed as a result of (i) any material breach by the Optionee of any agreement between the Optionee and the Company; (ii) the conviction of, indictment for or plea of nolo contendere by the Optionee to a felony or a crime involving moral turpitude; or (iii) any material misconduct or willful and deliberate non-performance (other than by reason of disability) by the Optionee of the Optionee's duties to the Company.

(d) Other Termination. If the Optionee's employment or other service relationship terminates for any reason other than the Optionee's death, the Optionee's disability or Cause, and unless otherwise determined by the Administrator, any portion of this Stock Option outstanding on such date may be exercised, to the extent exercisable on the date of termination, for a period of six months from the date of termination or until the Expiration Date, if earlier.

Any portion of this Stock Option that is not exercisable on the date of termination shall terminate and be of no further force or effect on the date that is three months following the date of termination, or the Expiration Date if earlier; provided that if the Administrator determines to accelerate the exercisability of any such portion of the Stock Option during such period, such Stock Option shall remain exercisable for the applicable period set forth in this Section 3. The Administrator's determination of the reason for termination of the Optionee's employment or other service relationship shall be conclusive and binding on the Optionee and his or her representatives or legatees.

4. Incorporation of Plan. Notwithstanding anything herein to the contrary, this Stock Option shall be subject to and governed by all the terms and conditions of the Plan, including the powers of the Administrator set forth in Section 2(b) of the Plan. Capitalized terms in this Agreement shall have the meaning specified in the Plan, unless a different meaning is specified herein.

5. Transferability. This Agreement is personal to the Optionee, is non-assignable and is not transferable in any manner, by operation of law or otherwise, other than by will or the laws of descent and distribution. This Stock Option is exercisable, during the Optionee's lifetime, only by the Optionee, and thereafter, only by the Optionee's legal representative or legatee.

6. Tax Withholding. The Optionee shall, not later than the date as of which the exercise of this Stock Option becomes a taxable event for Federal income tax purposes, pay to the Company or make arrangements satisfactory to the Administrator for payment of any Federal, state, and local taxes required by law to be withheld on account of such taxable event. The Company shall have the authority to cause the minimum required tax withholding obligation to be satisfied, in whole or in part, by withholding from shares of Stock to be issued to the Optionee a number of shares of Stock with an aggregate Fair Market Value that would satisfy the minimum withholding amount due.

7. No Obligation to Continue Employment. Neither the Company nor any Subsidiary is obligated by or as a result of the Plan or this Agreement to continue the Optionee in employment and neither the Plan nor this Agreement shall interfere in any way with the right of the Company or any Subsidiary to terminate the employment of the Optionee at any time.

8. Integration. This Agreement constitutes the entire agreement between the parties with respect to this Stock Option and supersedes all prior agreements and discussions between the parties concerning such subject matter.

9. Data Privacy Consent. In order to administer the Plan and this Agreement and to implement or structure future equity grants, the Company, its subsidiaries and affiliates and certain agents thereof (together, the "Relevant Companies") may process any and all personal or professional data, including but not limited to Social Security or other identification number, home address and telephone number, date of birth and other information that is necessary or desirable for the administration of the Plan and/or this Agreement (the "Relevant Information"). By entering into this Agreement, the Optionee (i) authorizes the Company to collect, process, register and transfer to the Relevant Companies all Relevant Information; (ii) waives any privacy rights the Optionee may have with respect to the Relevant Information; (iii) authorizes the Relevant Companies to store and transmit such information in electronic form; and (iv) authorizes the transfer of the Relevant Information to any jurisdiction in which the Relevant Companies consider appropriate. The Optionee shall have access to, and the right to change, the Relevant Information. Relevant Information will only be used in accordance with applicable law.

10. Notices. Notices hereunder shall be mailed or delivered to the Company at its principal place of business and shall be mailed or delivered to the Optionee at the address on file with the Company or, in either case, at such other address as one party may subsequently furnish to the other party in writing.

GLOBAL BLOOD THERAPEUTICS, INC.

By: _____
Name:
Title:

The foregoing Agreement is hereby accepted and the terms and conditions thereof hereby agreed to by the undersigned. Electronic acceptance of this Agreement pursuant to the Company's instructions to the Optionee (including through an online acceptance process) is acceptable.

Dated: _____

_____
Optionee's Signature

Optionee's name and address:

_____

_____

_____

RESTRICTED STOCK UNIT AWARD AGREEMENT
FOR COMPANY EMPLOYEES
UNDER GLOBAL BLOOD THERAPEUTICS, INC.
2017 INDUCEMENT EQUITY PLAN

Name of Grantee: _____

No. of Restricted Stock Units: _____

Grant Date: _____

Vesting Commencement Date: _____

Pursuant to the Global Blood Therapeutics, Inc. 2017 Inducement Equity Plan as amended through the date hereof (the "Plan"), Global Blood Therapeutics, Inc., a Delaware corporation (the "Company"), hereby grants an award of the number of Restricted Stock Units listed above (an "Award") to the Grantee named above. Each Restricted Stock Unit shall relate to one share of Common Stock, par value $0.001 per share (the "Stock") of the Company. For the avoidance of doubt, the Award is not issued under the Company's 2015 Stock Option and Incentive Plan, and does not reduce the share reserve under such equity plan. This Award is granted as an "employment inducement award" pursuant to the exemption provided by Rule 5635(c)(4) of the Marketplace Rules of the NASDAQ Stock Market, Inc.

1. Restrictions on Transfer of Award. This Award may not be sold, transferred, pledged, assigned or otherwise encumbered or disposed of by the Grantee, and any shares of Stock issuable with respect to the Award may not be sold, transferred, pledged, assigned or otherwise encumbered or disposed of until (i) the Restricted Stock Units have vested as provided in Paragraph 2 of this Agreement and (ii) shares of Stock have been issued to the Grantee in accordance with the terms of the Plan and this Agreement.

2. Vesting of Restricted Stock Units. The restrictions and conditions of Paragraph 1 of this Agreement shall lapse as follows: _____ (each such date, a "Vesting Date"), so long as the Grantee remains an employee or other service provider (including a consultant) of the Company or a Subsidiary on such Dates. The Administrator may at any time accelerate the vesting schedule specified in this Paragraph 2.

3. Termination of Employment or Service Relationship. If the Grantee's employment by or other service relationship with the Company and its Subsidiaries terminates for any reason (including death or disability) prior to the satisfaction of the vesting conditions set forth in Paragraph 2 above, any Restricted Stock Units that have not vested as of such date shall automatically and without notice terminate and be forfeited unless the Administrator otherwise determines, in its sole discretion, within three months following the date of termination, to accelerate all or any portion of such unvested Restricted Stock Units, and neither the Grantee nor any of his or her successors, heirs, assigns, or personal representatives will thereafter have any further rights or interests in such unvested Restricted Stock Units.

4. Issuance of Shares of Stock. As soon as practicable following each Vesting Date (but in no event later than two and one-half months after the end of the year in which the Vesting Date occurs), the Company shall issue to the Grantee the number of shares of Stock equal to the aggregate number of Restricted Stock Units that have vested pursuant to Paragraph 2 of this Agreement on such date and the Grantee shall thereafter have all the rights of a stockholder of the Company with respect to such shares.

5. Incorporation of Plan. Notwithstanding anything herein to the contrary, this Agreement shall be subject to and governed by all the terms and conditions of the Plan, including the powers of the Administrator set forth in Section 2(b) of the Plan. Capitalized terms in this Agreement shall have the meaning specified in the Plan, unless a different meaning is specified herein.

6. Tax Withholding. The Grantee shall, not later than the date as of which the receipt of this Award becomes a taxable event for Federal income tax purposes, pay to the Company or make arrangements satisfactory to the Administrator for payment of any Federal, state, and local taxes required by law to be withheld on account of such taxable event. The Company may, in its sole discretion, satisfy all or any portion of such withholding obligations relating to this Award by any of the means or by a combination of such means described in this Paragraph 6, subject to the other terms set forth herein. Provided that the Grantee makes an advance election, in accordance with procedures established by the Company (including its applicable insider trading policies), prior to the date upon which any portion of the Award vests to satisfy withholding obligations, as to which means or combination of means permitted hereunder Grantee elects, the Company shall allow the Grantee to irrevocably elect any of the following means or a combination of such means to satisfy such withholding obligations through, as applicable, a mandatory arrangement at a brokerage firm designated by the Company that is a member of the Financial Industry Regulatory Authority (a "FINRA Dealer"): (i) withholding from a "same day sale" commitment with the FINRA Dealer whereby the Grantee irrevocably elects to sell a portion of the shares of Stock to be delivered in connection with the settlement of this Award to satisfy such withholding obligation and the Grantee also elects to sell the remaining shares of Stock, and whereby the FINRA Dealer irrevocably commits to forward the proceeds necessary to satisfy the withholding obligation directly to the Company and to forward the remaining cash proceeds to the Grantee; (ii) causing the Grantee to tender a cash payment; (iii) permitting the Grantee to enter into a "same day sale to cover commitment" with the FINRA Dealer whereby the Grantee irrevocably elects to sell a portion of the shares of Stock to be delivered in connection with the settlement of this Award to satisfy such withholding obligation and whereby the FINRA Dealer irrevocably commits to forward the proceeds necessary to satisfy the withholding obligation directly to the Company; or (iv) if authorized or required by the Compensation Committee of the Board, by withholding a number of shares of Stock with an aggregate Fair Market Value equal to such minimum tax withholding obligation. If the Grantee fails to make an election in advance as required by the Company's procedures, or if the Company's insider trading compliance officer determines that the Company's insider trading policies and procedures would prohibit or prevent the Grantee from making any such election, the Grantee shall be deemed to have elected the "same day sale to cover commitment" method under clause (iii) of this Paragraph 6 to satisfy Grantee's withholding obligations.

7. Section 409A of the Code. This Agreement shall be interpreted in such a manner that all provisions relating to the settlement of the Award are exempt from the requirements of Section 409A of the Code as "short-term deferrals" as described in Section 409A of the Code.

8. No Obligation to Continue Employment. Neither the Company nor any Subsidiary is obligated by or as a result of the Plan or this Agreement to continue the Grantee in employment and neither the Plan nor this Agreement shall interfere in any way with the right of the Company or any Subsidiary to terminate the employment of the Grantee at any time.

9. Integration. This Agreement constitutes the entire agreement between the parties with respect to this Award and supersedes all prior agreements and discussions between the parties concerning such subject matter.

10. Data Privacy Consent. In order to administer the Plan and this Agreement and to implement or structure future equity grants, the Company, its subsidiaries and affiliates and certain agents thereof (together, the "Relevant Companies") may process any and all personal or professional data, including but not limited to Social Security or other identification number, home address and telephone number, date of birth and other information that is necessary or desirable for the administration of the Plan and/or this Agreement (the "Relevant Information"). By entering into this Agreement, the Grantee (i) authorizes the Company to collect, process, register and transfer to the Relevant Companies all Relevant Information; (ii) waives any privacy rights the Grantee may have with respect to the Relevant Information; (iii) authorizes the Relevant Companies to store and transmit such information in electronic form; and (iv) authorizes the transfer of the Relevant Information to any jurisdiction in which the Relevant Companies consider appropriate. The Grantee shall have access to, and the right to change, the Relevant Information. Relevant Information will only be used in accordance with applicable law.

11. Notices. Notices hereunder shall be mailed or delivered to the Company at its principal place of business and shall be mailed or delivered to the Grantee at the address on file with the Company or, in either case, at such other address as one party may subsequently furnish to the other party in writing.

GLOBAL BLOOD THERAPEUTICS, INC.

By: _____

Name:
Title:

The foregoing Agreement is hereby accepted and the terms and conditions thereof hereby agreed to by the undersigned. Electronic acceptance of this Agreement pursuant to the Company's instructions to the Grantee (including through an online acceptance process) is acceptable.

Dated: _____

_____

Grantee's Signature

Grantee's name and address:

_____

_____

_____

Global Blood Therapeutics, Inc.
Amended and Restated Severance and Change in Control Policy

Adopted on July 23, 2015

(amended and restated on January 6, 2016, July 5, 2017, July 26, 2017, December 13, 2017, March 13, 2018, July 23, 2019, October 16, 2019, January 7, 2020, May 26, 2020 and November 30, 2020)

Benefits in Connection with a Sale Event.

In connection with a Sale Event (as defined in the Global Blood Therapeutics, Inc. 2015 Stock Option and Incentive Plan (as may be amended or restated, the "2015 Plan")), employees of Global Blood Therapeutics, Inc. and its subsidiaries and affiliates (collectively, the "Company") will be entitled to receive the following benefits in the event of a termination of their employment or other service relationship with the Company (or its successor or acquirer) without Cause (as defined below) or for Good Reason (as defined below) within one (1) year after the closing of the Sale Event (the "Change in Control Period"), subject to each such employee's execution and non-revocation of a severance agreement within sixty (60) days following the date of such termination, including a general release of claims acceptable to the Company or its successor or acquirer:

- Full acceleration of vesting of all outstanding equity-based awards, including stock options and restricted stock units, under the 2015 Plan, the Company's 2017 Inducement Equity Plan, and such additional equity incentive plans, arrangements and agreements (as each may be further amended or restated) covering employees of the Company as the Company's Board of Directors may adopt and approve from time to time (collectively, "Awards"), and for the sake of clarity, for any Awards accelerated in such manner that contain conditions and restrictions relating to the attainment of performance goals, such performance goals will be deemed achieved at one hundred percent (100%) of target levels; and
- Payment of (a) severance in a lump sum in the amounts set forth below, (b) lump sum target incentive bonus payouts in the amounts set forth below, equal to (i) a percentage, as set forth below, of the employee's Target Incentive Bonus for the year in which the closing of the Sale Event occurred plus (ii) a prorated incentive bonus payout for the portion of the year in which the closing of the Sale Event occurred, prorated based on employee's Target Incentive Bonus and the date of termination of their employment or other service relationship with the Company and (c) if the employee was participating in the Company's group health plan immediately prior to the date of termination of his or her employment and elects COBRA health continuation, payment of a monthly cash payment for the period set forth below or the employee's COBRA health continuation period, whichever ends earlier, in an amount equal to the monthly employer contribution that the Company would have made to provide health insurance to the employee if the employee had remained employed by the Company, including, if applicable, the monthly employer contribution to a health savings account: [1]

[1] Benefits in the below table are reduced by Statutory Benefits as set forth in the "General Provisions" section below.

Position	Severance (Amount of Base Salary)	Incentive Bonus	Benefits Continuation
Chief Executive Officer	18 months	150% Target Incentive Bonus and prorated Target Incentive Bonus	18 months
Senior Management Team ("SMT") members	12 months	100% Target Incentive Bonus and prorated Target Incentive Bonus	12 months
Senior Vice Presidents and Vice Presidents (other than SMT members)	9 months	100% Target Incentive Bonus and prorated Target Incentive Bonus	9 months
All Other Employees	6 months	100% Target Incentive Bonus and prorated Target Incentive Bonus	6 months

Benefits Not in Connection with a Sale Event.

Certain designated employees of the Company who execute a participation letter in substantially the form attached hereto as Exhibit A will be entitled to receive the following benefits in the event of a termination of their employment or other service relationship with the Company (or its successor or acquirer) without Cause or for Good Reason outside of the Change in Control Period, subject to each such employee's execution and non-revocation of a severance agreement within sixty (60) days following the date of such termination, including a general release of claims acceptable to the Company or its successor or acquirer:

- Payment of (a) severance in a lump sum in the amounts set forth below, (b) lump sum target incentive bonus payouts in the amounts set forth below, equal to (i) a percentage, as set forth below, of the employee's Target Incentive Bonus for the year in which such termination of employment or other service relationship occurred plus (ii) a prorated incentive bonus payout for the portion of the year in which such termination of employment or other service relationship occurred, prorated based on employee's Target Incentive Bonus and the date of termination of their employment or other service relationship with the Company and (c) if the employee was participating in the Company's group health plan immediately prior to the date of termination of his or her employment and elects COBRA health continuation, payment of a monthly cash payment for the period set forth below or the employee's COBRA health continuation period, whichever ends earlier, in an amount equal to the monthly employer contribution that the Company would have made to provide health insurance to the employee if the employee had remained employed by the Company, including, if applicable, the monthly employer contribution to a health savings account: [2]

[2] Benefits in the below table are reduced by Statutory Benefits as set forth in the "General Provisions" section below.

Position	Severance (Amount of Base Salary)	Incentive Bonus	Benefits Continuation
Chief Executive Officer	12 months	100% Target Incentive Bonus and prorated Target Incentive Bonus	12 months
SMT members	12 months	N/A	12 months

General Provisions.

For purposes of this Amended and Restated Severance and Change in Control Policy (this "Policy"), SMT members shall include (i) each individual who is then employed by the Company as an executive officer and (ii) such other employees of the Company as may be designated by the Compensation Committee of the Board as SMT members for purposes of this Policy from time to time, which individuals specified in clauses (i) and (ii) shall each continue to be considered SMT members for purposes of general severance and change in control severance benefits so long as they are employed with the Company as SMT members; provided that (a) if any such individual is employed by the Company in any other capacity (other than serving as a SMT member), such individual will be eligible for benefits under this Policy in accordance with their then-applicable level of service as provided above; (b) any individual employed as the Company's Chief Executive Officer shall be eligible for the general severance and change in control severance benefits applicable to the Chief Executive Officer only so long as such individual is employed with the Company as the Chief Executive Officer (and if at any time such individual remains employed by the Company but is not serving as the Chief Executive Officer, e.g., serving as a non-CEO SMT member, such individual will be eligible for benefits under this Policy in accordance with his or her then-applicable level of service as provided above) and (c) any SMT member shall cease to be considered an SMT member for purposes of this Policy upon the termination of such individual's employment with the Company (except to the extent such termination triggers such individual's entitlement to general severance or change in control severance benefits in accordance with this Policy).

The amounts payable pursuant to this Policy shall be paid or commence to be paid within 60 days following the date of termination of employment, provided that if the 60-day period begins in one calendar year and ends in a second calendar year, such payments shall be paid or commence to be paid in the second calendar year by the last day of such 60-day period.

Upon the consummation of a Sale Event, to the extent Section 280G of the Internal Revenue Code is applicable to an employee, such employee shall be entitled to receive either: (a) payment of the full amounts set forth above to which the employee is entitled or (b) payment of such lesser amount that does not trigger excise taxes under Section 280G, whichever results in the employee receiving a higher amount after taking into account all federal, state, and local income, excise and employment taxes.

For purposes of this Policy, "Base Salary" shall mean the greater of (i) the base salary, at the annualized rate, in effect immediately prior to the date of termination or (ii) the base salary, at the annualized rate, in effect immediately prior to the Sale Event, as applicable.

For purposes of this Policy, “Cause” shall mean (i) the employee’s dishonest statements or acts with respect to the Company, or any current or prospective customers, suppliers, vendors or other third parties with which such entity does business, including without limitation, the employee engaging in misappropriation of funds or financial accounting improprieties; (ii) the employee’s commission of (A) a felony or (B) any misdemeanor involving moral turpitude, deceit, dishonesty or fraud; (iii) the employee’s continued non-performance of his or her duties to the Company which has continued for thirty (30) or more days following written notice of such non-performance by the Company; (iv) the employee’s material violation of the Company’s Code of Business Conduct and Ethics or of any of the Company’s other written employment, compliance or other policies as in effect from time to time; (v) the employee’s material violation of any provision of any agreement(s) between the employee and the Company relating to noncompetition, nonsolicitation, confidentiality, nondisclosure and/or assignment of inventions; or (vi) the employee’s failure to cooperate with a bona fide internal investigation or an investigation by regulatory or law enforcement authorities, after being instructed by the Company to cooperate, or the willful destruction or failure to preserve documents or other materials known to be relevant to such investigation or the inducement of others to fail to cooperate or to produce documents or other materials in connection with such investigation.

For purposes of this Policy, “Good Reason” shall mean that the employee followed the “Good Reason Process” following the occurrence of (a) a material diminution in the employee’s job responsibilities (provided that a change in the employee’s job title or reporting relationship shall not be deemed a material diminution in the employee’s job responsibilities), (b) a material diminution in the employee’s base salary or (c) the relocation of the employee’s principal place of business to a location that is more than twenty-five (25) miles from the employee’s then-current location of employment. “Good Reason Process” shall mean that (i) the employee reasonably determines in good faith that a “Good Reason” condition has occurred; (ii) the employee notifies the Company (or its successor) in writing of the first occurrence of the Good Reason condition within 60 days of the first occurrence of such condition; (iii) the employee cooperates in good faith with the Company’s (or its successor’s) efforts, for a period not less than 30 days following such notice (the “Cure Period”), to remedy the condition; (iv) notwithstanding such efforts, the Good Reason condition continues to exist; and (v) the employee terminates his employment within 60 days after the end of the Cure Period. If the Company or its successor cures the Good Reason condition during the Cure Period, Good Reason shall be deemed not to have occurred.

For purposes of this Policy, “Target Incentive Bonus” shall mean the greater of (i) the target bonus in effect immediately prior to the date of termination or (ii) the target bonus in effect immediately prior to the Sale Event, as applicable.

This Policy shall be administered by the Company, and the Company shall have the power and authority to interpret the terms and provisions of this Policy, to make all determinations it deems advisable for the administration of this Policy, to decide all disputes arising in connection with this Policy and to otherwise supervise administration of this Policy. The Company retains the right to amend, revise, change or end this Policy at any point in the future; provided that this Policy may not be amended or terminated during the period commencing on the date that it enters into a definitive agreement that if consummated, would result in a Sale Event and ending on the earlier of (i) one (1) year after a Sale Event and (ii) the termination of the definitive agreement without the consummation of a Sale Event. This Policy does not change the “at-will” employment status of any employee.

In the event an employee of the Company is party to an agreement or other arrangement with the Company that provides greater benefits than set forth in this Policy, such employee shall be entitled to receive the payments or benefits under such other agreement or arrangement and shall not be eligible to receive any payments or benefits under this Policy, provided that the definition of Cause set forth herein shall continue to apply to the eligibility to receive such other benefits.

If due to the termination of an employee's relationship with the Company that would trigger any benefits under this Policy, the employee would also qualify for any statutory benefits under applicable employment legislation (including but not limited to, statutory notice, statutory severance, or similar statutory indemnities related to termination, collectively "Statutory Benefits") under applicable employment laws, the benefits described under this Policy shall be reduced by such Statutory Benefits.

The payments under this Policy are intended either to be exempt from Section 409A of the Internal Revenue Code of 1986, as amended ("Section 409A") under the short-term deferral, separation pay, or other applicable exception, or to otherwise comply with Section 409A. This Policy shall be administered in a manner consistent with such intent. For purposes of Section 409A, all payments under this Policy shall be considered separate payments. To the extent that any payment or benefit described in this Policy constitutes "non-qualified deferred compensation" under Section 409A, and to the extent that such payment or benefit is payable upon an employee's termination of employment, then such payments or benefits shall be payable only upon such employee's "separation from service" (determined in accordance with the presumptions set forth in Treasury Regulation Section 1.409A-1(h)). Notwithstanding any provision to the contrary, to the extent an employee is considered a specified employee under Section 409A and would be entitled during the six-month period beginning on such employee's separation from service to a payment that is not otherwise excluded under Section 409A, such payment will not be made until the earlier of (i) the date six months and one day after the employee's separation from service or (ii) the employee's death. This Policy may be amended as may be necessary to fully comply with Section 409A and all related rules and regulations in order to preserve the payments and benefits provided hereunder. The Company makes no representation or warranty and shall have no liability to any employee or any other person if any provisions of this Policy are determined to constitute deferred compensation subject to Section 409A but do not satisfy an exemption from, or the conditions of, such Section.

EXHIBIT A

PARTICIPATION LETTER

[DATE]

[PARTICIPANT NAME]
[ADDRESS]

Dear [PARTICIPANT]:

The Board of Directors of Global Blood Therapeutics, Inc. (the "Company") has designated you as eligible for benefits not in connection with a Sale Event (the "Non-Sale Benefits") as set forth in the Company's Amended and Restated Severance and Change in Control Policy as may be amended from time to time (the "Policy"). As set forth in the Policy, there are certain eligibility requirements for such Non-Sale Benefits including, but not limited to, your execution of a participation letter as set forth herein.

You agree that to the extent any benefits to which you may be eligible under the Policy are contingent on the termination of your employment or other service relationship by the Company (or a successor or acquirer) without "cause," such term shall mean Cause as defined in the Policy. For the avoidance of doubt, the Cause definition in the Policy supersedes any other definition of such term which may apply to you.

This letter and the Policy constitute the entire agreement between you and the Company with respect to the subject matter hereof and supersede in all respects any and all prior agreements (oral or written) between you and the Company concerning such subject matter. In the event of a conflict between the terms of this letter and the terms of the Policy, the terms of the Policy shall apply.

Congratulations on being selected to be eligible for Non-Sale Benefits under the Policy.

GLOBAL BLOOD THERAPEUTICS, INC.

By: _____
Name:
Title:

AGREED TO AND ACCEPTED

_____
[Participant Name]

Exhibit 10.16

GLOBAL BLOOD THERAPEUTICS, INC.

NON-EMPLOYEE DIRECTOR COMPENSATION POLICY

The purpose of this Non-Employee Director Compensation Policy (the "Policy") of Global Blood Therapeutics, Inc., a Delaware corporation (the "Company"), is to provide a total compensation package that enables the Company to attract and retain, on a long-term basis, high-caliber directors who are not employees or officers of the Company. In furtherance of this purpose, effective as of January 1, 2021 (the "Effective Date"), all non-employee directors shall be paid compensation for services provided to the Company as set forth below:

Cash Retainers

Annual Retainer for Board Membership: $45,000 for general availability and participation in meetings and conference calls of our Board of Directors (the "Board"). Additional $25,000 for service as lead independent director or non-executive Chairperson of the Board. No additional compensation for attending individual Board meetings.

Additional Annual Retainers for Committee Membership and Service as Chairperson:

Audit Committee Chairperson:	$20,000
Audit Committee member:	$10,000
Compensation Committee Chairperson:	$15,000
Compensation Committee member:	$ 7,500
Nominating and Corporate Governance Committee Chairperson:	$10,000
Nominating and Corporate Governance Committee member:	$ 5,000
Commercial Committee Chairperson:	$15,000
Commercial Committee member:	$ 7,500
Research and Development Committee Chairperson:	$15,000
Research and Development Committee member:	$ 7,500

No additional compensation for attending individual committee meetings.

All cash retainers will be paid quarterly, in arrears, or upon the earlier resignation or removal of the non-employee director. Cash retainers owing to non-employee directors shall be annualized, meaning that with respect to non-employee directors who join the Board during the calendar year, such amounts shall be pro-rated based on the number of calendar days served by such director.

Equity Retainers

All grants of equity retainer awards to non-employee directors pursuant to this Policy will be automatic and nondiscretionary and will be made in accordance with the following provisions:

(a) Value. For purposes of this Policy, "Value" means with respect to (i) any award of stock options the grant date fair value of the option (i.e., Black-Scholes Value) determined in accordance with the reasonable assumptions and methodologies employed by the Company for calculating the fair value of options under ASC 718; and (ii) any award of restricted stock and restricted stock units the product of (A) the average closing market price on The NASDAQ Global Select Market (or such other market on which the Company's common stock, par value $0.001 per share ("Common Stock") is then principally listed) of one share of Common Stock over the trailing 20-trading day period ending on the trading day immediately preceding the grant date, and (B) the aggregate number of shares pursuant to such award.

(b) Revisions. The Compensation Committee of the Board (the "Compensation Committee") in its discretion may change and otherwise revise the terms of awards to be granted under this Policy, including, without limitation, the number of shares subject thereto, for awards of the same or different type granted on or after the date the Compensation Committee determines to make any such change or revision.

(c) Initial Equity Grants: One-time equity grants to each new non-employee director upon his/her election to the Board after the Effective Date of (i) an option to purchase shares of Common Stock, with a Value of $415,000, an exercise price per share equal to the closing price of a share of Common Stock on the date of grant and a term of ten years, provided that the maximum number of shares of Common Stock subject to each such option shall be 11,200 shares and (ii) a grant of restricted stock units with a Value of $415,000, provided that the maximum number of shares of Common Stock subject to each such grant of restricted stock units shall be 7,200 shares. Such initial option grant shall vest in equal monthly installments during the 36 months following the date upon which the director is first elected to the Board and such initial restricted stock unit grant shall vest in equal annual installments during the three years following the date upon which the director is first elected to the Board, in each case subject to the director's continued service on the Board through each applicable vesting date unless the Board determines that the circumstances warrant continuation of vesting.

(d) On the date of each Annual Meeting of Stockholders: Annual equity grants to each non-employee director serving on the Board immediately following the Company's annual meeting of stockholders consisting of (i) an option to purchase shares of Common Stock, with a Value of $207,500, an exercise price per share equal to the closing price of a share of Common Stock on the date of grant and a term of ten years, provided that the maximum number of shares of Common Stock subject to each such option shall be 5,600 shares and (ii) restricted stock units with a Value of $207,500, provided that the maximum number of shares of Common Stock subject to each such grant of restricted stock units shall be 3,600 shares. Such annual option grant shall vest 1/12th on each month following the grant date on the same day of the month as the grant date (and if there is no corresponding day, on the last day of the applicable month) for 11 months and the remaining 1/12th on the earlier of (A) the one-year anniversary of the grant date or (B) the Company's next annual meeting of stockholders, and such annual restricted stock unit grant shall

vest on the earlier of (1) the one-year anniversary of the grant date or (2) the Company's next annual meeting of stockholders, in each case subject to the director's continued service on the Board through each applicable vesting date unless the Board determines that the circumstances warrant continuation of vesting. If a new non-employee director joins our Board on a date other than the date of the Company's annual meeting of stockholders, then such non-employee director will be granted a pro-rata portion of the annual equity grants based on the time between such non-employee director's appointment and the Company's next annual meeting of stockholders, on the first eligible grant date following such non-employee director's appointment to our Board.

(e) Additional Equity Grants: In addition to the foregoing, non-employee directors may also be granted such additional stock options or restricted stock units in such amounts and on such dates as the Board may recommend.

(f) Sale Event Acceleration. Upon the consummation of a Sale Event (as defined in the Company's 2015 Stock Option and Incentive Plan, as may be amended, restated or otherwise modified from time to time), the vesting of all outstanding unvested stock options and restricted stock units granted to each non-employee director under this Policy shall accelerate in full.

(g) General. The form of option agreement will give directors up to one year following cessation of service as a director to exercise the options (to the extent vested at the date of such cessation), provided that the director has not been removed for cause. All of the foregoing option grants will have an exercise price equal to the fair market value of a share of Common Stock on the date of grant.

Expenses

The Company shall reimburse all reasonable out-of-pocket expenses incurred by non-employee directors in attending Board and committee meetings.

Amended and Restated Version Approved by the Board of Directors on September 8, 2016.
Amended: December 19, 2018.
Amended and Restated Version Approved by the Board of Directors on June 3, 2019.
Amended and Restated Version Approved by the Board of Directors on March 24, 2020.
Amended and Restated Version Approved by the Board of Directors on December 10, 2020.

Exhibit 21.1

SUBSIDIARIES OF REGISTRANT

Not applicable.

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

The Board of Directors
Global Blood Therapeutics, Inc.:

We consent to the incorporation by reference in the registration statements (No. 333-206329, 333-210475, 333-215732, 333-222803, 333-226051, 333-229392, 333-232427, 333-236042, 333-242336 and 333-252557) on Form S-8, and the registration statement (No. 333-241036) on Form S-3 ASR of Global Blood Therapeutics, Inc. and subsidiaries of our report dated February 24, 2021, with respect to the consolidated balance sheets of Global Blood Therapeutics, Inc. and subsidiaries as of December 31, 2020 and 2019, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for each of the years in the three-year period ended December 31, 2020, and the related notes, and the effectiveness of internal control over financial reporting as of December 31, 2020, which report appears in the December 31, 2020 annual report on Form 10-K of Global Blood Therapeutics, Inc. and subsidiaries.

Our report refers to a change in the method of accounting for leases as of January 1, 2019 due to the adoption of FASB Accounting Standards Update 2016-02, *Leases (Topic 842)*.

/s/ KPMG LLP

San Francisco, California
February 24, 2021

Exhibit 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO RULES 13a-14(a) AND 15d-14(a) OF THE SECURITIES EXCHANGE ACT,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Ted W. Love, certify that:

1. I have reviewed this Annual Report on Form 10-K of Global Blood Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 24, 2021

By: /s/ Ted W. Love
Ted W. Love, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER
PURSUANT TO RULES 13a-14(a) AND 15d-14(a) OF THE SECURITIES EXCHANGE ACT,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Jeffrey Farrow, certify that:

1. I have reviewed this Annual Report on Form 10-K of Global Blood Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 24, 2021

By: /s/ Jeffrey Farrow
Jeffrey Farrow
Chief Financial Officer
(Principal Financial Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Global Blood Therapeutics, Inc. (the "Company") on Form 10-K for the year ended December 31, 2020, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Ted W. Love, President and Chief Executive Officer of the Company, hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, to my knowledge that:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 24, 2021

By: /s/ Ted W. Love
Ted W. Love, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Global Blood Therapeutics, Inc. (the "Company") on Form 10-K for the year ended December 31, 2020, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Jeffrey Farrow, Chief Financial Officer of the Company, hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, to my knowledge that:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 24, 2021

By: /s/ Jeffrey Farrow
Jeffrey Farrow
Chief Financial Officer
(Principal Financial Officer)