Global Blood Therapeutics, Inc.
Form 10-K
March 29, 2016

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549
Form 10-K
(Mark One)

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

For the fiscal year ended December 31, 2015
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.)
400 East Jamie Court, Suite 101 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	Name of Each Exchange on Which Registered
Common Stock, $.001 par value	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 ý
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 ý
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 ý No ¨
Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted 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 and post such files). Yes ý No ¨
Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ¨
Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer" "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer ¨	Accelerated filer ¨

Non-accelerated filer ý (Do not check if a smaller reporting company) Smaller reporting company ¨
Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act.) Yes ¨ No ý
The registrant did not have a public float on the last business day of its most recently completed second fiscal quarter because there was no public market for the registrant's common equity as of such date.
As of March 21, 2016, the registrant had 30,527,075 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 2016 Annual Meeting of Stockholders, to be filed subsequent to the date hereof with the Securities and Exchange Commission (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, 2015.

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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. 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,” “wo 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: our capital resources, commercial market estimates, the potential safety, efficacy or other therapeutic benefits of our product candidates, 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 our product candidates, our future research and development efforts, patent protection, effects of healthcare reform, 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, "Global Blood Therapeutics," "Company," "we," "our," and "us" means Global Blood Therapeutics, Inc.

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PART I

Item 1. Business

Overview

We are a clinical-stage biopharmaceutical company dedicated to discovering, developing and commercializing novel therapeutics to treat grievous blood-based disorders with significant unmet need. We are developing our initial product candidate, GBT440, as an oral, once-daily therapy for sickle cell disease, or SCD, and are currently evaluating GBT440 in SCD subjects in an ongoing Phase 1/2 clinical trial. SCD is a genetic disease marked by red blood cell, or RBC, destruction and occluded blood flow and hypoxia, leading to anemia, stroke, multi-organ failure, severe pain crises, and shortened patient life span. GBT440 inhibits abnormal hemoglobin polymerization, the underlying mechanism of RBC sickling. In our clinical trials of GBT440 in SCD subjects, we observed reduced markers of red blood cell destruction, improvements in anemia, improvements in markers of tissue oxygenation, reduced numbers of sickled RBCs, and reduced markers of inflammation. In addition to GBT440 for the treatment of SCD, we intend to evaluate GBT440 for the treatment of hypoxemic pulmonary disorders and intend initially to conduct a Phase 2a proof of concept study of idiopathic pulmonary fibrosis subjects. We are also engaged in other research and development activities targeted towards hereditary angioedema, or HAE. We own and have exclusively licensed rights to our portfolio of product candidates in the United States, Europe and other major markets. We own or co-own one issued U.S. patent that covers the composition of matter for GBT440, which is due to expire in 2032 (absent any applicable patent term extensions), and we own or co-own additional pending patent applications in the United States and selected foreign countries.

SCD is a genetic blood disorder caused by a single point mutation in the beta-chain of hemoglobin, which results in the formation of abnormal hemoglobin known as sickle hemoglobin, or HbS. Normally, oxygenated RBCs , travel from the lung through blood vessels. Hemoglobin, the oxygen carrying protein inside red blood cells, releases oxygen at the tissues. In SCD, when oxygen is released at the tissues, HbS becomes sticky and aggregates into polymers, or long, rigid rods within an RBC, much like a “sword within a balloon.” The RBC assumes a sickled shape and becomes inflexible, which can cause blockage in small blood vessels. These polymers destroy RBCs and block blood flow, resulting in decreased oxygen delivery to tissues. Beginning in early childhood, SCD patients suffer many clinical consequences, including unpredictable and recurrent episodes, or crises, of severe chronic and acute pain, anemia, stroke, spleen failure, pulmonary hypertension, acute chest syndrome, liver disease, kidney failure, other morbidities, and premature death. These consequences are directly related to reduced blood flow and insufficient oxygen delivery. A 2014 publication noted that in the United States, SCD resulted in a shortened patient life expectancy by approximately 25 to 30 years even with available therapies.

Current treatment options for SCD are limited to hydroxyurea, or HU, blood transfusions and bone marrow transplantation. The utilization of these treatments is significantly limited due to their suboptimal efficacy and significant toxicity. As a result, patients with SCD continue to suffer serious morbidity and premature mortality.

We believe there is a significant unmet medical need for a novel SCD therapy 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;
- 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.

GBT440’s therapeutic approach was inspired by the natural activity of fetal hemoglobin, or HbF. HbF, which is present during fetal development and in early infancy until it is replaced with adult hemoglobin, has an inherently increased oxygen affinity that allows a fetus to extract oxygen from the mother’s blood. Typically, newborns with SCD do not experience RBC sickling until approximately six to nine months of age, after which HbF is usually no longer expressed. Additionally, it has been observed that rare individuals who have inherited both the HbS mutation as well as a gene deletion 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 polymers from forming. GBT440 is a novel, investigational drug that increases hemoglobin's affinity for oxygen by binding to the alpha-chain of hemoglobin. GBT440 has been observed to keep a proportion of sickle hemoglobin in its oxygenated state, which cannot participate in polymerization. Similar to HbF, by diluting total HbS with a proportion of GBT440-bound hemoglobin, GBT440 prevents hemoglobin polymer formation.

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In December 2014, we initiated our randomized, placebo-controlled, double-blind, single and multiple ascending dose Phase 1/2 clinical trial of GBT440 in healthy subjects and subjects with SCD. The study is being conducted in three parts: Part A (single dose administration), Part B (multiple dose administration, daily for 15 days in healthy subjects and 28 days in SCD subjects), and Part C (multiple dose administration, daily for 90 days in SCD subjects). We are evaluating the safety, tolerability, pharmacokinetics, or PK, and pharmacodynamics, or PD, of GBT440, as well as exploratory markers of SCD activity, including anti-hemolytic effects and SCD-related clinical effects. We reported initial results from our Phase 1/2 clinical trial at the American Society of Hematology meeting in December 2015. Among the 30 SCD subjects who received multiple doses of GBT440 (700mg or 500mg once a day), improvement in hemolytic parameters and tissue oxygenation as evidenced by declines in unconjugated bilirubin, lactate dehydrogenase (LDH), reticulocyte counts, and erythropoietin levels, improvements in anemia as evidenced by an increase in hemoglobin (Hb) levels, as well as a marked reduction in sickled RBCs in the peripheral blood were observed from baseline (Day -1) to Day 28. We believe the initial observations from this trial demonstrate the potential for GBT440 to serve as a disease-modifying therapy for SCD. Subject to data from one or more cohorts in Part C, we intend to engage in discussions with U.S. and European regulatory authorities to define the future development plan for GBT440. In 2015, the FDA granted Fast Track Designation and Orphan Drug Designation for GBT440 for the treatment of SCD.

We believe there is a significant market opportunity in SCD. The U.S. Centers for Disease Control, or CDC, estimates the prevalence of SCD at 90,000 to 100,000 individuals in the United States, where newborn screening is mandatory. It is estimated that the prevalence of SCD in Europe is approximately 60,000. The global incidence of SCD is estimated to be 250,000 to 300,000 births annually. One study estimated that in the United States, the average annual cost for the care of an adult patient with the most common genotype of SCD exceeds $200,000, and the cumulative lifetime costs exceed $8.0 million over an assumed 50-year lifespan, driven primarily by hospital admissions, physician fees, clinic and emergency department visits, and the costs of diagnostic procedures and outpatient consultations.

Beyond SCD, building on positive data from preclinical models of hypoxemia, we plan to investigate GBT440 in a Phase 2a proof of concept clinical trial in idiopathic pulmonary fibrosis, or IPF, patients with hypoxemia. Results from this clinical trial will guide further clinical development in IPF as well as other chronic and acute hypoxemic pulmonary disorders.

Additionally, in 2015 we nominated GBT018713, a proprietary, small molecule kallikrein inhibitor, for development as an orally administered therapy intended for the prevention of hereditary angioedema, or HAE, attacks. All currently marketed therapeutics for HAE must be administered intravenously or by subcutaneous injection. As a result, we believe that the availability of a safe and effective oral agent targeting a validated mechanism that prevents HAE attacks would have the potential to transform the treatment paradigm for this disease. We plan to complete toxicology studies to enable the filing of an Investigational New Drug (IND) application, submit an IND, and initiate a Phase 1 study for GBT018713 in 2016.

To execute on this opportunity, we have assembled a team of employees, management and directors rich in scientific experience and capabilities in drug discovery, development and commercialization. Our management has a successful track record in developing and commercializing drug candidates. In aggregate, our management team has contributed to 18 drug approvals, including Avastin, CellCept, Herceptin, INTEGRILIN, Kaletra, Kyprolis and Rituxan. We intend to leverage this expertise and experience to rapidly advance the development of GBT440 for SCD, determine the potential of GBT440 in hypoxemic pulmonary disorders initially in IPF, pursue an IND filing for GBT18713 in HAE, and advance other product candidates that we may identify and develop.

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Our Development Pipeline

The following table summarizes our development programs, potential indications, and their current stages of development:

BT440 for the Treatment of Sickle Cell Disease

We are developing GBT440 as a once-daily, oral therapy for patients with SCD. We are investigating GBT440's potential to inhibit the abnormal polymerization of hemoglobin, which is the underlying mechanism of red blood cell sickling and leads to the associated complications that characterize SCD. We have designed a clinical program for GBT440 targeted at the treatment of adults, adolescents, children and infants across all SCD genotypes. In December 2014, we initiated our first clinical trial of GBT440, in which we are evaluating GBT440 in both healthy subjects and SCD subjects. Because we have designed this trial to assess safety and tolerability, as well as PK, PD and other exploratory endpoints, including anti-hemolytic and anti-sickling effects, we characterize the trial as a Phase 1/2 clinical trial.

Sickle Cell Disease Overview

SCD is a grievous disease that can lead to hemolytic anemia (the destruction of RBCs within blood vessels), vaso-occlusion (blocked blood flow to tissues), progressive multi-organ damage and early death. Beginning in childhood, patients 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 with 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 (a medical emergency due to refractory penile erection) and premature death. A 2014 publication noted that in the United States SCD results in a decrease of approximately 25 to 30 years in life expectancy.

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 sickle hemoglobin, or HbS. Hemoglobin is a protein in RBCs that carries oxygen from the lungs to the body's tissues and returns carbon dioxide from the tissues back to the lungs. Hemoglobin accomplishes this diametric function by binding and then releasing oxygen through allosterism, a process by which the hemoglobin molecule changes 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. Oxyhemoglobin, the high oxygen affinity form of hemoglobin, is formed in the lungs during respiration, when oxygen binds to the hemoglobin molecule, while 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 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

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consequence, the normally round and flexible RBC becomes rigid and elongated 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; and
- HbS/ßthal, where one gene is HbS, and the other is Beta thalassemia.

Market Opportunity in SCD

The CDC estimates the prevalence of SCD at 90,000 to 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. It is estimated that the prevalence of SCD in Europe is approximately 60,000. The global incidence of SCD is estimated to be 250,000 to 300,000 births annually. SCD is concentrated in populations of African, Middle Eastern and South Asian descent. SCD is a standard part of mandatory newborn screening in the United States. 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. We believe that because of this common mechanism, GBT440 may show activity across all SCD genotypes, although all of the subjects studied to date have involved the HbSS genotype.

SCD is associated with high treatment costs. One study estimated that in the United States, the average annual cost for the care of an adult HbSS SCD patient exceeds $200,000 and the cumulative lifetime cost exceeds $8.0 million over an assumed 50-year lifespan, driven primarily by hospital admissions, physician fees, clinic and emergency department visits and the costs of diagnostic procedures and outpatient consultations. As a result, we believe that a safe and effective oral treatment for SCD would be well received by patients, physicians and payors.

Current Treatment Options and Their Limitations

SCD remains a significant unmet medical need. HU, 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 3 or more painful crises per year. HU is the only therapeutic approved for SCD, and there is no approved therapeutic for SCD in pediatric patients in the United States. The use of HU is significantly limited by its side effect profile, variable patient responses and concerns of long-term toxicity. HU’s side effects include impairment of fertility and the suppression of white blood cells (neutropenia) and platelets (thrombocytopenia), which place patients at risk for infection and bleeding.

In addition to HU treatment, 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, however, 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

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risks, including an approximately 5% mortality rate. Despite the current standard of care, including HU, 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 is 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;
- 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.

Overview of Hemoglobin Biology and GBT440's Mechanism of Action

As described above, hemoglobin accomplishes its diametric function of transporting oxygen from the lungs to the body's tissues and returning 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 (O2 % saturation) on the vertical axis relative to the amount of oxygen dissolved in blood, indicated as the oxygen tension, or partial pressure of oxygen (pO2) measured in millimeters of mercury (mmHg), on the horizontal axis.

We have demonstrated in preclinical models that our novel hemoglobin modifiers, including GBT440, bind to hemoglobin, resulting in increased oxygen affinity. The effect of these compounds on the measured OEC is a shift of the curve to the left on the horizontal axis, as shown in the graph below. 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 GBT440.

In various 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, could potentially delay the polymerization of HbS and prevent the sickling of RBCs, which may be able to ameliorate many, if not all, of the clinical manifestations of this disease. 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 GBT440.

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 deletion 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.

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Based on these observations, we believe that to delay polymerization of HbS, GBT440 would need to bind to only approximately 10-30% of the total hemoglobin in a patient's blood. One theoretical concern with increasing the affinity of hemoglobin for oxygen, however, is that excessive oxygen affinity could prevent hemoglobin from releasing oxygen into the tissues, thus causing hypoxia. Based on HbF data, our animal toxicology studies, and our ongoing clinical trial, we believe our target modification of the total hemoglobin in a patient's blood would not adversely compromise oxygen delivery to the tissues.

Ongoing Phase 1/2 Clinical Trial of GBT440

In December 2014, we initiated our first clinical trial of GBT440, a randomized, placebo-controlled, double-blind, single and multiple ascending dose study in which we are evaluating the safety, tolerability, PK and PD of GBT440 in both healthy subjects and subjects with SCD. We refer to this trial as study GBT440-001. The trial is currently being conducted at Guy's Hospital in London, United Kingdom, and is designed to enroll between 96 and 128 subjects, randomized 6:2 (GBT440:placebo) in approximately 15 cohorts. The study is being conducted in three parts: Part A (single dose administration), Part B (multiple dose administration, daily for 15 days in healthy subjects and 28 days in SCD subjects), and Part C (multiple dose administration, daily for 90 days in SCD subjects). We also intend to evaluate exploratory markers of SCD activity, including anti-hemolytic effects, and SCD-related clinical effects. We are evaluating GBT440's ability to prevent the hemolysis or destruction of RBCs in SCD subjects by measuring the blood levels of bilirubin and LDH, as well as reticulocyte counts. Bilirubin and LDH are released when RBCs undergo hemolysis, and reticulocytes are young RBCs that are released by the bone marrow in response to the ongoing hemolysis; thus we believe that lower levels of bilirubin and LDH and reduced reticulocyte counts represent potential markers for decreased hemolysis. We believe that findings of anti-sickling activity may translate into an improvement in anemia and may indicate a decrease in RBC damage and an improvement in RBC function which could lead to a reduction in or prevention of the downstream effects such as pain episodes, leg ulcers and organ damage associated with RBC sickling in SCD patients. We anticipate that some of the data generated in this Phase 1/2 clinical trial could be used to support early proof-of-concept regarding the anti-sickling and clinical benefit of GBT440 in SCD patients.

We reported initial results from our Phase 1/2 clinical trial at the American Society of Hematology meeting in December 2015, which are detailed below. Based on the November 20, 2015 data cut, we have dosed 48 subjects in Part A single dose administration cohorts: 40 healthy volunteers (30 of whom received GBT440 and ten of whom received placebo) and eight SCD subjects (six of whom received GBT440 and two of whom received placebo). Additionally, in Part B multiple dose administration cohorts, we have dosed 59 subjects, comprised of 24 healthy volunteers (18 of whom received GBT440 and six of whom received placebo) and 35 SCD subjects (26 of whom received GBT440 and 9 of whom received placebo). All 24 healthy volunteers (in 3 dose cohorts) have completed 15-day dosing (18 of whom received GBT440 and 6 of whom received placebo). In 35 SCD subjects, three GBT440 dose levels have been administered for 28 days: 16 of 16 planned subjects have received 700 mg (12 of whom received GBT440 and 4 of whom received placebo); 14 of 16 subjects have received 500 mg (10 of whom received GBT440 and 4 of whom received placebo) and 5 of 8 subjects have received 1000 mg (enrollment is ongoing with the treatment assignment blinded as of November 20, 2015). We initiated the first cohort in the Part C 90-day dose administration in SCD subjects in December 2015.

Overall, the most commonly reported adverse events, or AEs, across SCD subjects included headache, back pain, pain, rhinitis, fatigue and sickle cell crisis (this includes both SCD subjects receiving GBT440 and those receiving placebo, as the treatment assignments for all subjects were blinded as of the data cutoff). To date, no drug-related serious adverse events, or SAEs, have been reported. No SAEs were reported in the single dose cohorts or in healthy subjects who received multiple doses of GBT440. A total of five SAEs were reported in SCD subjects in the multiple dose cohorts. All of the reported SAEs occurred after completion of the treatment period (during follow-up) and were considered by the investigator to be unrelated or unlikely to be related to the study drug, and all were consistent with SCD (sickle cell anemia with crisis or infection with hemolysis). One of these SAEs involving a sickle cell crisis requiring hospitalization was reported in a placebo subject; the treatment assignment was unblinded by the principal investigator.

No subject in the single dose cohorts discontinued the study drug due to an AE. Adverse events leading to dose modification in the multiple dose cohorts included two healthy subjects who discontinued study drug due to AEs; one healthy subject discontinued the study drug on Day 12 due to an AE (Grade 1/mild generalized rash) and one healthy subject discontinued study drug on Day 7 due to a Grade 2/moderate headache; the events in both subjects resolved without treatment. Additionally, one subject each in the 700 mg cohort and 500 mg cohort had dose reductions. Specifically, for the subject in the 700 mg cohort, GBT440 or placebo was reduced on Day 11 due to AEs of Grade 1 nausea and stomach ache, which were considered possibly related to the study drug. For the subject in 500 mg cohort, GBT440 or placebo was reduced on Day 10 (after one day of dose interruption) and again on Day 17, in both cases in accordance with protocol-defined criteria for dose reduction due to a rapid rise in Hb (Hb increase of approximately 2 g/dL over approximately 7 days). The subject had no associated AEs, or signs or symptoms of blood hyperviscosity, but in fact had decreasing reticulocyte counts and erythropoietin levels consistent with improved oxygen delivery to tissues. No subjects with SCD discontinued study drug due to an AE.

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We have observed no AEs related to tissue hypoxia, renal, liver or immune functions. We observed a mild transient rash in a healthy subject in our open-label, non-randomized clinical pharmacology study, which we refer to as study GBT440-002, studying the absorption, metabolism and elimination of GBT440. In this study, subjects receive a loading dose of 2000 mg of GBT440 (Day 1), followed by 400 mg daily for four days (Days 2-5, with radiolabelled dosing on Day 5). The healthy volunteer subject developed a mildly pruritic, papular rash on the neck and extremities on Day 2 of dosing, which was not associated with any systemic findings. Due to rapid improvement by the next day, the subject continued dosing. The rash has resolved, and the subject completed all doses of GBT440 in study GBT440-002.

The pharmacokinetic data from SCD subjects shows a dose proportional increase in GBT440 exposure following single and multiple dosing. The half life is approximately three days in healthy subjects and approximately 1.6 days in SCD subjects. The shorter half life in SCD subjects may be due to higher RBC turnover in SCD.

Among the SCD subjects who received multiple doses of GBT440 (700 mg or 500 mg once a day) in study GBT440-001, improvement in hemolytic parameters and tissue oxygenation as evidenced by declines in unconjugated bilirubin, LDH, reticulocyte counts, and erythropoietin levels, improvements in anemia as evidenced by an increase in hemoglobin (Hb) levels, as well as a marked reduction in sickled RBCs in the peripheral blood, were observed from baseline (Day -1) to Day 28 (Figure 1).

The data showed that from baseline to Day 28:

- Markers of hemolysis decreased with GBT440 treatment, including unconjugated bilirubin (median decrease of 31% and 43% with GBT440 at 500 mg and 700 mg, respectively, compared with an increase of 2% in placebo) and LDH (median decrease of 20% and 12% with GBT440 500 and 700 mg, respectively, compared with a decrease of 7% with placebo).
- The median hemoglobin concentration increased rapidly with GBT440 treatment, with increases evident by Day 4, and absolute increases of 0.5 and 0.7 g/dL (500 mg and 700 mg, respectively) compared with a 0.1 g/dL decrease with placebo.
- The median reticulocyte count decreased by 31% and 37% (500 mg and 700 mg, respectively) with GBT440 compared with a 7% increase with placebo, indicating that the hemoglobin rise is due to decreased red blood cell destruction (hemolysis). Median erythropoietin levels decreased by 9 and 18 mU/mL (500 mg and 700 mg, respectively) with GBT440 treatment compared with an increase of 28 mU/mL with placebo.
- Median sickle cell counts decreased by 56% and 46% (500 mg and 700 mg, respectively) with GBT440 treatment as compared with a 14% increase with placebo. Consistent with previously reported experience, our emerging data showed high inter- and intra-subject variability in circulating sickle cell counts.
- Inflammatory soluble adhesion molecules for the 700 mg dose cohort showed promising trends in improvement including P-Selectin (median decrease of 19% compared with increase of 20% in placebo) and ICAM-1 (median decrease of 6% compared with increase of 33% in placebo). Data for the 500 mg dose cohort has not yet been analyzed. A reduction in inflammation with GBT440 treatment is consistent with a reduction in red blood cell damage and downstream endothelial injury.

Figure 1: Peripheral Blood Smear of a GBT440-Treated Subject at Baseline (Day -1) and Day 28

Representative images from GBT440 treated subject

Day -1 Day 28 (GBT440 700 mg)

While these data are early, we are encouraged by the expanding clinical evidence demonstrating that GBT440 was well tolerated over 28 days of dosing and that GBT440 improves hemolytic anemia, reduces red blood cell damage, reduces inflammation, and improves oxygen delivery. While the exact cause is currently under investigation, we believe that the decline in hemoglobin after Day 22 reflects multiple factors including variability, blood drawing, and the bone marrow resetting from previous decades of hemolysis due to potential improvement in RBC lifespan with GBT440. We believe that longer term

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treatment (90 days) will be informative. Overall, we believe these data continue to support the potential for GBT440 to serve as a disease-modifying therapy for SCD. We are currently enrolling SCD subjects in additional cohorts: 1000 mg for 28 days and 700 mg for 90 days to corroborate our initial clinical findings. In addition, we plan to evaluate one additional cohort in eight SCD subjects (six active, two placebo) with Hb sickle cell (HbSC) or HbS/ thalassemia, to further understand the role of GBT440 in these SCD genotypes. We expect to receive data from these additional subjects in the second half of 2016. In addition, we anticipate to initiate a PK study in pediatric subjects with SCD in the first half of 2016.

Subsequent Clinical and Regulatory Path for GBT440

Subject to additional data from one or more of the multiple dose cohorts of our Phase 1/2 clinical trial in SCD subjects, we intend to engage in discussions with U.S. and European regulatory authorities to define the future development plan for GBT440. The objectives of these regulatory interactions will include discussion of study design for additional clinical trials, trial endpoints and the development of GBT440 in other patient populations, including pediatrics.

We believe GBT440 may hold significant potential for SCD patients and could become the first mechanism-based and disease-modifying therapeutic for this grievous disease. In 2015, the FDA granted Fast Track Designation status and Orphan Drug Designation status for GBT440 for the treatment of SCD.

Evaluation of GBT440 and Analogs in Hypoxemic Pulmonary Disorders

In hypoxemic pulmonary disorders, where the lungs cannot supply adequate oxygen to the blood, we believe that hemoglobin modifiers that left-shift the OEC have the potential to enable increased oxygen uptake in the lungs, resulting in improved oxygen delivery to tissues. The primary goal in treating patients affected by these disorders is to increase hemoglobin oxygen affinity in order to transfer more oxygen into the blood to compensate for the reduced oxygen absorption associated with the underlying lung disease. Supplemental oxygen therapy is a well-established lifesaving treatment in acute and chronic hypoxemic conditions, but is associated with a number of risks, including local and systemic side effects and places a significant burden on the patients quality of life due to the demand of the delivery equipment and ultimately psycho-social decline. Accordingly, we believe a drug that improves oxygen uptake and delivery, thereby providing benefits similar to oxygen therapy without the associated risks and burden to patients, could fill a significant unmet medical need.

We are evaluating our proprietary compounds in a variety of disorders in which hypoxemia is believed to play a key role in disease progression and adverse patient outcomes, including idiopathic pulmonary fibrosis, or IPF, and other chronic and acute lung disorders. Since GBT440 is intended to address the hypoxemic aspects of IPF, we believe that GBT440 could be administered potentially in combination with other therapeutics focused on slowing the rate of disease progression, such as pirfenidone and nintedanib.

IPF is a fatal disease characterized by irreversible, progressive scarring of the lungs, which leads to their deterioration. IPF causes shortness of breath and destruction of healthy lung tissue, resulting in hypoxemia, tissue hypoxia, and ultimately organ failure. The prognosis is poor for patients with IPF, which occurs primarily in people over 50 years old, with a median survival time from diagnosis of three to five years.

We have observed in a mouse model of hypoxia (Study 1) that oral dosing with a hemoglobin-modifying analog of GBT440 may potentially provide protection against extreme hypoxia (5% oxygen, far lower than 21% atmospheric oxygen), as shown by improvements in survival (as measured by heart rate < 60 mmHg) and hypoxemia in treated animals compared to control. We believe this is based upon the compound’s effect on increased hemoglobin oxygen affinity. The results of this study are summarized in the graph below:

Study 1: Tolerance of animals to 5% O2 hypoxia

Based on the results of Study 1, we initiated two additional animal studies in disease models of acute (Study 2) and chronic (Study 3) lung injury, where we also observed improvements in hypoxemia and survival in animals treated with a hemoglobin-modifying analog of GBT440 compared to controls.

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In the acute lung injury model (Study 2), lipopolysaccharide, or LPS (a potent pro-inflammatory bacterial endotoxin), was used to induce lung injury. Additionally, animals were exposed to 5% O2 producing hypoxemia. In the chronic lung injury model (Study 3), bleomycin was used to induce lung injury for 14 days, resulting in increased fibrosis and hypoxemia over a period of two weeks. The animals were then treated, starting at day 8, with a GBT440 analog or control. The results of these studies are shown in the graphs below, which suggest that a hemoglobin-modifying agent such as GBT440 may improve oxygen uptake in a lung with diffuse injury characterized by acute inflammation or fibrosis.

Study 2: Tolerance of LPS-treated animals to 5% O2 hypoxia

Study 3: Effect of a GBT440 analog on arterial oxygen saturation levels in bleomycin-injured mice

Based on these results and subject to our filing and the clearance of an IND or CTA, we expect to initiate a Phase 2a clinical trial of GBT440 in a hypoxemic pulmonary disorder, specifically IPF, in the first half of 2016.

Oral Kallikrein Inhibitor in Hereditary Angioedema

We are also engaged in the discovery of small molecules to produce an oral prophylactic therapy for HAE. HAE is a rare, genetic disorder characterized by severe and potentially life-threatening systemic inflammation that is estimated to affect approximately 6,500 people in the United States and approximately one in 50,000 people globally. HAE is caused by a deficiency in a protein called C1-INH, whose role is to prevent the uncontrolled production of kallikrein in blood plasma. Kallikrein is an enzyme in blood that generates bradykinin, which in turn directly stimulates blood vessel swelling, leakage and tissue inflammation. This can lead to excruciating pain, tissue deformation, and in some cases, airway obstruction and death. Plasma kallikrein is a clinically validated target and serves as a key component in the regulation of inflammation and contact activation pathways. Kallikrein’s role in HAE is well established, and previous studies have demonstrated that kallikrein inhibition can reverse and/or prevent angioedema attacks.

All currently marketed therapeutics for HAE must be administered intravenously or by subcutaneous injection. As a result, we believe that the availability of a safe and effective oral prophylactic agent would have the potential to transform the treatment paradigm for this disease. We are currently conducting preclinical research to develop an orally available therapeutic that could potently and selectively inhibit plasma kallikrein for the treatment of HAE. We believe that the availability of a safe and effective oral agent targeting a validated mechanism that prevents HAE attacks would have the potential to transform the treatment paradigm for this disease. In 2015, we nominated GBT018713, a proprietary, small molecule kallikrein inhibitor, for development as an orally administered therapy intended for the prevention of HAE attacks. We plan to complete toxicology studies to enable the filing of an IND, submit an IND, and initiate a Phase 1 study for GBT018713 in 2016.

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Manufacturing

We do not own or operate, and currently have no 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 non-clinical research and our ongoing clinical trial of GBT440. We have not entered into long-term agreements with our current CMOs. We intend to continue to rely on CMOs for later-stage development and commercialization of GBT440, as well as the development and commercialization of any other product candidates that we may identify. Although we rely on CMOs, we have personnel and third-party consultants with extensive manufacturing experience to oversee the relationships with our contract manufacturers.

We believe the synthesis of the drug substance for GBT440 is reliable and reproducible from readily available starting materials, and the synthetic routes are amenable to large-scale production and do not require unusual equipment or handling in the manufacturing process. We have obtained an adequate supply of the drug substance for GBT440 from our CMOs to satisfy our immediate clinical and nonclinical demands. We have implemented improvements to our drug substance manufacturing process to further ensure production capacity adequate to meet future development and commercial demands.

Drug product formulation development work for GBT440 is in progress to support both adult and pediatric patient populations. We have contracted with a third-party manufacturer capable of both formulation development and drug product manufacturing. We plan to identify a second drug product manufacturer in the future to add further capacity and redundancy to our supply chain to support late-stage development and commercialization.

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 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 by filing patent applications directed to compositions and methods of treatment created or identified from our ongoing development of our product candidates. Our success will depend 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. We seek to obtain domestic and international patent protection, and endeavor to promptly file patent applications for new commercially valuable inventions.

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 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.

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 priority of invention.

Patents

Our patent portfolio includes three issued U.S. patents, two allowed U.S. patent applications, and several U.S. and foreign patent applications in various stages of prosecution. The issued patent (U.S. Patent No. 9,018,210) covering the composition of matter for GBT440 and analogs, which we may own jointly with and have exclusively licensed

from the Regents of the University of California, or the Regents, was granted on April 28, 2015 and is currently expected to expire in 2032 absent any applicable patent term extensions. The issued U.S. patents (U.S. Patent Nos. 8,952,171 and 9,012,450), covering the composition of matter for GBT440 analogs, were granted on February 10, 2015 and April 21, 2015, respectively, and are currently expected to expire in 2033 and 2032, respectively, absent any applicable patent term extensions. We also own jointly with and have exclusively licensed from the Regents, U.S. Patent No. 9,012,450. The risks associated with joint ownership of patent rights are more fully discussed under “Risk Factors-Risks Related to Our Intellectual Property.” The foreign patent applications covering the composition of matter for GBT440 and analogs, if issued, would in each case be expected to expire

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between 2032 and 2035, absent any applicable patent term extensions. Our patent applications fall into three major categories: (i) GBT440; (ii) GBT440 analogs and (iii) kallikrein modulators.

GBT440 patent portfolio. Our patent portfolio relating to GBT440 is comprised of ten patent families and includes patent applications covering certain compositions of matter, methods of use and certain polymorphs related to GBT440 pending in a variety of jurisdictions, including the United States, jurisdictions under the Patent Cooperation Treaty, or PCT, Argentina, and Taiwan. The issued U.S. patent (U.S. Patent No. 9,018,210) covering the composition of matter for GBT440 was granted on April 28, 2015 and is currently expected to expire in 2032, absent any applicable patent term extensions. Any patents that may issue from our other patent applications relating to GBT440 in the United States, if issued, would be expected to expire between 2032 and 2036, absent any applicable patent term extensions. Any patents that may issue from corresponding PCT and foreign patent applications, if issued, would also be expected to expire between 2032 and 2036, absent any applicable patent term extensions. Some of these pending patent applications are jointly owned by us and the Regents.

GBT440 analogs patent portfolio. Our patent portfolio relating to GBT440 analogs is comprised of eight patent families and includes patent applications covering certain compositions of matter and methods of use for GBT440 analogs pending in a variety of jurisdictions, including the United States, jurisdictions under the PCT, Argentina and Taiwan. The two issued U.S. patents (U.S. Patent No. 8,952,171 and U.S. Patent No. 9,012,450, respectively) covering the composition of matter for GBT440 analogs are currently expected to expire in 2033 and 2032, respectively, absent any applicable patent term extensions. Any patents that may issue from the other patent applications relating to GBT440 analogs in the United States, if issued, would be expected to expire between 2032 and 2035, absent any applicable patent term extensions. Any patents that may issue from corresponding PCT and foreign patent applications, if issued, would be expected to expire between 2032 and 2035, absent any applicable patent term extensions. Some of these pending patent applications are jointly owned by us and the Regents.

Kallikrein modulators patent portfolio. Our patent portfolio relating to kallikrein modulators is comprised of three patent families covering certain compositions of matter for kallikrein modulators pending in the United States, with potential foreign rights under the Paris Convention. Any patents that may issue from these applications, if issued, would be expected to expire between 2035 and 2036 absent any applicable patent term extensions.

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. In the future, if our product candidates receive FDA approval, we expect to apply for patent term extension on patents, if issued, covering those products, their methods of use and/or methods of manufacture.

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.

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Sales and Marketing

We intend to begin building a commercial infrastructure in the United States and Europe necessary to effectively support the commercialization of GBT440 when we believe a regulatory approval in a particular geography is likely. Because SCD is a rare disease in these geographic markets, with a concentrated prescribing audience and a small number of key opinion leaders who significantly influence the treatments prescribed for the relevant patient population, we believe that we can effectively address the market using our own targeted, specialty sales and marketing organization supported by internal sales personnel, an internal marketing group and distribution support. Additional capabilities important to the SCD and hematology marketplace include the management of key accounts such as managed care organizations, specialty pharmacies and government accounts.

Outside of the United States and core European markets, where appropriate, we may utilize strategic partners, distributors or contract sales forces to expand the commercial availability of GBT440. In addition, we believe the other indications that we may pursue with our product candidates can also be addressed with a small, dedicated sales force. We currently do not expect that we will require large pharmaceutical partners for the commercialization of our product candidates, although we may consider partnering in certain territories or indications or for other strategic purposes. We intend to evaluate our commercialization strategy as we advance our preclinical programs in other rare disease indications.

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 our product candidates is likely to increase.

In the area of SCD, we expect to face competition from HU (marketed as DROXIA or Hydrea by Bristol-Myers Squibb Company as well as in generic form), which is currently the only approved therapeutic for the treatment of SCD. Several companies are also developing product candidates for chronic treatment in SCD, including Selexys Pharmaceuticals Corporation (in collaboration with Novartis AG), which is engaged in the clinical development of SelG1, an anti-P-selectin monoclonal antibody, and Baxter International Inc./Shire plc, which has completed a Phase 2 clinical trial of Bax-555, an orally available small molecule compound that is also intended to work by increasing hemoglobin oxygen affinity. We also expect to face competition from one-time therapies for SCD, including hematopoietic stem cell transplantation, gene therapy and gene editing. In particular, Bellicum Pharmaceuticals, Inc. is conducting a Phase 1/2 clinical trial of BPX-501 as an adjunct T-cell therapy administered after allogeneic hematopoietic stem cell transplant in pediatric patients with orphan inherited blood disorders, and bluebird bio, Inc. is currently engaged in the clinical development of LentiGlobin BB305, 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 HSCs into the patient's bloodstream.

In IPF, we expect to face competition from the approved therapeutics, including pirfenidone (marketed by Genentech a member of the Roche Group as Esbriet in the U.S., Canada, EU, and other markets, Shionogi as Pirespa in Japan, and in generic form in certain markets) and nintedanib, marketed by Boehringer Ingelheim GmbH in the U.S. and EU as Ofev. In addition, there are a number of agents in clinical development for IPF, that are targeting various anti-fibrotic pathways including the following in Phase 2: Bristol-Myers Squibb's BMS-986020, a LPA-1 receptor antagonist, Promedior/Bristol-Myers Squibb's PRM-151, a recombinant human pentraxin-2 protein, Sanofi's SAR-156597, an IL-4/IL-13-targeting monoclonal antibody, AstraZeneca's tralokinumab, an anti-IL-13 receptor monoclonal antibody, Roche/Genentech's lebrikizumab, an anti-IL-13 monoclonal antibody, Galecto Biotech/Bristol-Myers Squibb's TD-139, a galectin-3 inhibitor, Biogen's BG-00011, an integrin alpha-V/beta-6 monoclonal antibody, and FibroGen's FG-3019, a connective tissue growth factor monoclonal antibody, and Prometic's PBI-4050, an oral agent also targeting connective tissue growth factor. Since GBT440's approach is to address the hypoxemic aspects of IPF, we believe that GBT440 could be administered potentially in combination with other disease modifying therapeutics such as pirfenidone and nintedanib.

In HAE, we expect to face competition from several FDA-approved therapeutics, including Cinryze, marketed by Shire plc in the United States and Europe for the prevention of angioedema attacks in adults and adolescents; Firazyr, marketed by Shire plc in the United States, Europe and certain other geographic territories for the treatment of acute angioedema attacks in adult patients; KALBITOR, marketed by Dyax Corp. for the resolution of acute attacks in adolescent and adult HAE patients; Berinert, marketed by CSL Behring for the treatment of acute abdominal, facial or laryngeal attacks of HAE in adults and adolescents; and Ruconest, marketed by Pharming Group NV in Europe and Salix Pharmaceuticals, Ltd. in the United States for the treatment of acute angioedema attacks in adult patients. We are also aware of companies, including Dyax Corp./Shire plc and Biocryst Pharmaceuticals, Inc., that are engaged in the clinical development of other product candidates, including a kallikrein monoclonal antibody and oral kallkrein inhibitors, respectively, for the treatment of HAE patients.

Many 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,

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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 also may 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.

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, 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 New Drug Application, or NDA, process before they may be legally marketed in the United States. The process generally involves the following:

- completion of extensive non-clinical studies in accordance with applicable regulations, including the FDA's GLP regulations;
- submission to the FDA of an IND application, 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 to accept it for filing;
- 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 non-clinical 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 non-clinical and clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for our product candidates will be granted on a timely basis, or at all. The data required to support an NDA is generated in two distinct development stages: non-clinical and clinical. The non-clinical 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. The sponsor must submit the results of the non-clinical studies, together with

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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 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.

A sponsor who wishes to conduct a clinical trial outside the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of an NDA. The FDA will accept a well-designed and well-conducted foreign clinical study not conducted under an IND if the study was conducted in accordance with good clinical practice, and the FDA is able to validate the data through an onsite inspection if the agency deems necessary.

Clinical trials

Clinical trials are generally conducted in three sequential phases, known as Phase 1, Phase 2 and Phase 3, and 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 drug.
- Phase 2 clinical trials typically involve studies in disease-affected patients to determine the dose 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 for its intended use, its safety in use, and to establish the overall benefit/risk relationship of the product 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. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the drug, findings from animal or in vitro testing that suggests a significant risk for human subjects, and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. 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

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and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

NDA and FDA review process

The results of non-clinical studies and of the 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 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 the Prescription Drug User Fee Act, or PDUFA, as amended, each NDA must be accompanied by a user fee. The FDA adjusts the PDUFA user fees on an annual basis. According to the FDA's fee schedule, effective through September 30, 2016, the user fee for an application requiring clinical data, such as an NDA, is approximately $2.4 million. PDUFA also imposes an annual product fee for human drugs (approximately $0.1 million) and an annual establishment fee (approximately $0.6 million) on facilities used to manufacture prescription drugs. 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. 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 Federal Food, Drug, and Cosmetic Act is not subject to an application fee unless the application includes an indication for other than a rare disease or condition. GBT440 for the treatment of sickle cell disease has been granted orphan drug designation and qualifies for an orphan user fee exemption.

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 must make a decision on accepting an NDA for filing within 60 days of receipt. Once the submission 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 has 10 months from the 60-day filing date in which to complete its initial review of a standard NDA and respond to the applicant, and six months from the 60-day filing date for an NDA designated for priority review. 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 to determine whether they comply with cGMPs. 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. The FDA will likely re-analyze the clinical trial data, which could result in extensive discussions between the FDA and the applicant during the review process. The review and evaluation of an NDA by the FDA is extensive and time consuming and may take longer than originally planned to complete, and we may not receive a timely approval, if at all.

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. A Complete Response Letter 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 an additional registrational Phase 3 clinical trial(s), and/or other significant and time-consuming requirements related to clinical trials, non-clinical 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, or withdraw the application. Even if such

data and information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data.

Orphan drug designation

Under the Orphan Drug Act, 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 and for which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for this type of disease or condition will be recovered from sales of the product. Orphan product designation must be requested before submitting an NDA. After the FDA grants orphan product

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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.

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 or obtain approval for the same product but for a different indication than that for which the orphan product has exclusivity. Orphan product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same product as defined by the FDA for the same indication we are seeking, or if our product candidate is determined to be contained within the competitor's product for the same indication or disease. 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 European Union, or EU, has similar, but not identical, requirements and benefits.

Expedited development and review programs

The FDA has a Fast Track program that is intended to expedite or facilitate the process for reviewing new drugs that meet certain criteria. Specifically, new drugs are eligible for Fast Track designation if they are intended to treat a serious or life threatening condition and non-clinical 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. The sponsor of a new drug may request the FDA to designate the drug as a Fast Track product at any time during the clinical development of the product prior to receiving NDA approval.

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. 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 in an effort to facilitate the review. A product may also be eligible for accelerated approval. An investigational drug may obtain accelerated approval if it treats a serious or life-threatening condition and generally provides a meaningful advantage over available therapies and demonstrates an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. If the FDA concludes that a drug shown to be effective can be safely used only if distribution or use is restricted, it will require such post-marketing restrictions, as it deems necessary to assure safe use of the drug.

Additionally, a drug may be eligible for designation as a breakthrough therapy if the drug is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. The benefits of breakthrough therapy designation include the same benefits as fast track designation, plus intensive guidance from 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, 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. The Food and Drug Administration Safety and

Innovation Act, which was signed into law on July 9, 2012, amended the FDCA to require that 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 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

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agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from non-clinical studies, early phase clinical trials, and/or other clinical development programs.

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, reporting of adverse experiences and complying with 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. 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 their first use. Further, if there are any modifications to the drug, including changes in indications, labeling, or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA or NDA supplement, which may require the applicant to develop additional data or conduct additional non-clinical studies and clinical trials.

The FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMP. 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 regulations. These manufacturers must comply with cGMP regulations 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 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, 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.

Other regulatory matters

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, 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.

For example, in the United States, sales, marketing and scientific/educational programs must also comply with state and federal fraud and abuse laws. These laws include the federal Anti-Kickback Statute, which makes it illegal for any person, including a prescription drug manufacturer (or a party acting on its behalf) to knowingly and willfully solicit, receive, offer, or pay any remuneration 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. Violations of this law are punishable by up to five years in prison, criminal fines, administrative civil money penalties and exclusion from participation in federal healthcare programs. In addition, the Patient Protection and Affordable Health Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, among other things, amends the intent requirement of the federal Anti-Kickback Statute and criminal healthcare fraud statutes created by the federal Health Insurance Portability and Accountability Act of 1996. A person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it. Moreover, the ACA provides that the government may assert that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

Moreover, although we would not submit claims directly to payors, drug manufacturers can be held liable under the federal False Claims Act, which prohibits anyone from knowingly presenting, or causing to be presented, for payment to federal programs (including Medicare and Medicaid) claims for items or services, including drugs, that are false or

fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services. 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. 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. Penalties for a False Claims Act violation include three times the actual damages sustained by the government, plus mandatory civil penalties of between $5,500 and $11,000 for each separate false

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claim, the potential for exclusion from participation in federal healthcare programs, and the potential implication of various federal criminal statutes.

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.

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The failure to comply with any of these laws or regulatory requirements subjects firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, recall or seizure of products, total or partial suspension of production, denial or withdrawal of product approvals, or refusal to allow a firm to enter into supply contracts, including government contracts. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Prohibitions or restrictions on sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

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 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.

U.S. patent term restoration and marketing exclusivity

Depending upon the timing, duration and specifics of the FDA approval 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 extension and the application for the extension must be submitted prior to the expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we intend to apply for restoration of patent term for one of our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA. The request for patent term extension must be filed within a very short time frame after approval of the drug by the FDA. Failure to meet this time frame negates any patent term extension available.

Marketing exclusivity provisions under the FDCA can also delay the submission or the approval of certain marketing applications. The FDCA provides 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 abbreviated new drug application, or 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 NDA holder. 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. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the

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non-clinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and efficacy. Orphan drug exclusivity, as described above, may offer a seven-year period of marketing exclusivity, except in certain circumstances. Pediatric exclusivity is another type of regulatory market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued "Written Request" for such a trial. The FDA issues a written request for pediatric clinical trials prior to approval of a NDA only where it determines that information relating to the use of a drug in a pediatric population, or part of the pediatric population, may produce health benefits in that population.

European Union drug development

In the EU, our future products 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 agencies has been obtained.

Similar to the United States, the various phases of non-clinical and clinical research in the EU are subject to significant regulatory controls. Although the EU Clinical Trials Directive 2001/20/EC 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.

The EU clinical trials legislation is currently undergoing a revision process mainly aimed at harmonizing and streamlining the clinical trials authorization process, simplifying adverse event reporting procedures, improving the supervision of clinical trials, and increasing their transparency.

European Union drug review and approval

In the European Economic Area, or EEA, (which is comprised of the 27 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 Community MA is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the European Medicines Agency, or EMA, 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 such as 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. 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.

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 another 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 the 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 SPC, and a draft of the labeling and package leaflet, which are sent to the other Member States (referred to as the Member States Concerned) for their approval. If the Member States Concerned raise no objections, based on a potential serious risk to public health, to the assessment, SPC,

labeling, or packaging proposed by the RMS, the product is subsequently granted a national MA in all the Member States (i.e., in the RMS and the Member States Concerned).

Under the above described procedures, before granting the 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.

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European Union new chemical entity exclusivity

In the EU, new chemical entities, sometimes referred to as new active substances, qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. The data exclusivity, if granted, prevents regulatory authorities in the EU from referencing the innovator's data to assess a generic application for eight years, after which generic marketing authorization can be submitted, and the innovator's data may be referenced, but not approved for two years. 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.

European Union orphan designation and exclusivity

In the EU, the European Commission, 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 affecting not more than 5 in 10,000 persons in the EU Community (or where it is unlikely that the development of the medicine would generate sufficient return to justify the investment) and for which no satisfactory method of diagnosis, prevention, or treatment has been authorized (or, if a method exists, the product would be a significant benefit to those affected).

In the EU, 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 medicinal product approval. 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. 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.

Rest of the world regulation

For other countries outside of the EU and the United States, such as countries in Eastern Europe, Latin America 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 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, commercial insurance and managed healthcare organizations. In the United States, no uniform policy of coverage and reimbursement for drug products exists. 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. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, 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, 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 the Department of Health and Human Services 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 average manufacturer price, or AMP, and adding a new rebate calculation for "line

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extensions" (i.e., new formulations, such as extended release formulations) of solid oral dosage forms of branded products, 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, to be phased-in by 2014. The CMS have proposed to expand Medicaid rebate liability to the territories of the United States as well.

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 Part 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 products for which we receive marketing approval. However, any negotiated prices for 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, with the exception of children's hospitals, these newly eligible entities will not be eligible to receive discounted 340B pricing on orphan drugs. In addition, 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.

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. An increasing emphasis on cost containment measures in the United States has increased and we expect 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 addition, in most 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. 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. Historically, products launched in the EU do not follow price structures of the United States and generally prices tend to be significantly lower.

Employees

As of December 31, 2015, we employed 55 full-time employees, including 40 in research and development and 15 general and administrative and no part-time employees, in the United States. 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.

Research and Development

Research and development expense recognized were $36.7 million for the year ended December 31, 2015, $16.3 million for the year ended December 31, 2014 and $12.9 million for the year ended December 31, 2013.

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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 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 400 East Jamie Court, Suite 100, South San Francisco, California 94080. Our telephone number is (650) 741-7700 and our e-mail address is investor@globalbloodtx.com. Our Internet website address is globalbloodtx.com. No portion of our website is incorporated by reference into this Annual Report on Form 10-K.

We completed our initial public offering, or IPO, in August 2015, in which we sold 6,900,000 shares of common stock, at a public offering price of $20.00 per share, the net proceeds of which totaled $126.2 million, after deducting underwriting discounts and commissions and offering expenses incurred by us. We qualify as an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, as amended, or the JOBS Act. As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. We would cease to be an emerging growth company on the date that is the earliest of: (i) the last day of the fiscal year in which we have total annual gross revenues of $1 billion or more; (ii) December 31, 2020; (iii) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC.

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 final prospectus filed with the SEC on August 12, 2015 under Rule 424(b) of the Securities Act of 1933, as amended, 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 at the SEC’s Public Reference Room at 100 F Street, N.E. Washington, D.C. 20549. In addition, the SEC maintains information for electronic filers (including Global Blood Therapeutics, Inc.) at its website at www.sec.gov. The public may obtain information regarding the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. 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.

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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 Our Financial Position and Need for Additional Capital

We are a clinical development-stage biopharmaceutical company 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 only one product candidate in clinical development and have not generated any 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 clinical development-stage biopharmaceutical company with 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 our lead product candidate, GBT440, which is our only product candidate in clinical development.

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, 2015 and 2014 were $46.4 million and $20.8 million, respectively. As of December 31, 2015, we had an accumulated deficit of $98.5 million. We have not generated any revenue since our inception, 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:

- continue to advance GBT440 in clinical development;
- establish and maintain manufacturing and supply relationships with third parties that can provide adequate supplies (in amount and quality) of GBT440 to support further clinical development and, if approved, commercialization;
- seek and obtain regulatory and marketing approvals for GBT440;
- build a sales and marketing organization or enter into selected collaborations to commercialize GBT440, if approved;
- advance our other programs, including our programs for the clinical investigation of GBT440 in idiopathic pulmonary fibrosis (IPF) patients with hypoxemia and the development of a proprietary kallikrein inhibitor as an orally administered therapy intended for the prevention of hereditary angioedema (HAE) attacks, through preclinical and clinical development and commence development activities for any additional product candidates we may identify; and
- expand our organization to support our research, development and commercialization activities and our operations as a public company.

We have never generated any revenues from product sales and may never be able to develop or commercialize a marketable drug or achieve profitability. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our failure to achieve sustained profitability would depress the value of our company and could impair our ability to raise capital, expand our business, diversify our research and development pipeline, market GBT440 or 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 will require substantial additional funding to achieve our business goals. If we are unable to obtain this funding when needed and on acceptable terms, we could be forced to delay, limit or terminate 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 our product candidates and technologies.

We are currently advancing GBT440 through clinical development and conducting preclinical research activities in our other programs. Developing biopharmaceutical products is expensive and time-consuming, and we expect our

research and development expenses to increase substantially in connection with our ongoing activities, particularly as we advance GBT440 and other product candidates that we may identify and pursue in clinical trials. As of December 31, 2015 and 2014, we had working capital of $140.1 million and $51.1 million, respectively and capital resources consisting of cash and cash equivalents of $148.5 million and $52.1 million, respectively. Because the outcome of any clinical development and regulatory approval

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process is highly uncertain, we cannot reasonably estimate the actual capital amounts necessary to successfully complete the development, regulatory approval process and commercialization of GBT440 and any future product candidates.

In August 2015, we sold 6,900,000 shares of common stock in our IPO, the net proceeds of which totaled $126.2 million, after deducting underwriting discounts and commissions and offering expenses incurred by us. We expect that our existing cash and cash equivalents, will be sufficient to fund our operations through mid-2017. However, 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 GBT440 and 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:

- the time and cost necessary to complete our ongoing clinical trial that we characterize as a Phase 1/2 trial of GBT440, to initiate and complete any registrational clinical trials of GBT440 and to pursue regulatory approvals for GBT440, and the costs of post-marketing studies that could be required by regulatory authorities;
- the progress and results of our Phase 1/2 clinical trial of GBT440;
- the progress, timing, scope and costs of our nonclinical studies, clinical trials and other related activities, including the ability to enroll subjects in a timely manner for our Phase 1/2 clinical trial of GBT440 and potential future clinical trials;
- the costs of obtaining clinical and commercial supplies of GBT440 and any other product candidates we may identify and develop;
- our ability to advance our other programs, including our program for the clinical investigation of GBT440 in IPF patients with hypoxemia and the development of a proprietary kallikrein inhibitor as an orally administered therapy intended for the prevention of HAE attacks, through preclinical and clinical development, and the timing and scope of these development activities;
- our ability to successfully commercialize GBT440 and any other product candidates we may identify and develop;
- the manufacturing, selling and marketing costs associated with GBT440 and any other product candidates we may identify and develop, including the cost and timing of establishing our sales and marketing capabilities;
- the amount and timing of sales and other revenues from GBT440 and any other product candidates we may identify and develop, including the sales price and the availability of adequate third-party reimbursement;
- 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;
- 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 one or more of our research or development programs or the commercialization of any product candidates 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.

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 one or more jurisdictions for GBT440 or any other 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 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 not obtained regulatory approval for any product candidate, including GBT440, and it is possible that neither GBT440 nor any other product candidates we may seek to develop in the future will ever obtain regulatory approval.

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Applications for GBT440 or any other product candidates we may develop could fail to receive regulatory approval for many reasons, including but not limited to:

- our inability to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that GB440 or any other product candidate we may develop is safe and effective;
- the FDA or comparable foreign regulatory authorities may disagree with our plans regarding the pathways for approval or the design or implementation of our clinical trials;
- the population studied in the clinical program may not be sufficiently broad or representative to assure safety in the full population for which we seek approval;
- the FDA or comparable foreign regulatory authorities may require additional preclinical studies or clinical trials beyond those we anticipate;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from nonclinical studies or clinical trials;
- the data collected from clinical trials of GBT440 and other product candidates that we may identify and pursue may not be sufficient to support the submission of a new drug application, or NDA, or other submission for regulatory approval in the United States or elsewhere;
- 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 fail to approve the manufacturing processes, test procedures and specifications, or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may change in a manner that renders our clinical trial design or data insufficient for approval.

The lengthy approval process, as well as the unpredictability of the results of clinical trials, may result in our failing to obtain regulatory approval to market GBT440 and 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.

We are heavily dependent on the success of our lead product candidate, GBT440, and we have not identified other clinical development candidates within our other research programs, all of which are still in the preclinical development stage. If we are unable to successfully complete clinical development, obtain regulatory approval for, or commercialize GBT440, 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 preclinical and clinical development of GBT440, including conducting preclinical studies and clinical trials and providing general and administrative support for these operations. Our future success is dependent on our ability to successfully develop, obtain regulatory approval for, and commercialize GBT440. Before we can generate any revenues from sales of GBT440, we will be required to conduct additional clinical development, including, among other things, additional toxicology studies that may be required before we can conduct longer-term clinical trials and a larger registrational clinical trial if our ongoing clinical trial of GBT440 is successful, seek and obtain regulatory approval, secure adequate manufacturing supply to support larger clinical trials and commercial sales and build a commercial organization. Further, the success of GBT440 will depend on patent and trade secret protection, acceptance of GBT440 by patients, the medical community and third-party payors, its ability to compete with other therapies, healthcare coverage and reimbursement, and maintenance of an acceptable safety profile following approval, among other factors. If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize GBT440, which would materially harm our business.

GBT440 is currently our only product candidate to have advanced into what we characterize as a Phase 1/2 clinical trial, and it may be years before GBT440 can advance into a registrational study, if at all. All of our other programs are in an early stage of research and development. Although we have nominated for Investigational New Drug application, or IND, enabling toxicology studies a novel, small molecule, orally available kallikrein inhibitor product candidate for the prevention of angioedema attacks associated with HAE, the data generated in these studies may not be adequate to support the filing of an IND or for clinical evaluation, and we have not yet selected any other product

candidates that would enable the filing of an IND. We cannot be certain that GBT440 will be successful in clinical trials or receive regulatory approval. If we do not receive regulatory approval for, or otherwise fail to successfully commercialize, GBT440 or any other product candidate, we may need to spend significant additional time and resources to identify other product candidates, advance them through preclinical and clinical development and apply for regulatory approvals, which would adversely affect our business, prospects, financial condition and results of operations.

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The development of GBT440 as a potential disease-modifying anti-sickling agent represents a novel therapeutic approach to SCD treatment, and there is a risk that the outcome of our clinical trials will not be favorable.

We have concentrated our therapeutic product research and development efforts on developing novel, mechanism-based therapeutics for the treatment of grievous blood-based disorders with significant unmet need, including SCD, and our future success depends on the successful development of this therapeutic approach. The clinical trial requirements of the FDA and other regulatory agencies and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential product. At the moment, there is only one approved therapy for SCD, hydroxyurea, and there are no approved therapeutics directed toward preventing the polymerization of hemoglobin molecules as a mechanism to reduce RBC sickling in SCD patients. As a result, the design and conduct of clinical trials for a therapeutic that targets this mechanism in SCD are subject to unknown risks, and we may experience setbacks with our ongoing or planned clinical trials of GBT440 because of the limited clinical experience with its mechanism of action in SCD patients. In particular, regulatory authorities in the United States have not issued definitive guidance as to how to measure and achieve efficacy in SCD. Although we are evaluating exploratory endpoints, including anti-sickling and anti-hemolytic effects, changes in hemoglobin levels, and reticulocyte counts, for GBT440 in our Phase 1/2 clinical trial, regulators have not determined that such data signifies a clinically meaningful result in SCD patients or can support advancement into registrational trials or regulatory approval. We may not achieve our pre-specified endpoints in our Phase 1/2 clinical trial or in other clinical trials where there is limited or no regulatory guidance regarding appropriate clinical endpoints, which would decrease the probability of obtaining marketing approval for GBT440 or any other product candidate we may develop. Any inability to design clinical trials with protocols and endpoints acceptable to applicable regulatory authorities, and to obtain regulatory approvals for GBT440 and 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 an adequate safety or efficacy profile for GBT440 and other product candidates that we may pursue to justify proceeding to advanced clinical trials or an application for regulatory approval.

The results of nonclinical and preclinical studies and clinical trials of GBT440 and other 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 do not necessarily predict final results. For example, our preclinical studies and clinical trials of GBT440 to date have involved only one genotype of SCD, HbSS, and the results of these studies may not be replicated in other genotypes of SCD or in subsequent clinical trials. Additionally, any positive results generated in our Phase 1/2 clinical trial of GBT440 in adults would not ensure that we will achieve similar results in larger, registrational clinical trials or in clinical trials of GBT440 in pediatric populations. In addition, preclinical and clinical data are often susceptible to various interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval. Product candidates in later stages of clinical trials may fail to demonstrate the desired safety and efficacy despite having progressed through nonclinical studies and initial 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. Even if early stage clinical trials are successful, we may need to conduct additional clinical trials for product candidates in additional patient populations or under different treatment conditions before we are able to seek approvals from the FDA and regulatory authorities outside the United States to market and sell these product candidates. Our failure to demonstrate the required characteristics to support marketing approval for GBT440 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 submit GBT440 for marketing approval, the FDA and comparable foreign regulatory authorities will require that we conduct additional clinical trials and may impose additional requirements, the scope of which are not known at this time.

Before we can submit an NDA to the FDA for GBT440, we must successfully complete our ongoing clinical trial and one or more additional larger clinical trials. The FDA typically requires at least two pivotal, well-controlled clinical trials as a condition to the submission of an NDA and does not consider a single 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, such as effect on survival, organ function or patient reported outcomes and a confirmatory study would have been difficult to conduct on ethical grounds. Although we characterize our current clinical trial of GBT440 as a Phase 1/2 clinical trial because it is designed to evaluate exploratory endpoints that we believe may be clinically relevant to SCD patients, it is possible that, even if we achieve favorable results in our first clinical

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trial of GBT440, the FDA may require us to conduct one or more additional clinical trials, possibly involving a larger sample size or a different clinical trial design, before we can initiate a pivotal trial. The FDA may also require that we conduct additional toxicology studies before evaluating GBT440 in longer term clinical trials or impose a longer follow-up period for subjects treated with GBT440 prior to accepting an NDA submission.

It is possible that the FDA or the comparable foreign authorities may not consider the results of our ongoing and planned clinical trials to be sufficient for approval of GBT440 for SCD or IPF. If the FDA or comparable foreign regulatory authorities require additional clinical trials or data beyond that which we currently anticipate, we would incur increased costs and delays in the clinical development and marketing approval process, 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 and Marketing Authorization Application, or MAA, respectively, which may cause us to alter our development, regulatory and/or commercialization strategies.

We may encounter substantial delays in 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 our product candidates.

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

- delays in reaching, or any failure to reach, a consensus with regulatory agencies on study design;
- delays in reaching, or any failure to reach, 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, approval at 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 regulatory agencies, after an inspection of our clinical trial operations or study sites;
- failure by our CROs, 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 GCP, or applicable regulatory guidelines in other countries;
- delays in the testing, validation, manufacturing and delivery of sufficient quantities of our product candidates to the clinical sites;
- delays in having patients complete participation in a study or return for post-treatment follow-up;
- clinical trial sites or patients 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 our product candidates;
- occurrence of serious adverse events associated with the product candidate that are viewed to outweigh its potential benefits; or
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs 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. Such authorities may suspend or terminate a clinical trial due to a number of factors, 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 the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, and failure to demonstrate a benefit from using a drug. In addition, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional studies to bridge our modified product candidates to earlier versions.

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

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

Identifying and qualifying patients to participate in our ongoing and planned clinical trials of GBT440 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. Accordingly, there are limited patient pools from which to draw for clinical trials. For example, according to CDC estimates, the prevalence of SCD, for which GBT440 is being studied, is 90,000 to 100,000 individuals in the United States. Although genetic screening for SCD is mandatory for newborns in the United States, we may not be able to identify, recruit, and enroll a sufficient number of subjects to complete our clinical trials of GBT440 because of the perceived risks and benefits of GBT440, the availability of competing therapies and clinical trials, the proximity and availability of clinical trial sites for prospective patients and the subject referral practices of physicians. Further, if subjects in our clinical trials fail to comply with our dosing regimens, we may not be able to generate clinical data acceptable to the FDA in our trials. If patients are unwilling to participate in 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 GBT440 or our other product candidates, our costs may increase, and our ability to obtain regulatory approval and generate product revenue from 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 our product candidates, we may need to delay, limit or terminate our clinical development activities.

Clinical trials by their nature utilize a sample of the potential patient population. Our Phase 1/2 clinical trial of GBT440 is designed to enroll between 96 and 128 subjects. Accordingly, any rare and severe side effects of GBT440 may be uncovered only in later stages of our Phase 1/2 trial or only in any larger, subsequent trials that we may conduct. Many 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 preclinical toxicology study with GBT440 in non-humans and clinical trials involving other hemoglobin modifiers have shown a decrease in oxygen delivery to tissue when the percentage of modified hemoglobin is significant. Hemoglobin modifiers, by increasing HbS's affinity for oxygen, can cause a shift in oxygen levels, potentially resulting in tissue hypoxia. If GBT440 or any product candidates that we may develop are associated with tissue hypoxia or undesirable side effects in clinical trials or have characteristics that are unexpected, we may need to abandon their development or limit their development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective, which could adversely affect our business, prospects, financial condition and results of operations.

Although we intend to pursue expedited regulatory approval pathways for GBT440, it may not qualify for expedited development or, if it does qualify for expedited development, it may not actually lead to a faster development or regulatory review or approval process.

Although we believe there may be an opportunity to accelerate the development of GBT440 through one or more of the FDA's expedited programs, such as fast track, breakthrough therapy, accelerated approval or priority review, and we intend to pursue one or more of these expedited programs, we cannot be assured that GBT440 or any other product candidates that we may develop will qualify for such programs.

In October 2015, the FDA designated our investigation of GBT440 for the treatment of SCD as a Fast Track development program. Fast Track is a process designated to facilitate the development and expedite the review of drugs to treat serious conditions and that demonstrate the potential to address an unmet medical need. While Fast Track designation may provide more frequent access and communication with the FDA, it does not ensure that regulatory approval for GBT440 will occur on an expedited basis.

In addition, a drug may be eligible for designation as a breakthrough therapy if the drug is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more

clinically significant endpoints. Although breakthrough designation or access to any other expedited program may expedite the development or approval process, it does not change the standards for approval. If we apply for breakthrough therapy designation or any other expedited program for GBT440, the FDA may determine that GBT440, our proposed target indication or other aspects of our clinical development plans do not qualify for such expedited program. Even if we are successful in obtaining a breakthrough

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therapy designation or access to any other expedited program, we may not experience faster development timelines or achieve faster review or approval compared to conventional FDA procedures.

Furthermore, access to an expedited program may also be withdrawn by the FDA if it believes that the designation is no longer supported by data from our clinical development program. Additionally, qualification for Fast Track or any other expedited review procedure does not ensure that we will ultimately obtain regulatory approval for GBT440 or any other product candidate that we may develop in a timely manner, or at all.

Although the FDA has granted orphan drug designation to GBT440 for the treatment of SCD, we may not receive orphan drug designation for GBT440 in other jurisdictions or for other indications that we may pursue, or for 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 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 European Union, 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 European Medicines Agency, or EMA, grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the EU (or where it is unlikely that the development of the medicine would generate sufficient return to justify the investment) and for which no satisfactory method of diagnosis, prevention, or treatment is authorized or, if a method exists, the product would be of significant benefit to those affected by the condition. In December 2015, the FDA granted orphan drug designation for GBT440 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 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 has granted orphan drug designation to GBT440 for the treatment of SCD, we may apply for orphan drug designation for GBT440 in other jurisdictions or for other indications, or for product candidates we may develop, and applicable regulatory authorities may not grant us these additional designations. In addition, the exclusivity granted under any orphan drug designations that we have received or may receive may not effectively protect the product candidate from competition because different drugs can be approved for the same condition. 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, in that it is shown to be safer, more effective or makes a major contribution to patient care. 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.

Even if we receive regulatory approval for GBT440 or any other product candidate that we may develop, we will be subject to ongoing regulatory obligations and scrutiny and may be subject to product labeling and other post-marketing restrictions.

Even if a product candidate is approved, regulatory authorities may still impose significant restrictions on its indicated uses or marketing or impose ongoing requirements for potentially costly post-marketing studies. Furthermore, any new legislation addressing drug safety issues could result in delays or increased costs to assure compliance. If GBT440 or any other product candidates that we may develop are approved, they will each be subject to 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 the labeling claims that are necessary or desirable for the successful commercialization of our product candidates. For example, the development of GBT440 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 the desired age ranges, our business may suffer.

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In addition, manufacturers and manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to current Good Manufacturing Practices, or cGMP. As such, we and our contract manufacturers are subject to continual review and periodic inspections to assess compliance with cGMP and must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, and quality control. We will also be required to report certain adverse reactions and production problems, if any, to the FDA, and to comply with requirements concerning advertising and promotion for our products. The timing of our obligation to report adverse events would be triggered by the date we become aware of the adverse event as well as the nature of the event. We may fail to report adverse events we become aware of within the prescribed timeframe. We may also fail to appreciate that we have become aware of a reportable adverse event, especially if it is not reported to us as an adverse event or if it is an adverse event that is unexpected or removed in time from the use of our products. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. As such, we may not promote our products for indications or uses for which they do not have FDA approval.

If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing, or labeling of a product, a regulatory agency may impose restrictions or sanctions on that product or us, including requiring withdrawal of the product from the market. If we fail to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may:

- issue untitled or warning letters;
- impose civil or criminal penalties;
- impose injunctions;
- suspend regulatory approval;
- suspend any of our ongoing clinical trials;
- impose product recalls and 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.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenues from GBT440 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 harmed.

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 CRO who monitors our Phase 1/2 clinical trial of GBT440, to monitor and manage data for some of our ongoing nonclinical and all of our clinical programs. We rely on these parties for execution of our 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 cGMP or GCP, and Good Laboratory Practices, or GLP, 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, and other contractors. If we or any of our CROs or 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 require us to repeat or to perform additional nonclinical and clinical studies before approving our marketing applications, which would delay the regulatory approval process.

In addition, the execution of preclinical studies and clinical trials, and the subsequent compilation and analysis of the data produced, 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 as little as 30 days prior written notice of a material breach by us that is not cured within 30 days.

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Many of these agreements may also be terminated by such third parties under certain other circumstances, including our failure to comply with applicable laws. If any of our relationships with our third-party CROs terminates, we may not be able to enter into arrangements with alternative CROs or do so on commercially reasonable terms. In addition, our CROs are not our employees, and except for remedies available to us under our agreements with such CROs, we cannot control whether they devote sufficient time and resources to our programs. Furthermore, these third party CROs may also have relationships with other entities, some of which may be our competitors. If CROs 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 they obtain is compromised due to the failure to adhere to our protocols, regulatory requirements, or for other reasons, our development activities may be extended, delayed, or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. Switching or adding CROs involves additional cost, time and management resources and focus. CROs may also generate higher costs than anticipated.

Accordingly, our dependence on third-party CROs and other vendors 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 our product candidates for preclinical studies and clinical trials and expect to continue to do so for commercialization. Our business could be harmed if those third parties fail to provide us with sufficient quantities of drug product, or fail to do so at acceptable quality 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 Phase 1/2 clinical trial of GBT440 or any future clinical trials that we may conduct, and we lack the resources to manufacture any of our product candidates on a commercial scale. We rely, and expect to continue to rely, on third-party manufacturers to produce our product candidates for our clinical trials, as well as for commercial manufacture if any of our product candidates receives marketing approval. 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 also expect to rely on third parties for the manufacture of commercial supplies of GBT440 or any other product candidates, if approved.

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

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or non-renewal of the agreement by the third party at a time that is costly or inconvenient for us.

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 risks for the production of such materials and products. As a result, failure to meet the regulatory requirements for the production of those materials and products may affect the regulatory clearance of our contract manufacturers' facilities generally. If the FDA or a comparable foreign regulatory agency does not approve these facilities for the manufacture of our product candidates or if any agency withdraws its approval in the future, we may need to find alternative manufacturing facilities, which would negatively impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved.

GBT440 and any future product candidates that we may develop 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 clinical development or marketing approval. We are currently manufacturing GBT440 through third parties and have adequate supplies to conduct our ongoing Phase 1/2 clinical trial, but we have not yet

begun to produce the clinical supply of GBT440 for any larger registrational trials that we may conduct. 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 clinical development and commercialization activities. Our current and anticipated future dependence upon others for the manufacturing of our product candidates or marketed drugs may adversely affect our future profit margins and our ability to commercialize any product candidates that receive marketing approval on a timely and competitive basis.

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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 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 cGMP, 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 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 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 our product candidates.

We or our contract manufacturers must supply all necessary documentation in support of an NDA or MAA on a timely basis and must adhere to GLP and cGMP regulations enforced by the FDA and other regulatory agencies through their facilities inspection program. Some of our contract manufacturers have never produced a commercially approved pharmaceutical product and therefore have not obtained the requisite regulatory authority approvals to do so. 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 of our product candidates or any of our other potential products. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidates or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted. 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 the regulatory requirements. If these facilities do not pass a pre-approval plant inspection, regulatory approval of the products may not be granted or may be substantially delayed until any violations are corrected to the satisfaction of the regulatory authority, if ever.

The regulatory authorities also may, at any time following approval of a product for sale, 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 may be costly and/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 an NDA supplement or MAA variation, or equivalent foreign regulatory filing, which could result in further delay. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

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 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, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we rely on third parties to manufacture GBT440 and conduct other aspects of our clinical development activities, 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, material transfer agreements, collaborative research agreements, consulting agreements or other similar agreements 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, such as trade secrets. 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 become known by our competitors, are inadvertently 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

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discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

In addition, these agreements typically restrict the ability of certain collaborators, CROs, manufacturers and consultants to publish data potentially relating to our trade secrets. Our academic collaborators typically have rights to publish data, provided that we are notified in advance and may delay publication for a specified time in order to secure our intellectual property rights arising from the collaboration. In other cases, publication rights are controlled exclusively by us, although in some cases we may share these rights with other parties. We also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development partnerships or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of these agreements, independent development or publication of information including our trade secrets in cases where we do not have proprietary or otherwise protected rights at the time of publication. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain sufficient intellectual property protection for 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 GBT440 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 we may exclusively license or own solely and jointly with others, particularly patents, in the United States and other countries with respect to our product candidates and technology. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our product candidates.

Obtaining and enforcing biopharmaceutical patents is costly, time consuming 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.

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 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 highly uncertain. Our pending and future patent applications may not result in patents being issued that protect our 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.

Moreover, we may be subject to a third-party preissuance submission of prior art to the United States Patent and Trademark Office, or the 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 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 current or future product candidates.

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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 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 recently enacted and is currently implementing wide-ranging patent reform legislation. 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 15, 2013, under the Leahy-Smith America Invents Act, or the Leahy-Smith Act, enacted on September 16, 2011, the United States has moved to a first to file system. The Leahy-Smith Act also includes a number of significant changes that affect the way patent applications will be 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 act and new regulations on specific patents discussed herein have not been determined and would need to be reviewed. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act 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.
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 GBT440 or any future product candidates that we may develop.
We cannot assure that GBT440 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 GBT440 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 GBT440 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 intellectual property rights with respect to our 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 in order 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 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 and time consuming to litigate and would divert management's attention from our core business. Any of these events could harm our business significantly.

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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 our products 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 may infringe our patents or other intellectual property. Although we are not currently involved in any litigation, if we were to initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, written description or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability is 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. Our defense of litigation or 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 ability to 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 our product candidates to market.

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. 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, in September 2015 we secured exclusive rights from the Regents of the University of California, or the Regents, for certain patents and patent applications that they may own related to GBT440 and GBT440 analogs. To the extent that the Regents may be a co-owner of any of these patents and patent applications, some countries will require the consent of our other co-owner(s) to our agreement with the Regents and the consent of the Regents to our agreements with our other co-owner(s). Additionally, in the United States, each co-owner may be required to be joined as a

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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, 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. 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.

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 an outside firm and rely on our outside counsel to pay these fees due to non-U.S. patent agencies. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ 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, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business.

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

Filing, prosecuting and defending patents on 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 outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and may also export infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

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Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions, 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.

Risks Related to Commercialization

Even if GBT440 or any other product candidate that we may develop receives marketing approval, their commercial success will depend upon the degree of market acceptance by physicians, patients, third-party payors and others in the medical community.

If GBT440 or other product candidates that we may pursue receives marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. If our product candidates do 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 our product candidates, in addition to treating these target indications, also provide incremental health benefits to patients. Our efforts to educate the medical community and third-party payors about the benefits of our product candidates may require significant resources and may never be successful. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and potential advantages compared to alternative treatments, such as, in the case of GBT440, hydroxyurea;
- our ability to offer our drugs for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments, including future alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the availability of products and their ability to meet market demand, including a reliable supply for long-term daily treatment;
- the strength of marketing and distribution support;
- the availability of third-party coverage and adequate reimbursement;
- the clinical indications for which the product is approved;
- the prevalence and severity of any side effects and overall safety profile; and
- any restrictions on the use of our drugs together with other medications.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unsuccessful in commercializing our product candidates when approved by health authorities.

Although some of our employees have experience with commercializing products while employed at other companies, we as a company have no experience selling and marketing our product candidates and we currently have no marketing or sales organization. To successfully commercialize any products that may result from our development programs, we will need to develop these capabilities, either on our own or with others. If our product candidates receive regulatory approval, we intend to establish a sales and marketing organization with technical expertise and supporting distribution capabilities to commercialize our product candidates in major markets, which will be expensive, difficult and time consuming. Any failure or delay in the development of our internal sales, marketing, and distribution capabilities would adversely impact the commercialization of our products.

Further, given our lack of prior experience in marketing and selling biopharmaceutical products, 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 our product candidates. As such, we may be required to hire substantially more sales representatives to adequately support the commercialization of our product candidates or we may incur excess costs as a result of hiring more sales representatives than necessary. With respect to certain geographical markets, we may 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 our future products, if any, and we are unable to develop the necessary marketing capabilities on our own, we will be unable to generate sufficient

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product revenue to sustain our business. We may be competing with companies that currently have extensive and well-funded marketing and sales operations. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.
The insurance coverage and reimbursement status of newly-approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for new or current products could limit our ability to market those products and decrease our ability to generate revenue.
Our target patient populations are small, and accordingly the pricing, coverage and reimbursement of our product candidates, if approved, must be adequate to support our commercial infrastructure. Our per-patient prices must be sufficient to recover our development and manufacturing costs and potentially achieve profitability. Accordingly, the availability and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford expensive treatments, such as ours, assuming approval. Sales of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors. If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our product candidates. 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 products. In the United States, the principal decisions about reimbursement for new medicines are typically 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 Medicaid or Medicare. However, the practices and requirements relating to the 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.
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 pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In general, the prices of medicines under such systems are 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. 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.
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 our product candidates. We expect to experience pricing pressures in connection with the sale of any of our product candidates, 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. As a result, 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 may be sold, and drug pricing and other healthcare costs continue to be subject to intense political and social pressures which we anticipate will continue and escalate on a global basis. As a result, our business and reputation 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.
In light of the large population of patients with SCD who reside in foreign countries, our ability to generate meaningful revenues in those jurisdictions may be limited due to the strict price controls and reimbursement

limitations imposed by governments outside of the United States.

In some countries, particularly in the EU, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. 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. If reimbursement of our product candidates is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory

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levels, our business could be harmed, possibly materially, based on the large population of patients with SCD who reside in foreign countries.

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 initiatives to contain healthcare costs. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or the Health Care Reform Law, 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. The Health Care Reform Law, among other things, 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 promoted a new Medicare Part D coverage gap discount program.

In addition, other legislative changes have been proposed and adopted in the United States since the Health Care Reform Law was enacted. On August 2, 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers up to 2% per fiscal year. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, delayed for another two months the budget cuts mandated by these sequestration provisions of the Budget Control Act of 2011. On March 1, 2013, the President signed an executive order implementing sequestration, and on April 1, 2013, the 2% Medicare payment reductions went into effect. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

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 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 may compete with our product candidates. 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 staff and experienced 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 our potential product candidates uneconomical or obsolete, and we may not be successful in marketing our product candidates against competitors.

If the market opportunities for 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.

We focus our research and product development on treatments for chronic blood diseases, with an initial focus on SCD. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, 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 these diseases. 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 potentially addressable patient population for each of our product candidates may be limited or may not be amenable to treatment with our product candidates,

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and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business. Further, even if we obtain significant market share for our product candidates, because the potential target populations are small, we may never achieve profitability despite obtaining such significant market share.

Risks Related to Our Business and Industry

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, research and development, clinical, financial and business development expertise of our executive officers, as well as the other members of our scientific and clinical teams. 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 and clinical personnel and, if we progress the development of our drug pipeline toward scaling up for commercialization, 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 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. 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 expect to expand our product development capabilities and potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

As our development progresses, we expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of research, drug development, regulatory affairs and, if any of our product candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated 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 and train additional 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 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 would be impaired.

Although a substantial amount of our effort will focus on the continued clinical testing, potential approval and commercialization of GBT440, 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. With the exception of GBT440, all of our other potential product candidates remain in the preclinical development stage. 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;

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- 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 or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;
- 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 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 GBT440.

If successful product liability claims are brought against us, we may incur substantial liability and costs. If the use of our product candidates harms patients, or is perceived to harm patients even when such harm is unrelated to 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 use of our product candidates in clinical trials and the sale of any 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 our product candidates may induce adverse events. 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 FDA warnings on product labels;
- the inability to commercialize our product candidates; and
- decreased demand for 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 clinical programs; however, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If and when we obtain marketing approval for product candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. 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 product candidates. Such events could subject us to costly litigation, require us to pay substantial amounts of money to injured patients, delay, negatively impact or end our opportunity to receive or maintain regulatory approval to market our product candidates, if approved, or require us to suspend or abandon our commercialization efforts of any approved product candidates. Even in a circumstance in which we do not believe that an adverse event is related to our products, the investigation into the circumstance may be time-consuming or inconclusive. These investigations 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.

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

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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 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 certain programs or product candidates or for indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs for product candidates, including GBT440, 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 royalty 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 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 arrangements with pharmaceutical or biotechnology companies for the development or commercialization of GBT440 and potential future product candidates. We may enter into these arrangements on a selective basis depending on the merits of retaining commercialization rights for ourselves as compared to entering into selective collaboration arrangements with leading pharmaceutical or biotechnology companies for our product candidates, both in the United States and internationally. We will face, to the extent that we decide to enter into collaboration agreements, significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator'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 candidate, the costs and complexities of manufacturing and delivering a 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, collaboration arrangements are complex and time consuming to negotiate, document and implement, and we have not previously established our ability to do so successfully. We may not be successful in our efforts to establish and implement 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 future collaborations that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations. Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable product candidate and, in some cases, termination of the collaboration arrangement. These disagreements can be difficult to resolve if neither of the parties has final

decision-making authority under the collaboration agreement. Collaborations with pharmaceutical or biotechnology companies and other third parties often are terminated or allowed to expire by the other party. Any such termination or expiration would adversely affect us financially and could harm our business reputation.

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Our 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.

We currently have no international operations, but our business strategy incorporates potential international expansion as we seek to obtain regulatory approval for, and commercialize, GBT440 in patient populations outside the United States. If GBT440 is approved, we may hire sales representatives and conduct physician and patient association outreach activities outside of the United States. Doing business internationally involves a number of risks, including but not limited to:

- multiple, conflicting, and changing laws and regulations such as privacy regulations, 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 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 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 U.S. Foreign Corrupt Practices Act, its books and records provisions, or its anti-bribery provisions.

Any of these factors could significantly harm our future international expansion and operations and, consequently, our results of operations.

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

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets which biotechnology companies such as ourselves rely upon for sources of capital. In the past, global financial crises caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn 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 suppliers, possibly resulting in supply disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

We or the third parties upon whom we depend may be adversely affected by earthquakes or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Earthquakes 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. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and 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.

Our internal computer systems, or those of our CROs, CMOs, or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our drug development programs.

Despite the implementation of security measures, our internal computer systems and those of our CROs, CMOs, and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption

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of our drug development programs. For example, the loss of data from completed or ongoing clinical trials or preclinical studies for any of our product candidates could 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.

Risks Related to Our Equity Securities

If we are unable to implement and maintain effective internal control over financial reporting in the future, the accuracy and timeliness of our financial reporting may be adversely affected

As a public company, we are subject to Section 404, or Section 404, of the Sarbanes-Oxley Act of 2002, or Sarbanes Oxley, and the related rules of the SEC, which generally requires our management and independent registered public accounting firm to report on the effectiveness of our internal control over financial reporting. Company responsibilities required by Sarbanes Oxley include establishing and maintaining corporate oversight and adequate internal control over financial reporting and disclosure controls and procedures. Effective internal controls are necessary for us to produce reliable financial reports and are important to help prevent financial fraud.

Beginning with the second annual report that we will be required to file with the SEC, Section 404 requires an annual management assessment of the effectiveness of our internal control over financial reporting. Once we are no longer an emerging growth company under the JOBS Act or, if prior to such date, we opt to no longer take advantage of the applicable exemption, we will be required to include an opinion from our independent registered public accounting firm on the effectiveness of our internal control over financial reporting.

To date, we have never conducted a review of our internal control over financial reporting for the purpose of providing the reports required by Section 404. During the course of our review and testing, we may identify significant deficiencies and be unable to remediate them before we must provide the required reports. For example, during the course of our audit for the years ended December 31, 2014 and 2013, we identified a material weakness in our internal control over financial reporting related to an insufficient number of qualified personnel within our accounting function to adequately segregate duties, a lack of sufficient review and approval procedures of manual journal entries posted to the general ledger and inadequate review procedures over general ledger accounting reconciliations. While we believe we have fully remediated the material weakness in our internal controls, if additional 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 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, as a public company we are required to file accurate and timely quarterly and annual reports with the SEC under the Exchange Act. Any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from The NASDAQ Global Select Market or other adverse consequences that would materially harm our business.

We are an “emerging growth company,” and will be able to avail ourselves of reduced disclosure requirements applicable to emerging growth companies, which could make our common stock less attractive to investors.

We are an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, as amended, or the JOBS Act, and we intend to take advantage of some of the exemptions from reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. We will remain an emerging growth company until the earliest of (1) December 31, 2020, (2) the last day of the fiscal year in which we have total annual gross revenue of at least $1.0 billion, (3) the last day of the fiscal year in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th and

(4) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period. We cannot predict if investors will find our common stock less attractive because we may rely on certain reporting exemptions available to emerging growth companies. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

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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 IPO in August 2015 and is likely to continue to be volatile. For example, our common stock traded at a high of $57.00 on September 8, 2015 and a low of $28.73 on December 8, 2015. Our stock price could be subject to wide fluctuations in response to a variety of factors, including the following:

- adverse results or delays in preclinical studies or clinical trials;
- reports of adverse events in other treatments for SCD or other indications that we may pursue, or clinical trials of such products;
- any delay in filing an IND or NDA for any of our product candidates that we may develop and any adverse development or perceived adverse development with respect to the FDA's review of that IND or NDA;
- failure to develop successfully and commercialize GBT440 or any other product candidates that we may develop;
- adverse regulatory decisions affecting our product candidates or development programs;
- inability to obtain additional funding;
- our failure to prosecute, maintain or enforce our intellectual property rights;
- changes in laws or regulations applicable to future products;
- inability to obtain adequate product supply for 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 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;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- 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 Global Select Market 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 may negatively affect the market price of our common stock, regardless of our actual operating performance. 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:

- the timing and cost of, and level of investment in, research and development activities relating to our product candidates, which may change from time to time;
- the timing and success or failure of clinical trials for 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 regulatory approval for our product candidates, and the timing and scope of any such approvals we may receive;

- the cost of manufacturing 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 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 our product candidates, should they receive approval, which may vary significantly;
- future accounting pronouncements or changes in our accounting policies;

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- the risk/benefit profile, cost and reimbursement policies with respect to our products candidates, if approved, and existing and potential future drugs that compete with our product candidates; and
- the changing and volatile U.S., European and global economic environments.

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 revenue or 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 revenue and/or earnings 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.

Pursuant to our 2015 Stock Option and Incentive Plan, or the 2015 Plan, we are authorized to grant stock options and other equity-based awards to our employees, directors and consultants. 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, 50,000 shares of our common stock were initially reserved for future issuance pursuant to our 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 (i) 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 by the maximum amount each year, 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. If our stockholders sell, or if the market perceives that our stockholders intend to sell, substantial amounts of our common stock in the public market, the price of our common stock could decline significantly.

The lock-up agreements pertaining to our IPO expired on February 8, 2016. As a result, persons who were our stockholders prior to our IPO continue to hold a substantial number of shares of our common stock that many of them are now able to sell in the public market. Significant portions of these shares are held by a small number of 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 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 and executive officers may in the future establish programmed selling plans under Rule 10b5-1 of the Securities Exchange Act of 1934, as amended, 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.

Additionally, certain holders of our common stock, or their transferees, have rights to require us to file one or more registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. If we were to register the resale of these shares, they could be freely sold in the public market. If these

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additional shares are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

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 own approximately 69% of our outstanding voting stock as of March 21, 2016, 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 cash resources and may not use them effectively.

We have broad discretion in the application of our existing cash and cash equivalents. We expect to use our existing cash and cash equivalents to continue the clinical development of GBT440, to fund the research and development of our other programs, and for working capital and general corporate purposes. Our failure to apply our existing cash and cash equivalents 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. In addition, our existing cash and cash equivalents may not be sufficient for our anticipated uses, and we may need additional resources to progress our product candidates to the stage we expect.

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.

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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. Our prior equity offerings and other changes in our stock ownership may have resulted in ownership changes. In addition, we have experienced an ownership change as a result of our initial public offering and may experience subsequent shifts in our stock ownership, 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 be 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.

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.

If we fail to maintain a proper and effective system of disclosure controls and procedures and internal controls, our ability to produce accurate and timely financial statements or comply with applicable regulations could be impaired, which could result in sanctions or other penalties that would harm our business.

We are subject to the reporting requirements of the Securities Exchange Act of 1934, the Sarbanes-Oxley Act and the rules and regulations of The NASDAQ Global Select Market. The Sarbanes-Oxley Act requires, among other things, that we establish and maintain effective disclosure controls and procedures and internal controls over financial reporting. Commencing with our fiscal year ending December 31, 2016, we must perform system and process evaluation and testing of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting in our Form 10-K filing for that year, as required by Section 404 of the Sarbanes-Oxley Act. This will require that we incur substantial additional professional fees and internal costs to expand our accounting and finance functions and that we expend significant management efforts. Previously we have never been required to test our internal controls within a specified period and, as a result, we may experience difficulty in meeting these reporting requirements in a timely manner.

We may discover weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If that were to happen, the market price of our stock could decline and we could be subject to sanctions or investigations by NASDAQ, the SEC or other regulatory authorities.

We will incur significant costs as a result of operating as a new public company, and our management will devote substantial time to new compliance initiatives.

As a public company, we will incur significant legal, accounting, and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act, as well as rules subsequently implemented by the SEC and The NASDAQ Global Select Market have imposed various requirements on public companies. In July 2010, the

Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act, was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas such as “say on pay” and pay parity. Recent legislation permits smaller “emerging growth companies” to

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implement many of these requirements over a longer period and up to five years from the pricing of our IPO. We have elected to take advantage of this legislation but cannot guarantee that we will not be required to implement these requirements sooner than budgeted or planned and thereby incur unexpected expenses. Stockholder activism, the current political environment, and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, 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 these compliance initiatives. Moreover, these 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 the Sarbanes-Oxley Act and rules adopted by the SEC and by NASDAQ, would likely result in increased costs to us as we respond to their requirements.

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. 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 28,000 square feet of space pursuant to two separate noncancelable operating leases. In 2012 we entered into a noncancelable operating lease for approximately 16,000 square feet that expires in April 2018; and in 2014 we assumed a second noncancelable operating lease from a neighboring tenant for approximately 12,000 square feet that expires in April 2018. We believe that our existing facilities are sufficient for our current needs.

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. Although the results of litigation and claims cannot be predicted with certainty, we do not believe we are party to any claim or litigation the outcome of which, if determined adversely to us, would individually or in the aggregate be reasonably expected to have a material adverse impact on our financial position, results of operations or cash flows. Regardless of the outcome, litigation can have an adverse effect on us because of defense and settlement costs, diversion of management resources and other factors.

Item 4. Mine Safety Disclosures

Not applicable.

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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. The following table sets forth the range of high and low quarterly sales prices per share of our common stock for the periods noted, as reported on The NASDAQ Global Select Market:

	Prices	
	High	Low
2015		
Third Quarter (from August 12, 2015)	$57.00	$33.01
Fourth Quarter	$55.74	$28.73

On March 21, 2016, the last reported sale price on The NASDAQ Global Select Market for our common stock was $15.83.

Recent Sales of Unregistered Securities

During the year ended December 31, 2015, 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, 2015.

Holders of Common Stock

As of March 21, 2016, there were 26 holders of record of 30,527,075 outstanding shares of our common stock.

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' cumulative 4-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 8/12/2015 to 12/31/2015.

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$100 investment in stock or index	August 12, 2015	December 31, 2015
Global Blood Therapeutics, Inc.	$100	$74.99
NASDAQ Composite Index	$100	$97.66
NASDAQ Biotechnology Index	$100	$88.17
NASDAQ Pharmaceutical Index	$100	$89.36

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

Initial Public Offering

Use of Proceeds

In August 2015, we completed an initial public offering (the IPO) of 6,900,000 shares of common stock at a price of $20.00 per share. We received net proceeds of $126.2 million, net of underwriting discounts and commissions, and offering expenses incurred by us.

None of the expenses associated with the IPO were paid to directors, officers, or persons owning 10% or more of any class of equity securities, or to their associates, or to our affiliates, other than payments in the ordinary course of business to officers for salaries. Goldman, Sachs & Co. and Morgan Stanley & Co. LLC acted as joint book-running managers, and Cowen and Company and Wedbush PacGrow acted as co-managers for the offering.

Shares of our common stock began trading on the NASDAQ Global Select Market on August 12, 2015. The shares were registered under the Securities Act on a Registration Statement on Form S-1 (Registration No. 333-205563), which was declared effective by the SEC on August 11, 2015.

There has been no material change in the planned use of proceeds from our IPO as described in our final prospectus dated August 12, 2015, filed with the SEC pursuant to Rule 424(b)(4) under the Securities Act of 1933, as amended.

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Item 6. Selected Financial Data

The information set forth below for the three years ended December 31, 2015 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 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:

	Years Ended December 31,		
(In thousands, except for share and per share data)	2015	2014	2013
Summary of Operations Data:			
Operating Expenses			
Research and development	$36,657	$16,324	$12,855
General and administrative	9,671	3,855	2,309
Related party expenses	65	332	499
Total operating expenses	46,393	20,511	15,663
Loss from operations	(46,393)	(20,511)	(15,663)
Change in fair value of Series A redeemable convertible preferred stock liability	—	(297)	(2,455)
Interest income	33	1	2
Net loss	$(46,360)	$(20,807)	$(18,116)
Net loss attributable to common stockholders	$(50,540)	$(23,772)	$(19,851)
Net loss per share attributable to common stockholders, basic and diluted	$(3.95)	$(14.20)	$(16.14)
Weighted-average number of shares used in computing net loss per share attributable to common stockholders, basic and diluted (1)	12,806,697	1,673,919	1,230,241

(1) Refer to Note 13, "Net Loss per Share Attributable to Common Stockholders" in the Notes to Financial Statements included in Part II, Item 8 of this annual report on Form 10-K for an explanation of the method used to compute basic and diluted net loss attributable to common stockholders and the weighted-average number of shares used in computation of the per share amounts.

	As of December 31,		
(in thousands)	2015	2014	2013
Selected Balance Sheet Data:			
Cash and cash equivalents	$148,502	$52,069	$3,278
Working capital (deficit)	140,097	51,056	(36)
Total assets	153,074	55,756	6,172
Accumulated deficit	(98,465)	(49,328)	(28,047)
Total stockholders' equity (deficit)	140,795	(49,326)	(25,974)

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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 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 wel 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 clinical-stage biopharmaceutical company dedicated to discovering, developing and commercializing novel therapeutics to treat grievous blood-based disorders with significant unmet need. We are developing our initial product candidate, GBT440, as an oral, once-daily therapy for sickle cell disease, or SCD, and are currently evaluating GBT440 in SCD subjects in an ongoing Phase 1/2 clinical trial. SCD is a genetic disease marked by red blood cell, or RBC, destruction and occluded blood flow and hypoxia, leading to anemia, stroke, multi-organ failure, severe pain crises, and shortened patient life span. GBT440 inhibits abnormal hemoglobin polymerization, the underlying mechanism of RBC sickling. In our clinical trials of GBT440 in SCD subjects, we observed reduced markers of red blood cell destruction, improvements in anemia, improvements in markers of tissue oxygenation, reduced numbers of sickled RBCs, and reduced markers of inflammation. In addition to GBT440 for the treatment of SCD, we intend to evaluate GBT440 for the treatment of hypoxemic pulmonary disorders and intend initially to conduct a Phase 2a proof of concept study of idiopathic pulmonary fibrosis subjects. We are also engaged in other research and development activities targeted towards hereditary angioedema, or HAE. We own and have exclusively licensed rights to our portfolio of product candidates in the United States, Europe and other major markets. We own or co-own one issued U.S. patent that covers the composition of matter for GBT440, which is due to expire in 2032 (absent any applicable patent term extensions), and we own or co-own additional pending patent applications in the United States and selected foreign countries.

Since our inception in 2011, we have devoted substantially all of our resources to identifying and developing our product candidates, including conducting clinical trials and preclinical studies and providing general and administrative support for these operations.

Prior to our initial public offering, or IPO, we had funded our operations primarily from the issuance and sale of redeemable convertible preferred stock. In August 2015, we completed our IPO pursuant to which we issued 6,900,000 shares of our common stock at a price of $20.00 per share, which included 900,000 shares sold pursuant to the exercise of the underwriters' option to purchase additional shares. We received $126.2 million from the IPO, net of underwriting discounts and commissions, and offering expenses incurred by us.

We have never been profitable and have incurred net losses in each year since inception. Our net losses were $46.4 million for the year ended December 31, 2015 and $20.8 million for the year ended December 31, 2014. As of December 31, 2015 we had an accumulated deficit of $98.5 million. To date, we have not generated any revenue. We do not expect to receive any revenue from any product candidates that we develop until we obtain regulatory approval and commercialize our products or enter into collaborative agreements with third parties. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We had cash and cash equivalents totaling $148.5 million as of December 31, 2015.

Recent Developments

The Regents of the University of California License Agreement

In September 2015, we executed an agreement with the Regents of the University of California, or the Regents, for an exclusive license to those rights the Regents may own in certain patents and patent applications relating to GBT440 and GBT440 analogs, and in exchange have committed to pay a royalty of less than 1% on future net sales. We are

solely responsible, in consultation with the Regents, for preparing, filing, prosecuting and maintaining these patents and patent applications.

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Critical Accounting Polices and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with United States generally accepted accounting principles, or U.S. GAAP. The preparation of these 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 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.

Accrued Research and Development Costs

We record accrued expenses for estimated costs of our research and development activities conducted by third-party service providers, which include the conduct of preclinical studies and clinical trials and contract manufacturing activities. We record the estimated costs of research and development activities based upon the estimated amount of services provided but not yet invoiced, and include these costs in accrued liabilities in the balance sheet and within research and development expense in the statement of operations and comprehensive loss. These costs are a significant component of our research and development expenses. We record accrued expenses for these costs based on the estimated amount of work completed and in accordance with agreements established with these third parties. We estimate the amount of work completed through discussions with internal personnel and external service providers as to the progress or stage of completion of the services and the agreed-upon fee to be paid for such services. We make significant judgments and estimates in determining the accrued balance in each reporting period. As actual costs become known, we adjust our accrued estimates. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed, the number of subjects enrolled and the rate of patient enrollment may vary from our estimates and could result in us reporting amounts that are too high or too low in any particular period. Our accrued expenses are dependent, in part, upon the receipt of timely and accurate reporting from clinical research organizations and other third-party service providers. To date, there have been no material differences between our accrued liabilities and actual expenses.

Stock-Based Compensation

We use the Black-Scholes-Merton option pricing model to estimate the fair value of options granted under our equity incentive plans and rights to acquire stock granted under our Employee Stock Purchase Plan (ESPP). The Black-Scholes-Merton option valuation model requires the use of assumptions, including the expected term of the award and the expected stock price volatility. We used the "simplified" method, which is based on the mid-point between the vesting date and the end of the contractual term, for the expected option term. We use peer company price volatility to estimate expected stock price volatility due to the limited trading history for our common stock since our IPO in August 2015. The comparable companies were chosen based on their similar size, stage in life cycle, or area of specialty. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our stock price becomes available.

Restricted stock purchases (RSPs) are measured based on the fair market values of the underlying stock on the dates of grant.

Stock-based compensation expense was calculated based on awards ultimately expected to vest and was reduced for estimated forfeitures at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differed from those estimates. We estimated annual forfeiture rates for stock options and RSPs based on our historical forfeiture experience.

The estimated fair value of stock options and RSPs is expensed on a straight-line basis over the service period of the grant and the estimated fair value of performance-contingent options and RSPs is expensed using an accelerated method over the term of the award once we determine that it is probable that those performance milestones will be achieved. Compensation expense for RSPs that contain performance conditions is based on the grant date fair value of

the award. Compensation expense is recorded over the requisite service period based on management's best estimate as to whether it is probable that the shares awarded are expected to vest. We assess the probability of the performance indicators being met on a continuous basis.

Fair value of each share of underlying common stock is based on the closing price of our common stock as reported on the date of grant. Prior to our IPO, the fair values of the shares of common stock underlying our share-based awards were estimated on each grant date by our board of directors. In order to determine the fair value of our common stock underlying option grants, our board of directors considered, among other things, contemporaneous valuations of our common stock prepared by an

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unrelated third-party valuation firm in accordance with the guidance provide by the American Institute of Certified Public Accountants Practice Guide, Valuation of Privately-Held-Company Equity Securities Issued as Compensation. Given the absence of a public trading market for our common stock, our board of directors exercised their judgment and considered a number of objective and subjective factors to determine the best estimate of the fair value of our common stock, including: our stage of development; progress of our research and development efforts; the rights, preferences and privileges of our preferred stock relative to those of our common stock; equity market conditions affecting comparable public companies and the lack of marketability of our common stock.

Compensation expense for purchases under the ESPP is recognized based on the fair value of the common stock on the date of offering, less the purchase discount percentage provided for in the plan.

Stock-based compensation expense was $3.2 million for the year ended December 31, 2015, $0.4 million for the year ended December 31, 2014 and $0.1 million for the year ended December 31, 2013. As of December 31, 2015, we had $11.4 million of total unrecognized stock-based compensation costs, net of estimated forfeitures, which we expect to recognize over a weighted-average period of 1.8 years.

We have not recognized, and we do not expect to recognize in the near future, any tax benefit related to employee stock-based compensation expense as a result of the full valuation allowance on our deferred tax assets including deferred tax assets related to our net operating loss carryforwards.

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 periodically 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.

As of December 31, 2015, our total deferred tax assets, less our total deferred tax liabilities, were $36.1 million. Due to our lack of earnings history and uncertainties surrounding our ability to generate future taxable income, the net deferred tax assets have been fully offset by a valuation allowance. The deferred tax assets were primarily comprised of federal and state tax net operating losses and tax credit carryforwards.

Utilization of the net operating loss (NOL) carryforwards may be subject to a substantial annual limitation due to ownership changes that may have occurred or that could occur in the future, as required by Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, and similar state provisions. These ownership change limitations may limit the amount of NOL carryforwards and other tax attributes that can be utilized annually to offset future taxable income and tax, respectively. In general, an “ownership change” as defined by Section 382 of the Code results from a transaction or series of transactions over a three-year period resulting in an ownership change of more than 50 percentage points (by value) of the outstanding stock of a company by certain stockholders. Since our formation, we have raised capital through the issuance of capital stock on several occasions, which separately or combined with the purchasing stockholders’ subsequent disposition of those shares, may have resulted in such ownership changes, or could result in ownership changes in the future.

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Results of Operations

Comparison of the years ended December 31, 2015, 2014 and 2013

	Year Ended December 31,			Change 2015/2014		2014/2013	
(in thousands, except percentages)	2015	2014	2013	$	%	$	%
Operating expenses:							
Research and development	$36,657	$16,324	$12,855	$20,333	125 %	$3,469	27 %
General and administrative	9,671	3,855	2,309	5,816	151	1,546	67
Related party expenses	65	332	499	(267)	(80)	(167)	(33)
Total operating expenses	46,393	20,511	15,663	25,882	126	4,848	31
Loss from operations	(46,393)	(20,511)	(15,663)	(25,882)	126	(4,848)	31
Change in fair value of Series A redeemable convertible preferred stock liability	—	(297)	(2,455)	297	(100)	2,158	(88)
Interest income	33	1	2	32	*	(1)	(50)
Net loss	$(46,360)	$(20,807)	$(18,116)	$(25,553)	123 %	$(2,691)	15 %

* Change is not meaningful

Research and development expenses

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

- employee-related expenses, which include salaries, benefits and stock-based compensation;
- expenses incurred under agreements with consultants, third-party contract organizations, and investigative clinical trial sites that conduct research and development activities on our behalf;
- laboratory and vendor expenses related to the execution of preclinical studies, nonclinical studies and clinical trials;
- the costs related to production of clinical supplies, including fees paid to contract manufacturers;
- licensing of intellectual property rights; 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 has historically been our investment in research and development activities, including the clinical development of GBT440. We allocate research and development salaries, benefits, stock-based compensation and indirect costs to GBT440 and other product candidates that we may pursue on a program-specific basis, and we include these costs in the program-specific expenses.

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 our 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 the successful development of our product candidates 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.

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The following table summarizes our research and development expenses incurred during the respective periods:

	Years Ended December 31,			Change 2015/2014		2014/2013	
(in thousands, except percentages)	2015	2014	2013	$	%	$	%
Costs incurred by development program:							
GBT440 for the treatment of SCD	$26,875	$8,867	$7,555	$18,008	203 %	$1,312	17 %
Oral treatment for HAE	8,908	5,069	4,261	3,839	76 %	808	19 %
Other preclinical programs	874	2,388	1,039	(1,514)	(63)%	1,349	130 %
Total research and development expenses	$36,657	$16,324	$12,855	$20,333	125 %	$3,469	27 %

Research and development expenses increased by $20.3 million, or 125%, to $36.7 million for the year ended December 31, 2015 from $16.3 million for the year ended December 31, 2014. The increase was primarily due to increased external expenses related to our SCD program for GBT440 as we initiated our Phase 1/2 clinical trial in early 2015 of $13.5 million and license fees for intellectual property rights to GBT440 from the Regents of $4.5 million, as well as increased expenses related to preclinical efforts for our HAE program of $3.8 million. These increases were partially offset by decreases in expenses from other preclinical programs of $1.5 million that were deemphasized.

Research and development expenses increased by $3.5 million, or 27%, to $16.3 million for the year ended December 31, 2014 from $12.9 million for the year ended December 31, 2013. The increase was primarily due to $1.3 million related to our SCD program for GBT440 as we conducted pre-IND testing and prepared to launch our Phase 1/2 clinical trial, $0.8 million related to our HAE program as we expanded our chemistry research efforts in seeking a clinical candidate and $1.4 million as we explored other research programs to add to our potential product candidate pipeline.

General and administrative expenses

General and administrative expenses consist of personnel costs, allocated facilities costs and other expenses for outside professional services, including legal, patent, human resources, audit and accounting services. Personnel costs consist of salaries, benefits and stock-based compensation. Allocated expenses consist of expenses for rent and maintenance of facilities, depreciation and amortization expense and other supplies. We expect to incur additional expenses in the future as a result of operating as a public company, including expenses related to compliance with the rules and regulations of the Securities and Exchange Commission, The NASDAQ Global Select Market, additional insurance expenses, investor relations activities and other administrative and professional services.

General and administrative expenses increased by $5.8 million, or 151%, to $9.7 million for the year ended December 31, 2015 from $3.9 million for the year ended December 31, 2014. The increase was primarily due to an increase of $2.9 million in salaries and benefits and recruiting expenses as we expanded our business management team and a net increase of $2.9 million in other general and administrative expenses, such as professional and consulting services, due to the growth of our operations.

General and administrative expenses increased by $1.5 million, or 67%, to $3.9 million for the year ended December 31, 2014 from $2.3 million for the year ended December 31, 2013. The increase was primarily due to a $0.8 million increase in salaries and benefits as we expanded our business management team, a $0.5 million increase in patent and professional services as our business grew in its second full year of operations and a $0.2 million increase in other general and administrative expenses due to the growth of our operations.

Related party expenses

Related party expenses represent fees for management and advisory services provided by Third Rock Ventures, LLC, or TRV, a related party due to its significant equity ownership.

Related party expenses decreased by $0.3 million, or 80%, to $0.1 million for the year ended December 31, 2015 from $0.3 million for the year ended December 31, 2014, and decreased by $0.2 million, or 33%, to $0.3 million for the year ended December 31, 2014 from $0.5 million for the year ended December 31, 2013. The decreases were

primarily due to a reduction in management services provided from TRV as we expanded our internal business management team.

Change in fair value of Series A redeemable convertible preferred stock liability

The change in the fair value of the Series A redeemable convertible preferred stock liability was zero for the year ended December 31, 2015 compared to a $0.3 million expense for the year ended December 31, 2014 due to the settlement of Series A

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redeemable convertible preferred stock liability in October 2014, at which time we were no longer under any obligation to issue additional shares of Series A redeemable convertible preferred stock.

The change in fair value of Series A redeemable convertible preferred stock liability was $0.3 million for the year ended December 31, 2014, compared to a $2.5 million expense for the year ended December 31, 2013. The change in both periods represents the increase in fair value of the Series A redeemable convertible preferred stock liability associated with our obligation to issue additional shares of Series A redeemable convertible preferred stock.

Income Taxes

As of December 31, 2015, we had net operating loss carryforwards of approximately $82.1 million to offset future federal income taxes, if any, through 2035, and approximately $80.0 million that may offset future state income taxes, if any, through 2035. 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, 2015, we recorded a 100% valuation allowance against our deferred tax assets of approximately $36.1 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.

Liquidity and Capital Resources

We are not profitable and have incurred losses and negative cash flows from operations each year since our inception. Prior to our IPO, our operations were financed primarily by net proceeds from the sale and issuance of convertible preferred stock. In August 2015, we completed our IPO pursuant to which we issued 6,900,000 shares of our common stock at a price to the public of $20.00 per share, which included the exercise in full of the underwriters' option to purchase additional shares. We received proceeds of $126.2 million, net of underwriting discounts and commissions, and offering expenses incurred by us. As of December 31, 2015, we had $148.5 million in cash and cash equivalents. Our primary use of cash is to fund operating expenses, which consist primarily of research and development expenditures. Cash used to fund operating expenses 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 until mid-2017. 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 will continue to require additional financing to advance GBT440 through clinical development, to develop other potential product candidates from our research programs and to fund operations for the foreseeable future. We will 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:

- the time and cost necessary to complete our ongoing clinical trial that we characterize as a Phase 1/2 trial of GBT440, to initiate and complete any registrational clinical trials of GBT440 and to pursue regulatory approvals for GBT440, and the costs of post-marketing studies that could be required by regulatory authorities;
- the progress and results of our Phase 1/2 clinical trial of GBT440;
- the progress, timing, scope and costs of our nonclinical studies, clinical trials and other related activities, including the ability to enroll subjects in a timely manner for our Phase 1/2 clinical trial of GBT440 and potential future clinical trials;
- the costs of obtaining clinical and commercial supplies of GBT440 and any other product candidates we may identify and develop;
- our ability to advance our other programs, including our program for the development of GBT440 in hypoxemic pulmonary disorders and the development of an orally available kallikrein inhibitor for the prevention of HAE attacks, through IND-enabling studies and clinical development, and the timing and scope of these development activities;
- our ability to successfully commercialize GBT440 and any other product candidates we may identify and develop;

- the manufacturing, selling and marketing costs associated with GBT440 and any other product candidates we may identify and develop, including the cost and timing of expanding our sales and marketing capabilities;

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- the amount and timing of sales and other revenues from GBT440 and any other product candidates we may identify and develop, including the sales price and the availability of adequate third-party reimbursement;
- 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;
- 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 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 our product candidate, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated clinical studies and research and development activities.

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

	Year Ended December 31,		
(in thousands)	2015	2014	2013
Cash used in operating activities	$(30,890)	$(20,121)	$(14,700)
Cash used in investing activities	(993)	(383)	(940)
Cash provided by financing activities	128,316	69,295	15,279
Net increase (decrease) in cash and cash equivalents	$96,433	$48,791	$(361)

Cash flows from operating activities

Net cash used in operating activities was $30.9 million for the year ended December 31, 2015, consisting of a net loss of $46.4 million, which was offset by non-cash charges for the fair value of stock issued for the license agreement entered into with the Regents of $4.5 million, for stock-based compensation of $3.2 million, and for depreciation and amortization expense of $0.9 million. The change in our net operating assets and liabilities was due primarily to an increase in accrued expenses related to an increase in our research and development activities of $2.8 million, in accounts payable as a result of timing of payments of $2.7 million, and in accrued compensation related to our headcount of $1.4 million.

Net cash used in operating activities was $20.1 million for the year ended December 31, 2014, consisting of a net loss of $20.8 million, which was offset by non-cash charges for depreciation and amortization expense of $0.7 million, for stock-based compensation of $0.4 million and for remeasurement of our Series A redeemable convertible preferred stock liability of $0.3 million. The change in our net operating assets and liabilities was due primarily to an increase in our prepaid expenses for the advance payments made in connection with our Phase 1/2 clinical trial of GBT440 and deposits for the manufacturing of clinical trial materials of $0.8 million, an increase in other current assets related to our funding obligations for our Phase 1/2 clinical trial of $0.3 million and a decrease in accounts payable due to timing of payments of $0.3 million, which was partially offset by an increase in accrued expenses primarily related to an increase in our research and development activities of $0.6 million and an increase in accrued compensation related to an increase in our headcount of $0.3 million.

Cash used in operating activities was $14.7 million for the year ended December 31, 2013, consisting of a net loss of $18.1 million, which was offset by non-cash charges for the remeasurement of the Series A redeemable convertible preferred stock liability of $2.5 million, for depreciation and amortization expense of $0.5 million and for stock-based compensation of $0.1 million. The change in our net operating assets and liabilities was due primarily to an increase in accrued compensation related to an increase in our headcount of $0.5 million and an increase in our accrued expenses related to an increase in our research and development activities of $0.2 million, which were partially offset by a decrease in accounts payable due to timing of payments of $0.5 million.

Cash flows from investing activities

Net cash used in investing activities for the year ended December 31, 2015, 2014 and 2013 was primarily related to our purchase of property and equipment for our office and laboratory facilities.

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Cash flows from financing activities

Net cash provided by financing activities was $128.3 million for the year ended December 31, 2015, $69.3 million for the year ended December 31, 2014 and $15.3 million for the year ended December 31, 2013. The cash provided by financing activities in 2015 was primarily related to net proceeds of $126.2 million from our IPO in August 2015 and proceeds of $2.1 million from the purchase of restricted stock. The cash provided by financing activities in 2014 was primarily related to net proceeds of $68.8 million from the issuance of redeemable convertible preferred stock and proceeds from restricted stock purchases of $0.4 million. The cash provided by financing activities in 2013 was primarily related to net proceeds from the issuance of redeemable convertible preferred stock of $15.2 million.

Off-Balance Sheet Arrangements

As of December 31, 2015, we had no off-balance sheet arrangements as defined in Item 303(a)(4) of Regulation S-K as promulgated by the SEC.

Contractual Obligations and Other Commitments

The following table summarizes our contractual obligations as of December 31, 2015:

	Payments Due by Period				
(in thousands)	Total	Less Than 1 Year	1 to 3 Years	4 to 5 Years	More Than 5 Years
Operating lease obligations	$2,704	$1,209	$1,495	$—	$—
Total contractual obligations	$2,704	$1,209	$1,495	$—	$—

We have excluded from the above table $1.0 million in contractual obligations related to uncertain tax positions as we cannot make a reasonably reliable estimate of the period of cash settlement.

Recent Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the Financial Accounting Standards Board ("FASB") or other standards setting bodies that are adopted by us as of the specified effective date. Unless otherwise discussed, we believe that the impact of recently issued standards that are not yet effective will not have a material impact on our financial statements upon adoption.

In August 2014, the FASB issued ASU No. 2014-15, Disclosure of Uncertainties about an Entity’s Ability to Continue as a Going Concern. ASU 2014-15 requires management to evaluate whether there is substantial doubt about an entity’s ability to continue as a going concern and to provide related footnote disclosures. In doing so, companies will have reduced diversity in the timing and content of footnote disclosures than under today’s guidance. ASU 2014-15 is effective for us in the first quarter of 2017 with early adoption permitted. We do not believe the impact of adopting ASU 2014-15 on our financial statements will be material.

In November 2015, the FASB issued ASU No. 2015-17, Balance Sheet Classification of Deferred Taxes, which amends existing guidance to require that deferred income tax liabilities and assets be classified as noncurrent in a classified balance sheet, and eliminates the prior guidance which required an entity to separate deferred tax liabilities and assets into a current amount and a noncurrent amount in a classified balance sheet. The standard is effective for us in fiscal year 2017. Early adoption is permitted. As permitted by ASU 2015-17, we early-adopted this standard and applied it retrospectively to all periods of the tax provision presented. As we have full valuation allowance against the deferred assets and liabilities, there is no impact to the financial statements. We have reflected the change of this pronouncement in Note 10, "Income Taxes", in the Notes to Financial Statements included in Part II, item 8 of this annual report on Form 10-K.

In February 2016, the FASB issued ASU No. 2016-02, Leases. The new standard requires lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight-line basis over the term of the lease. A lessee is also required to record a right-of-use asset and a lease liability for all leases with a term of greater than 12 months regardless of their classification. Leases with a term of 12 months or less will be accounted for similar to existing guidance for operating leases. The standard is effective for interim and annual periods beginning after December 15, 2018, with early adoption permitted. We are currently in the process of evaluating the impact the adoption of this new standard will have on our financial position or results of operations.

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Item 7.A 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 had cash and cash equivalents of $148.5 million as of December 31, 2015 and $52.1 million as of December 31, 2014, which consist of bank deposits and money market funds. Such interest-earning instruments carry a degree of interest rate risk; however, historical fluctuations in interest income have not been significant. We had no outstanding debt as of December 31, 2015 and 2014.

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Item 8. Financial Statements and Supplementary Data

GLOBAL BLOOD THERAPEUTICS, INC.
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Years Ended December 31, 2015 and 2014

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Report of Independent Registered Public Accounting Firm

The Board of Directors

Global Blood Therapeutics, Inc.:

We have audited the accompanying balance sheets of Global Blood Therapeutics, Inc. as of December 31, 2015 and 2014, and the related statements of operations and comprehensive loss, redeemable convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the years in the three year period ended December 31, 2015. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Global Blood Therapeutics, Inc. as of December 31, 2015 and 2014, and the results of its operations and its cash flows for each of the years in the three year period ended December 31, 2015, in conformity with U.S. generally accepted accounting principles.

(signed) KPMG LLP

San Francisco, California

March 29, 2016

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GLOBAL BLOOD THERAPEUTICS, INC.
Balance Sheets
(In thousands, except share and per share amounts)

	December 31, 2015	2014
Assets		
Current assets:		
Cash and cash equivalents	$148,502	$52,069
Prepaid expenses	1,222	1,135
Other assets, current	1,096	389
Total current assets	150,820	53,593
Property and equipment, net	2,114	2,023
Restricted cash	140	140
Total assets	$153,074	$55,756
Liabilities, Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)		
Current liabilities:		
Accounts payable	$3,361	$541
Payable due to related party	—	14
Accrued liabilities	4,400	948
Accrued compensation	2,242	847
Other liabilities, current	720	187
Total current liabilities	10,723	2,537
Other liabilities, noncurrent	1,556	384
Total liabilities	12,279	2,921
Commitments and contingencies (Note 12)		
Redeemable convertible preferred stock, $0.001 par value: zero and 69,363,168 shares authorized at December 31, 2015 and 2014, respectively; zero and 69,113,168 shares issued and outstanding at December 31, 2015 and 2014, respectively; aggregate liquidation preference of zero and $103,289 at December 31, 2015 and 2014, respectively.	—	102,161
Stockholders' equity (deficit):		
Preferred stock, $0.001 par value, 5,000,000 and zero shares authorized at December 31, 2015 and 2014, respectively, and none issued and outstanding as of December 31, 2015 and 2014.	—	—
Common stock, $0.001 par value, 150,000,000 and 94,000,000 shares authorized at December 31, 2015 and 2014, respectively; 29,359,800 and 1,954,488 shares issued and outstanding at December 31, 2015 and 2014, respectively.	29	2
Additional paid-in capital	239,231	—
Accumulated deficit	(98,465)	(49,328)
Total stockholders' equity (deficit)	140,795	(49,326)
Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)	$153,074	$55,756

See accompanying notes.

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GLOBAL BLOOD THERAPEUTICS, INC.
Statements of Operations and Comprehensive Loss
(In thousands, except share and per share amounts)

	Year Ended December 31, 2015	2014	2013
Operating expenses:			
Research and development	$36,657	$16,324	$12,855
General and administrative	9,671	3,855	2,309
Related party expenses	65	332	499
Total operating expenses	46,393	20,511	15,663
Loss from operations	(46,393)	(20,511)	(15,663)
Change in fair value of Series A redeemable convertible preferred stock liability	—	(297)	(2,455)
Interest income	33	1	2
Net loss and comprehensive loss	$(46,360)	$(20,807)	$(18,116)
Net loss attributable to common stockholders	$(50,540)	$(23,772)	$(19,851)
Net loss per share attributable to common stockholders, basic and diluted	$(3.95)	$(14.20)	$(16.14)
Weighted-average number of shares used in computing net loss per share attributable to common stockholders, basic and diluted	12,806,697	1,673,919	1,230,241

See accompanying notes.

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GLOBAL BLOOD THERAPEUTICS, INC.
Statements of Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)
(In thousands, except share amounts)

	Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount			
Balance at December 31, 2012	13,663,168	$9,451	971,418	$1	$444	$(9,794)	$(9,349)
Issuance of Series A redeemable convertible preferred stock, net of $15 in issuance costs	15,250,000	15,235	—	—	—	—	—
Remeasurement of fair value and settlement of Series A redeemable convertible preferred stock liability	—	1,804	—	—	3,081	—	3,081
Accretion of redeemable convertible preferred stock to redemption value	—	1,735	—	—	(1,598)	(137)	(1,735)
Vesting of restricted stock purchase	—	—	412,386	—	6	—	6
Common stock issued on exercise of stock options	—	—	4,285	—	1	—	1
Stock-based compensation expense	—	—	—	—	138	—	138
Net loss	—	—	—	—	—	(18,116)	(18,116)
Balance at December 31, 2013	28,913,168	28,225	1,388,089	1	2,072	(28,047)	(25,974)
Issuance of Series A redeemable	21,000,000	20,591	—	—	—	—	—

convertible preferred stock, net of $393 derivative liability and $16 in issuance costs

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Issuance of Series B redeemable convertible preferred stock, net of $146 in issuance costs	19,200,000	47,854	—	—	—	—	—
Settlement of fair value of Series A redeemable convertible preferred stock liability	—	2,526	—	—	—	—	—
Accretion of redeemable convertible preferred stock to redemption value	—	2,965	—	—	(2,491)	(474)	(2,965)
Vesting of restricted stock purchase	—	—	411,333	1	20	—	21
Common stock issued on exercise of stock options	—	—	155,066	—	49	—	49
Stock-based compensation expense	—	—	—	—	350	—	350
Net loss	—	—	—	—	—	(20,807)	(20,807)
Balance at December 31, 2014	69,113,168	102,161	1,954,488	2	—	(49,328)	(49,326)
Accretion of redeemable convertible preferred stock to redemption value	—	4,180	—	—	(1,403)	(2,777)	(4,180)
Conversion of Series A and B redeemable convertible preferred stock into	(69,113,168)	(106,341)	19,746,614	20	106,321	—	106,341

common stock							
Issuance of common stock upon initial public offering, net of issuance costs	—	—	6,900,000	7	126,223	—	126,230
Common stock issued for license	—	—	85,714	—	4,492	—	4,492
Common stock issued on exercise of stock options	—	—	89,549	—	45	—	45
Vesting of restricted stock purchases	—	—	583,435	—	330	—	330

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Stock-based compensation expense	—	—	—	3,223	—	3,223
Net loss	—	—	—	—	(46,360)	(46,360)
Balance at December 31, 2015	$—	29,359,800	$29	$239,231	$(98,465)	$140,795

See accompanying notes.

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GLOBAL BLOOD THERAPEUTICS, INC.
Statements of Cash Flows
(In thousands)

	Year Ended December 31,		
	2015	2014	2013
CASH FLOWS FROM OPERATING ACTIVITIES:			
Net loss	$(46,360)	$(20,807)	$(18,116)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	873	666	534
Loss on disposal of fixed assets	33	—	
Remeasurement of Series A redeemable convertible preferred stock liability	—	297	2,455
Stock-based compensation	3,223	350	138
Fair value of stock issued for license	4,492	—	—
Changes in operating assets and liabilities:			
Prepaid expenses	(87)	(753)	(73)
Other assets, current	22	(323)	149
Accounts payable	2,705	(304)	(465)
Payable due to related party	(14)	(115)	(68)
Accrued liabilities	2,834	599	183
Accrued compensation	1,395	271	494
Other liabilities, current	19	17	38
Other liabilities, noncurrent	(25)	(19)	31
Net cash used in operating activities	(30,890)	(20,121)	(14,700)
CASH FLOWS FROM INVESTING ACTIVITIES:			
Purchase of property and equipment	(993)	(323)	(940)
Increase in restricted cash	—	(60)	—
Net cash used in investing activities	(993)	(383)	(940)
CASH FLOWS FROM FINANCING ACTIVITIES:			
Proceeds from issuance of common stock, net of issuance costs	126,230	—	—
Proceeds from issuance of redeemable convertible preferred stock, net of issuance costs	—	68,838	15,235
Proceeds from sale of restricted stock	2,108	408	43
Repurchase of unvested restricted stock purchases	(67)	—	—
Proceeds from the exercise of common stock options	45	49	1
Net cash provided by financing activities	128,316	69,295	15,279
Net increase (decrease) in cash and cash equivalents	96,433	48,791	(361)
Cash and cash equivalents at beginning of period	52,069	3,278	3,639
Cash and cash equivalents at end of period	$148,502	$52,069	$3,278
SUPPLEMENTAL DISCLOSURES OF NON-CASH FINANCING INFORMATION:			
Remeasurement and settlement of fair value of Series A redeemable convertible preferred stock liability	$—	$2,526	$4,885
Accretion of Series A redeemable convertible preferred stock	$4,180	$2,965	$1,735

See accompanying notes.

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GLOBAL BLOOD THERAPEUTICS, INC.
Notes to Financial Statements
1. Organization and Basis of Presentation
Global Blood Therapeutics Inc. (the “Company”, “we”, “us”, and “our”) was incorporated in Delaware in February 2011 and commenced operations in May 2012. We are a clinical-stage biopharmaceutical company dedicated to discovering, developing and commercializing novel therapeutics to treat grievous blood-based disorders with significant unmet need. Our primary activities have been establishing our facilities, recruiting personnel, conducting development of our product candidates, including clinical trials, and raising capital. Our principal operations are based in South San Francisco, California, and we operate in one segment.
Reverse Stock Split
In July 2015, our Board of Directors approved an amendment to our amended and restated certificate of incorporation to effect a reverse split of our issued and outstanding common stock at a 1-for-3.5 ratio, which was effected on July 30, 2015. The par value and authorized shares of common stock and convertible preferred stock were not adjusted as a result of the reverse split. All issued and outstanding common stock, options to purchase common stock and per share amounts contained in the financial statements have been retroactively adjusted to reflect the reverse stock split for all periods presented. The financial statements have also been retroactively adjusted to reflect a proportional adjustment to the conversion ratio for each series of preferred stock that was effected in connection with the reverse stock split.
Initial Public Offering
On August 11, 2015, our registration statement on Form S-1 (File No. 333-205563) relating to our initial public offering (“IPO”) of common stock became effective. The IPO closed on August 17, 2015 at which time we issued 6,900,000 shares of our common stock at a price of $20.00 per share. We received $126.2 million, net of underwriting discounts and commissions, and offering expenses incurred by us. Upon the closing of our IPO, all outstanding shares of our redeemable convertible preferred stock converted by their terms into 19,746,614 shares of common stock. See Note 6, “Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit).”
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 research and development activities. As of December 31, 2015, we had an accumulated deficit of $98.5 million. We expect to incur additional losses in the future to conduct product research and development and we anticipate the need to raise additional capital to fully implement our business plan. We intend to raise such capital through the issuance of additional equity, and potentially through borrowings, and strategic alliances with partner companies. However, if such financing is not available at adequate levels or when it will be required, we will need to reevaluate our operating plans. We believe that our existing cash and cash equivalents will be sufficient to fund our cash requirements through mid-2017.
2. Summary of Significant Accounting Policies
Basis of Presentation
The accompanying financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America (“U.S. GAAP”).
Use of Estimates
The preparation of the accompanying 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 financial statements, and the reported amounts of 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.
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.

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Concentration of Credit Risk
Financial instruments that potentially subject us to a concentration of credit risk consist of cash and cash equivalents. Our cash and cash equivalents are held by a financial institution in the United States. Amounts on deposit may at times exceed federally insured limits. We believe that the financial institution is financially sound, and accordingly, minimal credit risk exists with respect to the financial institution.
Fair Value Measurement
The carrying amounts of certain financial instruments, including cash equivalents, restricted cash, accounts payable and accrued liabilities approximate fair value due to their relatively short maturities.
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, 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 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 money market funds held by our financial institution as collateral for our letter of credit under our facility lease.
Accruals of Research and Development Costs
We record accruals for estimated costs of research, preclinical, 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. 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 actual costs through discussions with internal personnel and external service providers as to the progress or stage of completion of the services and the agreed-upon fee to be paid for such services. We make significant judgments and estimates in determining the accrual balance in each reporting period. As actual costs become known, we adjust our accruals. We have not experienced any material deviations between accrued clinical trial expenses and actual clinical trial expenses. However, actual services performed, number of subjects enrolled, and the rate of subject enrollment may vary from our estimates, resulting in adjustments to clinical trial expense in future periods. Changes in these estimates that result in material changes to our accruals could materially affect our results of operations.
Leases
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 balance sheet. Incentives granted under our facilities leases, including 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.

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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. There have been no items qualifying as other comprehensive income (loss) and, therefore, for all periods presented, our comprehensive income (loss) was the same as our net loss.
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.
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 statements of operations and comprehensive loss is based on options ultimately expected to vest, taking into consideration estimated forfeitures. Stock-based compensation expense is revised in subsequent periods, if necessary, if actual forfeitures differ from these estimates. When estimating forfeitures, we consider historic voluntary termination behaviors as well as trends of actual option forfeitures. For options granted to nonemployees, we revalue the unearned portion of the stock-based compensation and at each reporting period end the resulting change in fair value is recognized in the statements of operations and comprehensive loss over the period the related services are rendered.
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. Our policy is to recognize interest and penalties related to the underpayment of income taxes as a component of income tax expense or benefit. To date, there have been no interest or penalties charged in relation to the unrecognized tax benefits.
Net Loss per Share Attributable to Common Stockholders
Basic net loss per share attributable to common stockholders is calculated by dividing the net loss attributable to common stockholders by the weighted average number of shares of common stock outstanding during the period, without consideration of common stock equivalents. The net loss attributable to common stockholders is calculated by adjusting our net loss for the accretion on the redeemable convertible preferred stock. Diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders, since the effects of potentially dilutive securities are antidilutive given our net loss.
Recent Accounting Pronouncements
In August 2014, the FASB issued ASU No. 2014-15, Disclosure of Uncertainties about an Entity’s Ability to Continue as a Going Concern. ASU 2014-15 requires management to evaluate whether there is substantial doubt about an entity’s ability to continue as a going concern and to provide related footnote disclosures. In doing so, companies will have reduced diversity in the timing and content of footnote disclosures than under today’s guidance. ASU 2014-15 is effective for us in the first quarter of 2017 with early adoption permitted. We do not believe the impact of adopting

ASU 2014-15 on our financial statements will be material.

In November 2015, the FASB issued ASU No. 2015-17, Balance Sheet Classification of Deferred Taxes, which amends existing guidance to require that deferred income tax liabilities and assets be classified as noncurrent in a classified balance sheet, and eliminates the prior guidance which required an entity to separate deferred tax liabilities and assets into a current

amount and a noncurrent amount in a classified balance sheet. The standard is effective for us in fiscal year 2017. Early adoption is permitted. As permitted by ASU 2015-17, we early-adopted this standard and applied it retrospectively to all periods of the tax provision presented. As we have full valuation allowance against the deferred assets and liabilities, there is no impact to the financial statements. We have reflected the change resulting from this pronouncement in Note 10, Income Taxes.

In February 2016, the FASB issued ASU No. 2016-02, Leases. The new standard requires lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight-line basis over the term of the lease. A lessee is also required to record a right-of-use asset and a lease liability for all leases with a term of greater than 12 months regardless of their classification. Leases with a term of 12 months or less will be accounted for similar to existing guidance for operating leases. The standard is effective for interim and annual periods beginning after December 15, 2018, with early adoption permitted. We are currently in the process of evaluating the impact the adoption of this new standard will have on our financial position or results of operations.

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 financial statements on a recurring basis (at least annually). Financial instruments include cash and cash equivalents, restricted cash, accounts payable and accrued liabilities that approximate fair value due to their relatively short maturities.

Assets and liabilities recorded at fair value on a recurring basis in the 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 and liabilities measured at fair value on a recurring basis:

	December 31, 2015			
(in thousands)	Total	Level 1	Level 2	Level 3
Financial Assets:				
Money market funds	$148,642	$148,642	$—	$—
Total financial assets	$148,642	$148,642	$—	$—

	December 31, 2014			
(in thousands)	Total	Level 1	Level 2	Level 3
Financial Assets:				
Money market funds	$52,209	$52,209	$—	$—
Total financial assets	$52,209	$52,209	$—	$—

Our financial instruments consist of Level 1 assets. Where quoted prices for identical assets are available in an active market, securities are classified as Level 1. Level 1 assets consist of highly liquid money market funds, which as of

December 31, 2015 and 2014 includes $140,000 of funds that are collateral for our facility lease that are included within restricted cash. There were no unrealized gains and losses in our investments in these money market funds.

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The following table sets forth a summary of the changes in the fair value of our Level 3 financial instruments as follows:

(in thousands)	Series A Redeemable Convertible Preferred Stock Liability
Balance at January 1, 2014	$1,836
Net increase in fair value upon revaluation	297
Recognition of fair value of liability due to new obligation for Series A financing in April 2014	393
Settlement of tranche liability due to issue of Series A redeemable convertible preferred shares	(2,526)
Balance at December 31, 2014	$—

The Series A redeemable convertible preferred stock liability stemmed from the initial sale of Series A redeemable convertible preferred stock wherein we were obligated to sell additional shares in subsequent closings contingent upon the achievement of certain development milestones. The subsequent closings were deemed to be freestanding financial instruments that were outside our control. We estimated the fair value of this liability using Black-Scholes-Merton Option Pricing models that include the assumptions of probability of the financing occurring, stock price per share, expected term, and discount rate. The change in fair value was recognized as a gain or loss in the statements of operations and comprehensive loss, with final settlement of the liability in 2014 upon the issuance of the final tranche of convertible preferred stock.

4. Balance Sheet Components

Property and Equipment

Property and equipment consist of the following:

	December 31,	
(in thousands)	2015	2014
Laboratory equipment	$3,151	$2,611
Computer equipment	596	472
Leasehold improvements	340	245
Construction-in-progress	129	—
Total property and equipment	4,216	3,328
Less: accumulated depreciation and amortization	(2,102)	(1,305)
Property and equipment, net	$2,114	$2,023

Depreciation and amortization expense was $0.9 million for the year ended December 31, 2015, $0.7 million for the year ended December 31, 2014 and $0.5 million for the year ended December 31, 2013.

Accrued Liabilities

Accrued liabilities consist of the following:

	December 31,	
(in thousands)	2015	2014
Accrued clinical and manufacturing expenses	$4,025	$749
Accrued professional and consulting services	287	153
Other	88	46
Total accrued liabilities	$4,400	$948

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Other liabilities, noncurrent

Other noncurrent liabilities consists of the following:

(in thousands)	December 31, 2015	2014
Restricted shares subject to repurchase, noncurrent	$1,470	$273
Deferred rent, noncurrent	86	111
Total other liabilities, noncurrent	$1,556	$384

5. Common Stock

Common Stock Reserved for Issuance

We have reserved sufficient shares of common stock for issuance upon the exercise of stock options 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, 2015, no common stock dividends had been declared by the board of directors.

We have reserved shares of common stock, on an as-converted basis, for future issuance as follows:

	December 31, 2015	2014
Series A redeemable convertible preferred stock outstanding, as converted	—	14,260,904
Series B redeemable convertible preferred stock outstanding, as converted	—	5,485,710
Restricted shares subject to future vesting	1,097,288	1,121,979
Options issued and outstanding	2,058,787	954,567
Shares available for future grant under the 2015 Plan	1,014,485	651,816
Employee stock purchase plan	50,000	—
Total	4,220,560	22,474,976

Common Stock Issued for License Agreement

In September, 2015, we executed an agreement with the Regents of the University of California, or the Regents, for an exclusive license to those rights the Regents may own in certain patents and patent applications relating to GBT440 and GBT440 analogs, and in exchange have committed to pay a royalty of less than 1% on future net sales. In connection with this agreement we issued 85,714 shares of our common stock with an estimated fair value of $4.5 million, which was recorded in research and development expense in our statement of operations.

Restricted Stock

In May 2012, we issued 1,345,709 shares of restricted common stock to founders at $0.0035 per share of which 1,249,282 were subject to future vesting. Under the related stock purchase agreements, we have the right to repurchase the common stock which right lapses according to individual vesting schedules. In order to vest, the holders are required to provide continued service to us. Upon vesting, the appropriate amounts are transferred from liabilities to additional paid-in capital. If the holder of any unvested restricted common stock is terminated for any reason, we have the right to repurchase the unvested shares at the stockholder’s original purchase price. As such, the shares subject to future vesting are not deemed outstanding for accounting purposes until the shares vest.

We have issued stock awards to employees under the 2012 Stock Option and Grant Plan. Under the related stock purchase agreements, we have the right to repurchase the common stock at the lower of fair value and the stockholders’ original purchase price which right lapses according to individual vesting schedules. In order to vest, the holders are required to provide continued service to us. Upon vesting, the appropriate amounts are transferred from liabilities to additional paid in capital. If the holder of any unvested restricted common stock is terminated for any reason, we have the right to repurchase the unvested shares at the stockholder’s original purchase price. As such, the shares subject to future vesting are not deemed outstanding for accounting purposes until the shares vest.

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Restricted shares subject to repurchase and related liability were as follows:

(in thousands except share data)	December 31, 2015	2014
Restricted shares subject to repurchase:		
Shares issued to founders	6,250	174,150
Shares issued pursuant to the 2012 Stock Option and Grant Plan	1,091,038	947,829
Total restricted shares subject to repurchase	1,097,288	1,121,979
Liability pertaining to restricted shares subject to repurchase		
Other liabilities, current	$677	$163
Other liabilities, noncurrent	1,470	273
Total liabilities pertaining to shares subject to repurchase	$2,147	$436

6. Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)

Following the IPO in August 2015, all of our outstanding shares of our redeemable convertible preferred stock were converted into 19,746,614 shares of common stock and the related carrying value was reclassified to common stock and additional paid-in capital. Accordingly, there were no shares of redeemable convertible preferred stock outstanding as of December 31, 2015.

As of December 31, 2014 redeemable convertible preferred stock consisted of the following:

(in thousands, except share amounts)	Shares Authorized	Shares Issued and Outstanding	Net Carrying Value	Aggregate Liquidation Preference
Series A	50,163,168	49,913,168	$54,273	$55,254
Series B	19,200,000	19,200,000	47,888	48,035
Total redeemable convertible preferred stock	69,363,168	69,113,168	$102,161	$103,289

Prior to the conversion of our convertible preferred stock upon our IPO, the significant provisions of each series of the redeemable convertible preferred stock were as follows:

Liquidation

Upon liquidation, dissolution, or winding up of the Company (whether voluntary or involuntary) or Deemed Liquidation Event (as defined below), before any distribution or payment was to be made to the holders of any Series A redeemable convertible preferred stock or common stock, the holders of Series B redeemable convertible preferred stock would have been entitled to be paid out of our assets legally available for distribution, an amount equal to the original issue price of the Series B redeemable convertible preferred stock plus any dividends accrued, but unpaid thereon, whether or not declared, together with any other dividends declared but unpaid thereon. The holders of Series A redeemable convertible preferred stock would have been entitled to receive, prior and in preference to any distribution of any of the Company's assets legally available for distribution to the holders of common stock, an amount equal to the respective original issue price of Series A of redeemable convertible preferred stock, plus any dividends accrued, but unpaid thereon, whether or not declared, together with any other dividends declared but unpaid thereon. The original issue price was $2.50 for the Series B and $1.00 for the Series A redeemable convertible preferred stock.

Voting

Each holder of shares of redeemable convertible preferred stock was entitled to the number of votes equal to the number of shares of common stock into which such shares of redeemable convertible preferred stock could have been converted and had voting rights and powers equal to the voting rights and powers of the common stock, and except as provided by law or by other provisions of the Certificate of Incorporation, voted together with the common stock as a single class on an as-converted basis on all matters as to which holders of common stock had the right to vote.

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The holders of Series A redeemable convertible preferred stock, voting separately as a single class, were entitled to elect three members of the Company's Board of Directors. All remaining members of the Company's Board of Directors were elected by the holders of the common stock and any other series or class of voting stock, including the Series A and B redeemable convertible preferred stock, exclusively and voting together as a single class.

Conversion

The holders of redeemable convertible preferred stock were subject to certain optional and mandatory conversion rights.

(i) Optional Conversion Rights: Each share of redeemable convertible preferred stock were convertible, at the option of the holder, into such number of fully paid shares of common stock as was determined by dividing the Original Issue Price by the Conversion Price in effect at the time of conversion.

(ii) Mandatory Conversion Rights: Upon either (a) for each of Series A and Series B redeemable convertible preferred stock the date and time, or the occurrence of an event, specified by vote or written consent of holders of at least a majority of the then outstanding shares of Series A redeemable convertible preferred stock or Series B redeemable convertible preferred stock or (b) the closing of the sale of shares of common stock to the public in a qualified initial public offering, all outstanding shares of redeemable convertible preferred stock were automatically to be converted into shares of common stock, at the then effective conversion rate.

Dividends

Series A and Series B redeemable convertible preferred stock accrued dividends at a rate per annum of $0.08 and $0.20 per share, respectively. Dividends were cumulative and accrued on a day-to-day basis. Dividends were payable only when and if declared by the Board of Directors. No dividends were declared as of December 31, 2014 or through the conversion date in 2015.

Redemption

The Series A redeemable convertible preferred stock was redeemable, at the election of majority of the holders of Series A redeemable convertible preferred stock, on or after the later to occur of the redemption in full of all outstanding shares of Series B redeemable convertible preferred stock and the seventh anniversary of the Series A preferred stock issue date (or May 2019), in three annual installments at the original issue price of $1.00 per share, plus any unpaid accruing dividends (whether or not declared).

The Series B redeemable convertible preferred stock was redeemable at the election of majority of the holders of Series B redeemable convertible preferred stock, on or after the seventh anniversary of the Series B preferred stock issue date (or December 2021), in three annual installments at the original issue price of $2.50 per share, plus any unpaid accruing dividends (whether or not declared). As only the passage of time was required for Series A and Series B to become redeemable, the Company was accreting the carrying value of Series A and Series B to their redemption value over the period from the date of issuance to May 2019 and December 2021, respectively, (the earliest redemption dates). In the event of a change of control of the Company, proceeds would have been distributed in accordance with the liquidation preferences set forth in its Amended and Restated Certificate of Incorporation unless the holders of redeemable convertible preferred stock had converted their preferred shares into common shares. Therefore, redeemable convertible preferred stock was classified outside of stockholders' equity (deficit) on the accompanying balance sheets, as Series A and Series B preferred could have been redeemed and as events triggering the liquidation preferences were not solely within the Company's control.

Accretion of redeemable convertible preferred stock was $4.2 million for the year ended December 31, 2015, $3.0 million for the year ended December 31, 2014 and $1.7 million for the year ended December 31, 2013. The accretion was recorded as an offset to the additional paid in capital until such balance was depleted and any remaining accretion was recorded to accumulated deficit.

7. Series A Redeemable Convertible Preferred Stock Liability

The Company recorded the redeemable convertible preferred stock liability incurred in connection with its Series A redeemable convertible preferred stock as a derivative financial instrument liability at the fair value on the date of issuance, and remeasured on each subsequent balance sheet date. The Series A preferred stock liability stems from the

initial sale of Series A redeemable convertible preferred stock wherein the Company was obligated to sell additional shares in subsequent closings contingent upon the achievement of certain development milestones. The subsequent closings were deemed to be freestanding financial instruments that were outside the control of the Company. The changes in fair value were recognized as a gain or loss

in the statements of operations and comprehensive loss and liability is remeasured at each reporting period and settlement of the related Series A tranche closings. The Company estimated the fair value of this liability using the Black Scholes option pricing model that include assumptions of probability of achievement of the development milestones or funding of the financing, stock price per share, expected term and risk-free interest rate.

At December 31, 2015 and 2014, there were no outstanding obligations related to the Series A redeemable convertible preferred stock liability as all obligations were settled in the Tranche 4 closing of the issuance of Series A redeemable convertible preferred stock in October 2014. For the years ended December 31, 2015, 2014 and 2013, the Company recorded a total charge of zero, $297,000 and $2.5 million, respectively, for the changes in the fair value of the Series A redeemable convertible preferred stock liability in the statement of operations and comprehensive loss. For the years ended December 31, 2015, 2014 and 2013, the Company recorded zero, $2.5 million and $1.8 million, respectively, as the settlement of the outstanding obligation/right of the Series A redeemable convertible preferred stock liability in redeemable convertible preferred stock.

8. Stock-based awards

2015 Stock Option and Incentive Plan

In July 2015, the Company adopted the 2015 Stock Option and Incentive Plan (the “2015 Plan”). Under the 2015 Plan, 1,430,000 shares of our common stock were initially 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. 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 four-year period but may be granted with different vesting terms. As of December 31, 2015, there were 1,014,485 shares available for us to grant under the 2015 Plan.

2012 Stock Option and Grant Plan

In 2012, the Company adopted the 2012 Stock Option and Grant Plan (the “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 employees, officers, directors, or consultants of ours. Previously we had initially reserved 2,785,713 shares of common stock for issuance under the 2012 Plan. On April 9, 2015 we increased the number of shares available under the 2012 Plan by 1,000,000 to a total of 3,785,713 shares. Awards granted under the 2012 Plan expire no later than 10 years from the date of grant. For incentive stock options and nonstatutory 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, the optionee directly or by attribution owns 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. Upon adoption of the 2015 Plan, no new awards or grants are permitted under the 2012 Plan.

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Stock Option Activity
The following table summarizes activity under the Company's stock option plans, including the 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, 2014	954,567	0.38	9.0	
Options granted	1,611,581	11.54		
Options exercised	(89,549)	0.50		
Options canceled	(417,812)	2.40		
Outstanding — December 31, 2015	2,058,787	$8.71	9.0	$50,910
Vested and exercisable — December 31, 2015	382,057	$2.93	7.9	$11,266
Vested and expected to vest — December 31, 2015	1,934,062	$8.53	8.9	$48,095

The aggregate intrinsic values of options outstanding, vested and exercisable, and vested and expected to vest were calculated as the difference between the exercise price of the options and the fair value our common stock as of December 31, 2015. The total intrinsic value of options exercised was $427,000 for the year ended December 31, 2015, $35,000 for the year ended December 31, 2014 and zero for the year ended December 31, 2013. The weighted-average estimated fair value of stock options granted was $8.56 for the year ended December 31, 2015, $0.34 for the year ended December 31, 2014 and $0.31 for the year ended December 31, 2013.

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,		
	2015	2014	2013
Expected term (in years)	5.3-6.3	6.0-6.1	6.0-6.1
Volatility	73.8%-87.6%	80.7%-93.0%	79.8%-86.6%
Risk-free interest rate	1.5%-1.8%	1.89%-2.10%	1.12%-1.31%
Dividend yield	—	—	—

The fair value of the shares of common stock underlying stock options before our IPO was determined by our Board of Directors. Prior to our IPO in August 2015, because there was no public market for our common stock, the Board of Directors determined fair value of the common stock at the time of grant of the option by considering a number of objective and subjective factors including important developments in our operations, valuations performed by an independent third party, sales of convertible preferred stock, actual operating results and financial performance, the conditions in the biotechnology industry and the economy in general, the stock price performance and volatility of comparable public companies, and the lack of liquidity of our common stock, among other factors.

In determining the fair value of the options granted, we used the Black-Scholes-Merton option-pricing model and assumptions discussed below. Each of these inputs is subjective and generally requires significant judgment to determine.

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 had very limited historical information to develop reasonable expectations about future exercise patterns and post-vesting employment termination behavior for our stock option grants.

Expected Volatility—Prior to the IPO in August 2015, we were privately held and did not have any trading history for our common stock; accordingly, the expected volatility was estimated based on the average volatility for comparable publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants. 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

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GLOBAL BLOOD THERAPEUTICS, INC.
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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. Sufficient trading history does not yet exist for our common stock, therefore the estimate of expected volatility is based on the volatility of other companies with similar products under development, market, size and other factors.
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.
Stock Options Granted to Non-employees with Service-Based Vesting Valuation Assumptions
Stock-based compensation related to stock options granted to non-employees is recognized as the stock options are earned. The fair value of the stock options granted is calculated at each reporting date using the Black-Scholes option-pricing model with the following assumptions:

	Year Ended December 31,		
	2015	2014	2013
Expected term (in years)	4.0-9.9	5.0-9.9	5.0-9.4
Volatility	73.4%-91.2%	77.6%-82.3%	79.7%-88.1%
Risk-free interest rate	0.8-2.7%	1.5%-2.7%	0.9%-2.6%
Dividend yield	—	—	—

Performance-Contingent Stock Options Granted to Employees Valuation Assumptions
On April 9, 2015, our Board of Directors granted a total of 227,139 performance-contingent awards to members of our senior management team, with an exercise price of $3.40 per share, which the Board of Directors determined was the fair market value on the grant date.
The awards have dual triggers of vesting based upon the successful achievement of four corporate operating milestones within specified timelines, as well as a requirement for continued employment. When a performance goal is deemed to be probable of achievement, time-based vesting and recognition of stock-based compensation expense commences. In the event any of the corporate operating milestones are not achieved by the specified timelines, such vesting tranche will terminate and no longer be exercisable with respect to that portion of the shares. As of December 31, 2015, we determined that the achievement of the requisite performance conditions was not probable and, as a result, no compensation cost was recognized for the performance-contingent awards.
The fair value of employee performance-contingent options was estimated at the date of grant using a Black-Scholes-Merton option-pricing model with the following assumptions:

	Year Ended December 31, 2015
Expected term (in years)	1.8-2.4
Volatility	77.2%-79.1%
Risk-free interest rate	0.5%-0.8%
Dividend yield	— %

Restricted Stock Purchases
When Restricted Stock Purchases ("RSPs") are granted, the individual purchases the shares at the grant date fair value of the underlying common stock. The purchase of the stock is subject to forfeiture prior to vesting at the lower of fair value and the original purchase price. The award is treated similarly to an early exercise of stock options for accounting purposes.

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A summary of our non-vested restricted stock for the year ended December 31, 2015 is as follows:

	Year Ended December 31, 2015
Outstanding — January 1,	1,121,979
Granted:	
Serviced-based vesting conditions	433,568
Performance-contingent awards	99,285
Market-condition awards	99,285
Vested	(583,435)
Repurchased by Company	(73,394)
Outstanding — December 31,	1,097,288

Service-based awards—RSPs granted during the years ended December 31, 2015, 2014 and 2013 generally vest over four years, subject to the individual holder's continued service relationship with us. The estimated weighted-average grant date fair value of restricted stock issued was $2.20 per share for the year ended December 31, 2015, $0.33 per share for the year ended December 31, 2014 and $0.23 per share for the year ended December 31, 2013.

The restricted common stock granted to an employee is valued using the Black-Scholes-Merton option-pricing model based on the common stock fair value at the time of the grant. For restricted common stock issued to consultants, we remeasure the fair value of the restricted shares as they vest at each reporting period using the Black-Scholes-Merton option-pricing model reflecting the remaining vesting period.

Performance-contingent award—On April 9, 2015, our Board of Directors granted a performance-contingent restricted stock purchase to our Chief Executive Officer shares of 99,285 restricted common stock with a purchase price of $3.40 per share, which the Board of Directors determined was the fair market value on the grant date. The estimated weighted-average grant-date fair value of the performance-contingent restricted stock purchase was $1.38.

This awards has dual triggers of vesting based upon the successful achievement of four corporate operating milestones within specified timelines, as well as a requirement for continued employment. When a performance goal is deemed to be probable of achievement, time-based vesting and recognition of stock-based compensation expense commences. In the event any of the corporate operating milestones are not achieved by the specified timelines, such vesting tranche will terminate and no longer be exercisable with respect to that portion of the shares. As of December 31, 2015, we determined that the achievement of the requisite performance conditions was not probable and, as a result, no compensation cost was recognized for the performance-contingent awards.

Market-condition award—On April 9, 2015, our Board of Directors granted a market-condition award to our Chief Executive Officer of 99,285 shares of restricted common stock, with a purchase price of $3.40 per share, which the Board of Directors determined was the fair market value on the grant date. The market-condition award does not vest until our market capitalization (determined based on the number of shares of common stock outstanding multiplied by the closing market price for our common stock as reported on NASDAQ) exceeds at least $2.0 billion for 20 consecutive trading days on or before the date twenty-four (24) months after the closing of our IPO.

The fair value of the market-condition award of $0.70 was determined on the grant date utilizing a lattice model that was prepared by a third party valuation firm with an expected term of 2.4 years. In August 2015, we began to recognize compensation costs for this award concurrent with the closing of our IPO.

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Notes to Financial Statements

Employee Stock Purchase Plan
In July 2015, we adopted the 2015 Employee Stock Purchase Plan (the "2015 ESPP"). Under the 2015 ESPP, 50,000 shares of our common stock were initially reserved for employee purchases of our common stock under terms and provisions established by the Board of Directors and approved by our stockholders. 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 provides for offering periods of six months in duration. The purchase periods end on either January 31st or July 31st. Contributions under the 2015 ESPP are limited to a maximum of 15% of an employee's eligible compensation.
The fair values of the rights granted under the 2015 ESPP were calculated using the following assumptions:

	Year Ended December 31, 2015	
Expected term (in years)	0.5	
Volatility	65.8	%
Risk-free interest rate	0.2	%
Dividend yield	—	%

Stock-Based Compensation Expense
Total stock-based compensation recognized by our research and development function and our general and administrative function was as follows:

	Year Ended December 31,		
(in thousands)	2015	2014	2013
Research and development	$2,031	$248	$113
General and administrative	1,192	102	25
Total stock-based compensation expense	$3,223	$350	$138

Total stock-based compensation recognized by employees and non-employees was as follows:

	Year Ended December 31,		
(in thousands)	2015	2014	2013
Employee	$2,359	$333	$136
Non-employee	864	17	2
Total stock-based compensation expense	$3,223	$350	$138

Unrecognized Stock-Based Compensation Expense and Weighted-Average Remaining Amortization Period
As of December 31, 2015 the unrecognized stock-based compensation cost, net of expected forfeitures, 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)
Options	$10,354	2.9
Restricted stock purchases	973	2.5
ESPP	34	.1
Total stock-based compensation expense	$11,361	1.83

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Notes to Financial Statements

9. 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. Prior to 2015, we had not provided any contributions to the plan. We made contributions to the Plan for eligible participants, and recorded contribution expenses of $33,000 for the year ended December 31, 2015, $19,000 for the year ended December 31, 2014 and $11,000 for the year ended December 31, 2013.

10. Income Taxes

No provision for income taxes was recorded for the years ended December 31, 2015 and 2014. We have incurred net operating losses for all the periods presented. We have not reflected any benefit of such net operating loss carryforwards in the accompanying financial statements. We have established a full valuation 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,	
	2015	2014
Federal statutory income tax rate	34.0 %	34.0 %
Non-deductible changes in fair value	(4.8)	(0.6)
Federal and state tax credits	1.4	2.4
Change in valuation allowance	(30.6)	(35.8)
Provision for Taxes	0.0 %	0.0 %

The components of the deferred tax assets and liabilities are as follows:

	December 31,	
(in thousands)	2015	2014
Deferred tax assets:		
Net operating loss carryforwards	$32,561	$17,651
Tax credits	2,584	1,630
Accruals and reserves	696	374
Stock based compensation	464	122
Gross deferred tax assets	36,305	19,777
Valuation allowance	(36,147)	(19,495)
Net deferred tax assets	158	282
Deferred tax liabilities:		
Property and equipment	(158)	(282)
Net deferred tax	$—	$—

In November 2015, the FASB issued ASU 2015-17, Balance Sheet Classification of Deferred Taxes, related to balance sheet classification of deferred taxes. The ASU requires that deferred tax assets and liabilities be classified as noncurrent in the statement of financial position, thereby simplifying the current guidance that requires an entity to separate deferred assets and liabilities into current and noncurrent amounts. We have early-adopted the ASU as of December 31, 2015 on a prospective basis and our statement of financial position as of this date reflects the revised classification of current deferred tax assets and liabilities as noncurrent.

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, 2015 and 2014 due to the uncertainty of realizing future tax benefits from its net operating loss carryforwards and other deferred tax assets. The valuation allowance increased by approximately $16.7 million and $8.9 million during the year ended December 31, 2015 and 2014, respectively. The increase in the valuation allowance is mainly related to the increase in net operating loss carryforwards incurred during the respective taxable years.

At December 31, 2015, we had net operating loss carryforwards for Federal income tax purposes of $82.1 million which are available to offset future taxable income, if any, through 2035 and net operating loss carryforwards for state income tax purposes of $80.0 million which are available to offset future taxable income, if any, through 2035. The net deferred tax asset

above does not include any amounts attributable to excess stock option deductions. As of December 31, 2015, we had research and development tax credit carryforwards of approximately $2.3 million and $1.7 million available to reduce future taxable income, if any, for federal and state income tax purposes, respectively. If not utilized, the federal credit carryforwards will begin expiring in 2031, and the state credits carryforward indefinitely.

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 before utilization. We have not utilized any NOL carryovers through December 31, 2015. In addition, our deferred tax assets are subject to full valuation allowance, and thus no benefit for deferred tax assets are recorded on our books. Our ability to use the remaining NOL carryforwards may be further limited if we experience a Section 382 ownership change as a result of future changes in our stock ownership.

No liability related to uncertain tax positions is recorded on the financial statements. 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:

	December 31,	
(in thousands)	2015	2014
Balance at beginning of year	$634	$352
Additions based on tax positions related to current year	371	282
Decreases for prior period tax positions	$—	$—
Unrecognized tax benefit - December 31	$1,005	$634

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 income tax returns in the United States and California. 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.

11. Related Party Transactions

Our majority investors are investment funds controlled by Third Rock Ventures, LLC (“TRV”) and two members of our Board of Directors are also partners in TRV. Management and advisory fee expense incurred with TRV was $65,000 for the year ended December 31, 2015, $332,000 for the year ended December 31, 2014, and $499,000 for the year ended December 31, 2013 for services which we requested from TRV. Our outstanding payable to TRV was zero as of December 31, 2015 and $14,000 as of December 31, 2014.

12. Commitments and Contingencies

Facilities

In 2012, we entered into a noncancelable operating lease for approximately 16,000 square feet of laboratory and office space in South San Francisco, California for an initial term of 66 months. We recognize minimum rent payments under the facility operating lease on a straight-line basis over the term of the lease.

In October 2014, we assumed the noncancelable operating lease from a neighboring tenant for approximately 12,000 square feet of adjacent laboratory and office space on substantially the same economic terms as our primary facility operating lease. We anticipate that related lease payments will expire in April 2018.

Future aggregate minimum lease payments under the noncancelable operating leases are as follows (in thousands):

Year ending December 31,	Amount
2016	$1,209
2017	1,115

2018	380
Total	$2,704

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Through February 2015, we were a party to a Space Sharing Agreement and a Shared Services Agreement with a biotechnology company that is also majority-owned by TRV. Under these agreements, specified expenses were shared equally between the two companies at cost and not subject to any markup or markdown. Under these agreements, we recorded reimbursements of $33,000 for the year ended December 31, 2015, $234,000 for the year ended December 31, 2014 and $107,000 for the year ended December 31, 2013. We have a receivable of $24,000 from these reimbursements which are included within other current assets on the balance sheets as of December 31, 2014.

Rent expense for the facility operating lease consisted of the following:

	Year Ended December 31,		
(in thousands)	2015	2014	2013
Minimum rental	$971	$554	$554
Net reimbursement under Space Sharing Agreement	(10)	(54)	(52)
Facility rental expense, net	$961	$500	$502

Indemnifications

We indemnify each of our directors and officers for certain events or occurrences, subject to certain limits, while the director 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 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 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.

Other

Liabilities for loss contingencies arising from claims, assessments, litigation, fines, and penalties and other sources are recorded when it is probable that a liability has been incurred and the amount can be reasonably estimated. Legal costs incurred in connection with loss contingencies are expensed as incurred.

13. Net Loss per Share Attributable to Common Stockholders

The following table sets forth the computation of the basic and diluted net loss per share attributable to common stockholders during the years ended December 31, 2015, 2014 and 2013:

	Year Ended December 31,		
(in thousands, except share and per share data)	2015	2014	2013
Numerator:			
Net loss	$(46,360)	$(20,807)	$(18,116)
Accretion and dividends on redeemable convertible preferred stock	(4,180)	(2,965)	(1,735)
Net loss attributable to common stockholders	$(50,540)	$(23,772)	$(19,851)
Denominator:			
Weighted average common shares outstanding	12,806,697	1,673,919	1,230,241
Net loss per share attributable to common stockholders, basic and diluted	$(3.95)	$(14.20)	$(16.14)

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Since the Company was in a loss position for all periods presented, basic net loss per share attributable to common stockholders is the same as diluted net loss per share for all periods as the inclusion of all potential common shares outstanding would have been anti-dilutive. Potentially dilutive securities that were not included in the diluted per share calculations because they would be anti-dilutive were as follows:

	December 31,		
	2015	2014	2013
Redeemable convertible preferred stock	—	19,746,614	8,260,906
Options to purchase common stock	2,058,787	954,567	618,923
Restricted stock subject to future vesting	1,097,288	1,121,979	691,117
2015 ESPP	9,491	—	—
Total	3,165,566	21,823,160	9,570,946

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Selected Quarterly Financial Information (unaudited)

The following table provides the selected quarterly financial data for 2015 and 2014:

	Quarter Ended							
(in thousands, except per share amounts)	December 31, 2015	September 30, 2015	June 30, 2015	March 31, 2015	December 31, 2014	September 30, 2014	June 30, 2014	March 31,2014
Loss from operations	$(15,598)	$(14,775)	$(8,600)	$(7,420)	$(5,314)	$(5,200)	$(5,128)	$(4,869)
Net loss	$(15,585)	$(14,764)	$(8,594)	$(7,417)	$(5,313)	$(5,222)	$(5,165)	$(5,107)
Net loss attributable to common shareholders	$(15,585)	$(15,551)	$(10,747)	$(8,657)	$(6,214)	$(5,987)	$(5,876)	$(5,695)
Net loss per share attributable to common shareholders - basic and diluted [(1)]	$(0.53)	$(0.90)	$(4.84)	$(4.22)	$(3.27)	$(3.53)	$(3.68)	$(3.81)

(1) The full year net loss per share of common stock, basic and diluted, may not equal the sum of the quarters due to weighting of outstanding shares.

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Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

We carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and our Vice President of Finance and Administration, of the effectiveness of our "disclosure controls and procedures" as of the end of the period covered by this report, pursuant to Rules 13a-15(b) and 15d-15(b) under the Securities Exchange Act of 1934, as amended, or the Exchange Act. In connection with that evaluation, our Chief Executive Officer and our Vice President of Finance and Administration concluded that our disclosure controls and procedures were effective and designed to provide reasonable assurance that the information required to be disclosed is recorded, processed, summarized and reported within the time periods specified in the SEC rules and forms as of December 31, 2015. For the purpose of this review, 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. In designing and evaluating the disclosure controls and procedures, our management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and our management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Management's Annual Report on Internal Control Over Financial Reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our registered public accounting firm due to a transition period established by the rules of the SEC for newly public companies.

Prior Material Weakness in Internal Control over Financial Reporting

A material weakness is a deficiency, or a combination of deficiencies, in internal controls over financial reporting, such that there is a reasonable possibility that a material misstatement of our financial statements will not be prevented or detected and corrected on a timely basis.

In connection with the audit of our financial statements for the years ended December 31, 2014 and December 31, 2013, we identified control deficiencies in the design and operation of our internal control over financial reporting that aggregated to a material weakness. The material weakness identified in our internal control over financial reporting related to a lack of sufficient number of qualified personnel within our accounting function to adequately segregate duties, a lack of sufficient review and approval of manual journal entries posted to the general ledger and a lack of adequate review procedures over general ledger account reconciliations.

Management's Remediation Activities

With the oversight of senior management and our audit committee, we implemented measures designed to improve our internal control over financial reporting in 2015 to remediate this material weakness, including the following:

- We formalized our internal control documentation and strengthened supervisory reviews by our management; and
- We added additional accounting personnel and implemented appropriate segregation of duties amongst accounting personnel.

We believe these steps, which are now fully implemented, have remediated the material weakness previously identified and have enhanced our internal control over financial reporting, as well as our disclosure controls and procedures. However, 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.

Changes in Internal Control over Financial Reporting

Except as otherwise described under "Management's Remediation Activities," there have been no other 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

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quarter ended December 31, 2015 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.

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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 2016 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2015.

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 http://www.ir.globalbloodtx.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 2016 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2015.

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 2016 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2015.

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 2016 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2015.

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 2016 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2015.

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PART IV

Item 15. Exhibits and Financial Statement Schedules

(a) The following documents are filed as part of this report:

(1) FINANCIAL STATEMENTS

The financial statements filed as part of this Annual Report on Form 10-K are listed in the "Index to Financial Statements" under Part II, Item 8 of this Annual Report on Form 10-K.

(2) FINANCIAL STATEMENT SCHEDULES

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 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.

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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: March 29, 2016

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 John Schembri, 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)	March 29, 2016
/s/ John Schembri John Schembri	Vice President, Finance and Administration (Principal Financial and Accounting Officer)	March 29, 2016
/s/ Michael W. Bonney Michael W. Bonney	Director	March 29, 2016
/s/ Willie L. Brown, Jr. Willie L. Brown, Jr.	Director	March 29, 2016
/s/ Charles Homcy Charles Homcy, M.D.	Director	March 29, 2016
/s/ Scott W. Morrison Scott W. Morrison	Director	March 29, 2016
/s/ Deval L. Patrick Deval L. Patrick	Director	March 29, 2016
/s/ Mark L. Perry Mark L. Perry	Director	March 29, 2016

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/s/ Glenn F. Pierce Glenn F. Pierce, M.D., Ph.D.	Director	March 29, 2016
/s/ Philip A. Pizzo Philip A. Pizzo, M.D.	Director	March 29, 2016

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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	Amended and Restated Investors' Rights Agreement by and among the Registrant and certain of its stockholders dated December 22, 2014	S-1	7/8/2015	4.2	
4.3	First Amendment to Amended and Restated Investors' Rights Agreement by and among the Registrant and certain of its stockholders dated January 26, 2016				X
10.1#	2012 Stock Option and Grant Plan and forms of award agreements thereunder	S-1	7/8/2015	10.2	
10.2#	2015 Stock Option and Incentive Plan and forms of award agreements thereunder	S-1/A	7/31/2015	10.3	
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 Eleanor L. Ramos, M.D., dated March 8, 2014	S-1	7/8/2015	10.4	
10.5#	Employment Offer Letter Agreement by and between the Registrant and Hing L. Sham, Ph.D., dated June 19, 2014				X
10.6#	Termination Letter Agreement by and between the Registrant and Uma Sinha, Ph.D., dated July 14, 2015				X
10.7	Lease Agreement by and between the Registrant and ARE-East Jamie Court, LLC, dated June 29, 2012, as amended by letter amendment dated June 29, 2012	S-1	7/8/2015	10.5	
10.8		S-1	7/8/2015	10.6	

	Assignment and Assumption of Lease by and between the Registrant and Myokardia, Inc., dated as of October 22, 2014			
10.9	Lease Agreement by and between the Registrant (as assignee of Myokardia, Inc.) and ARE-East Jamie Court, LLC, dated June 29, 2012	S-1	7/8/2015	10.7
10.10	Form of Indemnification Agreement by and between the Registrant and each of its directors and officers	S-1	7/31/2015	10.8
10.11#	2015 Employee Stock Purchase Plan	S-8	8/12/2015	99.3
10.12#	Senior Executive Cash Incentive Bonus Plan	8-K	1/12/2016	10.1

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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.INS	XBRL Instance Document	X
101.SCH	XBRL Taxonomy Extension Schema Document	X
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document	X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document.	X
101.LAB	XBRL Taxonomy Extension Label Linkbase Document.	X
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document.	X

Represents management compensation plan, contract or arrangement.

* 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.