Global Blood Therapeutics, Inc.
Form 424B5
February 22, 2017
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Filed Pursuant to Rule 424(b)(5)
Registration No. 333-214088

PROSPECTUS SUPPLEMENT

(To Prospectus dated October 28, 2016)

5,102,041 Shares

Common Stock

We are offering 5,102,041 shares of our common stock.

Our common stock is listed on The NASDAQ Global Select Market under the symbol GBT. On February 21, 2017, the last reported sale price of our common stock was $28.50 per share.

We are an emerging growth company as that term is used in the Jumpstart Our Business Startups Act of 2012 and, as such, have elected to rely on certain reduced public company disclosure requirements. See Prospectus Supplement Summary Implications of Being an Emerging Growth Company.

Investing in our common stock involves risks. See Risk Factors beginning on page S-11 of this prospectus supplement and under similar headings in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus.

Neither the Securities and Exchange Commission nor any other regulatory body has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

	PER SHARE	TOTAL
Public Offering Price	$ 24.50	$ 125,000,005
Underwriting Discounts and Commissions(1)	$ 1.33	$ 6,785,715
Proceeds to Global Blood Therapeutics, Inc. (before expenses)	$ 23.17	$ 118,214,290

(1) See Underwriting for a description of compensation payable to the underwriter.

If all of the shares are not sold at the public offering price, the underwriter may change the offering price and may offer shares from time to time for sale in negotiated transactions or otherwise, at market prices prevailing at the time of sale, at prices related to such prevailing market prices or otherwise.

Delivery of the shares of common stock is expected to be made on or about February 27, 2017. We have granted the underwriter an option for a period of 30 days to purchase up to an additional 765,306 shares of our common stock. If the underwriter exercises the option in full, the total underwriting discounts and commissions payable by us will be $7,803,572 and the total proceeds to us, before expenses, will be $135,946,430.

Sole Book-Running Manager

Cantor Fitzgerald & Co.

The date of this prospectus supplement is February 21, 2017.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is part of the registration statement that we filed with the Securities and Exchange Commission, or the SEC, using a shelf registration process and consists of two parts. The first part is this prospectus supplement, including the documents incorporated by reference, which describes the specific terms of this offering. The second part, the accompanying prospectus, including the documents incorporated by reference, gives more general information, some of which may not apply to this offering. Generally, when we refer to the prospectus, we are referring to both parts combined. This prospectus supplement may add to, update or change information in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement or the accompanying prospectus.

If information in this prospectus supplement is inconsistent with the accompanying prospectus or with any document incorporated by reference that was filed with the SEC before the date of this prospectus supplement, you should rely on this prospectus supplement. This prospectus supplement, the accompanying prospectus and the documents incorporated by reference into each include important information about us, the securities being offered and other information you should know before investing in our securities. You should also read and consider information in the documents we have referred you to in the sections of this prospectus supplement entitled Where You Can Find More Information and Incorporation of by Reference and the accompanying prospectus entitled Where You Can Find Additional Information and Incorporation by Reference.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

We take no responsibility for, and can provide no assurances as to the reliability of, any information that is in addition to or different from that contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. We are not offering to sell these securities in any jurisdiction where the offer or sale is not permitted. You should not assume that the information contained or incorporated by reference in this prospectus supplement or the accompanying prospectus is accurate as of any date other than as of the date of this prospectus supplement or the accompanying prospectus, as the case may be, or in the case of the documents incorporated by reference, the date of such documents regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or any sale of our securities. Our business, financial condition, liquidity, results of operations and prospects may have changed since those dates.

Unless the context suggests otherwise, all references to us, our, GBT, we, the Company and similar designations to Global Blood Therapeutics, Inc. and, where appropriate, our subsidiaries. We use various trademarks and trade names in our business, including without limitation our corporate name and logo. All other trademarks or trade names referred to in this prospectus are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus may be referred to without the ® and symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

No action is being taken in any jurisdiction outside the United States to permit a public offering of the securities or possession or distribution of this prospectus supplement or the accompanying prospectus in that jurisdiction. Persons who come into possession of this prospectus supplement or the accompanying prospectus

in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus supplement or the accompanying prospectus applicable to that jurisdiction.

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CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the information and documents incorporated by reference herein and therein, contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. These statements are often, but are not always, made through the use of words or phrases such as may, will, could, should, expects, intends, plans, antici believes, estimates, predicts, projects, potential, continue, and similar expressions, or the negative of these ter similar expressions. Accordingly, these statements involve estimates, assumptions, risks and uncertainties which could cause actual results to differ materially from those expressed in them. Any forward-looking statements are qualified in their entirety by reference to the factors discussed throughout this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein, and in particular those factors referenced in the sections entitled Risk Factors.

This prospectus supplement, the accompanying prospectus and the information and documents incorporated by reference herein and therein contain forward-looking statements that are based on our management s belief and assumptions and on information currently available to our management. These statements relate to future events or our future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

- the timing and the success of our ongoing Phase 3 clinical trial of GBT440 in adult and adolescent patients with sickle cell disease, or SCD, and our ongoing Phase 1 and Phase 2a clinical trials of GBT440 for the potential treatment of idiopathic pulmonary fibrosis, or IPF;

- the timing and success of our planned additional clinical trials of GBT440 in other chronic and acute hypoxemic pulmonary disorders and of any other product candidates we may develop in our target indications;

- our ability to enroll patients in our clinical trials at the pace that we project;

- whether the results of our trials will be sufficient to support domestic or foreign regulatory approvals for GBT440 or any other product candidates we may develop in our target indications;

- our ability to obtain, including under any expedited development or review programs, and maintain regulatory approval of GBT440 or any other product candidates we may develop;

- our ability to advance any other programs through preclinical and clinical development, and the timing and scope of these development activities;

our expectations regarding the use of our existing capital resources and any proceeds we may receive from the sale of securities offered under this prospectus supplement;

the benefits of the use of GBT440 or any other product candidates we may identify and develop;

our ability to successfully commercialize GBT440 or any other product candidates we may identify and pursue, if approved;

the rate and degree of market acceptance of GBT440 or any other product candidates we may identify and pursue;

our ability to maintain, or to recognize the anticipated benefits of, orphan drug designation for GBT440 or to obtain orphan drug designation for any other product candidates we may identify and pursue in the United States, Europe or any other jurisdiction;

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our expectations regarding government and third-party payor coverage and reimbursement;

our ability to manufacture GBT440 in conformity with the FDA s requirements and to scale up manufacturing of GBT440 to commercial scale;

our ability to successfully build a specialty sales force and commercial infrastructure;

our ability to compete with companies currently producing or engaged in the clinical development of treatments for the disease indications that we pursue;

our reliance on third parties to conduct our clinical trials;

our reliance on third-party contract manufacturers to manufacture and supply our product candidates for us;

our ability to retain and recruit key personnel;

our ability to obtain and maintain intellectual property protection for GBT440 or any other product candidates we may identify and pursue;

our estimates of our expenses, ongoing losses, future revenue, capital requirements and our needs for or ability to obtain additional financing;

our expectations regarding the time during which we will be an emerging growth company under the Jumpstart Our Business Startups Act of 2012, as amended, or the JOBS Act;

our financial performance; and

developments and projections relating to our competitors or our industry.

These forward-looking statements are neither promises nor guarantees of future performance due to a variety of risks and uncertainties, many of which are beyond our control, which could cause actual results to differ materially from those indicated by these forward-looking statements, including, without limitation the risk factors and cautionary statements described in other documents that we file from time to time with the SEC, specifically under Item 1A: Risk Factors and elsewhere in our most recent Annual Report on Form 10-K for the period ended December 31, 2015 and our most recent Quarterly Reports on Form 10-Q for the quarters ended March 31, 2016, June 30, 2016, and September 30, 2016 and our Current Reports on Form 8-K, and the section of this prospectus supplement and the accompanying prospectus entitled Risk Factors.

The forward-looking statements in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference represent our views as of their respective dates. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we assume no obligation to update or revise any forward-looking statements except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the dates on which they were made.

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference also contain estimates, projections and other information concerning our industry, our business, and the markets for certain disease treatments, 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.

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PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information contained elsewhere or incorporated by reference in this prospectus supplement and the accompanying prospectus and does not contain all of the information that you should consider before investing in our securities. Before investing in our common stock, you should carefully read this entire prospectus supplement and the accompanying prospectus, including the sections titled Risk Factors, our consolidated financial statements and related notes and the information in our filings with the U.S. Securities and Exchange Commission, or the SEC, incorporated by reference in this prospectus supplement and the accompanying prospectus. This prospectus supplement may add to, update or change information in the accompanying prospectus. Unless the context suggests otherwise, all references to us, our, GBT, we, the Company and similar designations refer to Global Blood Therapeutics, Inc. and, where appropriate, our subsidiaries.

Our Company

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 lead product candidate is GBT440, an oral, once-daily therapy that modulates hemoglobin s affinity for oxygen, which we believe inhibits hemoglobin polymerization in sickle cell disease, or SCD, and improves hypoxemia in idiopathic pulmonary fibrosis, or IPF. We are developing GBT440 for SCD. We are currently evaluating GBT440 in SCD in a Phase 3 clinical trial of GBT440 in adult and adolescent patients with SCD. In addition, we are evaluating the safety and pharmacokinetics of single and multiple doses of GBT440 in a Phase 2a clinical trial of adolescent patients with SCD. In 2015, the FDA granted Fast Track Designation and Orphan Drug Designation for GBT440 for the treatment of SCD, and in November 2016 we were granted Orphan Drug Designation in Europe for GBT440 for the treatment of SCD.

SCD is a genetic blood disorder 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 that causes sickling of RBCs. In our clinical trials of GBT440 in SCD patients, we observed reduced markers of red blood cell destruction, improvements in anemia, improvements in markers of tissue oxygenation, and reduced numbers of sickled RBCs.

In addition to SCD, in our development program to evaluate GBT440 for the potential treatment of IPF, which is a hypoxemic pulmonary disorder, we are conducting two Phase 2a clinical trials of GBT440 in IPF patients, as well as a complementary Phase 1 clinical trial of GBT440 in healthy volunteers under hypoxic conditions and exercise conditions that maximally stress heart and lung function. We expect to announce data from these Phase 2a and Phase 1 clinical trials in the second half of 2017. We are also engaged in other preclinical research and development activities.

We own or jointly own and have exclusively licensed rights to our portfolio of product candidates in the United States, Europe and other major markets. We own three issued U.S. patents that cover the composition of matter of GBT440, methods of use of GBT440 and a polymorph of GBT440. These patents are due to expire in 2032, 2034 and 2035, respectively (absent any applicable patent term extensions). We own or co-own additional pending patent applications in the United States and multiple foreign countries relating to GBT440.

We have never been profitable and have incurred net losses in each year since inception. Our net losses were $55.3 million and $30.8 million for the nine months ended September 30, 2016 and 2015, respectively. As of September 30, 2016 we had an accumulated deficit of $153.7 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.

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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. As of September 30, 2016, we had $217.8 million of cash and cash equivalents.

Overview of Sickle Cell Disease

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 is the protein inside RBCs that carries oxygen and releases oxygen at the tissues. In SCD, when oxygen is released, HbS becomes sticky and aggregates into polymers, or long, rigid rods within an RBC, much like a sword within a balloon. The RBC assume a sickled shape and becomes inflexible, which can destroy RBCs, cause blockage in small blood vessels, block blood flow, and decrease oxygen delivery to tissues. As a result, 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. According to a 2014 publication, in the United States, SCD shortens patient life expectancy by approximately 25 to 30 years even with available medical care.

Current treatment options for SCD are limited to one approved therapy for adults known as hydroxyurea, 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.

Our Lead Product Candidate

GBT440 s therapeutic approach was inspired by the natural activity of fetal hemoglobin, or HbF. HbF is present during fetal development and in early infancy until it is replaced with adult hemoglobin, and 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% sickled hemoglobin, or HbS, in their blood. HbF dilutes the concentration of deoxygenated HbS that can participate in hemoglobin polymerization, and thereby significantly reduces the formation of hemoglobin polymers.

GBT440 is a novel, proprietary 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

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in its oxygenated state, where it cannot participate in polymerization. Similar to HbF, by diluting total HbS with a proportion of GBT440-bound hemoglobin, GBT440 prevents hemoglobin polymer formation. Based on its mechanism of action, we believe that GBT440 can reduce the physical and clinical manifestations of SCD.

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 patients with SCD. The clinical trial was conducted in three parts: single dose administration, followed by multiple dose administration, daily for 15 days in healthy subjects and 28 days in SCD subjects, and then followed by multiple dose administration, daily for up to six months in SCD subjects. In this clinical trial, we evaluated the safety, tolerability, pharmacokinetics, and pharmacodynamics of GBT440, as well as exploratory markers of SCD activity, including anti-hemolytic effects and SCD-related clinical effects. We reported initial results from this clinical trial at the American Society of Hematology, or ASH, meeting in December 2015. We reported additional results from this clinical trial at the European Hematological Association meeting in June 2016 and at the ASH meeting in December 2016. Among the 41 SCD subjects who received multiple doses of GBT440 (at doses of either 1000mg, 900mg, 700mg or 500mg per day) for 28 days up to six months, 100% of study subjects demonstrated a hematologic response to GBT440 therapy, as evidenced by improvements in one or more markers of hemolysis and anemia (hemoglobin, unconjugated bilirubin and percentage reticulocyte counts). In addition, all study cohorts showed marked reductions in irreversibly sickled cells in the peripheral blood from baseline, and, all study subjects treated for 90 days to up to six months showed sustained improvement in bilirubin and percentage reticulocyte counts, continued reductions in sickled RBCs and a median 1.0 g/dL increase in hemoglobin. As a result, this Phase 1/2 clinical trial demonstrated GBT440 s pharmacological mechanism of action and linear, dose-proportional pharmacokinetics. In this clinical trial, GBT440 was well tolerated through six months of dosing; the most common treatment-related adverse events were mild to moderate headaches and gastrointestinal disorders, which occurred in similar rates in the placebo arms.

Following discussions with the FDA that concluded successfully in October 2016, we have initiated a randomized, double-blind, placebo-controlled, multi-national Phase 3 clinical trial of GBT440 in SCD that we refer to as the HOPE study. The HOPE study is designed to enroll up to 400 adult and adolescent SCD patients, age 12 years and older, who have had at least one episode of vaso-occlusive crisis in the previous year. The HOPE study is being conducted in two parts: the initial Part A, which will compare two dose levels of GBT440 (900 mg and 1500 mg) versus placebo, and will include up to 150 patients; followed by Part B, which will include 250 patients randomized to placebo or a dose of GBT440 selected based on the results of Part A. The main objectives of Part A are to select the optimal dose, define the final secondary endpoints for Part B and qualify the Patient Reported Outcome, or PRO, instrument. The primary efficacy endpoint of the HOPE study is the proportion of patients who achieve a >1 g/dL increase in hemoglobin at 24 weeks of treatment compared to baseline. Key secondary efficacy endpoints include the effect of GBT440 on SCD symptom exacerbation, which will be measured by our PRO instrument, in addition to overall SCD symptoms as compared to placebo. We will also assess traditionally defined vaso-occlusive crisis as well as hospitalizations and red blood cell transfusions as secondary endpoints.

Market Opportunity in 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 individuals. 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. 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 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.

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Given the concentrated prescriber base for SCD and the small number of key opinion leaders who significantly influence the treatments for this patient population, we intend to promote GBT440 with a specialty sales force in the United States and Europe. We are also evaluating options for commercializing GBT440 in other significant markets due to the concentration of SCD patient populations in sub-Saharan Africa, the Middle East, South Asia and Latin America.

Additional Opportunities

We are also studying the potential for GBT440 to treat IPF, which is a fatal disease characterized by irreversible, progressive scarring of the lungs. As an IPF patient s lung scarring worsens, the lungs cannot properly transport oxygen into the bloodstream and, as a result, the body s tissues do not get the oxygen they need. The cause of IPF is unknown and there is no cure. Progression of lung scarring inevitably results in hypoxemia causing shortness of breath and a decline in overall function; eventually the use of supplemental oxygen is necessary. Ultimately, the progressive worsening of lung function over time, leads to organ dysfunction, frequent hospitalizations and death. IPF typically affects individuals over the age of 50, and the median survival after diagnosis is approximately 2 to 3 years.

Hypoxemia, which means abnormally low levels of oxygen in the blood, is a common finding in IPF. Hypoxemia is the underlying cause of patients symptoms of breathlessness and fatigue, and contributes to adverse patient outcomes. GBT440 has been shown to increase oxygen saturation in animal models of pulmonary fibrosis and severe hypoxemia. Based on these findings, GBT is now conducting three clinical trials of GBT440 as a potential treatment for hypoxemia in a broad range of subjects with IPF.

In June 2016, we initiated our first Phase 2a clinical trial of GBT440 in IPF. This trial is a randomized, placebo-controlled study of GBT440 that is evaluating the safety, tolerability, pharmacokinetics and effect on hypoxemia of GBT440 in patients with IPF who have hypoxemia on exertion. In November 2016, we initiated our second Phase 2a clinical trial of GBT440 in IPF, an open-label study to evaluate the safety and efficacy of GBT440 for the treatment of hypoxemia in IPF patients who are on supplemental oxygen at rest. We have named this second Phase 2a clinical trial the ZEPHYR study. In addition, in February 2017, we initiated a Phase 1 clinical study to evaluate the physiologic effects of GBT440 in healthy volunteers under hypoxic conditions and exercise conditions that maximally stress heart and lung function, to support our understanding of GBT440 s effects on hypoxemia and complement our ongoing Phase 2a program.

We believe there is a significant market opportunity in IPF. It is estimated that there are less than 150,000 patients with IPF in the United States.

Management

We have assembled a team of employees, directors and scientific founders 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 team has contributed to 18 drug approvals, including Avastin®, Herceptin®, Kaletra®, Kyprolis®, Ravicti® 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 starting with IPF, and advance other product candidates that we may identify and develop.

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Our Strategy

Our strategy is to use our expertise in blood biology to build a multi-product company leading in the discovery, development and commercialization of novel medicines for grievous blood-based disorders. Key elements of our strategy include:

- rapidly advancing GBT440 for the treatment of SCD;
- rapidly advancing GBT440 for the treatment of IPF patients with hypoxemia, as well as in other chronic and acute hypoxemic pulmonary disorders; and
- evaluating opportunities to advance other product candidates.

Financial Overview

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. Our operating expenses increased during the first three quarters of 2016 as compared to the same periods in the prior year, they continued to increase during the remainder of 2016, and we expect they will continue to increase significantly thereafter, particularly as we continue our Phase 3 HOPE study of GBT440 for the treatment of SCD and our ongoing Phase 1 and 2a clinical trials of GBT440 for the treatment of SCD or IPF, incur start-up and other costs related to advancing our clinical development programs in SCD and IPF and expand our manufacturing operations as we advance our clinical trials and prepare for potential commercialization. As of December 31, 2016, we had approximately $92.1 million in cash and cash equivalents and $105.3 million in short and long-term marketable securities. This amount is unaudited and preliminary, and does not present all information necessary for an understanding of our financial condition as of December 31, 2016. The review of our financial statements for the year ended December 31, 2016 is ongoing and could result in changes to this amount. Our financial statements for the year ended December 31, 2016 will not be available until after this offering is completed, and consequently will not be available to you prior to investing in this offering.

Our Development Pipeline

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

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Corporate History and Information

We were incorporated under the laws of the State of Delaware in February 2011. Our principal executive office is located at 400 East Jamie Court, Suite 101, South San Francisco, California, and our telephone number is (650) 741-7700. Our website address is *www.globalbloodtx.com*. We do not incorporate the information on or accessible through our website into this prospectus supplement or the accompanying prospectus, and you should not consider any information on, or that can be accessed through, our website as part of this prospectus supplement or the accompanying prospectus.

Implications of Being an Emerging Growth Company

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 have elected to take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

- reduced disclosure about our executive compensation arrangements;
- no non-binding advisory votes on executive compensation or golden parachute arrangements; and
- exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting.

We may take advantage of these exemptions for up to five years from our initial public offering or such earlier time that we are no longer an emerging growth company. 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 $1.0 billion or more; (ii) December 31, 2020; (iii) the date on which we have issued more than $1.0 billion in nonconvertible debt during the previous three years; or (iv) the last day of the fiscal year in which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission, or SEC, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th. We may choose to take advantage of some but not all of these exemptions. We have taken advantage of reduced reporting requirements in this prospectus. Accordingly, the information contained herein may be different from the information you receive from other public companies in which you hold stock. Also, we have irrevocably elected to opt out of the exemption for the delayed adoption of certain accounting standards and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

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THE OFFERING

Common stock offered by us	5,102,041 shares
Common stock outstanding immediately following the offering	41,618,171 shares
Option to purchase additional shares	We have granted the underwriter an option for a period of 30 days to purchase an additional 765,306 shares of our common stock.
Use of proceeds	We intend to use the net proceeds from this offering and our existing capital resources, consisting of cash and cash equivalents and marketable securities, to fund our clinical development of GBT440 for the treatment of SCD, including our Phase 3 HOPE study and our ongoing Phase 2a clinical trial and planned clinical pharmacology studies, our Phase 1 and Phase 2a clinical trials of GBT440 for the treatment of IPF and other hypoxemic pulmonary disorders, our other research and development activities, and for working capital and general corporate purposes. See Use of Proceeds for additional information.
Risk factors	Investing in our securities involves risks. See Risk Factors beginning on page S-11 of this prospectus supplement.
NASDAQ Global Select Market symbol	GBT

The number of shares of our common stock to be outstanding after the offering is based on 36,516,130 shares of common stock outstanding as of September 30, 2016, and excludes:

- 2,703,252 shares of common stock issuable upon exercise of outstanding options as of September 30, 2016 at a weighted-average exercise price of $10.99 per share;
- 777,041 shares of restricted common stock which were subject to our right of repurchase as of September 30, 2016;
- 607,250 shares of common stock issuable upon exercise of options granted subsequent to September 30, 2016 at a weighted-average exercise price of $17.34 per share;

217,600 shares of common stock issuable upon the vesting of restricted stock units granted subsequent to September 30, 2016 pursuant to our 2015 Plan;

1,484,701 shares of common stock reserved for future issuance under our 2015 Stock Option and Incentive Plan, or the 2015 Plan, as of September 30, 2016; and

76,118 shares of common stock reserved for future issuance under our 2015 Employee Stock Purchase Plan, or the 2015 ESPP, as of September 30, 2016.

Except as otherwise indicated, all information in this prospectus supplement assumes no exercise by the underwriter of its option to purchase additional shares of our common stock.

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RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully consider the risks referenced below and described in the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, as well as other information we include or incorporate by reference into this prospectus supplement and the accompanying prospectus, before making an investment decision. Our business, financial condition or results of operations could be materially adversely affected by the materialization of any of these risks. The trading price of our securities could decline due to the materialization of any of these risks, and you may lose all or part of your investment. This prospectus supplement, the accompanying prospectus and the documents incorporated herein and therein by reference also contain forward-looking statements that involve risks and uncertainties. Actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks referenced below and described in the accompanying prospectus and the documents incorporated herein and therein by reference, including (i) our annual report on Form 10-K for the fiscal year ended December 31, 2015, (ii) our quarterly reports on Form 10-Q for the quarters ended March 31, 2016, June 30, 2016 and September 30, 2016 and (iii) other documents we file with the SEC that are deemed incorporated by reference into this prospectus supplement or the accompanying prospectus.

Risks Related to this Offering

We have broad discretion in the use of the net proceeds from this offering and our existing cash and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering, including for any of the purposes described in the section entitled Use of Proceeds, as well as our existing cash and cash equivalents, and you will be relying on the judgment of our management regarding such application. You will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. Our management might not apply the net proceeds or our existing cash in ways that ultimately increase the value of your investment. If we do not invest or apply the net proceeds from this offering or our existing cash in ways that enhance stockholder value, we may fail to achieve expected results, which could cause our stock price to decline. Pending their use, we may invest the net proceeds from this offering in investment-grade, interest-bearing securities. These investments may not yield a favorable return to our stockholders.

If you purchase our common stock in this offering, you will incur immediate and substantial dilution in the book value of your shares.

Investors purchasing shares of common stock in this offering will pay a price per share that substantially exceeds the as adjusted book value per share of our tangible assets as of September 30, 2016 after subtracting our liabilities. As a result, investors purchasing shares of common stock in this offering will incur immediate dilution of $16.34 per share, based on the difference between the public offering price of $24.50 per share, and the as adjusted net tangible book value per share of our outstanding common stock as of September 30, 2016.

This dilution is due to the substantially lower price paid by some of our investors who purchased shares prior to this offering as compared to the price offered to the public in this offering, and the exercise of stock options granted to our employees. In addition, as of September 30, 2016, options to purchase 2,703,252 shares of our common stock at a weighted-average exercise price of $10.99 per share were outstanding. The exercise of any of these options would result in additional dilution. As a result of the dilution to investors purchasing shares in this offering, investors may receive significantly less than the purchase price paid in this offering, if anything, in the event of our liquidation. Further, because we will need to raise additional capital to fund our future activities, we may in the future sell

substantial amounts of common stock or securities convertible into or exchangeable for common stock.

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These future issuances of common stock or common stock-related securities, together with the exercise of outstanding options and any additional shares issued in connection with acquisitions, if any, may result in further dilution. For a further description of the dilution that you will experience immediately after this offering, see Dilution.

Sales of a substantial number of shares of our common stock in the public market after this offering could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. We are unable to predict the effect that sales may have on the prevailing market price of our common stock.

In addition, the sale of substantial amounts of our common stock could adversely impact the price of our common stock. As of September 30, 2016, 36,516,130 shares of our common stock and options to purchase 2,703,252 shares of our common stock were outstanding. The sale or the availability for sale of a large number of shares of our common stock in the public market could cause the price of our common stock to decline.

We along with our directors and executive officers and certain of our principal stockholders, have agreed that for a period of 90 days (with respect to us and our executive officers and directors), or 45 days (with respect to certain of our principal stockholders) after the date of this prospectus supplement, subject to specified exceptions, including, with respect to certain of our principal stockholders, trades under existing 10b5-1 plans, we or they will not offer, sell, contract to sell, pledge or otherwise dispose of, directly or indirectly, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock. We and our directors and executive officers and certain of our principal stockholders may be released from these restrictions at the sole discretion of Cantor Fitzgerald & Co. Sales of stock by any of our directors, executive officers or principal stockholders could have a material adverse effect on the trading price of our common stock.

Certain holders of shares of our common stock are entitled to rights with respect to the registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

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, 2014 and 2013 were $46.4 million, $20.8 million and $18.1 million, respectively. Our net losses for the nine months ended

September 30, 2016 and 2015 were $55.3 million and $30.8 million respectively. As of September 30, 2016, we had an accumulated deficit of $153.7 million. Our operating expenses continued to

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increase during the remainder of 2016 as compared to the corresponding period in prior years, and we expect they will continue to increase significantly thereafter as we advance our pipeline. 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, for which we have initiated the Phase 3 HOPE study of GBT440 for the potential treatment of patients with SCD, have initiated a Phase 2a clinical trial of GBT440 for the potential treatment of low oxygen levels, also known as hypoxemia, in patients with idiopathic pulmonary fibrosis, or IPF, have initiated a Phase 1 clinical study to evaluate the physiologic effects of GBT440 in healthy volunteers under hypoxic conditions and exercise conditions that maximally stress heart and lung function and have additional Phase 1/2 clinical trials ongoing in SCD and IPF patients;

- 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 for any indication;

- build a sales and marketing organization or enter into selected collaborations to commercialize GBT440 for any indication, if approved;

- advance our other programs through nonclinical 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 maintain adequate cash reserves to advance our development programs or achieve approval to commercialize any products, or our failure to achieve sustained profitability would depress the value of our company and could impair our ability to raise capital, expand our business, 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, including by initiating a multi-national Phase 3 clinical trial of GBT440 that will enroll up to 400 patients with SCD, and by evaluating the safety and pharmacokinetics of single and multiple doses of GBT440 in a Phase 2a clinical trial of adolescent patients with SCD. We are also conducting two Phase 2a studies of GBT440 for the potential treatment of hypoxemia in patients with IPF, as well as a complementary Phase 1 clinical trial of GBT440 in healthy volunteers to evaluate the physiologic effects of GBT440 under hypoxic conditions and exercise conditions that maximally stress heart and lung function. GBT440 is our only product candidate, though, we are conducting nonclinical research activities in 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

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advance GBT440 and other product candidates that we may identify and pursue in clinical trials. As of September 30, 2016 and December 31, 2015, we had working capital of $208.1 million and $140.1 million, respectively and capital resources consisting of cash and cash equivalents of $217.8 million and $148.5 million, respectively. Because the outcome of any clinical development and regulatory approval 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 or any other future product candidates.

In August 2015, we sold 6,900,000 shares of common stock in our initial public offering, the net proceeds of which totaled $126.2 million, after deducting underwriting discounts and commissions and offering expenses incurred by us. In July 2016 we completed the sale of 6,667,228 shares of common stock in a follow-on offering, the net proceeds of which totaled $117.0 million, after deducting underwriting discounts and commissions and offering expenses. We expect that our existing capital resources consisting of cash and cash equivalents will be sufficient to fund our operations for at least the next twelve months.

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 or any other product candidates that we may identify and pursue. Moreover, such financing may result in dilution to stockholders, imposition of debt covenants and repayment obligations, or other restrictions that may affect our business. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans.

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

- the time and cost necessary to conduct and complete our Phase 3 HOPE study for the potential treatment of SCD, as well as to complete our ongoing Phase 2a clinical trial in this development program;

- the time and cost necessary to conduct and complete our ongoing clinical program of GBT440 for the potential treatment of hypoxemia in IPF, including the Phase 2a clinical trials of GBT440 that we initiated in June 2016 and November 2016, the Phase 1 clinical study of GBT440 that we initiated in February 2017 as well as other ongoing Phase 1 and Phase 2a clinical trials in this development program;

- the time and cost to conduct and complete any additional clinical studies required to pursue regulatory approvals for GBT440 for SCD, hypoxemia in IPF or any other indication, and the costs of post-marketing studies that could be required by regulatory authorities for any indication;

- the progress, data and results of our Phase 3 HOPE study, as well as of multiple other Phase 1, 1/2 and Phase 2a clinical trials of GBT440 for the potential treatment of SCD or hypoxemia in IPF patients, and our potential future clinical trials;

the progress, timing, scope and costs of our nonclinical studies, our clinical trials and other related activities, including our ability to enroll subjects in a timely manner for our Phase 3 HOPE study as well as our other multiple Phase 1and 2 clinical trials of GBT440 for SCD or hypoxemia in IPF patients, and our 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 development programs, including our program for the clinical investigation of GBT440 in SCD patients and in hypoxemia in IPF patients through nonclinical and clinical development, as well as any other potential product candidate programs we may identify and pursue, and the timing and scope of these development activities;

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our ability to successfully obtain any regulatory approvals from any regulatory authorities to market and sell GBT440 and any other product candidates we may identify and development in any territory(ies);

our ability to successfully commercialize GBT440 and any other product candidates we may identify and develop;

the manufacturing, selling and marketing costs associated with the potential commercialization of GBT440 and any other product candidates we may identify and develop, including the cost and timing of establishing our sales and marketing capabilities in any territory(ies);

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 of our lead product candidate GBT440 in 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 our lead product candidate, GBT440, or any future product candidates that we may identify and develop, our business will be substantially harmed.

We cannot commercialize a product until the appropriate regulatory authorities have reviewed and approved the product candidate. Approval by the FDA and comparable foreign regulatory authorities 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 our lead product candidate GBT440, and it is possible that neither GBT440 nor any other product candidates we may seek to develop in the future will ever obtain any regulatory approval.

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:

- we may not be able to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities (including the European Medicines Agency, or EMA) that GB440 or any other product candidates we may develop are safe and effective for any proposed indications;

- the FDA or comparable foreign regulatory authorities may disagree with our plans regarding the pathways and endpoints for approval or the design or implementation of our nonclinical studies or clinical trials;

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- the populations studied in our clinical programs may not be sufficiently broad or representative to assure safety or demonstrate efficacy in the full population for which we seek approval;

- the FDA or comparable foreign regulatory authorities may require additional nonclinical studies or clinical trials beyond those we anticipate;

- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data and results from our nonclinical studies or clinical trials;

- the data and results collected from nonclinical studies or clinical trials of GBT440 and any 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 any other submission for regulatory approval in any other jurisdiction;

- we may be unable to demonstrate to the FDA or comparable foreign regulatory authorities that a product candidate s risk-benefit ratio for its proposed indication is acceptable;

- the FDA or comparable foreign regulatory authorities may find deficiencies with or fail to approve the manufacturing processes, test procedures and specifications, or facilities of third-party manufacturers with which we contract and rely on for all clinical and commercial supplies of GBT440 and any other product candidates (if any); and

- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may change in a manner that renders our development or manufacturing efforts insufficient for approval.

The lengthy regulatory review and approval process, as well as the inherent unpredictability of the results of nonclinical and clinical trials, and our reliance on third-party manufacturers for any product candidates, 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 all of our other programs are still in the nonclinical development stage. If we are unable to successfully complete clinical development, obtain regulatory approval for, and 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 nonclinical and clinical development of our lead and initial product candidate GBT440, including conducting nonclinical studies and clinical trials and providing general and administrative support for these operations. We do not have any other clinical product candidates. Our future success is highly dependent on our ability to successfully develop, obtain regulatory approval for, and commercialize GBT440 for one or more potential indications. Before we can generate any revenues from sales of GBT440, we must conduct substantial additional clinical development (including, among others, multiple ongoing clinical studies and toxicology studies, and possibly additional future nonclinical studies and clinical trials to demonstrate safety and efficacy of GBT440 for any potential indication). In addition, we will need to seek and obtain

regulatory approval for any potential indication, secure an adequate manufacturing supply to support larger clinical trials and commercial sales and build a commercial organization. Further, the success of GBT440 as a potential commercial product will also 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, the status and availability of healthcare coverage and adequate reimbursement, and maintenance of an acceptable safety and efficacy profile following approval, among other factors. If we do not achieve all 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 clinical trials. We are developing GBT440 as an oral, once-daily therapy for the potential treatment of SCD, and are currently evaluating GBT440

in SCD patients in ongoing Phase 1/2a clinical trials and the HOPE Study, which is a recently initiated Phase 3 clinical trial in adult and adolescent SCD patients. In addition, we are conducting a Phase 1/2 program evaluating GBT440 for the potential treatment of hypoxemia in IPF.

All of our other programs are in an early, nonclinical stage of research and development, and we have no other product candidates in clinical trials. Out of our ongoing internal early-stage nonclinical research, we have not selected any other product candidates that would enable the filing of an IND. As a result, we are very dependent on our lead product candidate GBT440 for our business, prospects, financial condition and results of operations.

We are also very dependent on the data and results that we obtain over time from our most advanced clinical trial of our lead product candidate, GBT440. In late 2016, we initiated the HOPE study, which is designed to enroll up to 400 SCD patients, age 12 years and older, who have had at least one episode of vaso-occlusive crisis in the previous year. The primary endpoint of the HOPE study relates to the proportion of patients who achieve an increase in hemoglobin levels (compared to baseline) as pre-specified in the study protocol. We have not previously conducted any clinical study of GBT440 in SCD patients using this primary endpoint, and we do not believe this measure has been used as a primary endpoint for any registration studies for any other SCD therapies. In addition, the HOPE study will also use a new patient reported outcome, or PRO, instrument that we recently developed, and that has not been utilized before in any clinical studies, to generate data for a secondary endpoint in the HOPE study.

Our discussions with the FDA have focused on a pathway to full approval of GBT440 for the potential treatment of SCD patients based on the HOPE study, by meeting the primary endpoint and at least one key secondary endpoint. However, before being able to seek or to obtain full or conditional approval of GBT440 for the potential treatment of SCD, we may be required to conduct one or more additional clinical trials of GBT440, including one or more additional Phase 3 clinical trials or other studies. We do not have a special protocol assessment agreement in place with the FDA.

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

The development of GBT440 as a potential disease-modifying anti-sickling agent in SCD patients and as a treatment for hypoxemia in patients with IPF each represents novel therapeutic approaches, and there is a risk that the outcomes of our clinical trials will not be favorable or otherwise support any decision to seek or grant any regulatory approval.

We have concentrated our product research and development efforts on developing novel, mechanism-based therapeutics for the treatment of grievous blood-based disorders with significant unmet need, including SCD and IPF, and our future success depends on the successful development of this therapeutic approach. The clinical trial requirements of the FDA and other comparable regulatory agencies and the criteria these regulators use to determine the safety and efficacy of any product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential product. To date, there 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 red blood cell sickling in SCD patients. As a result, the design and conduct of clinical trials for a therapeutic such as GBT440 that targets this mechanism in SCD patients are subject to unknown risks, and we may experience setbacks with our ongoing or planned clinical trials of GBT440 in SCD because of the limited clinical

experience with its mechanism of action in these patients.

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In particular, regulatory authorities in the United States have not issued definitive guidance as to how to measure and achieve efficacy in treatments for SCD. Based on our discussion with the FDA regarding the design for the HOPE study, we have determined to measure change in hemoglobin levels as the primary endpoint in the HOPE study. This primary endpoint has not been used previously in a registration study for any SCD treatment. As a result, regulators have not determined that such data would signify a clinically meaningful result in SCD patients or would support seeking or obtaining regulatory approval.

With the exception of oxygen supplementation, there is currently no approved therapy to relieve low oxygenation in patients with hypoxemic pulmonary disorders such as IPF. Similar to our development program in SCD, the design and conduct of clinical trials for a therapeutic agent that targets this mechanism in IPF are subject to unknown risks, and we may experience setbacks with our ongoing or planned clinical trials of GBT440 because of the lack of clinical experience with its mechanism of action in IPF patients.

We may not achieve our pre-specified endpoints in the HOPE study, 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 any other product candidates that we may pursue, would have an adverse impact on our business, prospects, financial condition and results of operations.

Results of earlier studies may not be predictive of future clinical trial results, and initial studies may not establish 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 studies and clinical trials of GBT440, our other product candidates and future product candidates that we may pursue may not be predictive of the results of later-stage clinical trials, and interim results of a clinical trial may not necessarily predict final results. For example, our nonclinical studies and clinical trials to date of GBT440 in SCD have involved mostly one genotype of SCD, known as HbSS, and the results of these studies may not be replicated in other genotypes of SCD or in subsequent clinical trials. The HOPE study of GBT440 in SCD is not limited to only the HbSS genotype. Additionally, any positive results generated in our Phase 1/2 clinical trial of GBT440 in SCD in adults do not ensure that we will achieve similar results in the HOPE study, which will enroll both adult and adolescent populations, or our ongoing Phase 2a clinical trial of GBT440 in adolescents with SCD, or in any other potential indications for GBT440, such as IPF and other hypoxemic pulmonary disorders. Our later stage clinical trials, such as the HOPE study, may involve significantly broader patient populations than those in earlier clinical trials.

Product candidates in later stages of clinical trials, such as our recently initiated HOPE study, 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.

In addition, nonclinical and clinical data are often susceptible to various interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in nonclinical studies and clinical trials have nonetheless failed to obtain marketing approval, in part because of differing interpretations of data and results by regulatory authorities.

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.

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Before we are able to submit GBT440 for marketing approval, the FDA and comparable foreign regulatory authorities may impose additional requirements, the scope of which are not fully known at this time.

Before we can submit an NDA to the FDA for GBT440 for any potential indication, we must successfully complete our clinical trials including at least one or more additional larger clinical trials. The FDA typically requires at least two pivotal, well-controlled Phase 3 clinical trials as a condition to the submission of an NDA and does not usually consider a single Phase 3 clinical trial to be adequate to support product approval. The FDA will typically only consider relying on one pivotal trial if, in addition, other well-controlled studies of the drug exist (for example, for other dosage forms or in other populations) or if the pivotal trial is a multi-center trial that provides highly reliable and statistically strong evidence of an important clinical benefit, such as effect on survival, organ function or patient reported outcomes and a confirmatory study would have been difficult to conduct on ethical grounds.

Based on our discussions with the FDA regarding the design of the HOPE study of GBT440 in SCD patients, we believe that if the HOPE study meets the primary endpoint and at least one key secondary endpoint, the data and results from this Phase 3 clinical trial could form the basis for regulatory approval of GBT440 for SCD treatment. However, before being able to seek or to obtain full or even conditional approval of GBT440 for the treatment of SCD, we may be required to conduct additional clinical trials or nonclinical studies of GBT440, including one or more additional Phase 3 clinical trials or other studies. The FDA may also require a longer follow-up period for subjects treated with GBT440 prior to accepting an NDA submission. We do not have a special protocol assessment agreement in place with the FDA.

The FDA or the comparable foreign authorities may not consider the results of our ongoing (including our HOPE study in SCD patients), planned or potential future clinical trials, to be sufficient for approval of GBT440 for SCD patients or hypoxemia in IPF patients. 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 conducting or completing our clinical trials, which in turn will result in additional costs and may ultimately prevent successful or timely completion of the clinical development and commercialization of our lead product candidate or any other product candidates.

Before obtaining marketing approval from regulatory authorities for the sale of any our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates in humans. Clinical testing is expensive, time-consuming and uncertain as to outcome. We expect to conduct the HOPE study, which will enroll up to 400 SCD patients, at multiple clinical sites located in the United States, Europe, Africa and the Middle East, with top line data and results expected in the first half of 2019. In addition, we have multiple ongoing Phase 1/2 clinical studies of GBT440 for the potential treatment of SCD patients or hypoxemia in IPF patients. We cannot guarantee that the HOPE study or any other clinical trials for GBT440 or any other product candidates we may pursue 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 or failures in reaching a consensus with regulatory agencies on study design, including clinical endpoints sufficient to support an approval decision;

delays or failures in reaching agreement on acceptable terms with a sufficient number of prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;

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delays in obtaining required Institutional Review Board, or IRB, or ethics committee approval for each clinical trial site;

delays in recruiting a sufficient number of suitable patients to participate in our clinical trials;

imposition of a clinical hold by any regulatory authority, including if imposed due to safety concerns after an inspection of our clinical trial operations or study sites;

failure by our CROs, clinical sites, participating clinicians or patients, other third parties or us to adhere to clinical trial, regulatory or legal requirements;

failure to perform in accordance with the FDA s good clinical practices, or GCPs, or applicable regulatory requirements in other countries;

delays in the testing, validation, manufacturing and delivery of sufficient quantities of our product candidates or study related devices (such as the hand-held PRO instrument being used by patients in our HOPE study) to the clinical sites and patients;

delays in having patients enroll or complete participation in a study in accordance with applicable protocols, or return for post-treatment follow-up;

reduction in the number of participating clinical trial sites or patients, including by dropping out of a trial;

failure to address in an adequate or timely manner any patient safety concerns that arise during the course of a trial;

unanticipated costs or increases in costs of clinical trials of our product candidates;

the occurrence of serious adverse events or other safety concerns associated with our product candidates; or

changes in regulatory requirements and guidance that require amending or submitting new clinical protocols or obtaining additional IRB or other approvals to conduct or complete clinical studies of our product candidates.

We could also encounter delays if a clinical trial is suspended or terminated for any reason (which could occur as a result of termination by us, by the IRBs or ethics committees of the institutions in which such trials are being conducted, by an independent Safety Review Board for such trial, or by the FDA or other regulatory authorities). A clinical trial can be suspended or terminated for a wide variety of reasons, including failure to conduct the clinical trial

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

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, especially for the multi-national Phase 3 HOPE study, and any other product candidates that we may develop are critical to our success. Our clinical development efforts are initially focused on rare chronic blood diseases. For example, according to CDC estimates, the prevalence of SCD, for which GBT440 is being studied, is 90,000 to 100,000 individuals in the United States. For IPF, it is estimated that less than 150,000 people in the United States are affected. Accordingly, there are limited patient pools from which to draw for clinical trials in our target indications. The HOPE study is designed to enroll up to 400 adult and adolescent SCD patients in multiple study centers in the United States, Europe, Africa and the Middle East. We may not be able to identify, recruit, and enroll a sufficient number of subjects to complete the HOPE study or our other 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 subjects and the subject referral practices of physicians, among other factors.

Further, if subjects in our clinical trials fail to comply with our dosing regimens, we may not be able to generate clinical data acceptable to the FDA in our trials. For our HOPE study of GBT440 in adult and adolescent SCD patients, enrolled participants must use a patient reported outcomes, or PRO, instrument to complete very frequent patient surveys generating data relevant to a secondary endpoint. If HOPE study participants fail to comply consistently with these PRO-related steps and procedures, the quality of these study data and our ability to interpret these data and results could be impaired, and these data and results may not be acceptable to the FDA or comparable regulatory authorities or may be interpreted differently. If patients are unwilling or unable to participate in, complete or comply with the protocols for our studies for any reason, the timeline for recruiting subjects, conducting studies and obtaining regulatory approval of potential products may be delayed.

If we experience difficulties or delays in enrollment or are otherwise unable to successfully complete any clinical trial of GBT440, especially our the HOPE study, or any other product candidates we may pursue, our costs are likely to 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 only a small sample of the potential patient population. Our Phase 1/2 clinical program of GBT440 in SCD patients and IPF patients are providing only very limited experience of GBT440 in SCD patients and IPF patients. For example, our Phase 1/2a clinical trials of GBT440 in SCD are designed to enroll between 96 and 128 subjects, and our ongoing Phase 2a clinical trials of hypoxemia in IPF patients are designed to enroll only up to 49 subjects. In contrast, the Phase 3 HOPE study is designed to enroll up to 400 adult and adolescent SCD patients. However, even this larger trial design will enroll only a very small fraction of all patients with SCD. Any rare and severe side effects of GBT440 may be uncovered only in later stages of our ongoing clinical trials (such as our larger HOPE study), or only in trials involving different patient populations (such as pediatric patients or IPF patients), or only during post-approval studies or safety reporting. 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 nonclinical toxicology study with GBT440 in non-humans and clinical trials involving other hemoglobin modifiers (other than GBT440) have shown a decrease in oxygen delivery to tissue when a significant percentage of hemoglobin is modified. Hemoglobin modifiers, by increasing HbS s affinity for oxygen, can cause a shift in oxygen

levels, potentially resulting in tissue hypoxia. To date, clinical studies of GBT440 have not shown evidence of tissue hypoxia. However, if

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GBT440 or any other product candidates that we may develop are associated with tissue hypoxia or any other undesirable side effects or unexpected undesirable characteristics in clinical trials or nonclinical studies, we may need to abandon their development or limit their development to more narrow uses or subpopulations, which could adversely affect our business, prospects, financial condition and results of operations.

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

We believe there may be an opportunity to accelerate the development of our lead product candidate 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 for GBT440. However, we cannot be assured that GBT440 or any other product candidates that we may develop will qualify for or benefit from any such programs in the United States or any foreign regulatory jurisdictions.

In 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 review or approval for GBT440 will occur on an expedited basis, if at all.

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

Furthermore, access to an expedited program, if provided, may be withdrawn by the FDA or foreign regulatory authorities 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 ultimately we will obtain regulatory approval for GBT440 or any other product candidate that we may develop in a timely manner, or at all.

Although the FDA and the European Commission have each granted orphan drug designation to our lead product candidate GBT440 for the potential treatment of SCD, we may not receive orphan drug designation 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 in the future may not confer marketing exclusivity or other expected commercial benefits.

Our business strategy focuses on the development of product candidates for the treatment of rare, chronic blood disorders that may be eligible for FDA or 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 EMA recommends orphan drug designation to promote the development of medical products that

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are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the EU and for which no satisfactory method of diagnosis, prevention, or treatment is authorized (or in other very limited circumstances). In 2015 and 2016, respectively, the FDA and the European Commission (acting on a positive recommendation by the EMA) each granted orphan drug designation for 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 the same indication for that time period. The applicable period is seven years in the United States and 10 years in the EU. The EU exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

Although the FDA and the EMA have each granted orphan drug designation to GBT440 for the treatment of SCD, we may apply for orphan drug designation for GBT440 in other jurisdictions or for other indications, or for other product candidates we may develop and pursue in the future. Applicable regulatory authorities may not grant us these additional designations. In addition, the exclusivity granted under any orphan drug designations that we have received or may receive may not effectively protect the product candidate from competition because different drugs can be approved for the same condition. For example, in the United States, even after an orphan drug is approved, the FDA can subsequently approve another drug for the same condition if the FDA concludes that the later drug is clinically superior, or the FDA can approve a competitor application for the same drug for a different indication than the orphan drug designation. 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 our lead product candidate GBT440 or any other product candidate that we may develop and pursue, we will be subject to ongoing regulatory obligations and scrutiny and may be subject to significant restrictions relating to product labeling, distribution or other post-marketing requirements.

Even if a product candidate such as GBT440 is approved, regulatory authorities may still impose significant restrictions on its indicated uses, approved labeling, distribution or marketing or may impose ongoing requirements for potentially costly post-marketing studies. Furthermore, any new legislation addressing drug safety or other drug related issues could result in delays or increased costs to assure compliance. If GBT440 or any other product candidates that we may develop are approved, at a minimum they will each be subject to current standard ongoing regulatory requirements for labeling, packaging, storage, advertising, promotion, sampling, record-keeping and submission of safety and other post-market information, including both federal and state requirements in the United States. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization GBT440 or any other 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 this product candidate for the desired age ranges or other key labeling parameters, our business is likely to suffer.

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 s. For our lead product candidate GBT440 and any other product candidates we may pursue, we are wholly reliant on third-party contract manufacturers for clinical as well as any commercial supplies of product candidates and products. As such, we and our contract manufacturers are subject to continual review and periodic

inspections to assess compliance with cGMP requirements and must continue to

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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 comparable foreign regulatory authorities, and to comply with requirements concerning advertising and promotion for our products. In addition, we are subject to very rapid reporting obligations relating to any adverse events or serious adverse events relating to our product candidates and any approved products, if any. Our failure to report adverse events we become aware of within the prescribed timeframes could have serious negative consequences for our development programs, business and operations. In addition, any promotional communications or materials for prescription drugs are subject to a variety of complex legal and regulatory restrictions, including but not limited to consistency with the approved product s approved label. Failure to obey these standard marketing requirements for any approved product (if any) could have serious negative consequences for our commercialization activities (if any), business and operations.

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

issue untitled or warning letters;

impose civil or criminal penalties;

impose injunctions;

impose fines;

impose additional specialized restrictions on the company s activities and practices;

suspend regulatory approval;

suspend ongoing clinical trials;

seek voluntary product recalls and impose publicity requirements;

refuse to approve pending applications or supplements to approved applications submitted by us;

impose restrictions on our operations, including closing our contract manufacturers facilities; or

seize or detain products.

As a company, we have no experience with obtaining approval for, launching or commercializing any product candidates or products, or with complying with most of these complex ongoing regulatory requirements. It will take significant effort and management attention to address how to comply with these requirements in any jurisdiction for which we seek any product approval. Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity even if significant liabilities do not result. Any failure to comply with these complex ongoing regulatory requirements may significantly and adversely affect our ability to obtain approval for, launch, 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 significantly harmed.

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Risks Related to Our Reliance on Third Parties

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

We have relied upon and plan to continue to rely upon third-party CROs, including our CROs for our clinical trials of GBT440, to monitor and manage data for some of our ongoing nonclinical studies and for all of our clinical programs. We rely on these parties for execution of these nonclinical studies and clinical trials, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies and trials are conducted in accordance with the applicable protocol, legal, regulatory, and scientific standards and our reliance on the CROs does not relieve us of our regulatory responsibilities. We and our CROs and other vendors are required to comply with all applicable cGMPs, GCPs, and Good Laboratory Practices, or GLPs, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area, or EEA, and comparable foreign regulatory authorities. Regulatory authorities enforce these regulations through periodic inspections of study sponsors, principal investigators, study sites, manufacturing facilities, nonclinical testing facilities and other contractors. If we or any of our CROs or other vendors fail to comply with applicable regulations, the data generated in our nonclinical studies and clinical trials may be deemed unreliable and the applicable regulatory authorities may require us to repeat or to perform additional nonclinical and clinical studies before approving our marketing applications, which would delay the regulatory review and approval process, perhaps significantly.

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

Accordingly, our dependence on third-party CROs and other key 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 lead product candidate GBT440 and for any other product candidates we may pursue for nonclinical studies and clinical trials, and we expect to continue to do so for any product commercialization. Our business could be harmed if any of those third parties fail to provide us with sufficient quantities of drug product, or fail to do so at acceptable quality or quantity levels or prices.

We do not currently have, nor do we plan to acquire, the infrastructure or capability internally to manufacture drug supplies for our ongoing and planned clinical trials of GBT440 or any additional clinical trials

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that we may conduct for GBT440 or any other future product candidates, and we expect to always lack the resources to manufacture any of our product candidates on a commercial scale. We rely, and expect to continue to rely, wholly on third-party manufacturers to produce our product candidates for our clinical trials, including our HOPE study, as well as for commercial manufacture if GBT440 (or any of our product candidates, if any) 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 expect to rely on multiple third parties for the manufacture of commercial supplies of GBT440 or any other product candidates, if approved.

We may be unable to establish or maintain any agreements with third-party manufacturers for GBT440 or any other product candidates, or to do so on acceptable terms. Even if we are able to establish or maintain agreements with third-party manufacturers for GBT440 or any other product candidates, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach or termination of the manufacturing agreement by the third party or by us, including at a time that is costly or inconvenient for us;
- the inability of the third party to satisfy our ordering requirements as to quality, quantity and/or price;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the unwillingness of the third party to extend or renew terms with us when desired.

Furthermore, all of our contract manufacturers are engaged with other companies to supply and/or manufacture materials or products for such companies, which exposes our manufacturers to regulatory and market risks for the production of such materials and products. As a result, failure to meet the regulatory requirements for the production of those materials and products may affect the regulatory assessment or clearance of our contract manufacturers facilities generally, and industry consolidation, pricing or other market factors may cause our contract manufacturers to scale back, terminate or refuse to renew desired arrangements for our materials. If the FDA or a comparable foreign regulatory agency finds deficiencies in or does not approve these facilities for the manufacture of our product candidates or if any agency later finds deficiencies or withdraws its approval in the future, we may need to find alternative manufacturing facilities. Any of these factors could negatively impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved.

Our lead product candidate 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. Although we currently have adequate supplies to conduct our ongoing clinical trials, if we are unable to enter into relationships with additional contract manufacturers, or our current or future contract manufacturers cannot perform as agreed, we may

experience delays and incur additional costs in our clinical development and potential commercialization activities. Our current and anticipated future dependence upon others for the manufacturing of our product candidates and any 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.

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 lead product candidate GBT440, are subject to extensive regulation.

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Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical trials must be manufactured in accordance with cGMPs, or similar regulatory requirements outside the United States. These regulations govern manufacturing processes and procedures, including recordkeeping, and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of contaminants or to inadvertent changes in the properties or stability of our product candidates. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, suspension of production, seizures or voluntary recalls of product candidates or marketed drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect clinical or commercial supplies of GBT440 or any of our future product candidates.

Among other requirements, we or our contract manufacturers must supply all necessary documentation in support of an NDA or MAA seeking approval of a product candidate on a timely basis and must adhere to GLP and cGMP regulations enforced by the FDA and other regulatory agencies through their facilities inspection programs. Some of our contract manufacturers for GBT440 have never produced a commercially approved pharmaceutical product and therefore have not obtained the requisite regulatory authority pre-approval inspection or 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 lead product candidate GBT440. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of GBT440 or any of our future product candidates or the associated quality systems. Although we oversee the contract manufacturers, we cannot control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with these complex regulatory requirements. If these manufacturers, facilities, records or systems do not pass pre-approval inspections and reviews, regulatory approval of GBT440 or any of our other future product candidates may never be granted or may be substantially delayed.

In addition, at any time following approval of a product for sale, the regulatory authorities also may audit the manufacturing facilities of our third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that could be costly 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 a supplement to an NDA, MAA variation or equivalent foreign regulatory filing, which could result in further delay, uncertainty and costs. Regulatory agencies may also require additional clinical 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 programs, results and activities (including 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.

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

Because we rely on third parties to manufacture our lead product candidate GBT440 and to 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, other forms of agreement with any collaborators, CROs, manufacturers and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets and confidential information may become known by our competitors, may inadvertently be incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor s discovery of our trade secrets or confidential information, or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

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

Risks Related to Our Intellectual Property

If we or our licensors are unable to obtain and maintain sufficient intellectual property protection for 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 our lead product candidate 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, particularly patents, that we may exclusively license or own solely and jointly with others in the United States and other countries with respect to our product candidates and technology, including our lead product candidate GBT440. 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, uncertain and complex, and we or our licensors may not be able to file and prosecute all necessary or desirable patent applications, or maintain, enforce and license any patents that may issue from such patent applications, at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. We may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the rights to patents licensed to third parties. Therefore, these patents and applications may

not be prosecuted and enforced in a manner consistent with the best interests of our business. If our current or future licensors, licensees or collaboration partners fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our licensors, licensees or collaboration partners are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised.

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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 and will remain highly uncertain. The patent examination process may require us or our licensors, licensees or collaboration partners to narrow the scope of the claims of our or our licensors , licensees or collaboration partners pending and future patent applications, which may limit the scope of patent protection that may be obtained. Our pending and future patent applications may not result in patents being issued that protect our lead product candidate GBT440 or any future product candidates, in whole or in part, or which effectively prevent others from commercializing competitive product candidates. Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our patents by developing similar or alternative product candidates in a non-infringing manner, or by successful seeking to narrow or invalidate our patents or render them unenforceable. Our and our licensors , licensees or collaboration partners patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications, and then only to the extent the issued claims cover the technology.

We cannot assure you that all of the potentially relevant prior art relating to our patents and patent applications has been found. If such prior art exists, it can invalidate a patent or prevent a patent from issuing from a pending patent application. Moreover, we may be subject to a third-party preissuance submission of prior art to the United States Patent and Trademark Office, or 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 GBT440 or any future product candidates.

In addition, the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical product candidates, or limit the duration of the patent protection of our product candidates. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing drugs similar or identical to ours.

The United States has enacted 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.

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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 in 2011, the United States has moved to a first to file system similar to outside the United States. The Leahy-Smith Act also includes a number of significant changes that affect the way patent applications are prosecuted, and may also affect patent litigation. The effects of these changes are currently unclear as the USPTO must still implement various regulations, the courts have yet to address certain of these provisions and the applicability of the Leahy-Smith Act and new regulations remain to be issued. 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 our lead product candidate GBT440 or any future product candidates that we may develop.

We cannot assure that our lead product candidate 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 third-party intellectual property rights with respect to GBT440 or our future product candidates, that would cause us to incur substantial expenses and, if successful against us, could cause us to pay substantial damages, including treble damages and attorneys fees if we are found to be willfully infringing a third party s patents. We may also be required to indemnify parties with whom we have contractual relationships against such claims. If a patent infringement suit were brought against us, we could be forced to stop or delay research, development, manufacturing or sales of the product or product candidate that is the subject of the suit. As a result of patent infringement claims, or 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, uncertain, and time consuming to litigate, and would divert management s attention from our core business. Any of these events could harm our business significantly.

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

jurisdictions regarding our intellectual property rights with respect to our product candidates and technology.

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

Competitors or other parties may infringe our patents or other intellectual property. Although we are not currently involved in any 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, and there are multiple potential grounds for a validity challenge or an unenforceability assertion. The outcome following legal assertions of invalidity and unenforceability is often highly unpredictable.

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

In addition, our defense of litigation, interference or derivation proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our business and operations including our ability to 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 and operations including 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. 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 2015 we secured exclusive rights from the Regents of the University of California, or the Regents, for certain patents and patent applications that they jointly own with us related to our lead product candidate GBT440 and GBT440 analogs. Additionally, in the United States, each co-owner may be required to be joined as a party to any claim or action we may wish to bring to enforce these patent rights, which may limit our ability to pursue third-party infringement claims.

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

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

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

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

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

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

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. We employ outside firms and rely on them to pay many of these fees. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of complex procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market, with a material adverse effect on our business.

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

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

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

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

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

An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned to a first-to-file system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. A third party that files a patent application in the

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

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

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

Additionally, the U.S. Supreme Court has ruled on several patent cases in recent years, such as Association for Molecular Pathology v. Myriad Genetics, Inc. (Myriad I), Mayo Collaborative Services v. Prometheus Laboratories, Inc., and Alice Corporation Pty. Ltd. v. CLS Bank International, 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 decisions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. Similarly, the complexity and uncertainty of European patent laws has also increased in recent years. In addition, the European patent system is relatively stringent in the type of amendments that are allowed during prosecution. These changes could limit our ability to obtain new patents in the future that may be important for our business.

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Risks Related to Commercialization

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

If our lead product candidate GBT440 or other product candidates that we may pursue receives marketing approval, the product may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community and marketplace. If any approved product (if any) does not achieve an adequate level of acceptance, we may not generate significant revenue from drug sales and we may not become profitable. Before granting reimbursement approval, healthcare payors may require us to demonstrate that our product candidates, in addition to treating the target indication, 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 wide range of factors, including:

- the efficacy and potential advantages of our drugs compared to alternative treatments (for example, in SCD for GBT440 compared to hydroxyurea);
- our ability to offer our drugs for sale at competitive prices;
- the convenience and ease of administration of our drugs compared to alternative current and future treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the availability of drugs and their ability to meet market demand, including a reliable supply for long-term chronic treatment;
- the strength of marketing and distribution support;
- the availability of third-party coverage and adequate reimbursement;
- the clinical indications and approved labeling for which the drug is approved;
- the prevalence and severity of any side effects and overall safety profile of the drug; and

any restrictions on the use of the drug, including together with other medications.

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, as a company we 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, risky 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, if any are approved.

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 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 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 of government funded or private insurance coverage for our product candidates for any approved indications, and the extent of reimbursement by governmental and private payors, will be essential for most patients to be able to afford expensive treatments, such as we expect ours to be, 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 third party payors, like private health insurers, including health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, and government health administration authorities, like Medicare and Medicaid. 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 drug products. The process for determining whether a third-party payor will provide coverage for a product may be separate from the process for setting the reimbursement rate that the payor will pay for the product. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the FDA-approved products for a particular indication. Moreover, a third-party payor s decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. For example, the payor s reimbursement payment rate may not be adequate or may require co-payments that patients find unacceptably high. Additionally, coverage and reimbursement for products can differ significantly from payor to payor.

In the United States, significant decisions about reimbursement for new medicines are made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, as CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare and enters into contracts with drug manufacturers for discounted drug prices for Medicaid under the Medicaid Drug Rebate Program. 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 European Union, 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, or to meet other criteria for pricing approval. If reimbursement of our product candidates is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business and operations could be harmed, possibly materially, based on the large population of patients with SCD who reside in foreign countries.

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

Although we do not currently have any products on the market, our current and future operations may be directly, or indirectly through our prescribers, customers and third-party payors, subject to various U.S. federal and state healthcare laws and regulations. These laws may impact, among other things, our current business operations, including our clinical research activities, and proposed sales, marketing and education programs and constrain our business and financial arrangements and relationships with healthcare providers, physicians and other parties through which we market, sell and distribute our products for which we obtain marketing approval. We may also be subject to additional healthcare, statutory and regulatory requirements and enforcement by foreign regulatory authorities in jurisdictions in which we conduct our business. The laws that may affect our ability to operate include:

the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or paying any remuneration (including any kickback, bribe, or certain rebates), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, lease, order or

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recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under U.S. federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

the U.S. federal false claims and civil monetary penalties laws, including the civil False Claims Act, which, among other things, impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the U.S. federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;

the U.S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services; similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 and their implementing regulations, including the Final HIPAA Omnibus Rule, published in January 2013, which imposes certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without appropriate authorization by covered entities subject to the Final HIPAA Omnibus Rule, i.e. health plans, healthcare clearinghouses and healthcare providers, as well as their business associates that perform certain services for or on their behalf involving the use or disclosure of individually identifiable health information;

the U.S. federal Food, Drug and Cosmetic Act, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices;

the U.S. federal legislation commonly referred to as Physician Payments Sunshine Act, enacted as part of the ACA, and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children s Health Insurance Program to report annually to the CMS information related to certain payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members;

analogous state laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including, but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry s voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts; and

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European and other foreign law equivalents of each of the laws, including reporting requirements detailing interactions with and payments to healthcare providers.

Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from U.S. government funded healthcare programs, such as Medicare and Medicaid, or similar programs in other countries or jurisdictions, disgorgement, individual imprisonment, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, contractual damages, reputational harm, diminished profits, and the curtailment or restructuring of our operations. Further, defending against any such actions can be costly, time-consuming and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. If any of the physicians or other providers or entities with whom we expect to do business is found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment. If any of the above occur, it could adversely affect our ability to operate our business and our results of operations.

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

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or the Affordable Care Act, or the ACA, was passed, which substantially changes the way health care is financed by both governmental and private insurers, and significantly impacts the U.S. pharmaceutical industry. The provisions of the ACA of importance to the pharmaceutical and biotechnology industry are, among others, the following:

an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs agents and biologic agents, which is apportioned among these entities according to their market share in certain government healthcare programs;

an increase in the rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for branded and generic drugs, respectively;

a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts to negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer s outpatient drugs to be covered under Medicare Part D;

extension of manufacturers Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations, unless the drug is subject to discounts under the 340B drug discount program;

a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;

expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers Medicaid rebate liability;

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expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;

new requirements under the federal Physician Payments Sunshine Act for drug manufacturers to report information related to payments and other transfers of value made to physicians and teaching hospitals as well as ownership or investment interests held by physicians and their immediate family members;

a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;

creation of the Independent Payment Advisory Board, which, if and when impaneled, will have authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription drugs; and

establishment of a Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been judicial and Congressional challenges to numerous aspects of the ACA. In January, Congress voted to adopt a budget resolution for fiscal year 2017, or the Budget Resolution, that authorizes the implementation of legislation that would repeal portions of the ACA. The Budget Resolution is not a law, however, it is widely viewed as the first step toward the passage of repeal legislation. Further, on January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. Congress also could consider subsequent legislation to replace elements of the ACA that are repealed. We cannot predict how repeal efforts or any legislation passed to replace portions of the ACA will impact our business.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. After various complex legislative and executive branch actions, starting in 2013 Medicare payment reductions to providers of up to 2% per fiscal year went into effect through 2025, unless Congressional action is taken. Further, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which have resulted in several recent Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, reduce the price of drugs under Medicare and reform government program reimbursement methodologies for products. 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 lead product candidate GBT440 for the potential treatment of SCD or IPF. We have competitors both in the United States and internationally, including major multinational pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies. Many of our competitors have substantially greater financial, technical, and other resources, such as larger research and development, marketing and manufacturing organizations. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. As a result, these companies may obtain regulatory approval more rapidly than we are able to and may be more effective in selling and

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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.

Our initial research and product development efforts are focused on the potential of our lead and initial product candidate to treat SCD or hypoxemia in IPF. 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, 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, medical and clinical and technical operations 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 and geographic market is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. 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

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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 are filed for or 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 our lead product candidate 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 nonclinical 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;
- the market for a product candidate may change during our program so that such a product may become unreasonable to continue to develop;

a product candidate may on further study be shown to have harmful side effects, lack of potential efficacy or other characteristics that indicate it is unlikely to meet applicable regulatory criteria or remain reasonable to continue to develop;

a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and

a product candidate may not be accepted as safe and effective by patients, the medical community or third-party payors, if applicable.

If we fail to develop and successfully commercialize 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 our lead product candidate GBT440.

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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, including our lead product candidate GBT440, 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 warnings on product labels or additional restrictions imposed by regulatory authorities;

the recall of our product candidates;

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, but 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, but 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 can be time-consuming to address, could subject us to costly litigation, require us to pay substantial amounts of money to injured patients, can delay, negatively impact or end our opportunity to receive or maintain regulatory approval to market our product candidates, if approved, can require us to suspend or abandon our commercialization efforts of any approved product candidates, or can impair our ability to raise funds to pursue our development or commercialization efforts. Investigations of these events may interrupt our sales efforts, delay our regulatory approval process in other countries, or impact and limit the type of regulatory approvals our product candidates receive or maintain. As a result of these factors, a product liability claim, even if successfully defended, could have a material adverse effect on our business, financial condition or results of operations.

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

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials

and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

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

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

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

Because we have limited resources, we may forego or delay the pursuit of opportunities with programs or product candidates or for indications that later prove to have greater commercial potential than those we do pursue. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs for product candidates, including our lead product candidate 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 partnering arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate, or we may allocate internal resources to a product candidate in a therapeutic area in which it would have been more advantageous to enter into a partnering arrangement.

Any collaboration 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. To the extent that we decide to enter into collaboration agreements, we will face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for any 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

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consuming to negotiate, document and implement, and we have not previously established our ability to undertake these activities 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 us and 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, costly and time-consuming disputes or termination of the collaboration arrangement. These disagreements can be difficult to resolve successfully, and any such termination or expiration would adversely affect us financially and could harm our business reputation. Many collaborations in the pharmaceutical and biotechnology industries do not result in successful outcomes, for a wide variety of reasons.

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.

Our business strategy currently incorporates potential international expansion as we have initiated our multi-national Phase 3 HOPE study of our lead product candidate GBT440 for the potential treatment of SCD inside and outside the United States, and plan to seek to obtain regulatory approval to and commercialize GBT440 in patient populations inside and 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 sale or use of our products in various countries;
- additional potentially relevant third-party patent rights;
- complexities and difficulties in obtaining protection for and enforcing our intellectual property;
- difficulties in staffing and managing 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.

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

Among other matters, Trade Laws prohibit companies and their employees, agents, clinical research organizations, legal counsel, accountants, consultants, contractors, and other partners from authorizing, promising, offering, providing, soliciting, or receiving directly or indirectly, corrupt or improper payments or anything else of value to or from recipients in the public or private sector. Violations of Trade Laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We also expect our non-U.S. activities to increase in time. We engage third parties for clinical trials and/or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals. We can be held liable for the corrupt or other illegal activities of our personnel, agents, or partners, even if we do not explicitly authorize or have prior knowledge of such activities.

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

Our ability to invest in and expand our business and meet our financial obligations, to attract and retain third-party contractors and collaboration partners and to raise additional capital depends on our operating and financial performance, which, in turn, is subject to numerous factors, including the prevailing economic and political conditions and financial, business and other factors beyond our control, such as the rate of unemployment, the number of uninsured persons in the United States, the results of presidential elections, other political influences and inflationary pressures. For example, an overall decrease in or loss of insurance coverage among individuals in the United States as a result of unemployment, underemployment or the potential repeal of certain provisions of the ACA, may decrease the demand for healthcare services and pharmaceuticals. If fewer patients are seeking medical care because they do not have insurance coverage, we may experience difficulties in any eventual commercialization of our product candidates and our business, results of operations, financial condition and cash flows could be adversely affected.

In addition, certain events have caused, and may cause or contribute to global financial crises, which have triggered and may in the future lead to extreme volatility and disruptions in the capital and credit markets. For example, in June 2016, the United Kingdom, or the U.K., held a referendum in which voters supported the exit of the U. K. from the EU (commonly referred to as Brexit), which could cause disruptions to and create uncertainty surrounding our business, including affecting our existing relationships with third parties that conduct some of our nonclinical studies and clinical trials and our ability to enter into new relationships with vendors and other third-party contractors, which could have an adverse effect on our business, financial results and operations. The referendum is non-binding, but if passed into law, negotiations would commence to determine the future terms of the U.K. s relationship with the EU, including the terms of trade between the U.K. and the EU. Brexit has already and could continue to adversely affect European and/or worldwide economic and market conditions and could continue to contribute to instability in the global financial markets. The measures could also adversely affect our ability to raise additional capital, potentially disrupt the markets in which we currently conduct and plan to conduct operations and the tax jurisdictions in which we operate and adversely change tax benefits or liabilities in these or other jurisdictions. In addition, Brexit could lead to legal uncertainty and potentially divergent national laws and regulations as the U.K. determines which EU laws to replace or replicate, which may present difficulties for our clinical and regulatory strategy.

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 relationships with our contractors and potential collaboration partners. Any of the foregoing could harm our

business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

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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 third party vendors, 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 third party vendors are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our drug development programs. For example, the loss of data from completed or ongoing clinical trials or nonclinical 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 fail to maintain proper and effective systems of disclosure controls and internal controls over financial reporting to the extent required under applicable regulations, the accuracy and timeliness of our financial reporting may be adversely affected, and we could be subject to sanctions or other penalties that would harm our business.

As a public company, we are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, Section 404, or Section 404, of the Sarbanes-Oxley Act of 2002, or Sarbanes Oxley, and the rules and regulations of The NASDAQ Stock Market. Section 404 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 annual report on Form 10-K for the fiscal year ending December 31, 2016, 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 Jumpstart Our Business Startups Act of 2012, as amended, or 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. We expect to incur additional professional fees and internal costs to expand our accounting and finance functions and to expend significant management efforts in order to comply with these

requirements. 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.

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We are in the process of carrying out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and our Chief Financial Officer, of the effectiveness of our internal control over financial reporting for the purpose of providing the reports required by Section 404. These processes continue to be reviewed, and during the course of our subsequent review and testing, we may identify material weaknesses or significant deficiencies and be unable to remediate them before we must provide the required reports. If material weaknesses or significant deficiencies in our internal control over financial reporting are identified in the future, we may not detect or remediate errors on a timely basis and our consolidated financial statements may be materially misstated. We or our independent registered public accounting firm may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall. In addition, 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 JOBS Act, and we have elected 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 or (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.

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

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

- adverse results or delays in our nonclinical studies or clinical trials;
- reports of adverse events in other treatments for SCD, IPF 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 our lead product candidate 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;

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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. For example, negative publicity regarding drug pricing and price increases by pharmaceutical companies has negatively impacted, and may continue to negatively impact, the markets for biotechnology and pharmaceutical stocks. In the past, following periods of volatility in the market, securities class-action litigation has often been instituted against companies. Such litigation, if instituted against us, could result in substantial costs and diversion of management s attention and resources, which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

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

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

- 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;

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- 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;
- 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, in January 2017 our board of directors approved our 2017 Inducement Equity Plan, or 2017 Inducement Plan, to enable us and our subsidiaries to grant

non-qualified stock options and other equity-based awards to induce highly-qualified prospective officers and employees who are not currently employed by us or our subsidiaries to accept employment with us or our subsidiaries. The number of shares initially reserved for grant under the 2017 Inducement Plan is 300,000 shares, subject to adjustment for reorganization, recapitalization, stock dividend, stock split, or similar changes in our capital stock. In addition, we have reserved shares of common stock for issuance pursuant to our 2015 Employee Stock Purchase Plan, or 2015 ESPP, which number of shares will automatically increase each year on January 1, from January 1, 2016 to January 1, 2025, by the lesser of (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

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2015 Plan and the 2015 ESPP each year. If our board of directors elects to increase the number of shares available for future grant under the 2015 Plan, the 2017 Inducement Plan or the 2015 ESPP, our stockholders may experience additional dilution, and our stock price may fall.

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

Sales of a substantial number of shares of our common stock in the public market could occur at any time. A significant portion of our outstanding shares of common stock are held by a small number of stockholders, including our directors, officers and affiliates. 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, executive officers and certain affiliates have established or 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 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 owned approximately 62.9% of our outstanding common stock as of February 14, 2017, 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.

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;

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create a classified board of directors whose members serve staggered three-year terms;

specify that special meetings of our stockholders can be called only by our board of directors, the chairperson of our board of directors, our chief executive officer or our president;

prohibit stockholder action by written consent;

establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;

provide that our directors may be removed only for cause;

provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;

specify that no stockholder is permitted to cumulate votes at any election of directors;

expressly authorize our board of directors to modify, alter or repeal our amended and restated bylaws; and

require supermajority votes of the holders of our common stock to amend specified provisions of our amended and restated certificate of incorporation and amended and restated bylaws.

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

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

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

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

We have incurred substantial losses during our history and do not expect to become profitable in the near future and we may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire. Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an ownership change, generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation s ability to use its

pre-change net operating loss carryforwards, or NOLs, and other pre-change tax attributes (such as research tax credits) to offset its post-change income or taxes may be limited. We experienced an ownership change as a result of our IPO, however we do not believe that this ownership change will significantly limit our ability to use these pre-change NOL carryforwards. We may experience subsequent shifts in our stock ownership, including as a result of our follow-on offering in June 2016, some of which are outside of our control. As a result, if we earn net taxable income, our ability to use our pre-change NOL carryforwards to offset U.S. federal taxable income may become subject to limitations, which could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

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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.

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

As a public company, we 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 has 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 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 or increase in volatility. Further, if our operating results fail to meet the forecasts of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

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

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the IRS and the U.S. Treasury Department. Changes to tax laws (which

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changes may have retroactive application) could adversely affect our stockholders or us. In recent years, many such changes have been made and changes are likely to continue to occur in the future. We cannot predict whether, when, in what form, or with what effective dates, tax laws, regulations and rulings may be enacted, promulgated or decided, which could result in an increase in our, or our stockholders , tax liability or require changes in the manner in which we operate in order to minimize increases in our tax liability.

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USE OF PROCEEDS

We estimate that the net proceeds from our issuance and sale of shares of our common stock in this offering will be approximately $117.9 million ($135.6 million if the underwriter s option to purchase additional shares is exercised in full), after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering and our existing capital resources, consisting of cash and cash equivalents and marketable securities, to fund our clinical development of GBT440 for the treatment of SCD, including our Phase 3 HOPE study and our ongoing Phase 2a clinical trial and planned clinical pharmacology studies, our Phase 1 and Phase 2a clinical trials of GBT440 for the treatment of IPF and other hypoxemic pulmonary disorders, our other research and development activities, and for working capital and general corporate purposes.

Based on our current plans, we believe our cash and cash equivalents, together with the net proceeds to us from this offering, will be sufficient to fund our operations for at least the next 12 months.

We may also use a portion of the net proceeds to in-license, acquire or invest in new businesses, technology or assets. Although we have no specific agreements, commitments or understandings with respect to any in-license or acquisition, we evaluate such opportunities and engage in related discussions with other business entities from time to time.

This expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions. As of the date of this prospectus supplement, we cannot predict with certainty all of the particular uses for the net proceeds to be received upon the completion of this offering or the amounts that we will actually spend on the uses set forth above or the timing of such events. The amounts and timing of our actual expenditures and the extent of our preclinical and clinical development activities may vary significantly depending on numerous factors, including the progress of our development efforts, the status of and results from nonclinical studies and our ongoing clinical trials or any clinical trials we may commence in the future, our ability to take advantage of expedited programs or to obtain regulatory approval for GBT440 and any other product candidates we may identify and pursue, the timing and costs associated with the manufacture and supply of GBT440 and any other product candidates we may identify and pursue for clinical development or commercialization, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering.

Pending our use of the net proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation investments, including short-term and/or long-term, investment-grade, interest-bearing instruments and U.S. government securities.

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DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted to the extent of the difference between the price per share of our common stock in this offering and the as adjusted net tangible book value per share of our common stock immediately after this offering.

As of September 30, 2016, we had net tangible book value of approximately $210.1 million, or $5.75 per share of our common stock, based upon 36,516,130 shares of our common stock outstanding as of that date. Historical net tangible book value per share is equal to our total tangible assets, less total liabilities, divided by the number of outstanding shares of our common stock. Dilution in net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the net tangible book value per share of our common stock immediately after this offering.

After giving effect to the sale of 5,102,041 shares of common stock in this offering at the public offering price of $24.50 per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2016 would have been approximately $328.0 million, or approximately $7.88 per share of common stock. This represents an immediate increase in as adjusted net tangible book value of $2.13 per share to our existing stockholders and an immediate dilution of $16.62 per share to new investors participating in this offering.

Dilution per share to new investors is determined by subtracting net tangible book value per share after this offering from the public offering price per share paid by new investors. The following table illustrates this per share dilution:

Public offering price per share		$ 24.50
Historical net tangible book value per share as of September 30, 2016	$ 5.75	
Increase in net tangible book value per share attributable to new investors	2.13	
As adjusted net tangible book value per share after this offering		7.88
Dilution per share to new investors		$ 16.62

If the underwriter exercises in full its option to purchase up to an additional 765,306 shares of our common stock at the public offering price of $24.50 per share, the as adjusted net tangible book value after this offering would be $8.16 per share, representing an increase in net tangible book value of $2.40 per share to existing stockholders and immediate dilution of $16.34 per share to investors purchasing our common stock in this offering at the public offering price.

The foregoing table and discussion is based on 36,516,130 shares of common stock outstanding as of September 30, 2016 and includes and excludes:

- 2,703,252 shares of common stock issuable upon exercise of outstanding options as of September 30, 2016 at a weighted-average exercise price of $10.99 per share;

777,041 shares of restricted common stock which were subject to our right of repurchase as of September 30, 2016;

607,250 shares of common stock issuable upon exercise of options granted subsequent to September 30, 2016 at a weighted-average exercise price of $17.34 per share;

217,600 shares of common stock issuable upon the vesting of restricted stock units granted subsequent to September 30, 2016 pursuant to our 2015 Plan;

1,484,701 shares of common stock reserved for future issuance under the 2015 Plan as of September 30, 2016; and

76,118 shares of common stock reserved for future issuance under the 2015 ESPP as of September 30, 2016.

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To the extent that any options are exercised, new options are issued under our equity incentive plans, or we otherwise issue additional shares of common stock in the future (including shares issued in connection with acquisitions), there will be further dilution to new investors.

In addition, we may choose to raise additional capital due to market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

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PRICE RANGE OF COMMON STOCK

Our common stock began trading on The NASDAQ Global Select Market under the symbol GBT on August 12, 2015. Prior to that time, there was no public market for our common stock. The following table sets forth the high and low sale prices per share of our common stock, as reported on The NASDAQ Global Select Market, for the periods indicated:

	High	Low
Year ended December 31, 2015		
Third quarter (from August 12, 2015)	$ 57.00	$ 33.01
Fourth quarter	$ 55.74	$ 28.73
Year ended December 31, 2016		
First quarter	$ 31.97	$ 12.24
Second quarter	$ 27.99	$ 14.22
Third quarter	$ 24.10	$ 16.07
Fourth quarter	$ 23.80	$ 13.35
Year ending December 31, 2017		
First quarter (through February 21, 2017)	$ 29.10	$ 14.00

On February 21, 2017, the last reported sale price of our common stock as reported on The NASDAQ Global Select Market was $28.50 per share. As of February 20, 2017, there were approximately 23 record holders of our common stock. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees.

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DIVIDEND POLICY

We have never declared or paid dividends on our capital stock. We do not anticipate paying any dividends on our capital stock in the foreseeable future. We currently intend to retain all available funds and any future earnings to fund the development and growth of our business. Any future determination to declare dividends will be subject to the discretion of our board of directors and will depend on various factors, including applicable laws, our results of operations, financial condition, future prospects and any other factors deemed relevant by our board of directors. Investors should not purchase our common stock with the expectation of receiving cash dividends.

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UNDERWRITING

We have entered into an underwriting agreement with Cantor Fitzgerald & Co., as representative of the several underwriters, with respect to the common stock being offered hereby. Subject to the terms and conditions of the underwriting agreement, each of the underwriters has agreed to purchase from us the respective number of shares of common stock shown opposite its name below:

UNDERWRITERS	NUMBER OF SHARES
Cantor Fitzgerald & Co.	5,102,041
Total	5,102,041

The underwriting agreement provides that the obligation of the underwriters are subject to certain conditions precedent and that the underwriters have agreed to purchase all of the shares of common stock sold under the underwriting agreement if any of these shares are purchased.

We have agreed to indemnify the underwriters against specified liabilities, including liabilities under the Securities Act, and to contribute to payments the underwriters may be required to make in respect thereof.

The underwriters are offering the shares of common stock, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel and other conditions specified in the underwriting agreement. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Underwriting discounts and commissions and offering expenses. The underwriters are purchasing the 5,102,041 shares of common stock from us at $24.50 per share, which will result in $118,214,290 ($135,571,430 if the underwriter s option to purchase additional shares is exercised in full) of proceeds to us before expenses.

The underwriters may offer the shares of common stock from time to time for sale in one or more transactions on The NASDAQ Global Select Market, in the over-the-counter market, through negotiated transactions or otherwise at market prices prevailing at the time of sale, at prices related to prevailing market prices or at negotiated prices. In connection with the sale of the shares of common stock offered hereby, the underwriters may be deemed to have received compensation in the form of underwriting discounts. The underwriters may effect such transactions by selling shares of common stock to or through dealers, and such dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters and/or purchasers of shares of common stock for whom they may act as agents or to whom they may sell as principal.

We estimate that the total expenses of the offering payable by us, other than the underwriting discounts and commissions, will be approximately $350,000. We have also agreed to reimburse the underwriters for certain of their expenses in an amount up to $25,000 in the aggregate.

Option to purchase additional shares. We have granted the underwriter an option, exercisable for 30 days from the date of this prospectus supplement, to purchase, from time to time, in whole or in part, up to 765,306 of additional shares from us at the public offering price set forth on the cover page of this prospectus supplement, less underwriting discounts and commissions.

Discretionary accounts. The underwriters do not intend to confirm sales of shares of common stock to any accounts over which it has discretionary authority.

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Stabilization. In connection with this offering, the underwriters may engage in stabilizing transactions, overallotment transactions, syndicate covering transactions and purchases to cover positions created by short sales in accordance with Regulation M under the Exchange Act.

Stabilizing transactions permit bids to purchase shares of common stock so long as the stabilizing bids do not exceed a specified maximum, and are engaged in for the purpose of preventing or retarding a decline in the market price of the common stock while the offering is in progress.

Overallotment transactions involve sales by the underwriters of shares of common stock in excess of the number of shares of common stock the underwriters are obligated to purchase. This creates a syndicate short position which may be either a covered short position or a naked short position. In a covered short position, the number of shares of common stock overallotted by the underwriters, if any, is not greater than the number of shares of common stock that they may purchase in the option to purchase additional shares. In a naked short position, the number of shares of common stock involved is greater than the number of shares of common stock in the option to purchase additional shares, if any. The underwriters may close out any short position by exercising their option to purchase additional shares, if any, and/or purchasing shares of common stock in the open market.

Syndicate covering transactions involve purchases of common stock in the open market after the distribution has been completed in order to cover syndicate short positions. In determining the source of shares of common stock to close out the short position, the underwriters will consider, among other things, the price of shares of common stock available for purchase in the open market as compared with the price at which the underwriter may purchase shares of common stock through exercise of the option to purchase additional shares, if any. If the underwriters sells more shares of common stock than could be covered by exercise of the option to purchase additional shares, if any, and, therefore, has a naked short position, the position can be closed out only by buying shares of common stock in the open market. A naked short position is more likely to be created if the underwriters are concerned that after pricing there could be downward pressure on the price of the shares of common stock in the open market that could adversely affect investors who purchase in the offering.

These stabilizing transactions and syndicate covering transactions may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock in the open market may be higher than it would otherwise be in the absence of these transactions. Neither we nor the underwriters make any representation or prediction as to the effect that the transactions described above may have on the price of our common stock. These transactions may be effected on The NASDAQ Global Select Market, in the over-the-counter market or otherwise and, if commenced, may be discontinued at any time.

Passive market making. In connection with this offering, the underwriters may engage in passive market making transactions in our common stock on The NASDAQ Global Select Market in accordance with Rule 103 of Regulation M under the Exchange Act, during a period before the commencement of offers or sales of common stock and extending through the completion of the distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker s bid that bid must then be lowered when specified purchase limits are exceeded.

Lock-up agreements. We and our executive officers and directors have agreed that for a period of 90 days after the date of this prospectus, and certain of our principal stockholders have agreed that for a period of 45 days after the date of this prospectus (as applicable, the restricted period), without the prior written consent Cantor Fitzgerald & Co. on behalf of the underwriters, we and they will not:

offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of, directly or indirectly, any shares of common stock or any securities convertible into or exercisable or exchangeable for shares of common stock;

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file any registration statement with the Securities and Exchange Commission relating to the offering of any shares of common stock or any securities convertible into or exercisable or exchangeable for common stock; or

enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of our common stock;

whether any such transaction described above is to be settled by delivery of common stock or such other securities, in cash or otherwise. In addition, we and each such person agrees that, without the prior written consent of Cantor Fitzgerald & Co. on behalf of the underwriters, we or such other person will not, during the restricted period, make any demand for, or exercise any right with respect to, the registration of any shares of common stock or any security convertible into or exercisable or exchangeable for common stock.

The restrictions described in the immediately preceding paragraph do not apply to:

the sale of shares to the underwriters;

our issuance of common stock upon the exercise of an option or a warrant or the conversion of a security outstanding on the date of, and described in, this prospectus;

the transfer of common stock to us pursuant to the exercise of our right to repurchase certain shares in connection with the termination of employment or board service under agreements entered into pursuant to our equity incentive plans;

transactions by any person other than us relating to shares of common stock or other securities acquired in open market transactions after the completion of the offering of the shares; provided that no filing under Section 16(a) of the Securities Exchange Act of 1934, as amended (the Exchange Act), is required or voluntarily made in connection with subsequent sales of the common stock or other securities acquired in such open market transactions;

our sale or issuance of or entry into an agreement to sell or issue shares of common stock in connection with our acquisition of one or more businesses, products, assets or technologies or in connection with certain strategic transactions; provided, that, the aggregate number of shares of common stock that we may sell or issue or agree to sell or issue pursuant to this provision cannot exceed 5% of the total number of shares of common stock issued and outstanding immediately following the completion of this offering and provided further that each recipient of such shares pursuant to this provision must execute and deliver to the representatives, on or prior to such issuance, a lock-up agreement; or

the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares of common stock, provided that (i) such plan does not provide for the transfer of common stock during the restricted period and (ii) to the extent a public announcement or filing under the Exchange Act, if any, is

required or voluntarily made regarding the establishment of such plan, such announcement or filing shall include a statement to the effect that no transfer of common stock may be made under such plan during the restricted period.

In addition, the restrictions do not apply to certain of our principal stockholders with respect to the distribution of shares of common stock pursuant to a trading plan that is existing on the date of this prospectus supplement, provided that to the extent a public announcement or filing under the Exchange Act, if any, is required or voluntarily made regarding such distribution, such announcement or filing shall include a statement that such distribution is in accordance with an established trading plan.

Other Activities and Relationships. The underwriters and certain of their affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriters and certain of their affiliates have, from time to

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time, performed, and may in the future perform, various commercial and investment banking and financial advisory services for us and our affiliates, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and certain of their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve securities and/or instruments issued by us and our affiliates. If the underwriters or their respective affiliates have a lending relationship with us, they routinely hedge their credit exposure to us consistent with their customary risk management policies. The underwriters and their respective affiliates may hedge such exposure by entering into transactions which consist of either the purchase of credit default swaps or the creation of short positions in our securities or the securities of our affiliates, including potentially the common stock offered hereby. Any such short positions could adversely affect future trading prices of the common stock offered hereby. The underwriters and certain of their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Notice to Investors

Australia

This prospectus supplement and the accompanying prospectus are not a disclosure document for the purposes of Australia s Corporations Act 2001 (Cth) of Australia, or Corporations Act, has not been lodged with the Australian Securities & Investments Commission and is only directed to the categories of exempt persons set out below. Accordingly, if you receive this prospectus supplement in Australia:

A. You confirm and warrant that you are either:

sophisticated investor under section 708(8)(a) or (b) of the Corporations Act;

a sophisticated investor under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant s certificate to the company which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made;

a person associated with the company under Section 708(12) of the Corporations Act; or

professional investor within the meaning of section 708(11)(a) or (b) of the Corporations Act.

To the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor or professional investor under the Corporations Act, any offer made to you under this prospectus supplement is void and incapable of acceptance.

B. You warrant and agree that you will not offer any of the shares issued to you pursuant to this prospectus supplement for resale in Australia within 12 months of those shares being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

Canada

The shares of our common stock may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the shares of our common stock must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

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Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus supplement (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser s province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser s province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 (or, in the case of securities issued or guaranteed by the government of a non-Canadian jurisdiction, section 3A.4) of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

European Economic Area

In relation to each member state of the European Economic Area which has implemented the Prospectus Directive, each, a Relevant Member State, with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State, which is referred to as the Relevant Implementation Date, no offer of any securities which are the subject of the offering contemplated by this prospectus supplement has been or will be made to the public in that Relevant Member State other than any offer where a prospectus has been or will be published in relation to such securities that has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the relevant competent authority in that Relevant Member State in accordance with the Prospectus Directive, except that with effect from and including the Relevant Implementation Date, an offer of such securities may be made to the public in that Relevant Member State:

a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;

b) to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representative of the underwriters for any such offer; or

c) to any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of securities shall require the Company or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

For the purposes of this provision, the expression an offer to the public in relation to any securities in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe the securities, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State and the expression Prospectus Directive means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State.

Hong Kong

No securities have been offered or sold, and no securities may be offered or sold, in Hong Kong, by means of any document, other than to persons whose ordinary business is to buy or sell shares or debentures, whether as principal or agent; or to professional investors as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or in other circumstances which do not result in the document being a prospectus as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap. 32) of Hong Kong. No

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document, invitation or advertisement relating to the securities has been issued or may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance.

This prospectus supplement has not been registered with the Registrar of Companies in Hong Kong. Accordingly, this prospectus supplement may not be issued, circulated or distributed in Hong Kong, and the securities may not be offered for subscription to members of the public in Hong Kong. Each person acquiring the securities will be required, and is deemed by the acquisition of the securities, to confirm that he is aware of the restriction on offers of the securities described in this prospectus supplement and the relevant offering documents and that he is not acquiring, and has not been offered any securities in circumstances that contravene any such restrictions.

Israel

In the State of Israel this prospectus supplement shall not be regarded as an offer to the public to purchase shares of common stock under the Israeli Securities Law, 5728-1968, which requires a prospectus to be published and authorized by the Israel Securities Authority, if it complies with certain provisions of Section 15 of the Israeli Securities Law, 5728-1968, including, inter alia, if: (i) the offer is made, distributed or directed to not more than 35 investors, subject to certain conditions (the Addressed Investors); or (ii) the offer is made, distributed or directed to certain qualified investors defined in the First Addendum of the Israeli Securities Law, 5728-1968, subject to certain conditions (the Qualified Investors). The Qualified Investors shall not be taken into account in the count of the Addressed Investors and may be offered to purchase securities in addition to the 35 Addressed Investors. The Company has not and will not take any action that would require it to publish a prospectus in accordance with and subject to the Israeli Securities Law, 5728-1968. The Company and the underwriters have not and will not distribute this prospectus supplement or make, distribute or direct an offer to subscribe for our common stock to any person within the State of Israel, other than to Qualified Investors and up to 35 Addressed Investors.

Qualified Investors may have to submit written evidence that they meet the definitions set out in of the First Addendum to the Israeli Securities Law, 5728-1968. In particular, we may request, as a condition to be offered common stock, that Qualified Investors will each represent, warrant and certify to us and/or to anyone acting on our behalf: (i) that it is an investor falling within one of the categories listed in the First Addendum to the Israeli Securities Law, 5728-1968; (ii) which of the categories listed in the First Addendum to the Israeli Securities Law, 5728-1968 regarding Qualified Investors is applicable to it; (iii) that it will abide by all provisions set forth in the Israeli Securities Law, 5728-1968 and the regulations promulgated thereunder in connection with the offer to be issued common stock; (iv) that the shares of common stock that it will be issued are, subject to exemptions available under the Israeli Securities Law, 5728-1968: (a) for its own account; (b) for investment purposes only; and (c) not issued with a view to resale within the State of Israel, other than in accordance with the provisions of the Israeli Securities Law, 5728-1968; and (v) that it is willing to provide further evidence of its Qualified Investor status. Addressed Investors may have to submit written evidence in respect of their identity and may have to sign and submit a declaration containing, inter alia, the Addressed Investor s name, address and passport number or Israeli identification number.

Japan

The offering has not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948 of Japan, as amended), or FIEL, and the underwriters will not offer or sell any securities, directly or

indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means, unless otherwise provided herein, any person resident in Japan, including any corporation or other

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entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the FIEL and any other applicable laws, regulations and ministerial guidelines of Japan.

Singapore

This prospectus supplement has not been and will not be lodged or registered with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and any other document or material in connection with the offer or sale, or the invitation for subscription or purchase of the securities may not be issued, circulated or distributed, nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to the public or any member of the public in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (ii) to a relevant person as defined under Section 275(2), or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions, specified in Section 275 of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of any other applicable provision of the SFA. Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

a) a corporation (which is not an accredited investor as defined under Section 4A of the SFA) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries rights and interest in that trust shall not be transferable for six months after that corporation or that trust has acquired the Offer Shares under Section 275 of the SFA except:

i. to an institutional investor under Section 274 of the SFA or to a relevant person defined in Section 275(2) of the SFA, or to any person pursuant to an offer that is made on terms that such shares, debentures and units of shares and debentures of that corporation or such rights and interest in that trust are acquired at a consideration of not less than $200,000 (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets, and further for corporations, in accordance with the conditions, specified in Section 275 of the SFA;

ii. where no consideration is given for the transfer; or

iii. where the transfer is by operation of law.

Switzerland

The securities may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This prospectus supplement has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss

Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this prospectus supplement nor any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this prospectus supplement nor any other offering or marketing material relating to the offering, the Company or the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this prospectus supplement will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of securities.

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United Kingdom

This prospectus supplement is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended, which is referred to as the Order, and/or (ii) high net worth entities falling within Article 49(2)(a) to (d) of the Order and other persons to whom it may lawfully be communicated, each such person being referred to as a relevant person.

This prospectus supplement and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

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MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS FOR NON-U.S. HOLDERS

The following is a summary of the material U.S. federal income tax consequences of the ownership and disposition of our common stock to non-U.S. holders, but does not purport to be a complete analysis of all the potential tax considerations relating thereto. This summary is based upon the provisions of the Internal Revenue Code of 1986, as amended, or the Code, Treasury regulations promulgated thereunder, administrative rulings and judicial decisions, all as of the date hereof. These authorities may be changed or subject to differing interpretations, possibly with retroactive effect, so as to result in U.S. federal income tax consequences different from those set forth below. We have not sought any ruling from the Internal Revenue Service, or the IRS, with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS will agree with such statements and conclusions.

This summary also does not address the tax considerations arising under the laws of any U.S. state or local or any non-U.S. jurisdiction, U.S. federal estate or gift tax laws, the Medicare tax on net investment income or any alternative minimum tax consequences. In addition, this discussion does not address tax considerations applicable to an investor s particular circumstances or to investors that may be subject to special tax rules, including, without limitation:

banks, insurance companies or other financial institutions;

tax-exempt organizations;

dealers in securities or currencies;

traders in securities that elect to use a mark-to-market method of accounting for their securities holdings;

persons that own, or are deemed to own, more than five percent of our capital stock;

certain former citizens or long-term residents of the United States;

persons who hold our common stock as a position in a hedging transaction, straddle, conversion transaction or other risk reduction transaction;

persons who do not hold our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, for investment purposes);

S corporations, partnerships, or other entities or arrangements treated as partnerships for U.S. federal income tax purposes (or investors in any such entities);

persons deemed to sell our common stock under the constructive sale provisions of the Code;

regulated investment companies or real estate investment trusts;

pension plans;

controlled foreign corporations;

passive foreign investment companies; or

persons that acquire our common stock as compensation for services.

In addition, if a partnership, including any entity or arrangement classified as a partnership for U.S. federal income tax purposes, holds our common stock, the tax treatment of a partner in such partnership generally will depend on the status of the partner and upon the activities of the partnership. Accordingly, partnerships that hold our common stock, and partners in such partnerships, should consult their tax advisors.

You are urged to consult your tax advisor with respect to the application of the U.S. federal income tax laws to your particular situation, as well as any tax consequences of the purchase, ownership and disposition of our common stock arising under the U.S. federal estate or gift tax rules or under the laws of any U.S. state or local or any non-U.S. or other taxing jurisdiction or under any applicable tax treaty.

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Non-U.S. Holder Defined

For purposes of this discussion, you are a non-U.S. holder if you are a beneficial owner of our common stock that is for United States federal income tax purposes (i) a foreign corporation, (ii) a nonresident alien individual, (iii) a foreign estate, the income of which, if from sources without the United States and not effectively connected with the conduct of a trade or business within the United States, is not subject to tax in the United States, or (iv) a trust that has not made an election to be treated as a U.S. holder under applicable Treasury regulations and that either (A) is not subject to the primary jurisdiction of a court within the United States, or (B) is not subject to the substantial control of one or more United States persons.

Distributions

As discussed under Dividend Policy, above, we do not anticipate paying any dividends on our capital stock in the foreseeable future. If we were to make distributions on our common stock, those payments will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. To the extent those distributions exceed both our current and our accumulated earnings and profits, they will constitute a return of capital and will first reduce your basis in our common stock, but not below zero, and then will be treated as gain from the sale of stock, subject to the tax treatment described in the discussion below regarding taxable dispositions of our common stock. Any such distributions would also be subject to the discussions below regarding backup withholding and FATCA.

Subject to the discussion below regarding a dividend received by you that is effectively connected with the conduct of a U.S. trade or business, a dividend paid to you generally will be subject to U.S. withholding tax either at a rate of 30% of the gross amount of the dividend or such lower rate as may be specified by an applicable income tax treaty. In order to receive a reduced treaty rate, you must provide us with a valid IRS Form W-8BEN, IRS Form W-8-BEN-E or another appropriate version of IRS Form W-8 (or a successor form), in each case, certifying qualification for the reduced rate.

Dividends received by you that are effectively connected with the conduct of a U.S. trade or business (and, if required by an applicable income tax treaty, are attributable to a permanent establishment maintained by you in the United States) generally are exempt from such withholding tax. In order to obtain this exemption, you must provide us with a valid IRS Form W-8ECI or successor form or other applicable IRS Form W-8 properly certifying such exemption. Such effectively connected dividends, although not subject to withholding tax, are taxed at the same graduated rates applicable to U.S. persons, net of certain deductions and credits, subject to an applicable income tax treaty providing otherwise. In addition, if you are a corporate non-U.S. holder, you may also be subject to a branch profits tax at a rate of 30% or such lower rate as may be specified by an applicable income tax treaty on your earnings and profits in respect of such effectively connected dividend income.

If you are eligible for a reduced rate of withholding tax pursuant to a tax treaty, you may be able to obtain a refund of any excess amounts currently withheld if you file an appropriate claim for refund with the IRS.

Gain on Sale or Other Taxable Disposition of Common Stock

Subject to the discussion below regarding backup withholding and FATCA, a non-U.S. Holder generally will not be required to pay U.S. federal income tax on any gain realized upon the sale or other taxable disposition of our common stock unless:

the gain is effectively connected with the conduct of a U.S. trade or business (and, if required by an applicable income tax treaty, the gain is attributable to a permanent establishment maintained by you in the U.S.), in which case you will be required to pay tax on the net gain derived from the sale under regular graduated U.S. federal income tax rates, and for a non-U.S. holder that is a corporation, such non-U.S. holder may be subject to the branch profits tax on any earnings and profits attributable to such gains at a 30% rate or such lower rate as may be specified by an applicable income tax treaty;

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you are an individual who is present in the United States for a period or periods aggregating 183 days or more during the taxable year in which the sale or disposition occurs and certain other conditions are met, in which case you will be required to pay a flat 30% tax on the gain derived from the sale, which tax may be offset by certain U.S. source capital losses in the taxable year of disposition (even though you are not considered a resident of the United States) (subject to applicable income tax or other treaties); or

our common stock constitutes a U.S. real property interest by reason of our status as a U.S. real property holding corporation for U.S. federal income tax purposes, or a USRPHC, at any time within the shorter of the five-year period preceding the disposition or your holding period for our common stock. We believe that we are not currently and will not become a USRPHC. However, because the determination of whether we are a USRPHC depends on the fair market value of our U.S. real property relative to the fair market value of our other real property and business assets, there can be no assurance that we will not become a USRPHC in the future. Even if we become a USRPHC, however, as long as our common stock is regularly traded on an established securities market (as determined under the Code), such common stock will be treated as U.S. real property interests only if you actually or constructively hold more than five percent of such regularly traded common stock at any time during the applicable period that is specified in the Code.

Backup Withholding and Information Reporting

Generally, we must report annually to the IRS the amount of dividends paid to you, your name and address, and the amount of tax withheld, if any. A similar report will generally be sent to you. Pursuant to applicable income tax treaties or other agreements, the IRS may make these reports available to tax authorities in your country of residence.

Payments of dividends or of proceeds on the disposition of stock made to you may be subject to additional information reporting and backup withholding at the then applicable rate (currently 28%) unless you establish an exemption, for example by properly certifying your non-U.S. status on an IRS Form W-8BEN, IRS Form W-8BEN-E or another appropriate version of IRS Form W-8 (or a successor form). Notwithstanding the foregoing, backup withholding and information reporting may apply if either we or our paying agent has actual knowledge, or reason to know, that you are a U.S. person.

Backup withholding is not an additional tax; rather, the U.S. income tax liability of persons subject to backup withholding will be reduced by the amount of tax withheld. If withholding results in an overpayment of taxes, a refund or credit may generally be obtained from the IRS, provided that the required information is furnished to the IRS in a timely manner.

Foreign Account Tax Compliance Act (FATCA)

Provisions commonly referred to as FATCA may impose withholding tax on certain types of payments made to foreign financial institutions and certain other non-U.S. entities. The legislation imposes a 30% withholding tax on dividends on, or gross proceeds from the sale or other disposition of, our common stock paid to a foreign financial institution or to certain non-financial foreign entities, unless (i) the foreign financial institution undertakes certain diligence and reporting obligations, (ii) the non-financial foreign entity either certifies it does not have any substantial U.S. owners or furnishes identifying information regarding each substantial U.S. owner and such entity meets certain other specified requirements, or (iii) the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from these rules. If the payee is a foreign financial institution and is subject to the requirements in (i) above, it must enter into an agreement with the U.S. Treasury requiring, among other things, that it undertake to identify accounts held by certain U.S. persons or U.S.-owned foreign entities, annually report certain information about such accounts, and withhold 30% on payments to account holders whose actions prevent it from complying with

these reporting and other

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requirements. If the country in which a payee is resident has entered into an intergovernmental agreement with the United States regarding FATCA, that agreement may permit the payee to report to that country rather than to the U.S. Treasury. Under final regulations and published guidance, the obligation to withhold from payments made to a foreign financial institution or a foreign non-financial entity under FATCA with respect to dividends on our common stock are currently in effect, but with respect to the gross proceeds of a sale or other disposition of our common stock will not begin until January 1, 2019. Prospective investors should consult their tax advisors regarding FATCA.

The preceding discussion of U.S. federal income tax considerations is for general information only. It is not tax advice. Each prospective investor should consult its own tax advisor regarding the particular U.S. federal, state and local and non-U.S. tax consequences of purchasing, holding and disposing of our common stock, including the consequences of any proposed change in applicable laws.

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LEGAL MATTERS

Certain legal matters with respect to the securities offered by this prospectus supplement will be passed upon for us by Goodwin Procter LLP, San Francisco, California. Certain legal matters will be passed upon for the underwriters by Cooley LLP, San Diego, California.

EXPERTS

The financial statements of Global Blood Therapeutics, Inc. as of December 31, 2015 and 2014, and for each of the years in the three-year period ended December 31, 2015, are incorporated by reference herein and in reliance upon the report of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

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WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-3 under the Securities Act of 1933, as amended, or the Securities Act, with respect to the common stock offered by this prospectus supplement. This prospectus supplement, filed as part of the registration statement, does not contain all the information set forth in the registration statement and its exhibits and schedules, portions of which have been omitted as permitted by the rules and regulations of the SEC. For further information about us, we refer you to the registration statement and to its exhibits and schedules.

Statements contained in this prospectus supplement or the accompanying prospectus concerning the contents of any contract or any other document are not necessarily complete. If a contract or document has been filed as an exhibit to the registration statement, we refer you to the copy of the contract or document that has been filed. Each statement in this prospectus supplement or the accompanying prospectus relating to a contract or document filed as an exhibit is qualified in all respects by the filed exhibit. The reports and other information we file with the SEC can be read and copied at the SEC s Public Reference Room at 100 F Street, NE, Washington D.C. 20549. You may obtain information regarding the operation of the Public Reference Room by calling 1(800) SEC-0330. The SEC also maintains a web site (http://www.sec.gov) that contains reports, proxy and information statements and other information regarding issuers like us that file electronically with the SEC.

We are subject to the reporting and information requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and, as a result, we file periodic reports, proxy statements and other information with the SEC. These periodic reports, proxy statements and other information will be available for inspection and copying at the SEC s public reference room and the web site of the SEC referred to above. Copies of certain information filed by us with the SEC are also available on our website at www.globalbloodtx.com. Information contained on our website is not incorporated by reference into this prospectus supplement or the accompanying prospectus and, therefore, is not part of this prospectus supplement or the accompanying prospectus.

INCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference the information and reports we file with it, which means that we can disclose important information to you by referring you to these documents. The information incorporated by reference is an important part of this prospectus supplement and the accompanying prospectus, and information that we file later with the SEC will automatically update and supersede the information already incorporated by reference. We are incorporating by reference the documents listed below, which we have already filed with the SEC, and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, including all filings made after the date of the filing of this prospectus supplement, except as to any portion of any future report or document that is not deemed filed under such provisions, after the date of this prospectus supplement and prior to the termination of this offering:

Annual Report on Form 10-K for the year ended December 31, 2015, filed with the SEC on March 29, 2016;

The information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2015 from our definitive proxy statement on Schedule 14A (other than information furnished rather than filed), which was filed with the SEC on April 28, 2016;

Quarterly Reports on Form 10-Q filed with the SEC for the quarter ended March 31, 2016, filed with the SEC on May 12, 2016, the quarter ended June 30, 2016, filed with the SEC on August 10, 2016 and the quarter ended September 30, 2016, filed with the SEC on November 9, 2016;

Current Reports on Form 8-K filed with the SEC on January 5, 2016, January 12, 2016, February 8, 2016, April 4, 2016, June 10, 2016, June 17, 2016, September 19, 2016, October 24, 2016,

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November 10, 2016, November 28, 2016, November 30, 2016, December 5, 2016, January 20, 2017 and February 17, 2017 (in each case, except for information contained therein which is furnished rather than filed); and

The description of our common stock contained in our registration statement on Form 8-A (Registration No. 001-37539) filed with the SEC on August 11, 2015 under Section 12(b) of the Exchange Act, including any amendments or reports filed for the purpose of updating such description.

Upon request, we will provide, without charge, to each person, including any beneficial owner, to whom a copy of this prospectus is delivered, a copy of the documents incorporated by reference into this prospectus but not delivered with the prospectus. You may request a copy of these filings, and any exhibits we have specifically incorporated by reference as an exhibit in this prospectus, at no cost by writing or telephoning us at the following address: Global Blood Therapeutics, Inc., 400 East Jamie Court, Suite 101, South San Francisco, California 94080, Attention: Secretary, or by telephone request to (650) 741-7700.

You may also access these documents, free of charge on the SEC s website at www.sec.gov or on our website at www.globalbloodtx.com. Information contained on our website is not incorporated by reference into this prospectus, and you should not consider any information on, or that can be accessed from, our website as part of this prospectus supplement or the accompanying prospectus.

This prospectus supplement is part of a registration statement we filed with the SEC. We have incorporated exhibits into this registration statement. You should read the exhibits carefully for provisions that may be important to you.

You should rely only on the information incorporated by reference or provided in this prospectus supplement or the accompanying prospectus. We have not authorized anyone to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus supplement, the accompanying prospectus or in the documents incorporated by reference is accurate as of any date other than the date on the front of this prospectus supplement or those documents.

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PROSPECTUS

$250,000,000

Common Stock

Preferred Stock

Debt Securities

Warrants

Units

We may from time to time issue, in one or more series or classes, up to $250,000,000 in aggregate principal amount of our common stock, preferred stock, debt securities, warrants and/or units. We may offer these securities separately or together in units. We will specify in the accompanying prospectus supplement the terms of the securities being offered. We may sell these securities to or through underwriters and also to other purchasers or through agents. We will set forth the names of any underwriters or agents, and any fees, conversions or discount arrangements, in the accompanying prospectus supplement. We may not sell any securities under this prospectus without delivery of the applicable prospectus supplement.

You should read this document and any prospectus supplement or amendment carefully before you invest in our securities.

Our common stock is listed on The NASDAQ Global Select Market under the symbol GBT. On October 13, 2016, the closing price for our common stock, as reported on The NASDAQ Global Select Market, was $18.20 per share. Our principal executive office is located at 400 East Jamie Court, Suite 101, South San Francisco, California 94080.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties referenced under the heading Risk Factors contained in this prospectus beginning on page 2 and any applicable prospectus supplement, and under similar headings in the other documents that are incorporated by reference into this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this Prospectus is October 28, 2016.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC, using a shelf registration process. Under this shelf registration process, we may from time to time sell any combination of the securities described in this prospectus in one or more offerings for an aggregate offering price of up to $250,000,000.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide one or more prospectus supplements that will contain specific information about the terms of the offering. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and the accompanying prospectus supplement together with the additional information described under the heading Where You Can Find More Information beginning on page 28 of this prospectus.

You should rely only on the information contained in or incorporated by reference in this prospectus, any accompanying prospectus supplement or in any related free writing prospectus filed by us with the SEC. We have not authorized anyone to provide you with different information. This prospectus and the accompanying prospectus supplement do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in the accompanying prospectus supplement or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information appearing in this prospectus, any prospectus supplement, the documents incorporated by reference and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

Unless the context suggests otherwise, all references to us, our, GBT, we, the Company and similar designations refer to Global Blood Therapeutics, Inc. and, where appropriate, our subsidiaries.

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RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully consider the risks referenced below and described in the documents incorporated by reference in this prospectus and any prospectus supplement, as well as other information we include or incorporate by reference into this prospectus and any applicable prospectus supplement, before making an investment decision. Our business, financial condition or results of operations could be materially adversely affected by the materialization of any of these risks. The trading price of our securities could decline due to the materialization of any of these risks, and you may lose all or part of your investment. This prospectus and the documents incorporated herein by reference also contain forward-looking statements that involve risks and uncertainties. Actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks referenced below and described in the documents incorporated herein by reference, including (i) our annual report on Form 10-K for the fiscal year ended December 31, 2015, which is on file with the SEC and is incorporated herein by reference, (ii) our quarterly reports on Form 10-Q for the quarters ended March 31, 2016 and June 30, 2016, which are incorporated by reference into this prospectus, and (iii) other documents we file with the SEC that are deemed incorporated by reference into this prospectus.

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CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the documents that we incorporate by reference, contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. These statements are often, but are not always, made through the use of words or phrases such as may, will, could, should, expects, intends, plans, anticipates, believes, estimates, predicts, pr and similar expressions, or the negative of these terms, or similar expressions. Accordingly, these statements involve estimates, assumptions, risks and uncertainties which could cause actual results to differ materially from those expressed in them. Any forward-looking statements are qualified in their entirety by reference to the factors discussed throughout this prospectus, and in particular those factors referenced in the section Risk Factors.

This prospectus contains forward-looking statements that are based on our management s belief and assumptions and on information currently available to our management. These statements relate to future events or our future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

- the timing and the success of our ongoing Phase 1/2 clinical trial of GBT440 in healthy adult subjects and sickle cell disease, or SCD, patients and our ongoing Phase 2a clinical trials of GBT440 in adolescent SCD patients and in idiopathic pulmonary fibrosis, or IPF, patients;

- the timing and success of our planned additional clinical trials of GBT440 in other chronic and acute hypoxemic pulmonary disorders and of any other product candidates we may develop in our target indications;

- our ability to enroll patients in our clinical trials at the pace that we project;

- whether the results of our trials will be sufficient to support domestic or foreign regulatory approvals for GBT440 or any other product candidates we may develop in our target indications;

- our ability to obtain, including under any expedited development or review programs, and maintain regulatory approval of GBT440 or any other product candidates we may develop;

- our ability to advance our other programs, through preclinical and clinical development, and the timing and scope of these development activities;

our expectations regarding the use of our existing capital resources and any proceeds we may receive from the sale of securities offered under this prospectus;

the benefits of the use of GBT440 or any other product candidates we may identify and develop;

our ability to successfully commercialize GBT440 or any other product candidates we may identify and pursue, if approved;

the rate and degree of market acceptance of GBT440 or any other product candidates we may identify and pursue;

our ability to maintain, or to recognize the anticipated benefits of, orphan drug designation for GBT440 or to obtain orphan drug designation for any other product candidates we may identify and pursue in the United States, Europe or any other jurisdiction;

our expectations regarding government and third-party payor coverage and reimbursement;

our ability to manufacture GBT440 in conformity with the FDA s requirements and to scale up manufacturing of GBT440 to commercial scale;

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- our ability to successfully build a specialty sales force and commercial infrastructure;
- our ability to compete with companies currently producing or engaged in the clinical development of treatments for the disease indications that we pursue;
- our reliance on third parties to conduct our clinical trials;
- our reliance on third-party contract manufacturers to manufacture and supply our product candidates for us;
- our ability to retain and recruit key personnel;
- our ability to obtain and maintain intellectual property protection for GBT440 or any other product candidates we may identify and pursue;
- our estimates of our expenses, ongoing losses, future revenue, capital requirements and our needs for or ability to obtain additional financing;
- our expectations regarding the time during which we will be an emerging growth company under the Jumpstart Our Business Startups Act of 2012, as amended, or the JOBS Act;
- our financial performance; and
- developments and projections relating to our competitors or our industry.

These forward-looking statements are neither promises nor guarantees of future performance due to a variety of risks and uncertainties, many of which are beyond our control, which could cause actual results to differ materially from those indicated by these forward-looking statements, including, without limitation the risk factors and cautionary statements described in other documents that we file from time to time with the SEC, specifically under Item 1A: Risk Factors and elsewhere in our most recent Annual Report on Form 10-K for the period ended December 31, 2015 and our most recent Quarterly Reports on Form 10-Q for the quarters ended March 31, 2016 and June 30, 2016, and our Current Reports on Form 8-K, and the section of any accompanying prospectus supplement entitled Risk Factors.

The forward-looking statements in this prospectus and the documents incorporated by reference represent our views as of their respective dates. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we assume no obligation to update or revise any forward-looking statements except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the dates on which they were made.

This prospectus and the documents incorporated by reference also contain 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.

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THE COMPANY

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, and reduced numbers of sickled RBCs. In addition to GBT440 for the treatment of SCD, we are evaluating GBT440 for the treatment of hypoxemic pulmonary disorders. In June 2016, we initiated clinical sites and subsequently began enrolling subjects in a Phase 2a clinical trial of GBT440 in idiopathic pulmonary fibrosis, or IPF, and we expect to initiate an additional Phase 2 clinical trial of GBT440 in a hypoxemic pulmonary disorder in the second half of 2016. We are also engaged in other pre-clinical research and development activities. We own or jointly own and have exclusively licensed rights to our portfolio of product candidates in the United States, Europe and other major markets. We own two issued U.S. patents that cover the composition of matter of GBT440, which are due to expire in 2032 and 2035, respectively (absent any applicable patent term extensions), and we own or co-own additional pending patent applications in the United States and selected foreign countries.

We have never been profitable and have incurred net losses in each year since inception. Our net losses were $34.3 million and $16.0 million for the six months ended June, 2016 and 2015, respectively. As of June 30, 2016 we had an accumulated deficit of $132.7 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. As of June 30, 2016, we had $231.9 million of cash and cash equivalents.

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.

We were incorporated under the laws of the State of Delaware in February 2011. Our principal executive office is located at 400 East Jamie Court, Suite 101, South San Francisco, California 94080, and our telephone number is (650) 741-7700. Our website address is *www.globalbloodtx.com*. We do not incorporate the information on or accessible through our website into this prospectus, and you should not consider any information on, or that can be accessed through, our website as part of this prospectus. Our common stock trades on The NASDAQ Global Select Market under the symbol GBT .

We use various trademarks and trade names in our business, including without limitation our corporate name and logo. All other trademarks or trade names referred to in this prospectus are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus may be referred to without the ® and symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

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RATIO OF EARNINGS TO FIXED CHARGES

Our ratio of earnings to fixed charges for recently completed fiscal years and any required interim periods will be specified in a prospectus supplement or in a document that we file with the SEC and incorporate by reference in the future, if and when required.

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USE OF PROCEEDS

We intend to use the net proceeds from the sale of any securities offered under this prospectus for general corporate purposes unless otherwise indicated in the applicable prospectus supplement. General corporate purposes may include research and development and clinical development costs to support the advancement of our product candidates and the expansion of our product candidate pipeline; repayment and refinancing of debt; working capital; and capital expenditures. We may temporarily invest the net proceeds in a variety of capital preservation instruments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities, or may hold such proceeds as cash, until they are used for their stated purpose. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion over the allocation of net proceeds.

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SECURITIES WE MAY OFFER

This prospectus contains summary descriptions of the securities we may offer from time to time. These summary descriptions are not meant to be complete descriptions of each security. The particular terms of any security will be described in the applicable prospectus supplement.

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DESCRIPTION OF CAPITAL STOCK

The following description of our common stock and preferred stock, together with the additional information we include in any applicable prospectus supplements, summarizes the material terms and provisions of the common stock and preferred stock that we may offer under this prospectus. The following description of our capital stock does not purport to be complete and is subject to, and qualified in its entirety by, our certificate of incorporation and bylaws, which are exhibits to the registration statement of which this prospectus forms a part, and by applicable law. The terms of our common stock and preferred stock may also be affected by Delaware law.

Authorized Capital Stock

Our authorized capital stock consists of 150,000,000 shares of common stock, par value $0.001 per share, and 5,000,000 shares of preferred stock, par value $0.001 per share, all of which are undesignated preferred stock. As of October 11, 2016, we had 37,303,171 shares of common stock outstanding and no shares of preferred stock outstanding.

Common Stock

The holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of the stockholders. The holders of our common stock do not have any cumulative voting rights. Holders of our common stock are entitled to receive ratably any dividends declared by our board of directors out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding preferred stock. Our common stock has no preemptive rights, conversion rights or other subscription rights or redemption or sinking fund provisions.

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in all assets remaining after payment of all debts and other liabilities and any liquidation preference of any outstanding preferred stock. All outstanding shares are fully paid and nonassessable.

When we issue shares of common stock under this prospectus, the shares will fully be paid and nonassessable and will not have, or be subject to, any preemptive or similar rights.

Undesignated Preferred Stock

Our board of directors is authorized to issue up to 5,000,000 shares of undesignated preferred stock in one or more series without stockholder approval. Our board of directors may determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock.

The purpose of authorizing our board of directors to issue preferred stock in one or more series and determine the number of shares in the series and its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. Examples of rights and preferences that the Board may fix are:

- dividend rights;
- conversion rights;

voting rights;

terms of redemption;

liquidation preferences;

sinking fund terms; and

the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of common stock.

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The existence of authorized but unissued shares of undesignated preferred stock may enable our board of directors to render more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of us or our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer, stockholder or stockholder group. The rights of holders of our common stock described above, will be subject to, and may be adversely affected by, the rights of any preferred stock that we may designate and issue in the future. The issuance of shares of undesignated preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

We will incorporate by reference as an exhibit to the registration statement, which includes this prospectus, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering. This description and the applicable prospectus supplement will include:

- the title and stated value;
- the number of shares authorized;
- the liquidation preference per share;
- the purchase price;
- the dividend rate, period and payment date, and method of calculation for dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;
- any listing of the preferred stock on any securities exchange or market;

whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price, or how it will be calculated, and the conversion period;

whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price, or how it will be calculated, and the exchange period;

voting rights, if any, of the preferred stock;

preemptive rights, if any;

restrictions on transfer, sale or other assignment, if any;

whether interests in the preferred stock will be represented by depositary shares;

a discussion of any material United States federal income tax considerations applicable to the preferred stock;

the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;

any limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and

any other specific terms, preferences, rights or limitations of, or restrictions on, the preferred stock.

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When we issue shares of preferred stock under this prospectus, the shares will fully be paid and nonassessable and will not be subject to any preemptive or similar rights.

Antitakeover Effects of Delaware Law and Provisions of our Restated Certificate of Incorporation and Amended and Restated Bylaws

Certain provisions of the Delaware General Corporation Law and of our restated certificate of incorporation and amended and restated bylaws could have the effect of delaying, deferring or discouraging another party from acquiring control of us. These provisions, which are summarized below, are expected to discourage certain types of coercive takeover practices and inadequate takeover bids and, as a consequence, they might also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions are also designed in part to encourage anyone seeking to acquire control of us to first negotiate with our board of directors. These provisions might also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders might otherwise deem to be in their best interests. However, we believe that the advantages gained by protecting our ability to negotiate with any unsolicited and potentially unfriendly acquirer outweigh the disadvantages of discouraging such proposals, including those priced above the then-current market value of our common stock, because, among other reasons, the negotiation of such proposals could improve their terms.

Delaware Takeover Statute

We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a business combination with an interested stockholder for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or
- at or after the time the stockholder became interested, the business combination was approved by our board of directors and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

any merger or consolidation involving the corporation and the interested stockholder;

any sale, transfer, lease, pledge, exchange, mortgage or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;

subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;

subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; or

the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Provisions of our Restated Certificate of Incorporation and Amended and Restated Bylaws

Our restated certificate of incorporation and amended and restated bylaws include a number of provisions that may have the effect of delaying, deferring or discouraging another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Board composition and filling vacancies. In accordance with our restated certificate of incorporation, our board is divided into three classes serving staggered three-year terms, with one class being elected each year. Our restated certificate of incorporation also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of 75% or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only be filled by the affirmative vote of a majority of our directors then in office even if less than a quorum.

No written consent of stockholders. Our restated certificate of incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting. This limit may lengthen the amount of time required to take stockholder actions and would prevent the amendment of our bylaws or removal of directors by our stockholder without holding a meeting of stockholders.

Meetings of stockholders. Our bylaws provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our bylaws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance notice requirements. Our bylaws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days or more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. The notice must contain certain information specified in our bylaws.

Amendment to certificate of incorporation and bylaws. As required by the Delaware General Corporation Law, any amendment of our restated certificate of incorporation must first be approved by a majority of our board of directors, and if required by law or our restated certificate of incorporation, must thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment, and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, directors, limitation of liability and the amendment of our restated certificate of incorporation must be approved by not less than 75% of the outstanding shares entitled to vote on the amendment, and not less than 75% of the outstanding shares of each class entitled to vote thereon as a class. Our bylaws may be amended by the affirmative vote of a majority vote of the

directors then in office, subject to any limitations set forth in the bylaws; and may also be amended by the affirmative vote of at least 75% of the outstanding shares entitled to

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vote on the amendment, or, if the board of directors recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

Undesignated preferred stock. Our restated certificate of incorporation provides for authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to render more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of us or our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our restated certificate of incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

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DESCRIPTION OF DEBT SECURITIES

This section describes the general terms and provisions of our debt securities that we may issue from time to time. We may issue debt securities, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. While the terms we have summarized below will apply generally to any future debt securities we may offer under this prospectus, the applicable prospectus supplement or free writing prospectus will describe the specific terms of any debt securities offered through that prospectus supplement or free writing prospectus. The terms of any debt securities we offer under a prospectus supplement or free writing prospectus may differ from the terms we describe below. Unless the context requires otherwise, whenever we refer to the indentures, we also are referring to any supplemental indentures that specify the terms of a particular series of debt securities.

We will issue any senior debt securities under the senior indenture that we will enter into with the trustee named in the senior indenture. We will issue any subordinated debt securities under the subordinated indenture that we will enter into with the trustee named in the subordinated indenture. We have filed forms of these documents as exhibits to the registration statement, of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

The indentures will be qualified under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act. We use the term trustee to refer to either the trustee under the senior indenture or the trustee under the subordinated indenture, as applicable.

The following summaries of material provisions of the senior debt securities, the subordinated debt securities and the indentures are subject to, and qualified in their entirety by reference to, all of the provisions of the indenture applicable to a particular series of debt securities. We urge you to read the applicable prospectus supplement or free writing prospectus and any related free writing prospectuses related to the debt securities that we may offer under this prospectus, as well as the complete applicable indenture that contains the terms of the debt securities. Except as we may otherwise indicate, the terms of the senior indenture and the subordinated indenture are identical.

General

We will describe in the applicable prospectus supplement or free writing prospectus the terms of the series of debt securities being offered, including:

- the title;
- the principal amount being offered, and if a series, the total amount authorized and the total amount outstanding;
- any limit on the amount that may be issued;
- whether or not we will issue the series of debt securities in global form, and, if so, the terms and who the depository will be;

the maturity date;

whether and under what circumstances, if any, we will pay additional amounts on any debt securities held by a person who is not a United States person for tax purposes, and whether we can redeem the debt securities if we have to pay such additional amounts;

the annual interest rate, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;

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whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;

the terms of the subordination of any series of subordinated debt;

the place where payments will be payable;

restrictions on transfer, sale or other assignment, if any;

our right, if any, to defer payment of interest and the maximum length of any such deferral period;

the date, if any, after which, the conditions upon which, and the price at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;

the date, if any, on which, and the price at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder s option, to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;

whether the indenture will restrict our ability or the ability of our subsidiaries to:

incur additional indebtedness;

issue additional securities;

create liens;

pay dividends or make distributions in respect of our capital stock or the capital stock of our subsidiaries;

redeem capital stock;

place restrictions on our subsidiaries ability to pay dividends, make distributions or transfer assets;

make investments or other restricted payments;

sell or otherwise dispose of assets;

enter into sale-leaseback transactions;

engage in transactions with stockholders or affiliates;

issue or sell stock of our subsidiaries; or

effect a consolidation or merger;

whether the indenture will require us to maintain any interest coverage, fixed charge, cash flow-based, asset-based or other financial ratios;

a discussion of certain material or special United States federal income tax considerations applicable to the debt securities;

information describing any book-entry features;

provisions for a sinking fund purchase or other analogous fund, if any;

the applicability of the provisions in the indenture on discharge;

whether the debt securities are to be offered at a price such that they will be deemed to be offered at an original issue discount as defined in paragraph (a) of Section 1273 of the Internal Revenue Code of 1986, as amended;

the denominations in which we will issue the series of debt securities, if other than denominations of $1,000 and any integral multiple thereof;

the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars; and

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any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, including any additional events of default or covenants provided with respect to the debt securities, and any terms that may be required by us or advisable under applicable laws or regulations or advisable in connection with the marketing of the debt securities.

Conversion or Exchange Rights

We will set forth in the applicable prospectus supplement or free writing prospectus the terms on which a series of debt securities may be convertible into or exchangeable for our common stock, our preferred stock or other securities (including securities of a third-party). We will include provisions as to whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock, our preferred stock or other securities (including securities of a third-party) that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale

Unless we provide otherwise in the prospectus supplement or free writing prospectus applicable to a particular series of debt securities, the indentures will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of all or substantially all of our assets. However, any successor to or acquirer of such assets must assume all of our obligations under the indentures or the debt securities, as appropriate. If the debt securities are convertible into or exchangeable for other securities of ours or securities of other entities, the person with whom we consolidate or merge or to whom we sell all of our property must make provisions for the conversion of the debt securities into securities that the holders of the debt securities would have received if they had converted the debt securities before the consolidation, merger or sale.

Events of Default Under the Indenture

Unless we provide otherwise in the prospectus supplement or free writing prospectus applicable to a particular series of debt securities, the following are events of default under the indentures with respect to any series of debt securities that we may issue:

if we fail to pay interest when due and payable and our failure continues for 90 days and the time for payment has not been extended;

if we fail to pay the principal, premium or sinking fund payment, if any, when due and payable at maturity, upon redemption or repurchase or otherwise, and the time for payment has not been extended;

if we fail to observe or perform any other covenant contained in the debt securities or the indentures, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive notice from the trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and

if specified events of bankruptcy, insolvency or reorganization occur.

We will describe in each applicable prospectus supplement or free writing prospectus any additional events of default relating to the relevant series of debt securities.

If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the trustee if notice is given by such holders, may declare the unpaid principal, premium, if any, and accrued interest, if any, due and payable immediately. If an event of default specified in the last bullet point above occurs with respect to us, the unpaid principal, premium, if any, and accrued interest, if any, of each issue of debt securities then outstanding shall be due and payable without any notice or other action on the part of the trustee or any holder.

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The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indentures, if an event of default under an indenture shall occur and be continuing, the trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the trustee reasonable indemnity or security satisfactory to it against any loss, liability or expense. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, or exercising any trust or power conferred on the trustee, with respect to the debt securities of that series, provided that:

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and
- subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the debt securities of any series will have the right to institute a proceeding under the indentures or to appoint a receiver or trustee, or to seek other remedies if:

- the holder has given written notice to the trustee of a continuing event of default with respect to that series;
- the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request, and such holders have offered reasonable indemnity to the trustee or security satisfactory to it against any loss, liability or expense or to be incurred in compliance with instituting the proceeding as trustee; and
- the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities, or other defaults that may be specified in the applicable prospectus supplement or free writing prospectus.

We will periodically file statements with the trustee regarding our compliance with specified covenants in the indentures.

Modification of Indenture; Waiver

Subject to the terms of the indenture for any series of debt securities that we may issue, we and the trustee may change an indenture without the consent of any holders with respect to the following specific matters:

to fix any ambiguity, defect or inconsistency in the indenture;

to comply with the provisions described above under Description of Our Debt Securities Consolidation, Merger or Sale;

to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act;

to add to, delete from or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;

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to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided under Description of Our Debt Securities General, to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;

to evidence and provide for the acceptance of appointment hereunder by a successor trustee;

to provide for uncertificated debt securities and to make all appropriate changes for such purpose;

to add to our covenants such new covenants, restrictions, conditions or provisions for the benefit of the holders, to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default or to surrender any right or power conferred to us in the indenture; or

to change anything that does not materially adversely affect the interests of any holder of debt securities of any series.

In addition, under the indentures, the rights of holders of a series of debt securities may be changed by us and the trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, subject to the terms of the indenture for any series of debt securities that we may issue or as otherwise provided in the prospectus supplement or free writing prospectus applicable to a particular series of debt securities, we and the trustee may make the following changes only with the consent of each holder of any outstanding debt securities affected:

extending the stated maturity of the series of debt securities;

reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption or repurchase of any debt securities; or

reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Discharge

Each indenture provides that, subject to the terms of the indenture and any limitation otherwise provided in the prospectus supplement or free writing prospectus applicable to a particular series of debt securities, we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

register the transfer or exchange of debt securities of the series;

replace stolen, lost or mutilated debt securities of the series;

maintain paying agencies;

hold monies for payment in trust;

recover excess money held by the trustee;

compensate and indemnify the trustee; and

appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, any premium and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we otherwise specify in the applicable prospectus supplement or free writing prospectus, in denominations of $1,000

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and any integral multiple thereof. The indentures provide that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company or another depository named by us and identified in a prospectus supplement or free writing prospectus with respect to that series.

At the option of the holder, subject to the terms of the indentures and the limitations applicable to global securities described in the applicable prospectus supplement or free writing prospectus, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indentures and the limitations applicable to global securities set forth in the applicable prospectus supplement or free writing prospectus, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will make no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement or free writing prospectus the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series. If we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or

- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Trustee

The trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs.

Subject to this provision, the trustee is under no obligation to exercise any of the powers given it by the indentures at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement or free writing prospectus, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus

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supplement or free writing prospectus, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in the applicable prospectus supplement or free writing prospectus, we will designate the corporate trust office of the trustee as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement or free writing prospectus any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

Governing Law

The indentures and the debt securities will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act is applicable.

Ranking of Debt Securities

The subordinated debt securities will be subordinate and junior in priority of payment to certain of our other indebtedness to the extent described in a prospectus supplement or free writing prospectus. The subordinated indenture does not limit the amount of subordinated debt securities that we may issue. It also does not limit us from issuing any other secured or unsecured debt.

The senior debt securities will rank equally in right of payment to all our other senior unsecured debt. The senior indenture does not limit the amount of senior debt securities that we may issue. It also does not limit us from issuing any other secured or unsecured debt.

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DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplements, summarizes the material terms and provisions of the warrants that we may offer under this prospectus and the related warrant agreements and warrant certificates. While the terms summarized below will apply generally to any warrants that we may offer, we will describe the particular terms of any series of warrants in more detail in the applicable prospectus supplement. If we indicate in the prospectus supplement, the terms of any warrants offered under that prospectus supplement may differ from the terms described below. Specific warrant agreements will contain additional important terms and provisions and will be incorporated by reference as an exhibit to the registration statement, which includes this prospectus.

General

We may issue warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series. We may issue warrants independently or together with common stock, preferred stock and/or debt securities, and the warrants may be attached to or separate from these securities.

We will evidence each series of warrants by warrant certificates that we will issue under a separate warrant agreement. We will enter into the warrant agreement with a warrant agent. We will indicate the name and address of the warrant agent in the applicable prospectus supplement relating to a particular series of warrants.

We will describe in the applicable prospectus supplement the terms of the series of warrants, including:

- the offering price and aggregate number of warrants offered;
- the currency for which the warrants may be purchased;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;
- if applicable, the date on and after which the warrants and the related securities will be separately transferable;
- in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at, and currency in which, this principal amount of debt securities may be purchased upon such exercise;
- in the case of warrants to purchase common stock or preferred stock, the number of shares of common stock or preferred stock, as the case may be, purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;

the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreement and the warrants;

the terms of any rights to redeem or call the warrants;

any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;

the periods during which, and places at which, the warrants are exercisable;

the manner of exercise;

the dates on which the right to exercise the warrants will commence and expire;

the manner in which the warrant agreement and warrants may be modified;

federal income tax consequences of holding or exercising the warrants;

the terms of the securities issuable upon exercise of the warrants; and

any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

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DESCRIPTION OF UNITS

We may issue units comprised of shares of common stock, shares of preferred stock, debt securities and warrants in any combination. We may issue units in such amounts and in as many distinct series as we wish. This section outlines certain provisions of the units that we may issue. If we issue units, they will be issued under one or more unit agreements to be entered into between us and a bank or other financial institution, as unit agent. The information described in this section may not be complete in all respects and is qualified entirely by reference to the unit agreement with respect to the units of any particular series. The specific terms of any series of units offered will be described in the applicable prospectus supplement. If so described in a particular supplement, the specific terms of any series of units may differ from the general description of terms presented below. We urge you to read any prospectus supplement related to any series of units we may offer, as well as the complete unit agreement and unit certificate that contain the terms of the units. If we issue units, forms of unit agreements and unit certificates relating to such units will be incorporated by reference as exhibits to the registration statement, which includes this prospectus.

Each unit that we may issue will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date. The applicable prospectus supplement may describe:

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provisions of the governing unit agreement;
- the price or prices at which such units will be issued;
- the applicable United States federal income tax considerations relating to the units;
- any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units; and
- any other terms of the units and of the securities comprising the units.

The provisions described in this section, as well as those described under Description of Capital Stock, Description of Debt Securities and Description of Warrants will apply to the securities included in each unit, to the extent relevant and as may be updated in any prospectus supplements.

Issuance in Series

We may issue units in such amounts and in as many distinct series as we wish. This section summarizes terms of the units that apply generally to all series. Most of the financial and other specific terms of a particular series of units will

be described in the applicable prospectus supplement.

Unit Agreements

We will issue the units under one or more unit agreements to be entered into between us and a bank or other financial institution, as unit agent. We may add, replace or terminate unit agents from time to time. We will identify the unit agreement under which each series of units will be issued and the unit agent under that agreement in the applicable prospectus supplement.

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The following provisions will generally apply to all unit agreements unless otherwise stated in the applicable prospectus supplement:

Modification without Consent

We and the applicable unit agent may amend any unit or unit agreement without the consent of any holder:

- to cure any ambiguity; any provisions of the governing unit agreement that differ from those described below;
- to correct or supplement any defective or inconsistent provision; or
- to make any other change that we believe is necessary or desirable and will not adversely affect the interests of the affected holders in any material respect.

We do not need any approval to make changes that affect only units to be issued after the changes take effect. We may also make changes that do not adversely affect a particular unit in any material respect, even if they adversely affect other units in a material respect. In those cases, we do not need to obtain the approval of the holder of the unaffected unit; we need only obtain any required approvals from the holders of the affected units.

Modification with Consent

We may not amend any particular unit or a unit agreement with respect to any particular unit unless we obtain the consent of the holder of that unit, if the amendment would:

- impair any right of the holder to exercise or enforce any right under a security included in the unit if the terms of that security require the consent of the holder to any changes that would impair the exercise or enforcement of that right; or
- reduce the percentage of outstanding units or any series or class the consent of whose holders is required to amend that series or class, or the applicable unit agreement with respect to that series or class, as described below.

Any other change to a particular unit agreement and the units issued under that agreement would require the following approval:

- If the change affects only the units of a particular series issued under that agreement, the change must be approved by the holders of a majority of the outstanding units of that series; or

If the change affects the units of more than one series issued under that agreement, it must be approved by the holders of a majority of all outstanding units of all series affected by the change, with the units of all the affected series voting together as one class for this purpose.

These provisions regarding changes with majority approval also apply to changes affecting any securities issued under a unit agreement, as the governing document.

In each case, the required approval must be given by written consent.

Unit Agreements Will Not Be Qualified under Trust Indenture Act

No unit agreement will be qualified as an indenture, and no unit agent will be required to qualify as a trustee, under the Trust Indenture Act. Therefore, holders of units issued under unit agreements will not have the protections of the Trust Indenture Act with respect to their units.

Mergers and Similar Transactions Permitted; No Restrictive Covenants or Events of Default

The unit agreements will not restrict our ability to merge or consolidate with, or sell our assets to, another corporation or other entity or to engage in any other transactions. If at any time we merge or consolidate with, or

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sell our assets substantially as an entirety to, another corporation or other entity, the successor entity will succeed to and assume our obligations under the unit agreements. We will then be relieved of any further obligation under these agreements.

The unit agreements will not include any restrictions on our ability to put liens on our assets, nor will they restrict our ability to sell our assets. The unit agreements also will not provide for any events of default or remedies upon the occurrence of any events of default.

Governing Law

The unit agreements and the units will be governed by Delaware law.

Form, Exchange and Transfer

We will issue each unit in global i.e., book-entry form only. Units in book-entry form will be represented by a global security registered in the name of a depositary, which will be the holder of all the units represented by the global security. Those who own beneficial interests in a unit will do so through participants in the depositary s system, and the rights of these indirect owners will be governed solely by the applicable procedures of the depositary and its participants. We will describe book-entry securities, and other terms regarding the issuance and registration of the units in the applicable prospectus supplement.

Each unit and all securities comprising the unit will be issued in the same form.

If we issue any units in registered, non-global form, the following will apply to them.

The units will be issued in the denominations stated in the applicable prospectus supplement. Holders may exchange their units for units of smaller denominations or combined into fewer units of larger denominations, as long as the total amount is not changed.

Holders may exchange or transfer their units at the office of the unit agent. Holders may also replace lost, stolen, destroyed or mutilated units at that office. We may appoint another entity to perform these functions or perform them ourselves.

Holders will not be required to pay a service charge to transfer or exchange their units, but they may be required to pay for any tax or other governmental charge associated with the transfer or exchange. The transfer or exchange, and any replacement, will be made only if our transfer agent is satisfied with the holder s proof of legal ownership. The transfer agent may also require an indemnity before replacing any units.

If we have the right to redeem, accelerate or settle any units before their maturity, and we exercise our right as to less than all those units or other securities, we may block the exchange or transfer of those units during the period beginning 15 days before the day we mail the notice of exercise and ending on the day of that mailing, in order to freeze the list of holders to prepare the mailing. We may also refuse to register transfers of or exchange any unit selected for early settlement, except that we will continue to permit transfers and

exchanges of the unsettled portion of any unit being partially settled. We may also block the transfer or exchange of any unit in this manner if the unit includes securities that are or may be selected for early settlement.

Only the depositary will be entitled to transfer or exchange a unit in global form, since it will be the sole holder of the unit.

Payments and Notices

In making payments and giving notices with respect to our units, we will follow the procedures as described in the applicable prospectus supplement.

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PLAN OF DISTRIBUTION

We may sell securities:

through underwriters;

through dealers;

through agents;

directly to purchasers; or

through a combination of any of these methods or any other method permitted by law.

In addition, we may issue the securities as a dividend or distribution or in a subscription rights offering to our existing security holders.

We may directly solicit offers to purchase securities, or agents may be designated to solicit such offers. In the prospectus supplement relating to such offering, we will name any agent that could be viewed as an underwriter under the Securities Act and describe any commissions that we must pay to any such agent. Any such agent will be acting on a best efforts basis for the period of its appointment or, if indicated in the applicable prospectus supplement, on a firm commitment basis. This prospectus may be used in connection with any offering of our securities through any of these methods or other methods described in the applicable prospectus supplement.

The distribution of the securities may be effected from time to time in one or more transactions:

at a fixed price, or prices, which may be changed from time to time;

at market prices prevailing at the time of sale;

at prices related to such prevailing market prices; or

at negotiated prices.

Each prospectus supplement will describe the method of distribution of the securities and any applicable restrictions.

The prospectus supplement with respect to the securities of a particular series will describe the terms of the offering of the securities, including the following:

the name of the agent or any underwriters;

the public offering or purchase price;

any discounts and commissions to be allowed or paid to the agent or underwriters;

all other items constituting underwriting compensation;

any discounts and commissions to be allowed or paid to dealers; and

any exchanges on which the securities will be listed.

If any underwriters or agents are used in the sale of the securities in respect of which this prospectus is delivered, we will enter into an underwriting agreement, sales agreement or other agreement with them at the time of sale to them, and we will set forth in the prospectus supplement relating to such offering the names of the underwriters or agents and the terms of the related agreement with them.

In connection with the offering of securities, we may grant to the underwriters an option to purchase additional securities with an additional underwriting commission, as may be set forth in the accompanying prospectus supplement. If we grant any such option, the terms of such option will be set forth in the prospectus supplement for such securities.

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If a dealer is used in the sale of the securities in respect of which the prospectus is delivered, we will sell such securities to the dealer, as principal. The dealer, who may be deemed to be an underwriter as that term is defined in the Securities Act, may then resell such securities to the public at varying prices to be determined by such dealer at the time of resale.

If we offer securities in a subscription rights offering to our existing security holders, we may enter into a standby underwriting agreement with dealers, acting as standby underwriters. We may pay the standby underwriters a commitment fee for the securities they commit to purchase on a standby basis. If we do not enter into a standby underwriting arrangement, we may retain a dealer-manager to manage a subscription rights offering for us.

Agents, underwriters, dealers and other persons may be entitled under agreements which they may enter into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, and may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

If so indicated in the applicable prospectus supplement, we will authorize underwriters or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in the prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in the prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will not be subject to any conditions except that:

- the purchase by an institution of the securities covered under that contract shall not at the time of delivery be prohibited under the laws of the jurisdiction to which that institution is subject; and

- if the securities are also being sold to underwriters acting as principals for their own account, the underwriters shall have purchased such securities not sold for delayed delivery. The underwriters and other persons acting as our agents will not have any responsibility in respect of the validity or performance of delayed delivery contracts.

Offered securities may also be offered and sold, if so indicated in the prospectus supplement, in connection with a remarketing upon their purchase, in accordance with a redemption or repayment pursuant to their terms, or otherwise, by one or more remarketing firms, acting as principals for their own accounts or as agents for us. Any remarketing firm will be identified and the terms of its agreement, if any, with us and its compensation will be described in the applicable prospectus supplement. Remarketing firms may be deemed to be underwriters in connection with their remarketing of offered securities.

Certain agents, underwriters and dealers, and their associates and affiliates, may be customers of, have borrowing relationships with, engage in other transactions with, or perform services, including investment banking services, for us or one or more of our respective affiliates in the ordinary course of business.

In order to facilitate the offering of the securities, any underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the securities or any other securities the prices of which may be used to determine payments on such securities. Specifically, any underwriters may overallot in connection with the offering, creating a short position for their own accounts. In addition, to cover overallotments or to stabilize the price of the securities or

of any such other securities, the underwriters may bid for, and purchase, the securities or any such other securities in the open market. Finally, in any offering of the securities through a syndicate of underwriters, the underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the securities in the offering if the syndicate repurchases previously distributed securities in transactions to cover syndicate short positions, in stabilization transactions or otherwise. Any of these activities may stabilize or maintain the market price of the securities above independent market levels. Any such underwriters are not required to engage in these activities and may end any of these activities at any time.

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We may engage in at the market offerings into an existing trading market in accordance with Rule 415(a)(4) under the Securities Act. In addition, we may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement so indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter and, if not identified in this prospectus, will be named in the applicable prospectus supplement (or a post-effective amendment). In addition, we may otherwise loan or pledge securities to a financial institution or other third party that in turn may sell the securities short using this prospectus and an applicable prospectus supplement. Such financial institution or other third party may transfer its economic short position to investors in our securities or in connection with a concurrent offering of other securities.

Under Rule 15c6-1 of the Exchange Act, trades in the secondary market generally are required to settle in three business days, unless the parties to any such trade expressly agree otherwise. The applicable prospectus supplement may provide that the original issue date for your securities may be more than three scheduled business days after the trade date for your securities. Accordingly, in such a case, if you wish to trade securities on any date prior to the third business day before the original issue date for your securities, you will be required, by virtue of the fact that your securities initially are expected to settle in more than three scheduled business days after the trade date for your securities, to make alternative settlement arrangements to prevent a failed settlement.

The securities may be new issues of securities and may have no established trading market. The securities may or may not be listed on a national securities exchange. We can make no assurance as to the liquidity of or the existence of trading markets for any of the securities.

The specific terms of any lock-up provisions in respect of any given offering will be described in the applicable prospectus supplement.

The underwriters, dealers and agents may engage in transactions with us, or perform services for us, in the ordinary course of business for which they receive compensation.

The anticipated date of delivery of offered securities will be set forth in the applicable prospectus supplement relating to each offer.

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LEGAL MATTERS

Certain legal matters in connection with this offering will be passed upon for us by Goodwin Procter LLP, San Francisco, California. Any underwriters will also be advised about the validity of the securities and other legal matters by their own counsel, which will be named in the prospectus supplement.

EXPERTS

The financial statements of Global Blood Therapeutics, Inc. as of December 31, 2015 and 2014, and for each of the years in the three-year period ended December 31, 2015, have been incorporated by reference herein and in reliance upon the report of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of a registration statement that we have filed with the SEC. Certain information in the registration statement has been omitted from this prospectus in accordance with the rules of the SEC. We are subject to the information requirements of the Exchange Act and, in accordance therewith, file annual, quarterly and special reports, proxy statements and other information with the SEC. You may read and copy any document we file at the SEC s Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. You may call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room. These documents also may be accessed through the SEC s electronic data gathering, analysis and retrieval system, or EDGAR, via electronic means, including the SEC s home page on the Internet *(www.sec.gov*).

We have the authority to designate and issue more than one class or series of stock having various preferences, conversion and other rights, voting powers, restrictions, limitations as to dividends, qualifications, and terms and conditions of redemption. See Description of Capital Stock. We will furnish a full statement of the relative rights and preferences of each class or series of our stock which has been so designated and any restrictions on the ownership or transfer of our stock to any stockholder upon request and without charge. Written requests for such copies should be directed to Global Blood Therapeutics, Inc., 400 East Jamie Court, Suite 101, South San Francisco, California 94080, Attention: Secretary, or by telephone request to (650) 741-7700. Our website is located at *www.globalbloodtx.com*. Information contained on our website is not incorporated by reference into this prospectus and, therefore, is not part of this prospectus or any accompanying prospectus supplement.

I NCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference the information and reports we file with it, which means that we can disclose important information to you by referring you to these documents. The information incorporated by reference is an important part of this prospectus, and information that we file later with the SEC will automatically update and supersede the information already incorporated by reference. We are incorporating by reference the documents listed below, which we have already filed with the SEC, and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, including all filings made after the date of the filing of this registration statement and prior to the effectiveness of this registration statement, except as to any portion of any future report or document that is not deemed filed under such provisions, after the date of this prospectus and prior to the termination of this offering:

Annual Report on Form 10-K for the year ended December 31, 2015, filed with the SEC on March 29, 2016;

The information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2015 from our definitive proxy statement on Schedule 14A (other than information furnished rather than filed), which was filed with the SEC on April 28, 2016;

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Quarterly Reports on Form 10-Q filed with the SEC for the quarter ended March 31, 2016, filed with the SEC on May 12, 2016, and the quarter ended June 30, 2016, filed with the SEC on August 10, 2016;

Current Reports on Form 8-K filed with the SEC on January 5, 2016 (as to Item 5.02 only), January 12, 2016, February 8, 2016 (as to Item 5.02 only), April 4, 2016 (as to Item 5.02 and Exhibit 10.1 only), June 10, 2016, June 17, 2016 and September 19, 2016; and

The description of our common stock contained in our registration statement on Form 8-A (Registration No. 001-37539) filed with the SEC on August 11, 2015 under Section 12(b) of the Exchange Act, including any amendments or reports filed for the purpose of updating such description.

Upon request, we will provide, without charge, to each person, including any beneficial owner, to whom a copy of this prospectus is delivered, a copy of the documents incorporated by reference into this prospectus but not delivered with the prospectus. You may request a copy of these filings, and any exhibits we have specifically incorporated by reference as an exhibit in this prospectus, at no cost by writing or telephoning us at the following address: Global Blood Therapeutics, Inc., 400 East Jamie Court, Suite 101, South San Francisco, California 94080, Attention: Secretary, or by telephone request to (650) 741-7700.

You may also access these documents, free of charge on the SEC s website at *www.sec.gov* or on our website at *www.globalbloodtx.com*. Information contained on our website is not incorporated by reference into this prospectus, and you should not consider any information on, or that can be accessed from, our website as part of this prospectus or any accompanying prospectus supplement.

This prospectus is part of a registration statement we filed with the SEC. We have incorporated exhibits into this registration statement. You should read the exhibits carefully for provisions that may be important to you.

You should rely only on the information incorporated by reference or provided in this prospectus or any prospectus supplement. We have not authorized anyone to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus or in the documents incorporated by reference is accurate as of any date other than the date on the front of this prospectus or those documents.

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5,102,041 Shares

Common Stock

PROSPECTUS SUPPLEMENT

Sole Book-Running Manager

Cantor Fitzgerald & Co.

February 21, 2017