

Global Blood Therapeutics, Inc.
 Form 424B5
 March 12, 2018
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Filed Pursuant to Rule 424(b)(5)
 Registration No. 333-220127

CALCULATION OF REGISTRATION FEE

| Title of each class of securities to be registered | Amount to be registered(1) | Maximum offering price per share | Maximum aggregate offering price | Amount of registration fee(2) |
|---|-----------------------------------|---|---|--------------------------------------|
| Common stock, par value \$0.001 per share | 4,600,000 shares | \$54.00 | \$248,400,000 | \$30,925.80 |

- (1) Includes 600,000 shares of common stock issuable upon exercise of the underwriters' option to purchase additional shares of common stock.
- (2) This filing fee is calculated and being paid pursuant to Rule 457(r) of the Securities Act of 1933, as amended, and relates to our Registration Statement on Form S-3ASR (File No. 333-220127).

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PROSPECTUS SUPPLEMENT

(To Prospectus dated August 23, 2017)

4,000,000 Shares

Common Stock

Global Blood Therapeutics, Inc.

We are offering 4,000,000 shares of our common stock. Our common stock is listed on The Nasdaq Global Select Market under the symbol GBT. On March 8, 2018, the last reported sale price of our common stock on The Nasdaq Global Select Market was \$56.90 per share.

The underwriter has agreed to purchase our common stock from us at a price of \$52.35 per share.

The underwriter has agreed to reimburse certain of our expenses. See the section entitled Underwriting of this prospectus supplement.

Investing in our common stock involves risks. See the section entitled Risk Factors on page S-8 of this prospectus supplement.

We have granted the underwriters a 30-day option to purchase up to an additional 600,000 shares of common stock from us at a price of \$52.35 per share.

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.

The underwriter expects to deliver the shares of common stock to purchasers on or about March 13, 2018.

Wells Fargo Securities

Prospectus supplement dated March 8, 2018

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is part of the registration statement on Form S-3 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." If any statement in one of these documents is inconsistent with a statement in another document having a later date, the statement in the document having the later date modifies or supersedes the earlier statement.

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 refer 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, anticipates, believes, predicts, projects, potential, continue, 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 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 the Phase 3 and the Phase 2a HOPE-KIDS 1 Study, our ongoing clinical trials of voxelotor (previously known as GBT440) in adult and adolescent patients with sickle cell disease, or SCD;

the timing and success of our additional clinical trials of voxelotor, including in pediatric patients with SCD, 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 voxelotor 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 voxelotor 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;

the limitations of current treatment options for SCD;

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 voxelotor or any other product candidates we may identify and develop;

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

the potential market opportunity for, and rate and degree of market acceptance of, voxelotor 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 voxelotor 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 ability to maintain, or to recognize the anticipated benefits of, access to accelerated development and review programs through the FDA, such as the fast track and breakthrough therapy programs, or through the EMA's PRIME program, for voxelotor or any other product candidates we may identify and pursue;

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

our ability to manufacture voxelotor in conformity with the FDA's requirements and to scale up manufacturing of voxelotor 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 voxelotor or any other product candidates we may identify and pursue;

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

our financial performance;

developments and projections relating to our competitors or our industry;

our plans to explore strategic transactions to broaden our pipeline; and

our ability to implement our strategic plans for our business and technology.

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 year ended December 31, 2017 and our Current Reports on Form 8-K, and the section of this prospectus supplement and the accompanying prospectus entitled Risk Factors.

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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 common stock. Before investing in our common stock, you should carefully read this entire prospectus supplement and the accompanying prospectus, including the sections entitled 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 determined to discover, develop and deliver innovative treatments that provide hope to underserved patient communities. Our lead product candidate is voxelotor (previously known as 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. We are developing voxelotor for SCD.

We are currently evaluating voxelotor in SCD in a Phase 3 clinical trial in adult and adolescent patients with SCD. In addition, we are evaluating the safety and pharmacokinetics of single and multiple doses of voxelotor in a Phase 2a clinical trial of adolescent and pediatric patients with SCD, and in July 2017 we announced that we have expanded this open-label trial to include a new single-dose cohort in children aged 6-11. We expect to announce additional data from the initial dose cohort from this Phase 2a clinical trial in the first half of 2018 and topline results for the new single-dose cohort in the second half of 2018. In December 2015, the U.S. Food and Drug Administration, or FDA, granted Fast Track Designation and Orphan Drug Designation for voxelotor for the treatment of SCD and in November 2016 voxelotor was granted Orphan Drug Designation in Europe for the treatment of SCD. In June 2017, the European Medicines Agency, or EMA, granted PRIME designation for voxelotor for the treatment of SCD. The PRIME program is a new regulatory mechanism that provides for early and proactive EMA support to medicine developers to help patients benefit as early as possible from innovative new products that have demonstrated the potential to significantly address an unmet medical need. In September 2017, the FDA granted Rare Pediatric Disease designation to voxelotor for the treatment of SCD. In January 2018, the FDA granted Breakthrough Designation to voxelotor for the treatment of SCD. To date, voxelotor is the only SCD treatment to receive the FDA's Breakthrough Designation.

SCD is 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. Voxelotor inhibits abnormal hemoglobin polymerization, the underlying mechanism that causes sickling of RBCs. In our clinical trials to date of voxelotor 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.

We own or jointly own and have exclusively licensed rights to our product candidates in the United States, Europe and other major markets. We are the sole owner of issued U.S. patents covering voxelotor, including its composition of matter, methods of use, and a polymorph of voxelotor. These issued patents covering voxelotor will expire between 2032 and 2035, 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 our lead product candidate voxelotor.

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Beyond evaluation of voxelotor in SCD, we are also engaged in other research and development activities, all of which are currently in the pre-clinical phase. In addition, we regularly evaluate opportunities to in-license, acquire or invest in new business, technology or assets or engage in related discussions with other business entities.

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

We have never been profitable and have incurred net losses in each year since inception. Our net losses were \$117.0 million, \$82.5 million and \$46.4 million for the years ended December 31, 2017, December 31, 2016 and December 31, 2015, respectively. As of December 31, 2017, we had an accumulated deficit of \$298.0 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 December 31, 2017, we had \$198.3 million in cash and cash equivalents and \$131.1 million in marketable securities.

Corporate History and Information

We were incorporated under the laws of the State of Delaware in February 2011 and commenced operations in May 2012. Our principal executive office is located at 171 Oyster Point Blvd., Suite 300, South San Francisco, California 94080, and our telephone number is (650) 741-7700. Our website address is www.gbt.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.

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THE OFFERING

| | |
|--|--|
| Common stock offered by us | 4,000,000 shares |
| Option to purchase additional shares | Up to 600,000 shares |
| Common stock outstanding immediately following the offering | 50,131,723 shares (or 50,731,723 shares if the underwriters exercise their option to purchase additional shares in full) |
| 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 voxelotor for the treatment of SCD, including our ongoing Phase 3 HOPE study and our ongoing Phase 2a HOPE-KIDS 1 study, as well as future clinical trials, to build and expand our commercial organization in preparation for the potential approval and launch of voxelotor, to fund our other research and development activities, and for working capital and general corporate purposes. We may also use a portion of the net proceeds to in-license, acquire or invest in new business, technology or assets, although we have no material agreements, commitments or understandings in place. See Use of Proceeds for additional information. |
| Risk factors | Investing in our securities involves risks. See Risk Factors beginning on page S-8 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 46,131,723 shares of common stock outstanding as of December 31, 2017, and excludes: | |

394,736 shares of common stock issued in January 2018 in connection with the underwriters' exercise of their option to purchase additional shares in our previous follow-on offering;

2,945,901 shares of common stock issuable upon exercise of outstanding options as of December 31, 2017 at a weighted-average exercise price of \$17.50 per share;

241,617 shares of restricted common stock which were subject to our right of repurchase as of December 31, 2017;

650,708 shares of common stock issuable upon exercise of options granted subsequent to December 31, 2017 through March 1, 2018 at a weighted-average exercise price of \$59.59 per share;

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820,713 shares of common stock issuable upon the vesting of outstanding restricted stock units as of December 31, 2017;

425,535 shares of common stock issuable upon the vesting of restricted stock units granted subsequent to December 31, 2017 through March 1, 2018;

1,538,680 shares of common stock reserved for future issuance under our 2015 Stock Option and Incentive Plan, or the 2015 Plan, as of December 31, 2017;

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186,033 shares of common stock reserved for future issuance under our 2015 Employee Stock Purchase Plan, or the 2015 ESPP, as of December 31, 2017; and

170,000 shares of common stock reserved for future issuance under our 2017 Inducement Equity Plan, or the 2017 Inducement Plan, as of December 31, 2017.

Except as otherwise indicated, all information in this prospectus supplement assumes no exercise by the underwriters of their 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, 2017 and (ii) 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 marketable securities, 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 December 31, 2017 after subtracting our liabilities. As a result, investors purchasing shares of common stock in this offering will incur immediate dilution of \$43.47 per share, based on the difference between the public offering price of \$54.00 per share, and the as adjusted net tangible book value per share of our outstanding common stock as of December 31, 2017.

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 December 31, 2017, options to purchase 2,945,901 shares of our common stock at a weighted-average exercise price of \$17.50 per share were outstanding, and there were 820,713 shares of our common stock underlying restricted stock units subject to future vesting. The exercise of any of these options and the vesting of any shares underlying outstanding restricted stock units 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 December 31, 2017, 46,131,723 shares of our common stock and options to purchase 2,945,901 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 have agreed that for a period of 90 days after the date of this prospectus supplement, subject to specified exceptions, including, with respect to certain of our executive officers, 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 may be released from these restrictions at the sole discretion of Wells Fargo Securities, LLC. Sales of stock by any of our directors, executive officers 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 Business

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 changes may have retroactive application) could adversely affect our stockholders or us. In recent years, many such changes have been made and changes are likely to continue to occur in the future. For example, in December 2017, Congress passed the Tax Cuts and Jobs Act, which made broad and complex changes to the tax laws. We cannot predict whether, when, in what form, or with what effective dates, tax laws, regulations and rulings may be enacted, promulgated or decided, which could result in an increase in our, or our stockholders', tax liability or require changes in the manner in which we operate in order to minimize increases in our tax liability.

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

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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 and an ownership change as a result of our follow-on offerings, however we do not believe that these ownership changes will significantly limit our ability to use these pre-change NOL carryforwards. We may experience subsequent shifts in our stock ownership, including as a result of our future follow-on offering, some of which are outside of our control. As a result, if we earn net taxable income, our ability to use our pre-change NOL carryforwards to offset U.S. federal taxable income may become subject to limitations, which could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. In addition, pursuant to the Tax Cuts and Jobs Act of 2017 we may not use net operating loss carry-forwards to reduce our taxable income in any year by more than 80% and we may not carry back any net operating losses to prior years. These new rules apply regardless of the occurrence of an ownership change.

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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 \$208.9 million (\$240.3 million if the underwriters' 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 voxelotor for the treatment of SCD, including our ongoing Phase 3 HOPE study and our ongoing Phase 2a HOPE-KIDS 1 study, as well as future clinical trials, to build and expand our commercial organization in preparation for the potential approval and launch of voxelotor, to fund our other research and development activities, and for working capital and general corporate purposes.

We are working to diversify our pipeline, both through internal research as well as through business development efforts. We may therefore also use a portion of the net proceeds to in-license, acquire or invest in new businesses, technology or assets. Although we have no material agreements, commitments or understandings with respect to any in-license or acquisition, we have and plan to continue to evaluate such opportunities and engage in related discussions with other business entities from time to time.

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.

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 our ongoing clinical trials and nonclinical studies or any clinical trials we may commence in the future, our ability to take advantage of expedited programs or to obtain regulatory approval for voxelotor and any other product candidates we may identify and pursue, the timing and costs associated with the manufacture and supply of voxelotor and any other product candidates we may identify and pursue for clinical development or commercialization, our ability to successfully launch and commercialize voxelotor or any other product candidates if approved, any strategic transactions in which we may engage, 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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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 December 31, 2017, we had net tangible book value of approximately \$318.8 million, or \$6.91 per share of our common stock, based upon 46,131,723 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 4,000,000 shares of common stock in this offering at the public offering price of \$54.00 per share, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of December 31, 2017 would have been approximately \$527.7 million, or approximately \$10.53 per share of common stock. This represents an immediate increase in as adjusted net tangible book value of \$3.62 per share to our existing stockholders and an immediate dilution of \$43.47 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 | \$ 54.00 |
| Historical net tangible book value per share as of December 31, 2017 | \$ 6.91 |
| Increase in net tangible book value per share attributable to new investors | 3.62 |
| As adjusted net tangible book value per share after this offering | 10.53 |
| Dilution per share to new investors | \$ 43.47 |

If the underwriters exercise in full their option to purchase up to 600,000 additional shares of our common stock at the public offering price of \$54.00 per share, the as adjusted net tangible book value after this offering would be \$11.02 per share, representing an increase in net tangible book value of \$4.11 per share to existing stockholders and immediate dilution of \$42.98 per share to investors purchasing our common stock in this offering at the public offering price.

The foregoing table and discussion is based on 46,131,723 shares of common stock outstanding as of December 31, 2017, and excludes:

394,736 shares of common stock issued in January 2018 in connection with the underwriters' exercise of their option to purchase additional shares in our previous follow-on offering;

2,945,901 shares of common stock issuable upon exercise of outstanding options as of December 31, 2017 at a weighted-average exercise price of \$17.50 per share;

241,617 shares of restricted common stock which were subject to our right of repurchase as of December 31, 2017;

650,708 shares of common stock issuable upon exercise of options granted subsequent to December 31, 2017 through March 1, 2018 at a weighted-average exercise price of \$59.59 per share;

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820,713 shares of common stock issuable upon the vesting of outstanding restricted stock units as of December 31, 2017;

425,535 shares of common stock issuable upon the vesting of restricted stock units granted subsequent to December 31, 2017 through March 1, 2018;

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1,538,680 shares of common stock reserved for future issuance under our 2015 Stock Option and Incentive Plan, or the 2015 Plan, as of December 31, 2017;

186,033 shares of common stock reserved for future issuance under our 2015 Employee Stock Purchase Plan, or the 2015 ESPP, as of December 31, 2017; and

170,000 shares of common stock reserved for future issuance under our 2017 Inducement Equity Plan, or the 2017 Inducement Plan, as of December 31, 2017.

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.

Table of Contents**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 ended December 31, 2017 | | |
| First quarter | \$ 41.15 | \$ 14.00 |
| Second quarter | \$ 37.50 | \$ 25.65 |
| Third quarter | \$ 31.30 | \$ 24.03 |
| Fourth quarter | \$ 45.85 | \$ 29.45 |
| Year ending December 31, 2018 | | |
| First quarter (through March 8, 2018) | \$ 68.05 | \$ 38.80 |

On March 8, 2018, the last reported sale price of our common stock as reported on The Nasdaq Global Select Market was \$56.90 per share. As of March 8, 2018, there were approximately 17 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.

The transfer agent and registrar for our common stock is Continental Stock Transfer & Trust Company. The transfer agent's address is 1 State Street, 30th Floor, New York, NY 10004-1561 and its telephone number is (212) 509-4000.

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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

Wells Fargo Securities, LLC is acting as the underwriter for this offering. Subject to the terms and conditions set forth in an underwriting agreement among us and the underwriter, we have agreed to sell to the underwriter, and the underwriter has agreed to purchase from us, 4,000,000 shares of common stock.

Subject to the terms and conditions set forth in the underwriting agreement, the underwriter has agreed to purchase all of the shares sold under the underwriting agreement if any of these shares are purchased.

We have granted the underwriters a 30-day option to purchase up to an additional 600,000 shares of common stock from us at a price of \$52.35 per share.

We have agreed to indemnify the underwriter against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriter may be required to make in respect of those liabilities.

The underwriter is offering the shares, subject to prior sale, when, as and if issued to and accepted by it, subject to approval of legal matters by its counsel, including the validity of the shares, and other conditions contained in the underwriting agreement, such as the receipt by the underwriter of officers' certificates and legal opinions. The underwriter reserves the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commissions and Discounts

The underwriter has agreed to purchase the shares of our common stock from us at a price of \$52.35 per share, which will result in \$209.4 million of proceeds to us before expenses.

The expenses of the offering payable by us, not including the underwriting discounts, are estimated at \$0.5 million. We have agreed to reimburse the underwriter for expenses relating to clearing of this offering with the Financial Industry Regulatory Authority, Inc. in an amount up to \$25,000. The underwriter has agreed to reimburse certain of our expenses in connection with this offering in an amount up to \$719,700. Those expenses include up to \$719,700 payable to our third-party financial advisor, which is a FINRA member. The third party advisor is not acting as an underwriter and will not sell or offer to sell any securities or identify, solicit or engage directly with potential investors. In addition, the third party advisor will not underwrite or purchase any of the offered securities or otherwise participate in any such undertaking.

No Sales of Similar Securities

We have agreed that we will not, subject to specified exceptions, (1) 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, or otherwise transfer or dispose of, directly or indirectly, or file with the SEC a registration statement under the Securities Act relating to, any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock, or publicly disclose the intention to make any offer, sale, pledge, disposition or filing, (2) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the common stock or such other securities, or (3) file any registration statement (other than on Form S-8 or any successor form thereto with respect to securities issued or issuable under our equity incentive plans) with the SEC relating to the offering of any shares of common stock or any securities convertible into or exercisable or exchangeable for our common stock, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of common stock or such other securities, in cash or otherwise, without the prior written consent of Wells Fargo Securities, LLC for a period of 90 days after the date of this prospectus supplement.

Our directors and executive officers, and certain of our securityholders have entered into lock-up agreements with the underwriter prior to the commencement of this offering pursuant to which each of these persons or entities, subject to specified exceptions, for a period of 90 days after the date of this prospectus supplement, may not, without the prior written consent of Wells Fargo Securities, LLC, (1) offer,

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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 our common stock or any securities convertible into or exercisable or exchangeable for our common stock (including, without limitation, common stock or such other securities which may be deemed to be beneficially owned by such directors, executive officers, or other securityholders in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant), or publicly disclose the intention to make any offer, sale pledge or disposition, or (2) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the common stock or such other securities, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of common stock or such other securities, in cash or otherwise, or (3) make any demand for or exercise any right with respect to the registration of any shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock. We have agreed to indemnify the underwriter against certain liabilities, including liabilities under the Securities Act.

Our common stock is quoted on The Nasdaq Global Select Market under the symbol GBT.

Short Positions

In connection with the offering, the underwriter may purchase and sell our common stock in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriter of a greater number of shares than it is required to purchase in the offering. The underwriter must close out any short position by purchasing shares in the open market. A short position is more likely to be created if the underwriter is concerned that there may be downward pressure on the price of our common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of shares of common stock made by the underwriter in the open market prior to the completion of the offering.

Similar to other purchase transactions, the underwriter's purchases to cover the short sales 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 may be higher than the price that might otherwise exist in the open market. The underwriter may conduct these transactions on the Nasdaq in the over-the-counter market or otherwise.

Neither us nor the underwriter make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. In addition, neither we nor the underwriter make any representation that the underwriter will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Electronic Distribution

In connection with the offering, the underwriter or securities dealers may distribute prospectuses by electronic means, such as e-mail.

Other Relationships

The underwriter and its 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, financial and brokerage activities. The underwriter and its affiliates have engaged in, and may in the future engage in, investment banking and other commercial dealings in the ordinary course of business with us or our affiliates. They have received, or may in the future receive, customary fees and commissions for these transactions.

In addition, in the ordinary course of their business activities, the underwriter and its affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related

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derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriter and its affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Sales Outside the United States

No action has been taken in any jurisdiction (except the United States) that would permit a public offering of the common stock, or the possession, circulation or distribution of this prospectus supplement, the accompanying prospectus or any other material relating to us or our common stock in any jurisdiction where action for that purpose is required. Accordingly, the common stock may not be offered or sold, directly or indirectly, and none of this prospectus supplement, the accompanying prospectus or any other offering material or advertisements in connection with the offering of common stock may be distributed or published, in or from any country or jurisdiction except in compliance with any applicable rules and regulations of any such country or jurisdiction.

Each of the underwriters may arrange to sell shares of our common stock offered hereby in certain jurisdictions outside the United States, either directly or through affiliates, where they are permitted to do so. In that regard, Wells Fargo Securities, LLC may arrange to sell shares of our common stock in certain jurisdictions through an affiliate, Wells Fargo Securities International Limited, or WFSIL. WFSIL is a wholly-owned indirect subsidiary of Wells Fargo & Company and an affiliate of Wells Fargo Securities, LLC. WFSIL is a U.K. incorporated investment firm regulated by the Financial Conduct Authority. Wells Fargo Securities is the trade name for certain corporate and investment banking services of Wells Fargo & Company and its affiliates, including Wells Fargo Securities, LLC and WFSIL.

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.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus supplement and accompanying prospectus (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 of National Instrument 33-105 Underwriting Conflicts, or 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, or each, a Relevant Member State, with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State, or the Relevant Implementation Date, an offer of shares of common stock described in this prospectus supplement and accompanying prospectus may not be made to the public in that Relevant Member State except that an offer to the public

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in that Relevant Member State of any such shares of common stock may be made at any time under the following exemptions under the Prospectus Directive if they have been implemented in that Relevant Member State:

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

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

in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of shares of common stock shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospective Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

Each purchaser of shares of common stock described in this prospectus supplement and accompanying prospectus located within a Relevant Member State will be deemed to have represented, acknowledged and agreed that it is a qualified investor within the meaning of Article 2(1)(e) of the Prospectus Directive.

For the purpose of this provision, the expression an offer to the public in relation to any shares of common stock 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 shares of common stock to be offered so as to enable an investor to decide to purchase or subscribe for the shares of common stock, as the expression may be varied in the Relevant Member State, and the expression Prospectus Directive means Directive 2003/71/EC (and amendments thereto, including Directive 2010/73/EU), and includes any relevant implementing measure in the Relevant Member State.

United Kingdom

This prospectus supplement and the accompanying prospectus are only being distributed to, and are only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospective 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, or the Order, (ii) high net worth entities falling within Article 49(2)(a) to (d) of the Order or (iii) persons to whom it may otherwise lawfully be communicated (all such persons together being referred to as relevant persons). This prospectus supplement and accompanying prospectus are directed only at relevant persons and must not be acted on or relied on in the United Kingdom by persons who are not relevant persons. Any investment or investment activity to which this prospectus supplement and accompanying prospectus relates is available only to relevant persons, and will be engaged in only with relevant persons.

Each underwriter has represented and agreed that:

it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000, as amended, or the FSMA) received by it in connection with the issue or sale of the shares of common stock in circumstances in which Section 21(1) of the FSMA does not apply to the Company; and

it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the shares of common stock in, from or otherwise involving the United Kingdom.

Switzerland

This document as well as any other material relating to the shares of our common stock that are the subject of the offering contemplated by this prospectus supplement and accompanying prospectus do not

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constitute an issue prospectus pursuant to Article 652a or Article 1156 of the Swiss Code of Obligations. Our common stock will not be listed on the SWX Swiss Exchange and, therefore, the documents relating to our common stock, including, but not limited to, this document, do not claim to comply with the disclosure standards of the listing rules of SWX Swiss Exchange and corresponding prospectus schemes annexed to the listing rules of the SWX Swiss Exchange.

Our common stock is being offered in Switzerland by way of a private placement, i.e. to a small number of selected investors only, without any public offer and only to investors who do not purchase shares of our common stock with the intention to distribute them to the public. The investors will be individually approached by us from time to time.

This document as well as any other material relating to our common stock is personal and confidential and does not constitute an offer to any other person. This document may only be used by those investors to whom it has been handed out in connection with the offering described herein and may neither directly nor indirectly be distributed or made available to other persons without our express consent. It may not be used in connection with any other offer and shall in particular not be copied and/or distributed to the public in (or from) Switzerland.

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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,

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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.

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

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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;

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 24%) 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

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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 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 ANY TAX REFORM PROPOSALS PENDING IN THE U.S. CONGRESS.

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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 consolidated financial statements of Global Blood Therapeutics, Inc. as of December 31, 2017 and 2016, and for each of the years in the three-year period ended December 31, 2017, have been incorporated by reference herein 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

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.gbt.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.

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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, 2017, filed with the SEC on February 27, 2018;

Current Reports on Form 8-K filed with the SEC on January 9, 2018 (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., 171 Oyster Point Blvd., Suite 300, 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.gbt.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

Common Stock

Preferred Stock

Debt Securities

Warrants

Units

We may from time to time issue, in one or more series or classes, 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 August 21, 2017, the closing price for our common stock, as reported on The NASDAQ Global Select Market, was \$26.80 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.

This prospectus may not be used to offer or sell securities unless accompanied by a prospectus supplement.

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 August 23, 2017.

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ABOUT THIS PROSPECTUS

This prospectus is part of an automatic registration statement that we filed with the Securities and Exchange Commission, or the SEC, using a shelf registration process as a well-known seasoned issuer as defined in Rule 405 under the Securities Act of 1933, as amended, or the Securities Act. 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.

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 30 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, 2016, 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, 2017 and June 30, 2017, 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, 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 any accompanying prospectus supplement or the documents incorporated by reference herein, 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 3 clinical trial of GBT440 in adult and adolescent patients with sickle cell disease, or SCD, our ongoing Phase 2a clinical trial of adolescent and pediatric patients with 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 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;

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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 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, 2016 and our most recent Quarterly Reports on Form 10-Q for the quarters ended March 31, 2017 and June 30, 2017, and our Current Reports on Form 8-K to the extent incorporated by reference in this prospectus, 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. 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 and IPF. 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 GBT 440 in a Phase 2a clinical trial of adolescent and pediatric patients with SCD, and in July 2017 we announced that we have expanded this open-label trial to include a new single-dose cohort in children aged 6-11. In December 2015, the Food and Drug Administration, or FDA, granted Fast Track Designation and Orphan Drug Designation for GBT440 for the treatment of SCD, and in November 2016 GBT440 was granted Orphan Drug Designation in Europe for the treatment of SCD. In June 2017, the European Medicines Agency, or EMA, granted PRIME designation for GBT440 for the treatment of SCD. The PRIME program is a new regulatory mechanism that provides for early and proactive EMA support to medicine developers to help patients benefit as early as possible from innovative new products that have demonstrated the potential to significantly address an unmet medical need. SCD is 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 to date 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, we are conducting two Phase 2 clinical trials of GBT440 for the potential treatment of IPF, which is a hypoxemic pulmonary disorder. We are also conducting a Phase 1 study called Basecamp in healthy volunteers, which is intended to support our understanding of GBT440's effects on hypoxemia and complement our ongoing Phase 2a program in IPF. We are also engaged in other pre-clinical research and development activities. We own or jointly own and have exclusively licensed rights to our 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 GBT 440, 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 our lead product candidate GBT440.

We have never been profitable and have incurred net losses in each year since inception. Our net losses were \$47.2 million and \$34.3 million for the six months ended June 30, 2017 and 2016, respectively. As of June 30, 2017, we had an accumulated deficit of \$228.1 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, 2017, we had \$93.7 million in cash and cash equivalents and \$196.9 million in marketable securities.

We currently 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 \$1.07 billion or more; (ii) December 31, 2020; (iii) the date on which we have issued more than \$1.07 billion in nonconvertible debt during the previous three years; or (iv) the last day of the fiscal year in which we are deemed to become a large accelerated filer under the rules of the SEC, which means the aggregate market

value of our common stock that is held by non-affiliates equals or exceeds \$700 million as of the prior June 30th.

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Based on our calculation of the market value of our common stock that was held by non-affiliates as of June 30, 2017, on December 31, 2017, we will lose our status as an emerging growth company, our auditors will be required to formally attest to the effectiveness of our internal control over financial reporting pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, as amended, and we will no longer be able to take advantage of exemptions from reporting requirements available to emerging growth companies.

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 also use a portion of the net proceeds to acquire or invest in businesses, products and technologies that are complementary to our own, although we have no commitments or agreements with respect to any acquisitions as of the date of this prospectus. Pending these uses, we may 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 August 21, 2017, we had 43,764,503 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

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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.

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;

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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.

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.

Registration Rights

The holders of 3,451,337 shares of our common stock, or their permitted transferees, which we refer to as our registrable securities, are entitled to rights with respect to the registration of these securities under the Securities Act. These rights are provided under the terms of the investor rights agreement. The investor rights agreement includes demand registration rights, short-form registration rights and piggyback registration rights. All fees, costs and expenses incurred in connection with registrations under the investor rights agreement will be borne by us, and all selling expenses, including underwriting discounts and selling commissions, will be borne by the holders of the shares being registered.

Demand Registration Rights

The holders of our registrable securities are entitled to demand registration rights. Under the terms of the investor rights agreement, we will be required, upon the request of holders of at least 25% of our outstanding registrable securities, to file a registration statement with an anticipated offering amount of at least \$3.0 million and use commercially reasonable efforts to effect the registration of these shares for public resale. We are required to effect up to two registrations pursuant to this provision of the investor rights agreement.

Short Form Registration Rights

The holders of our registrable securities are also entitled to short form registration rights. Pursuant to the investor rights agreement, if we are eligible to file a registration statement on Form S-3, upon the request of holders of at least 25% of our outstanding registrable securities to sell registrable securities with an anticipated aggregate offering amount of at least \$1.0 million, we will be required to use our commercially reasonable efforts to effect a registration of such shares. We are required to effect up to two registrations in any twelve month period pursuant to this provision of the investor rights agreement.

Piggyback Registration Rights

The holders of our registrable securities are entitled to piggyback registration rights. If we register any of our securities either for our own account or for the account of other security holders, the holders of our outstanding registrable securities are entitled to include their shares in the registration. Subject to certain exceptions contained in the investor rights agreement, we and the underwriters may limit the number of shares included in the underwritten offering if the underwriters determine that marketing factors require a limitation of the number of shares to be underwritten.

Indemnification

Our investor rights agreement contains customary cross-indemnification provisions, under which we are obligated to indemnify holders of registrable securities in the event of material misstatements or omissions in the registration

statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions attributable to them.

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Expiration of Registration Rights

The registration rights granted under the investor rights agreement will terminate upon the earlier of (i) certain events constituting a sale of the company, (ii) at such time when all registrable securities could be sold under Rule 144 of the Securities Act or a similar exemption without limitation during a three-month period without registration or (iii) the third anniversary of our IPO.

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;

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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

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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 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;

in _____ at the market offering _____, within the meaning of Rule 415(a)(4) of the Securities Act, ; 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.

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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.

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 overallocate in connection with the offering, creating a short position for their own accounts. In addition, to cover overallocations or to stabilize the price of the securities or of any such other securities, the underwriters may bid for, and purchase, the securities or

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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.

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 consolidated financial statements of Global Blood Therapeutics, Inc. as of December 31, 2016 and 2015, and for each of the years in the three-year period ended December 31, 2016, have been incorporated by reference herein and in the registration statement 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.

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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, 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, 2016, filed with the SEC on March 13, 2017;

The information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2016 from our definitive proxy statement on Schedule 14A (other than information furnished rather than filed), which was filed with the SEC on April 28, 2017;

Quarterly Reports on Form 10-Q filed with the SEC for the quarter ended March 31, 2017, filed with the SEC on May 1, 2017; and the quarter ended June 30, 2017, filed with the SEC on August 7, 2017;

Current Reports on Form 8-K filed with the SEC on January 20, 2017, February 17, 2017, February 22, 2017, February 27, 2017, March 22, 2017, March 30, 2017, June 22, 2017, June 23, 2017, June 28, 2017, July 10, 2017 and August 1, 2017; 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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Global Blood Therapeutics, Inc.

4,000,000 Shares

Common Stock

PROSPECTUS SUPPLEMENT

March 8, 2018

Wells Fargo Securities