Global Blood Therapeutics, Inc.
Form 424B4
August 12, 2015
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Filed Pursuant to Rule 424(b)(4)
Registration No. 333-205563

PROSPECTUS

6,000,000 Shares

COMMON STOCK

Global Blood Therapeutics, Inc. is offering 6,000,000 shares of common stock. This is our initial public offering and no public market currently exists for our shares. The initial public offering price of our common stock is $20.00 per share.

Our common stock has been approved for listing on The NASDAQ Global Select Market under the symbol GBT.

We are an emerging growth company as that term is used in the Jumpstart Our Business Startups Act of 2012, as amended, and, as such, have elected to comply with certain reduced public company reporting requirements for this prospectus and future filings.

Investing in our common stock involves risks. See Risk Factors beginning on page 10.

PRICE $20.00 A SHARE

	Price to Public	Underwriting Discounts and Commissions[1]	Proceeds, Before Expenses, to Global Blood Therapeutics, Inc.
Per Share	$ 20.00	$ 1.40	$ 18.60
Total	$ 120,000,000	$ 8,400,000	$ 111,600,000

(1) The underwriters will receive compensation in addition to underwriting discounts and commissions. See Underwriting .

We have granted the underwriters an option to purchase up to 900,000 additional shares of our common stock. The underwriters can exercise this option at any time within 30 days after the date of this prospectus.

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

The underwriters expect to deliver the shares of common stock to purchasers on or about August 17, 2015.

Morgan Stanley **Goldman, Sachs & Co.**

Cowen and Company **Wedbush PacGrow**

August 11, 2015

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We and the underwriters have not authorized anyone to provide any information other than that contained in this prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We and the underwriters are not making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus is accurate only as of the date on the front cover of this prospectus. Our business, financial condition, results of operations and prospects may have changed since that date.

Until September 5, 2015 (the 25th day after the date of this prospectus), all dealers that effect transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealers obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

For investors outside of the United States: We have not, and the underwriters have not, done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than the United States. Persons outside of the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus outside of the United States.

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PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus and does not contain all of the information that you should consider in making your investment decision. Before investing in our common stock, you should carefully read this entire prospectus, including our financial statements and the related notes included elsewhere in this prospectus. You should also consider, among other things, the matters described under Risk Factors and Management s Discussion and Analysis of Financial Condition and Results of Operations, in each case appearing elsewhere in this prospectus. Unless otherwise stated, all references to us, our, GBT, we, the Company and similar designations refer to Global Blood Therapeutics, Inc.

Global Blood Therapeutics, Inc.

Our Company

We are a biopharmaceutical company dedicated to discovering, developing and commercializing novel therapeutics to treat grievous blood-based disorders. We are developing our initial product candidate, GBT440, as a once-daily, oral prophylactic therapy for sickle cell disease, or SCD, and are currently evaluating GBT440 in both healthy subjects and SCD patients in a randomized, placebo-controlled, double-blind Phase 1/2 clinical trial. SCD is a disease marked by severe pain crises, recurrent hospitalizations, multi-organ damage, and early mortality. GBT440 targets the underlying mechanism of red blood cell sickling, which we believe provides the potential to treat SCD rather than only its associated symptoms. In addition to GBT440 for the treatment of SCD, we are leveraging our deep scientific expertise in the chemical and biological mechanisms of blood-based disorders to target hypoxemic pulmonary disorders and hereditary angioedema, or HAE. We own rights to our product candidate portfolio in the United States, Europe and other major markets.

Overview of Sickle Cell Disease

SCD is a chronic, inherited blood disorder caused by a genetic mutation in the beta-chain of hemoglobin, which results in the formation of abnormal hemoglobin known as sickle hemoglobin, or HbS. Hemoglobin is contained within red blood cells, or RBCs. In its deoxygenated state, HbS has a propensity to polymerize, or bind together into long, rigid rods within an RBC, much like a sword within a balloon. Once HbS polymerizes, the RBC assumes a sickled shape and becomes inflexible, which can cause blockage in small blood vessels. Beginning in childhood, SCD patients suffer unpredictable and recurrent episodes or crises of severe pain due to blocked blood flow to organs, which often lead to psychosocial and physical disabilities. This blocked blood flow, combined with hemolytic anemia (the destruction of RBCs), can lead to multi-organ damage and early death.

We believe there is a significant unmet need in the treatment of SCD. Current treatment options for SCD are limited to hydroxyurea, or HU, blood transfusions and bone marrow transplantation. The utilization of these treatments is significantly limited due to their suboptimal efficacy and significant toxicity. As a result, patients with SCD continue to suffer serious morbidity and premature mortality. A 2014 publication noted that in the United States, SCD results in a decrease of approximately 25 to 30 years in life expectancy.

Our Product Candidate

GBT440 is a novel hemoglobin modifier that binds to hemoglobin molecules, which we have shown in preclinical models results in an increased affinity of hemoglobin for oxygen. In various studies of SCD, scientists have demonstrated that oxyhemoglobin, or hemoglobin in the oxygenated state, is a potent inhibitor of HbS polymerization. We therefore believe that increasing the proportion of oxyhemoglobin in blood could potentially delay the

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

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We believe that the natural activity of fetal hemoglobin, or HbF, as well as prior observations of the activity of other hemoglobin-modifying compounds, provide support for our approach to treating SCD with GBT440. By binding to and modifying hemoglobin, we believe GBT440 can delay the polymerization of HbS, thereby halting the progression of SCD. The results of our preclinical studies support our hypothesis that an appropriate modification of HbS is likely to prevent RBC sickling and could halt the progression of SCD without compromising oxygen delivery to the tissues.

In December 2014, we initiated our randomized, placebo-controlled, double-blind, single and multiple ascending dose Phase 1/2 clinical trial of GBT440 in healthy subjects and patients with SCD. In this trial, which is designed to enroll between 96 and 128 subjects across 12 cohorts, we are evaluating the safety, tolerability, pharmacokinetics, or PK, and pharmacodynamics, or PD, of GBT440, as well as exploratory markers of SCD activity, including anti-hemolytic effects and SCD-related clinical effects. As of July 31, 2015, we have dosed 48 subjects in six single dose cohorts, comprised of 40 healthy volunteers (30 of whom received GBT440 and ten of whom received placebo) and eight SCD patients (six of whom received GBT440 and two of whom received placebo). In the multiple dose arm of our trial, all 24 healthy volunteers have completed 15-day dosing, and eight SCD patients have completed 28-day dosing and are currently in the follow-up period. To date, there have been no serious adverse events among subjects treated with GBT440 in our Phase 1/2 clinical trial. One SCD patient who received placebo experienced an SCD-specific serious adverse event involving a sickle cell crisis. Among the six SCD patients who received multiple doses of GBT440, from baseline (Day -1) to Day 28, we have observed significant reductions in the number of sickled RBCs in all patients, which is the quintessential hallmark of the disease and the primary driver of disease pathology. We have also observed improvement in hemolysis markers as evidenced by declines in reticulocyte counts, unconjugated bilirubin and lactate dehydrogenase, or LDH, levels. Proof of concept was demonstrated within 15 days of once daily dosing with a rapid decline in hemolysis markers and improvement in anemia. We believe these initial data demonstrate the potential for GBT440 to serve as a disease-modifying therapy for SCD. Subject to data from one or more of the multiple dose cohorts of our Phase 1/2 clinical trial in SCD patients, we intend to engage in discussions with U.S. and European regulatory authorities to define the future development plan for GBT440.

Because available therapies in SCD are limited, the U.S. Food and Drug Administration, or the FDA, has suggested that the development of new therapies for SCD is an agency priority. As a result, we believe there may be an opportunity to accelerate the development of GBT440 through one or more of the FDA s expedited designation or approval programs. We believe that the data from SCD patients in our ongoing clinical trial, if positive, may provide an opportunity to demonstrate the beneficial effect of GBT440 on clinical parameters of hemolysis and resolution of anemia, which could potentially form the basis for qualification for expedited programs.

Market Opportunity in SCD

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

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

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We own or co-own one issued U.S. patent that covers the composition of matter for GBT440, which is due to expire in 2032 (absent any applicable patent term extensions), and we own or co-own additional pending patent applications in the United States and selected foreign countries.

Additional Opportunities

Beyond SCD, we plan to develop GBT440 or one or more of its analogs as a potential therapeutic for acute and chronic hypoxemic pulmonary disorders, including acute respiratory distress syndrome, or ARDS, and idiopathic pulmonary fibrosis, or IPF, where hypoxia is believed to play a key role in disease pathogenesis and adverse patient outcomes. These are conditions in which the lungs cannot supply adequate oxygen to the blood. Our pursuit of these indications is based on data from a mouse model of hypoxia, in which we observed that oral dosing with a hemoglobin-modifying analog of GBT440 increased survival during extreme hypoxia.

Additionally, we have identified several proprietary, small molecule kallikrein inhibitors in an effort to produce an orally administered therapy for the prevention of angioedema attacks, or episodes of severe swelling associated with HAE that may affect the face, airways, extremities or gastrointestinal tract. Kallikrein is an enzyme in blood that generates bradykinin, which in turn directly stimulates blood vessel swelling, leakage and tissue inflammation. All currently marketed therapeutics for HAE must be administered intravenously or by subcutaneous injection. As a result, we believe that a safe and effective oral prophylactic agent would have the potential to transform the treatment paradigm for this disease.

Management

We have assembled a team of employees, directors and scientific founders rich in scientific experience and capabilities in drug discovery, development and commercialization. Our management has a successful track record in developing and commercializing drug candidates. In aggregate, our team has contributed to 18 drug approvals, including Avastin, CellCept, Herceptin, INTEGRILIN, Kaletra, Kyprolis and Rituxan. We intend to leverage this expertise and experience to rapidly pursue the development of GBT440 and any other product candidates we may identify.

Our Strategy

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

- rapidly advance GBT440 for the treatment of SCD;
- explore the development of GBT440 and other hemoglobin modifiers in hypoxemic pulmonary disorders with significant unmet medical need;
- submit an Investigational New Drug application, or IND, and initiate clinical development for an oral kallikrein inhibitor in HAE;

retain global development and commercialization rights to product candidates in our core disease areas in major markets; and

evaluate opportunities to expand the scope of our product offerings.

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Our Development Pipeline

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

(1) We intend to initiate clinical development of GBT440 in pediatric populations and in other genotypes of SCD following the demonstration of proof-of-concept in our ongoing Phase 1/2 clinical trial.
(2) GBT440 and GBT440 analogs include patent rights jointly owned with third parties.

Risks Associated with Our Business

Our ability to implement our business strategy is subject to numerous risks that you should be aware of before making an investment decision. These risks are described more fully in the section entitled Risk Factors in this prospectus. These risks include, among others:

- We are a clinical development-stage company with a limited operating history, have incurred significant losses since our inception, and anticipate that we will continue to incur significant losses for the foreseeable future;
- Even if this offering is successful, we will need to raise additional funding before we can expect to generate any revenues from product sales;
- If we are unable to obtain regulatory approval for GBT440 or any other product candidates that we may identify or develop, our business will be substantially harmed;
- We are heavily dependent upon the success of GBT440, which is in the early stages of clinical development, and we have not identified any other clinical development candidates;
- Results of earlier studies may not be predictive of future clinical trial results, and we may fail to establish an adequate safety or efficacy profile to conduct advanced clinical trials or obtain regulatory approval for GBT440 or any other product candidates that we may pursue;
- If we are unable to obtain and maintain sufficient intellectual property protection for GBT440, our technologies, or any future product candidates, we may not be able to compete effectively in our markets;
- Our future success depends in part upon our ability to retain our key employees, consultants and advisors and to attract, retain and motivate other qualified personnel; and

In connection with the audit of our financial statements as of and for the years ended December 31, 2014 and 2013, we identified a material weakness in our internal control over financial reporting.

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Implications of Being an Emerging Growth Company

We qualify as an emerging growth company as defined in the Jumpstart Our Business Startups Act of 2012, as amended, or the JOBS Act. As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

- two years of audited financial statements in addition to any required unaudited interim financial statements with correspondingly reduced Management s Discussion and Analysis of Financial Condition and Results of Operations disclosure;
- reduced disclosure about our executive compensation arrangements;
- no non-binding advisory votes on executive compensation or golden parachute arrangements; and
- exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting.

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

Corporate History and Information

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

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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THE OFFERING

Common stock offered by us	6,000,000 shares
Common stock to be outstanding after this offering	27,808,457 shares
Underwriters option	We have granted the underwriters an option to purchase a maximum of 900,000 additional shares of common stock from us. The underwriters can exercise this option at any time within 30 days from the date of this prospectus.
Use of Proceeds	We estimate that we will receive net proceeds from the sale of shares of our common stock in this offering of approximately $109.4 million, or $126.1 million if the underwriters fully exercise their option to purchase additional shares, based on the initial public offering price of $20.00 per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use the net proceeds from this offering and our existing cash and cash equivalents to fund our clinical development of GBT440 for the treatment of SCD, including the completion of our ongoing Phase 1/2 clinical trial, planned clinical pharmacology studies and through the initiation of a pivotal clinical trial, our conducting of clinical trials of GBT440 or its analogs for the treatment of hypoxemic pulmonary disorders, our completion and filing of an IND and beginning a Phase 1/2 clinical trial of an oral kallikrein inhibitor for the treatment of HAE, our other research and development activities, and for working capital and general corporate purposes. See Use of Proceeds for additional information.
Risk Factors	You should read carefully Risk Factors beginning on page 10 and other information included in this prospectus for a discussion of factors that you should consider before deciding to invest in shares of our common stock.
Directed share program	At our request, the underwriters have reserved 5% of the shares of common stock to be issued by us and offered by this prospectus for sale, at the initial public offering price, to directors, officers, employees, business associates and related persons of Global Blood Therapeutics, Inc. The number of shares of common stock available for sale to the general public will be reduced to the extent these individuals purchase such reserved shares. Any reserved shares that are not so purchased will

	be offered by the underwriters to the general public on the same basis as the other shares offered by this prospectus.
NASDAQ Global Select Market symbol	GBT

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The number of shares of common stock to be outstanding after this offering is based on 21,808,457 shares of common stock outstanding as of March 31, 2015 and excludes:

- 1,190,051 shares of common stock issuable upon exercise of outstanding options as of March 31, 2015 at a weighted average exercise price of $0.81 per share;
- 985,338 shares of restricted common stock which were subject to our right of repurchase as of March 31, 2015;
- 882,557 shares of common stock issuable upon exercise of options granted subsequent to March 31, 2015 at a weighted-average exercise price of $4.21 per share and 607,853 shares of restricted common stock issued subsequent to March 31, 2015 at a purchase price of $3.40 per share;
- 445,620 shares of common stock reserved for future issuance under our 2012 Stock Option and Grant Plan, or the 2012 Plan, as of March 31, 2015;
- 1,430,000 shares of common stock reserved for future issuance under our 2015 Stock Option and Incentive Plan, or the 2015 Plan, which became effective upon the effectiveness of the registration statement of which this prospectus is a part; and
- 50,000 shares of common stock reserved for future issuance under our 2015 Employee Stock Purchase Plan, or the 2015 ESPP, which became effective upon the effectiveness of the registration statement of which this prospectus is a part.

Except as otherwise indicated, all information in this prospectus assumes or gives effect to:

- the conversion of all outstanding shares of our redeemable convertible preferred stock into an aggregate of 19,746,614 shares of our common stock upon the completion of this offering;
- no exercise of the outstanding options described above;
- no exercise by the underwriters of their option to purchase up to an additional 900,000 shares of our common stock in this offering;
- a one-for-3.5 reverse split of our common stock, which became effective on July 30, 2015; and

the filing of our restated certificate of incorporation and the adoption of our amended and restated bylaws, which will occur immediately prior to the completion of this offering.

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SUMMARY FINANCIAL DATA

The following tables present summary financial data for our business. We derived the following statements of operations data for the years ended December 31, 2013 and 2014 from our audited financial statements appearing elsewhere in this prospectus. We derived the statements of operations data for the three months ended March 31, 2014 and 2015 and the balance sheet data as of March 31, 2015 from our unaudited interim financial statements appearing elsewhere in this prospectus. We have prepared the unaudited interim financial statements on the same basis as our audited financial statements and, in the opinion of management, reflect all adjustments, consisting only of normal recurring adjustments, that are necessary for the fair statement of our unaudited interim financial statements. Our historical results are not necessarily indicative of the results that may be expected in the future, and our interim results are not necessarily indicative of the results to be expected for the full year or any other period. You should read this data together with our financial statements and related notes appearing elsewhere in this prospectus and the information under the captions Selected Financial Data and Management s Discussion and Analysis of Financial Condition and Results of Operations.

	Year Ended December 31,		Three Months Ended March 31,	
	2013	2014	2014	2015
			(unaudited)	
	(in thousands, except share and per share data)			
Summary of Operations Data:				
Operating expenses:				
Research and development	$ 12,855	$ 16,324	$ 3,877	$ 6,069
General and administrative	2,309	3,855	821	1,298
Related party expenses	499	332	171	53
Total operating expenses	15,663	20,511	4,869	7,420
Loss from operations	(15,663)	(20,511)	(4,869)	(7,420)
Change in fair value of Series A redeemable convertible preferred stock liability	(2,455)	(297)	(238)	
Interest income	2	1		3
Net loss	$ (18,116)	$ (20,807)	$ (5,107)	$ (7,417)
Net loss attributable to common stockholders	$ (19,851)	$ (23,772)	$ (5,695)	$ (8,657)
Net loss per share attributable to common stockholders, basic and diluted [1]	$ (16.14)	$ (14.20)	$ (3.81)	$ (4.22)
Weighted-average number of shares used in computing net loss per share attributable to common stockholders, basic and diluted[1]	1,230,241	1,673,919	1,496,607	2,052,874
		$ (1.51)		$ (0.34)

Pro forma net loss per share, basic and diluted (unaudited) [1]		
Weighted-average number of shares used in computing pro forma net loss per share, basic and diluted (unaudited) [1]	13,761,829	21,799,488

(1) See Notes 2 and 10 to our audited financial statements and Notes 2 and 7 to our unaudited interim condensed financial statements included elsewhere in this prospectus for an explanation of the calculations of our basic and diluted net loss per share attributable to common stockholders, pro forma net loss per share and the weighted-average number of shares used in the computation of the per share amounts.

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	As of March 31, 2015		
	Actual	Pro Forma [1] (unaudited) (in thousands)	Pro Forma As Adjusted [2]
Balance Sheet Data:			
Cash and cash equivalents	$ 45,800	$ 45,800	$ 155,150
Working capital	43,634	43,634	152,984
Total assets	50,477	50,477	159,827
Redeemable convertible preferred stock	103,396		
Accumulated deficit	(57,652)	(57,652)	(57,652)
Total stockholders (deficit) equity	(57,650)	45,746	155,096

(1) The pro forma column reflects the automatic conversion of all outstanding shares of our redeemable convertible preferred stock into 19,746,614 shares of our common stock immediately prior to the completion of this offering.

(2) The pro forma as adjusted column reflects the pro forma adjustments set forth above and the receipt of $109.4 million in net proceeds from our sale of shares of common stock in this offering at the initial public offering price of $20.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

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RISK FACTORS

Investing in our common stock involves a high degree of risk. You should consider carefully the following risks, together with all the other information in this prospectus, including our financial statements and notes thereto, before you invest in our common stock. If any of the following risks actually materializes, our operating results, financial condition and liquidity could be materially adversely affected. As a result, the trading price of our common stock could decline and you could lose part or all of your investment.

Risks Related to Our Financial Position and Need for Additional Capital

We are a clinical development-stage biopharmaceutical company with a limited operating history. We have incurred significant losses since our inception and anticipate that we will continue to incur losses for the foreseeable future. We have only one product candidate in clinical development and have not generated any revenue since our inception, which, together with our limited operating history, may make it difficult for you to assess our future viability.

We are a clinical development-stage biopharmaceutical company with a limited operating history upon which you can evaluate our business and prospects. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. To date, we have focused principally on developing our lead product candidate, GBT440, which is our only product candidate in clinical development.

We are not profitable and have incurred losses in each year since our inception in February 2011 and the commencement of our principal operations in May 2012. Our net losses for the years ended December 31, 2014 and 2013 were $20.8 million and $18.1 million, respectively and $7.4 million for the three months ended March 31, 2015. As of March 31, 2015, we had an accumulated deficit of $57.7 million. We have not generated any revenue since our inception, and have financed our operations solely through the sale of equity securities and convertible debt. We continue to incur significant research and development and other expenses related to our ongoing operations and expect to incur losses for the foreseeable future. We anticipate these losses will increase as we:

- continue to advance GBT440 in clinical development;
- establish and maintain manufacturing and supply relationships with third parties that can provide adequate (in amount and quality) supplies of GBT440 to support further clinical development and, if approved, commercialization;
- seek and obtain regulatory and marketing approvals for GBT440;
- build a sales and marketing organization or enter into selected collaborations to commercialize GBT440, if approved;
- advance our other programs through preclinical development and commence clinical development activities for any additional product candidates we may identify; and

expand our organization to support our research, development and commercialization activities and our operations as a public company.

We have never generated any revenues from product sales and may never be able to develop or commercialize a marketable drug or achieve profitability. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our failure to achieve sustained profitability would depress the value of our company and could impair our ability to raise capital, expand our business, diversify our research and development pipeline, market GBT440 or any other product candidates we may identify and pursue, if approved, or continue our operations. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders equity and working capital.

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

We are currently advancing GBT440 through clinical development and conducting preclinical research activities in our other programs. Developing biopharmaceutical products is expensive and time-consuming, and we expect our research and development expenses to increase substantially in connection with our ongoing activities, particularly as we advance GBT440 and other product candidates that we may identify and pursue in clinical trials. As of December 31, 2014 and March 31, 2015, we had working capital of $51.1 million and $43.6 million, respectively and capital resources consisting of cash and cash equivalents of $52.1 million and $45.8 million, respectively. Because the outcome of any clinical development and regulatory approval process is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development, regulatory approval process and commercialization of GBT440 and any future product candidates.

We estimate that the net proceeds from this offering will be approximately $109.4 million, based on the initial public offering price of $20.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We expect that the net proceeds from this offering, together with our existing cash and cash equivalents, will be sufficient to fund our operations through early 2017. However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings or other sources, such as strategic collaborations or license and development agreements. Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize GBT440 and other product candidates that we may identify and pursue. Moreover, such financing may result in dilution to stockholders, imposition of debt covenants and repayment obligations, or other restrictions that may affect our business. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans.

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

- the time and cost necessary to complete our ongoing clinical trial that we characterize as a Phase 1/2 trial of GBT440, to initiate and complete any pivotal clinical trials of GBT440 and to pursue regulatory approvals for GBT440, and the costs of post-marketing studies that could be required by regulatory authorities;
- the progress and results of our Phase 1/2 clinical trial of GBT440;
- the progress, timing, scope and costs of our nonclinical studies, clinical trials and other related activities, including the ability to enroll patients in a timely manner for our Phase 1/2 clinical trial of GBT440 and potential future clinical trials;
- the costs of obtaining clinical and commercial supplies of GBT440 and any other product candidates we may identify and develop;

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

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

the amount and timing of sales and other revenues from GBT440 and any other product candidates we may identify and develop, including the sales price and the availability of adequate third-party reimbursement;

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the cash requirements of any future acquisitions or discovery of product candidates;

the time and cost necessary to respond to technological and market developments;

the extent to which we may acquire or in-license other product candidates and technologies;

our ability to attract, hire and retain qualified personnel; and

the costs of maintaining, expanding and protecting our intellectual property portfolio.

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

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

If we are unable to obtain regulatory approval in one or more jurisdictions for GBT440 or any other product candidates that we may identify and develop, our business will be substantially harmed.

We cannot commercialize a product until the appropriate regulatory authorities have reviewed and approved the product candidate. Approval by the FDA and comparable foreign regulatory authorities is lengthy and unpredictable, and depends upon numerous factors. Approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate s clinical development and may vary among jurisdictions, which may cause delays in the approval or the decision not to approve an application. We have not obtained regulatory approval for any product candidate, including GBT440, and it is possible that neither GBT440 nor any other product candidates we may seek to develop in the future will ever obtain regulatory approval.

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

our inability to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that GB440 or any other product candidate we may develop is safe and effective;

the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;

the population studied in the clinical program may not be sufficiently broad or representative to assure safety in the full population for which we seek approval;

the FDA s or comparable foreign regulatory authorities requirement for additional preclinical studies or clinical trials;

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

the data collected from clinical trials of GBT440 and other product candidates that we may identify and pursue may not be sufficient to support the submission of a new drug application, or NDA, or other submission for regulatory approval in the United States or elsewhere;

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

the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications, or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and

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the approval policies or regulations of the FDA or comparable foreign regulatory authorities may change in a manner that renders our clinical trial design or data insufficient for approval.

The lengthy approval process, as well as the unpredictability of the results of clinical trials, may result in our failing to obtain regulatory approval to market GBT440 and other product candidates that we may pursue in the United States or elsewhere, which would significantly harm our business, prospects, financial condition and results of operations.

We are heavily dependent on the success of our lead product candidate, GBT440, and we have not identified other clinical development candidates within our other research programs, all of which are still in the preclinical development stage. If we are unable to successfully complete clinical development, obtain regulatory approval for, or commercialize GBT440, or experience delays in doing so, our business will be materially harmed.

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

GBT440 is currently our only product candidate to have advanced into what we characterize as a Phase 1/2 clinical trial, and it may be years before GBT can advance into a pivotal study, if at all. All of our other programs are in an early stage of research and development, and we have not yet selected any other product candidates for studies that would enable the filing of an Investigational New Drug application or for clinical evaluation. We cannot be certain that GBT440 will be successful in clinical trials or receive regulatory approval. If we do not receive regulatory approval for, or otherwise fail to successfully commercialize, GBT440, we may need to spend significant additional time and resources to identify other product candidates, advance them through preclinical and clinical development and apply for regulatory approvals, which would adversely affect our business, prospects, financial condition and results of operations.

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

We have concentrated our therapeutic product research and development efforts on developing novel, mechanism-based therapeutics for the treatment of grievous blood-based disorders, including SCD, and our future success depends on the successful development of this therapeutic approach. The clinical trial requirements of the FDA and other regulatory agencies and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential product. At the moment, there is only one approved therapy for SCD, hydroxyurea, and there are no approved therapeutics directed toward preventing the polymerization of hemoglobin molecules within RBCs as a mechanism to reduce RBC sickling in SCD patients. As a result, the design and conduct of clinical trials for a therapeutic that targets this mechanism in SCD are subject to unknown risks, and we may experience setbacks with our ongoing or planned clinical trials of GBT440 because of the limited clinical experience with its mechanism of

action in SCD patients. In particular, regulatory authorities in

the United States have not issued definitive guidance as to how to measure and achieve efficacy in SCD. Although we intend to evaluate exploratory endpoints, including anti-sickling and anti-hemolytic effects, changes in hemoglobin levels, and reticulocyte counts, for GBT440 in our Phase 1/2 clinical trial, regulators have not determined that such data signifies a clinically meaningful result in SCD patients or can support advancement into pivotal trials or regulatory approval. We may not achieve our pre-specified endpoints in our Phase 1/2 clinical trial or in other clinical trials where there is limited or no regulatory guidance regarding appropriate clinical endpoints, which would decrease the probability of obtaining marketing approval for GBT440 or any other product candidate we may develop. Any inability to design clinical trials with protocols and endpoints acceptable to applicable regulatory authorities, and to obtain regulatory approvals for GBT440 and other product candidates that we may pursue, would have an adverse impact on our business, prospects, financial condition and results of operations.

Results of earlier studies may not be predictive of future clinical trial results, and initial studies may not establish an adequate safety or efficacy profile for GBT440 and other product candidates that we may pursue to justify proceeding to advanced clinical trials or an application for regulatory approval.

The results of nonclinical and preclinical studies and clinical trials of GBT440 and other product candidates that we may pursue may not be predictive of the results of later-stage clinical trials, and interim results of a clinical trial do not necessarily predict final results. For example, our preclinical studies of GBT440 to date have involved only one genotype of SCD, HbSS, and the results of these studies may not be replicated in other genotypes of SCD or in human clinical trials. Additionally, any positive results generated in our Phase 1/2 clinical trial of GBT440 in adults would not ensure that we will achieve similar results in larger, pivotal clinical trials or in clinical trials of GBT440 in pediatric populations. In addition, preclinical and clinical data are often susceptible to various interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy despite having progressed through nonclinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier studies, and we cannot be certain that we will not face similar setbacks. Even if early stage clinical trials are successful, we may need to conduct additional clinical trials for product candidates in additional patient populations or under different treatment conditions before we are able to seek approvals from the FDA and regulatory authorities outside the United States to market and sell these product candidates. Our failure to demonstrate the required characteristics to support marketing approval for GBT440 or any other product candidate we may choose to develop in any ongoing or future clinical trials would substantially harm our business, prospects, financial condition and results of operations.

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

Before we can submit an NDA to the FDA for GBT440, we must successfully complete our ongoing clinical trial and one or more additional larger clinical trials. The FDA typically requires at least two pivotal, well-controlled clinical trials and does not consider a single clinical trial to be adequate to serve as a pivotal trial. The FDA will typically only consider relying on one pivotal trial if, in addition, other well-controlled studies of the drug exist (for example, for other dosage forms or in other populations) or if the pivotal trial is a multi-center trial that provides highly reliable and statistically strong evidence of an important clinical benefit, such as effect on survival, organ function or patient reported outcomes and a confirmatory study would have been difficult to conduct on ethical grounds. Although we characterize our current clinical trial of GBT440 as a Phase 1/2 clinical trial because it is designed to evaluate exploratory endpoints that we believe may be clinically relevant to SCD patients, it is possible that, even if we achieve

favorable results in our first clinical trial of GBT440, the FDA may require us to conduct an additional clinical trial, possibly involving a larger sample size or a different

clinical trial design, before we can initiate a pivotal trial. The FDA may also require that we conduct additional toxicology studies before evaluating GBT440 in longer term clinical trials or a longer follow-up period of subjects treated with GBT440 prior to accepting an NDA submission.

It is possible that the FDA or the comparable foreign authorities may not consider the results of our ongoing and planned clinical trials to be sufficient for approval of GBT440 for SCD. If the FDA or comparable foreign regulatory authorities require additional clinical trials or data beyond that which we currently anticipate, we would incur increased costs and delays in the clinical development and marketing approval process, which may require us to expend more resources than are available to us. In addition, it is possible that the FDA and the comparable foreign authorities may have divergent opinions on the elements necessary for a successful NDA and Marketing Authorization Application, or MAA, respectively, which may cause us to alter our development, regulatory and/or commercialization strategies.

We may encounter substantial delays in completing our clinical trials, which in turn will result in additional costs and may ultimately prevent successful or timely completion of the clinical development and commercialization of our product candidates.

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

- delays in reaching, or any failure to reach, a consensus with regulatory agencies on study design;
- delays in reaching, or failing to reach, agreement on acceptable terms with a sufficient number of prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- delays in obtaining required Institutional Review Board, or IRB, approval at each clinical trial site;
- delays in recruiting a sufficient number of suitable patients to participate in our clinical trials;
- imposition of a clinical hold by regulatory agencies, after an inspection of our clinical trial operations or study sites;
- failure by our CROs, other third parties or us to adhere to clinical trial, regulatory or legal requirements;
- failure to perform in accordance with the FDA s good clinical practices, or GCP, or applicable regulatory guidelines in other countries;

delays in the testing, validation, manufacturing and delivery of sufficient quantities of our product candidates to the clinical sites;

delays in having patients complete participation in a study or return for post-treatment follow-up;

clinical trial sites or patients dropping out of a trial;

delay or failure to address any patient safety concerns that arise during the course of a trial;

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

occurrence of serious adverse events associated with the product candidate that are viewed to outweigh its potential benefits; or

changes in regulatory requirements and guidance that require amending or submitting new clinical protocols.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by an independent Safety Review Board for such trial or by

the FDA or other regulatory authorities. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, and failure to demonstrate a benefit from using a drug. In addition, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional studies to bridge our modified product candidates to earlier versions.

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

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

Identifying and qualifying patients to participate in our ongoing and planned clinical trials of GBT440 and any other product candidates that we may develop are critical to our success. Our clinical development efforts are initially focused on rare chronic blood diseases. Accordingly, there are limited patient pools from which to draw for clinical trials. For example, according to CDC estimates, the prevalence of SCD, for which GBT440 is being studied, is 90,000 to 100,000 individuals in the United States. Although genetic screening for SCD is mandatory for newborns in the United States, we may not be able to identify, recruit, and enroll a sufficient number of patients to complete our clinical trials of GBT440 because of the perceived risks and benefits of GBT440, the availability of competing therapies and clinical trials, the proximity and availability of clinical trial sites for prospective patients and the patient referral practices of physicians. Further, if subjects in our clinical trials fail to comply with our dosing regimens, including the requirement that subjects in the multiple ascending dose cohorts of our Phase 1/2 clinical trial administer GBT440 orally on an outpatient basis, we may not be able to generate clinical data acceptable to the FDA in our trials. If patients are unwilling to participate in our studies for any reason, the timeline for recruiting patients, conducting studies and obtaining regulatory approval of potential products may be delayed.

If we experience difficulties or delays in enrollment or are otherwise unable to successfully complete any clinical trial of GBT440 or our other product candidates, our costs may increase, and our ability to obtain regulatory approval and generate product revenue from any of these product candidates will be impaired. Any of these occurrences would harm our business, prospects, financial condition and results of operations.

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

Clinical trials by their nature utilize a sample of the potential patient population. Our Phase 1/2 clinical trial of GBT440 is designed to enroll between 96 and 128 subjects, and to date, we have only begun to evaluate GBT440 in a limited number of subjects at a limited duration of exposure. Accordingly, any rare and severe side effects of GBT440 may be uncovered only in later stages of our Phase 1/2 trial or only in any larger, subsequent trials that we may conduct. Many product candidates that initially showed promise in early stage testing have later been found to cause side effects that prevented their further development. In particular, the development of tucaresol, a hemoglobin-modifying compound that was observed to have anti-hemolytic and anti-sickling effects in SCD patients, was discontinued by Burroughs Wellcome & Co. due to immune-related side effects. It is possible that GBT440,

which also binds to hemoglobin molecules, may result in similar or additional side effects. Moreover, a preclinical toxicology study with GBT440 in non-humans and clinical trials involving other hemoglobin modifiers have shown a decrease in oxygen delivery to tissue when the percentage of modified

hemoglobin is significant. Hemoglobin modifiers, by increasing HbS s affinity for oxygen, can cause a shift in oxygen levels, potentially resulting in tissue hypoxia. If GBT440 or any product candidates that we may develop are associated with tissue hypoxia or undesirable side effects in clinical trials or have characteristics that are unexpected, we may need to abandon their development or limit their development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective, which could adversely affect our business, prospects, financial condition and results of operations.

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

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

For example, a drug may be eligible for designation as a breakthrough therapy if the drug is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. Although breakthrough designation or access to any other expedited program may expedite the development or approval process, it does not change the standards for approval. If we apply for breakthrough therapy designation or any other expedited program for GBT440, the FDA may determine that GBT440, our proposed target indication or other aspects of our clinical development plans do not qualify for such expedited program. Even if we are successful in obtaining a breakthrough therapy designation or access to any other expedited program, we may not experience faster development timelines or achieve faster review or approval compared to conventional FDA procedures. Access to an expedited program may also be withdrawn by the FDA if it believes that the designation is no longer supported by data from our clinical development program. Additionally, qualification for any expedited review procedure does not ensure that we will ultimately obtain regulatory approval for GBT440 or any other product candidate that we may develop.

Even though we may apply for orphan drug designation for GBT440, we may not be able to obtain orphan drug marketing exclusivity for this product candidate or any of our other product candidates.

Our business strategy focuses on the development of product candidates for the treatment of rare, chronic blood disorders that may be eligible for FDA or European Union, or EU, orphan drug designation. Regulatory authorities in some jurisdictions, including the United States and the EU, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States. In the EU, the Committee for Orphan Medicinal Products of the European Medicines Agency, or EMA, grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the EU (or where it is unlikely that the development of the medicine would generate sufficient return to justify the investment) and for which no satisfactory method of diagnosis, prevention, or treatment is authorized or, if a method exists, the product would be of significant benefit to those affected by the condition.

Generally, if a drug with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug is entitled to a period of marketing exclusivity, which precludes

the FDA or the EMA from approving another marketing application for the same drug for that time period. The applicable period is seven years in the United States and 10 years in the EU. The EU exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if

the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

Although we may apply for orphan drug designation for GBT440 or other product candidates we may develop, applicable regulatory authorities may not grant us this designation. In addition, even if we obtain orphan drug exclusivity for GBT440 or any other product candidate that we may develop, that exclusivity may not effectively protect the candidate from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve another drug for the same condition if the FDA concludes that the later drug is clinically superior, in that it is shown to be safer, more effective or makes a major contribution to patient care. Any inability to secure orphan drug designation or the exclusivity benefits of this designation would have an adverse impact on our ability to develop and commercialize our product candidates.

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

Even if a product candidate is approved, regulatory authorities may still impose significant restrictions on its indicated uses or marketing or impose ongoing requirements for potentially costly post-marketing studies. Furthermore, any new legislation addressing drug safety issues could result in delays or increased costs to assure compliance. If GBT440 or any other product candidates that we may develop are approved, they will each be subject to ongoing regulatory requirements for labeling, packaging, storage, advertising, promotion, sampling, record-keeping and submission of safety and other post-market information, including both federal and state requirements in the United States. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates. For example, the development of GBT440 for the prophylactic treatment of SCD in pediatric patients is an important part of our current business strategy, and if we are unable to obtain regulatory approval for the desired age ranges, our business may suffer.

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

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

issue warning letters;

impose civil or criminal penalties;

impose injunctions;

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suspend regulatory approval;

suspend any of our ongoing clinical trials;

impose product recalls and publicity requirements;

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

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

seize or detain products or require a product recall.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenues from GBT440 or any future product candidates. If we are subject to regulatory sanctions or if regulatory approval for our product candidates is withdrawn or limited, our business, prospects, financial condition and results of operations would be harmed.

Risks Related to Our Reliance on Third Parties

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

We have relied upon and plan to continue to rely upon third-party CROs, including our CRO who monitors our Phase 1/2 clinical trial of GBT440 in London, UK, to monitor and manage data for some of our ongoing nonclinical and all of our clinical programs. We rely on these parties for execution of our nonclinical studies and clinical trials, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies and trials are conducted in accordance with the applicable protocol, legal, regulatory, and scientific standards and our reliance on the CROs does not relieve us of our regulatory responsibilities. We and our CROs and other vendors are required to comply with cGMP or GCP, and Good Laboratory Practices, or GLP, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area, or EEA, and comparable foreign regulatory authorities. Regulatory authorities enforce these regulations through periodic inspections of study sponsors, principal investigators, study sites, and other contractors. If we or any of our CROs or vendors fail to comply with applicable regulations, the data generated in our nonclinical studies and clinical trials may be deemed unreliable and the applicable regulatory authorities may require us to repeat or to perform additional nonclinical and clinical studies before approving our marketing applications, which would delay the regulatory approval process.

In addition, the execution of preclinical studies and clinical trials, and the subsequent compilation and analysis of the data produced, requires coordination among various parties. In order for these functions to be carried out effectively and efficiently, it is imperative that these parties communicate and coordinate with one another. These third parties may terminate their agreements with us upon as little as 30 days prior written notice of a material breach by us that is not cured within 30 days. Many of these agreements may also be terminated by such third parties under certain other

circumstances, including our failure to comply with applicable laws. If any of our relationships with our third-party CROs terminates, we may not be able to enter into arrangements with alternative CROs or do so on commercially reasonable terms. In addition, our CROs are not our employees, and except for remedies available to us under our agreements with such CROs, we cannot control whether they devote sufficient time and resources to our programs. Furthermore, these third party CROs may also have relationships with other entities, some of which may be our competitors. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our protocols, regulatory requirements, or for other reasons, our development activities may be extended, delayed, or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates.

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Switching or adding CROs involves additional cost, time and management resources and focus. CROs may also generate higher costs than anticipated.

Accordingly, our dependence on third-party CROs and other vendors may subject us to challenges, delays and costs that have a material adverse impact on our business, prospects, financial condition and results of operations.

We rely entirely on third parties for the manufacturing of our product candidates for preclinical studies and clinical trials and expect to continue to do so for commercialization. Our business could be harmed if those third parties fail to provide us with sufficient quantities of drug product, or fail to do so at acceptable quality levels or prices.

We do not currently have, nor do we plan to acquire, the infrastructure or capability internally to manufacture drug supplies for our ongoing Phase 1/2 clinical trial of GBT440 or any future clinical trials that we may conduct, and we lack the resources to manufacture any of our product candidates on a commercial scale. We rely, and expect to continue to rely, on third-party manufacturers to produce our product candidates for our clinical trials, as well as for commercial manufacture if any of our product candidates receives marketing approval. Although we generally do not begin a clinical trial unless we believe we have a sufficient supply of a product candidate to complete the trial, any significant delay or discontinuity in the supply of a product candidate, or the raw material components thereof, for an ongoing clinical trial due to the need to replace a third-party manufacturer could considerably delay the clinical development and potential regulatory approval of our product candidates, which could harm our business and results of operations. We also expect to rely on third parties for the manufacturing of commercial supply of GBT440 or any other product candidates, if approved.

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

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

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

GBT440 and any future product candidates that we may develop may compete with other product candidates and marketed drugs for access to manufacturing facilities. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We are currently manufacturing GBT440 through a third party and have adequate supplies to conduct our ongoing Phase 1/2 clinical trial, but we have not yet begun to produce the clinical supply of GBT440 for any larger pivotal trials that we may conduct. We do not currently have arrangements in place for redundant supply or a second source for bulk drug substance. If we are unable to enter into relationships with additional contract manufacturers, or our current or future contract manufacturers cannot perform as agreed, we may experience delays and incur additional costs in our clinical development and commercialization activities. Our current and anticipated future

dependence upon others for the manufacturing of our product candidates or marketed drugs may adversely affect our future profit margins and our ability to commercialize any product candidates that receive marketing approval on a timely and competitive basis.

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

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

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

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

Additionally, if supply from one approved manufacturer is interrupted, an alternative manufacturer would need to be qualified through an NDA supplement or MAA variation, or equivalent foreign regulatory filing, which could result in further delay. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

These factors could cause us to incur higher costs and could cause the delay or termination of clinical trials, regulatory submissions, required approvals, or commercialization of our product candidates. Furthermore, if our

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suppliers fail to meet contractual requirements and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials may be delayed or we could lose potential revenue.

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

Because we rely on third parties to manufacture GBT440 and conduct other aspects of our clinical development activities, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements or other similar agreements with any collaborators, CROs, manufacturers and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, such as trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor s discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

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

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain sufficient intellectual property protection for our product candidates, or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize product candidates similar or identical to ours, and our ability to successfully commercialize GBT440 and other product candidates that we may pursue may be impaired. Changes in patent policy and rules could impair our ability to protect our products and increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

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

Obtaining and enforcing biopharmaceutical patents is costly, time consuming and complex, and we may not be able to file and prosecute all necessary or desirable patent applications, or maintain, enforce and license any patents that may issue from such patent applications, at a reasonable cost or in a timely manner. It is also possible that we will fail to

identify patentable aspects of our research and development output before it is too late to obtain patent protection. We may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the rights to patents licensed to third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal, technological and factual questions and has in recent years been the subject of much litigation. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States, or vice versa. Further, we may not be aware of all third-party intellectual property rights potentially relating to our product candidates. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing or, in some cases, not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued that protect our product candidates, in whole or in part, or which effectively prevent others from commercializing competitive product candidates. Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our patents by developing similar or alternative product candidates in a non-infringing manner.

Moreover, we may be subject to a third-party preissuance submission of prior art to the United States Patent and Trademark Office, or the USPTO, or become involved in opposition, derivation, reexamination, *inter partes* review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize drugs without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

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

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

Assuming the other requirements for patentability are met, in the United States prior to March 15, 2013, the first to make the claimed invention is entitled to the patent, while outside the United States, the first to file a patent application is entitled to the patent. After March 15, 2013, under the Leahy-Smith America Invents Act, or the

Leahy-Smith Act, enacted on September 16, 2011, the United States has moved to a first to file system. The Leahy-Smith Act also includes a number of significant changes that affect the way patent applications will be prosecuted and may also affect patent litigation. The effects of these changes are currently unclear as the USPTO

must still implement various regulations, the courts have yet to address certain of these provisions and the applicability of the act and new regulations on specific patents discussed herein have not been determined and would need to be reviewed. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of patents that may issue from such patent applications, all of which could have a material adverse effect on our business and financial condition. Any further changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents and patent applications or narrow the scope of our potential patent protection.

We may become subject to claims alleging infringement of third parties patents or proprietary rights and/or claims seeking to invalidate our patents, which would be costly, time consuming and, if successfully asserted against us, delay or prevent the development and commercialization of GBT440 or any future product candidates that we may develop.

We cannot assure you that GBT440 or any future product candidates that we may develop will not infringe existing or future third-party patents. Because patent applications can take many years to issue and may be confidential for 18 months or more after filing, there may be applications now pending of which we are unaware and which may later result in issued patents that we may infringe by commercializing GBT440 or any future product candidates that we may develop. We may additionally be unaware of one or more issued patents that would be infringed by the manufacture, sale or use of GBT440 or any of our other product candidates.

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

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

Although we are not currently involved in any litigation, we may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our patents or other intellectual property. Although we are not currently involved in any litigation, if we were to initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is

invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, written description or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability is unpredictable.

Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference or derivation proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties, or enter into development partnerships that would help us bring our product candidates to market.

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

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

We may be subject to claims that former employees, collaborators or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. For example, inventorship disputes may arise from conflicting obligations of third parties involved in developing our product candidates or as a result of questions regarding co-ownership of potential joint inventions. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership or we may enter into agreements to clarify the scope of our rights in such intellectual property. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

We jointly own patents and patent applications with third parties. Our ability to exploit or enforce these patent rights, or to prevent the third party from granting licenses to others with respect to these patent rights, may be limited in some circumstances.

We jointly own certain patents and patent applications with third parties. In particular, the Regents of the University of California, or the Regents, have indicated that certain of our patents and patent applications relating to GBT440 and GBT440 analogs may have been jointly invented by us and employees of the university and, accordingly, may be jointly owned by us and the Regents. In the absence of an agreement with each co-owner of jointly owned patent rights, we will be subject to default rules pertaining to joint ownership. Some countries require the consent of all joint owners to exploit, license or assign jointly owned patents, and if we are unable to obtain that consent from the joint owner, we may be unable to exploit the invention or to license or assign our rights under these patents and patent

applications in those countries. In other countries, such as the United States, the joint owner could license or assign its rights under these patents and patent applications to another party without our consent and without any duty of accounting to us. Additionally, in the United States, the Regents may be required to be joined as a party to any claim or action we may wish to bring to enforce these patent rights, which may limit our ability to pursue third party infringement claims. We are currently in active discussions with

the Regents to obtain an exclusive license on commercially reasonable terms to the Regents interest in any GBT440 and GBT440 analog patent rights that we may jointly own with the Regents and anticipate that potential payments for the licensed rights may be scaled based on an independent third-party determination of inventorship. Based on these discussions to date, we believe the consideration for such licensed rights will not have a significant effect on our financial results or financial position. There is no assurance, however, that we will be able to obtain such a license on terms that we deem to be acceptable, or at all. If the Regents are deemed to be a joint owner of any patent rights relating to GBT440 or GBT440 analogs and we are unable to obtain an exclusive license to these rights, we may be required to seek and obtain the consent of the Regents to exploit these rights in connection with the commercialization of GBT440 or GBT440 analogs in certain foreign jurisdictions or to license or assign them to a third party, and we may not be able to prevent the Regents from granting licenses to these rights or assigning them to a third party in the United States.

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

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

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

We seek to protect our confidential proprietary information, in part, by confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and collaborators. These agreements are designed to protect our proprietary information. However, we cannot be certain that such agreements have been entered into with all relevant parties, and we cannot be certain that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. For example, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. We also seek to preserve the integrity and confidentiality of our confidential proprietary information by maintaining physical security of our premises and physical and electronic security of our information technology systems, but it is possible that these security measures could be breached. If any of our confidential proprietary information were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position.

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

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. We have systems in place to remind us to pay these fees, and we employ an outside firm and rely on our outside counsel to pay these fees due to non-

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U.S. patent agencies. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business.

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

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

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

Risks Related to Commercialization

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

If GBT440 or other product candidates that we may pursue receives marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant revenue from drug sales and we may not become profitable. Before granting reimbursement approval, healthcare payors may require us to demonstrate that our product candidates, in addition to treating these target indications, also provide incremental health benefits to patients. Our efforts to educate the medical community and third-party payors about the benefits of our product candidates may require significant resources and may never be successful. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

the efficacy and potential advantages compared to alternative treatments, such as, in the case of GBT440, hydroxyurea;

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our ability to offer our drugs for sale at competitive prices;

the convenience and ease of administration compared to alternative treatments, including future alternative treatments;

the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;

the availability of products and their ability to meet market demand, including a reliable supply for long-term daily treatment;

the strength of marketing and distribution support;

the availability of third-party coverage and adequate reimbursement;

the clinical indications for which the product is approved;

the prevalence and severity of any side effects and overall safety profile; and

any restrictions on the use of our drugs together with other medications.

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

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

Further, given our lack of prior experience in marketing and selling biopharmaceutical products, our initial estimate of the size of the required sales force may be materially more or less than the size of the sales force actually required to effectively commercialize our product candidates. As such, we may be required to hire substantially more sales representatives to adequately support the commercialization of our product candidates or we may incur excess costs as a result of hiring more sales representatives than necessary. With respect to certain geographical markets, we may enter into collaborations with other entities to utilize their local marketing and distribution capabilities, but we may be unable to enter into such agreements on favorable terms, if at all. If our future collaborators do not commit sufficient resources to commercialize our future products, if any, and we are unable to develop the necessary marketing

capabilities on our own, we will be unable to generate sufficient product revenue to sustain our business. We may be competing with companies that currently have extensive and well-funded marketing and sales operations. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

The insurance coverage and reimbursement status of newly-approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for new or current products could limit our ability to market those products and decrease our ability to generate revenue.

Our target patient populations are small, and accordingly the pricing, coverage and reimbursement of our product candidates, if approved, must be adequate to support our commercial infrastructure. Our per-patient prices must be sufficient to recover our development and manufacturing costs and potentially achieve

profitability. Accordingly, the availability and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford expensive treatments, such as ours, assuming approval. Sales of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors. If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, as CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicaid or Medicare. However, the practices and requirements relating to the payment of rebates by drug manufacturers for Medicaid purchases are determined by each state, and in some cases, if a company does not enter into a rebate agreement, its Medicaid sales will be subjected to a prior authorization procedure that requires state agency approval to qualify a doctor s prescription for reimbursement.

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

Moreover, increasing efforts by governmental and third-party payors, in the United States and abroad, to cap or reduce healthcare costs may cause such organizations to limit both coverage and level of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of any of our product candidates, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

In light of the large population of patients with SCD who reside in foreign countries, our ability to generate meaningful revenues in those jurisdictions may be limited due to the strict price controls and reimbursement limitations imposed by governments outside of the United States.

In some countries, particularly in the EU, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. To obtain coverage and reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If reimbursement of our product candidates is unavailable or limited in scope or amount,

or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially, based on the large population of patients with SCD who reside in foreign countries.

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

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or the Health Care Reform Law, was passed, which substantially changes the way health care is financed by both governmental and private insurers, and significantly impacts the U.S. pharmaceutical industry. The Health Care Reform Law, among other things, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs, and promoted a new Medicare Part D coverage gap discount program.

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

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

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

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

We focus our research and product development on treatments for chronic blood diseases, with an initial focus on SCD. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including the scientific literature, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. The effort to identify patients with diseases we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. Additionally, the potentially addressable patient population for each of our product candidates may be limited or may not be amenable to treatment with our product candidates, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business. Further, even if we obtain significant market share for our product candidates, because the potential target populations are small, we may never achieve profitability despite obtaining such significant market share.

Risks Related to Our Business and Industry

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

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

Recruiting and retaining qualified scientific and clinical personnel and, if we progress the development of our drug pipeline toward scaling up for commercialization, sales and marketing personnel, will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval for and commercialize our product candidates. Competition to hire qualified personnel in our industry is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. Furthermore, to the extent we hire personnel from competitors, we may be subject to allegations that they have been improperly solicited or that they have divulged proprietary or other confidential information, or that their former employers own their research output. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

We expect to expand our product development capabilities and potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could

disrupt our operations.

As our development progresses, we expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of research, drug development, regulatory affairs and, if

any of our product candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

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

Although a substantial amount of our effort will focus on the continued clinical testing, potential approval and commercialization of GBT440, a key element of our strategy is to pursue, develop and commercialize a portfolio of products utilizing proprietary discovery and development technology. We are seeking to do so through our internal research programs and may also selectively pursue commercially synergistic in-licensing or acquisition of additional assets. With the exception of GBT440, all of our other potential product candidates remain in the preclinical development stage. Research programs to identify product candidates require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for many reasons, including the following:

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

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

commercializing GBT440.

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

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

impairment of our business reputation;

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withdrawal of clinical trial participants;

costs due to related litigation;

distraction of management s attention from our primary business;

substantial monetary awards to patients or other claimants;

increased FDA warnings on product labels;

the inability to commercialize our product candidates; and

decreased demand for our product candidates, if approved for commercial sale.

We carry product liability insurance in amounts that we believe are sufficient in light of our current clinical programs; however, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If and when we obtain marketing approval for product candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. On occasion, large judgments have been awarded in class action lawsuits based on drugs or medical treatments that had unanticipated adverse effects. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business.

During the course of treatment, patients may suffer adverse events, including death, for reasons that may or may not be related to our product candidates. Such events could subject us to costly litigation, require us to pay substantial amounts of money to injured patients, delay, negatively impact or end our opportunity to receive or maintain regulatory approval to market our product candidates, if approved, or require us to suspend or abandon our commercialization efforts of any approved product candidates. Even in a circumstance in which we do not believe that an adverse event is related to our products, the investigation into the circumstance may be time-consuming or inconclusive. These investigations may interrupt our sales efforts, delay our regulatory approval process in other countries, or impact and limit the type of regulatory approvals our product candidates receive or maintain. As a result of these factors, a product liability claim, even if successfully defended, could have a material adverse effect on our business, financial condition or results of operations.

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

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting

damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

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

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

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

Because we have limited resources, we may forego or delay the pursuit of opportunities with certain programs or product candidates or for indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs for product candidates, including GBT440, may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate, or we may allocate internal resources to a product candidate in a therapeutic area in which it would have been more advantageous to enter into a partnering arrangement.

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

We may seek collaboration arrangements with pharmaceutical or biotechnology companies for the development or commercialization of GBT440 and potential future product candidates. We may enter into these arrangements on a selective basis depending on the merits of retaining commercialization rights for ourselves as compared to entering into selective collaboration arrangements with leading pharmaceutical or biotechnology companies for our product candidates, both in the United States and internationally. We will face, to the extent that we decide to enter into collaboration agreements, significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator s resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator s evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or comparable foreign regulatory authorities, the potential market for a product candidate, the costs and complexities of manufacturing and delivering a product candidate to patients, the potential of competing products, any uncertainty with respect to our ownership of technology, which can occur if there is a challenge to our ownership without regard to the merits of the challenge and industry and market conditions generally. Moreover, collaboration arrangements are complex and time consuming to negotiate, document and implement, and we have not previously established our ability to do so successfully. We may not be successful in our efforts to establish and implement collaborations or other alternative arrangements should we so chose to enter into such arrangements. The terms of any collaborations or other arrangements that we may establish may not be favorable to us.

Any future collaborations that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations. Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable product candidate and, in some cases, termination of the collaboration arrangement. These disagreements can be difficult to resolve if neither of the parties has final decision-making authority under the collaboration agreement. Collaborations with pharmaceutical or biotechnology companies and other third parties often are terminated or allowed to expire by the other party. Any such termination or expiration would adversely affect us financially and could harm our business reputation.

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

We currently have no international operations, but our business strategy incorporates potential international expansion as we seek to obtain regulatory approval for, and commercialize, GBT440 in patient populations

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outside the United States. If GBT440 is approved, we may hire sales representatives and conduct physician and patient association outreach activities outside of the United States. Doing business internationally involves a number of risks, including but not limited to:

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

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

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

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. The recent global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the recent global financial crisis, could result in a variety of risks to our business, including reduced ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

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

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

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currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

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

Despite the implementation of security measures, our internal computer systems and those of our third-party CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs. For example, the loss of clinical trial data for our product candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications or other data or applications relating to our technology or product candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of our product candidates could be delayed.

Risks Related to Our Equity Securities and This Offering

We have identified a material weakness in our internal control over financial reporting. If our remediation of this material weakness is not effective, or if we experience additional material weaknesses in the future or otherwise fail to maintain an effective system of internal controls in the future, we may not be able to accurately or timely report our financial condition or results of operations, which may adversely affect investor confidence in us and, as a result, the value of our common stock.

Prior to the completion of this offering, we have been a private company with limited accounting personnel to adequately execute our accounting processes and other supervisory resources with which to address our internal control over financial reporting. In connection with the audit of our financial statements as of and for the years ended December 31, 2014 and 2013, we identified a material weakness in our internal control over financial reporting. A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of our financial statements will not be prevented or detected on a timely basis. The material weakness related to a lack of sufficient number of qualified personnel within our accounting function to adequately segregate duties, a lack of sufficient review and approval of manual journal entries posted to the general ledger and a lack of adequate review procedures over general ledger account reconciliations.

We are implementing measures designed to improve our internal control over financial reporting to remediate this material weakness, including the following:

- We are formalizing our internal control documentation and strengthening supervisory reviews by our management; and

We are in the process of adding additional accounting personnel and segregating duties amongst accounting personnel.

We cannot assure you that the measures we have taken to date, and are continuing to implement, will be sufficient to remediate the material weakness we have identified or avoid potential future material weaknesses. If the steps we take do not correct the material weakness in a timely manner, we will be unable to conclude that we maintain effective internal control over financial reporting. Accordingly, there could continue to be a reasonable possibility that a material misstatement of our financial statements would not be prevented or detected on a timely basis.

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As a public company, we will be required to maintain internal control over financial reporting and to report any material weaknesses in such internal controls. Section 404 of the Sarbanes-Oxley Act requires that we evaluate and determine the effectiveness of our internal control over financial reporting and, beginning with our second annual report following this offering, which will be our year ending December 31, 2016, provide a management report on internal control over financial reporting. The Sarbanes-Oxley Act also requires that our management report on internal control over financial reporting be attested to by our independent registered public accounting firm, to the extent we are no longer an emerging growth company, as defined in the JOBS Act. We do not expect our independent registered public accounting firm to attest to our management report on internal control over financial reporting for so long as we are an emerging growth company.

We are in the process of designing and implementing the internal control over financial reporting required to comply with this obligation, which process will be time consuming, costly and complicated. If we identify any additional material weaknesses in our internal control over financial reporting, if we are unable to comply with the requirements of Section 404 in a timely manner, if we are unable to assert that our internal control over financial reporting is effective, or when required in the future, if our independent registered public accounting firm is unable to express an opinion as to the effectiveness of our internal control over financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports and the market price of our common stock could be adversely affected, and we could become subject to investigations by the stock exchange on which our securities are listed, the SEC, or other regulatory authorities, which could require additional financial and management resources.

We are an emerging growth company, and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies will make our common stock less attractive to investors.

We are an emerging growth company as defined in the Jumpstart Our Business Startups Act of 2012, as amended, or the JOBS Act, and we intend to take advantage of some of the exemptions from reporting requirements that are applicable to other public companies that are not emerging growth companies, including:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced Management s Discussion and Analysis of Financial Condition and Results of Operations disclosure;
- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor s report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- not being required to hold a non-binding advisory vote on executive compensation or obtain stockholder approval of any golden parachute payments not previously approved.

We cannot predict if investors will find our common stock less attractive because we will rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. We may take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the completion of this offering, (b) in which we have total annual gross revenue of at least $1.0 billion or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

Under Section 107(b) of the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected

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not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

The market price of our common stock may be highly volatile, and you may not be able to resell your shares at or above the initial public offering price.

Prior to this offering, there has not been a public market for our common stock. An active trading market for our common stock may not develop following this offering. You may not be able to sell your shares quickly or at the market price if trading in our common stock is not active. The initial public offering price for the shares was determined by negotiations between us and the representative of the underwriters and may not be indicative of prices that will prevail in the trading market.

The market price of our common stock is likely to be volatile. Our stock price could be subject to wide fluctuations in response to a variety of factors, including the following:

- adverse results or delays in preclinical studies or clinical trials;
- reports of adverse events in other SCD treatments or clinical trials of such products;
- inability to obtain additional funding;
- any delay in filing an IND or NDA for any of our product candidates that we may develop and any adverse development or perceived adverse development with respect to the FDA s review of that IND or NDA;
- failure to develop successfully and commercialize GBT440 or any other product candidates that we may develop;
- our failure to prosecute, maintain or enforce our intellectual property rights;
- changes in laws or regulations applicable to future products;
- inability to obtain adequate product supply for our product candidates or the inability to do so at acceptable prices;
- adverse regulatory decisions;
- introduction of new products, services or technologies by our competitors;

failure to enter into strategic collaborations;

failure to meet or exceed any financial projections that we or the investment community may provide;

the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;

announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;

disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;

additions or departures of key scientific or management personnel;

significant lawsuits, including patent or stockholder litigation;

changes in the market valuations of similar companies;

sales of our common stock by us or our stockholders in the future;

trading volume of our common stock; and

the other risks described in this Risk Factors section.

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In addition, companies trading in the stock market in general, and The NASDAQ Global Select Market in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. In the past, following periods of volatility in the market, securities class-action litigation has often been instituted against companies. Such litigation, if instituted against us, could result in substantial costs and diversion of management s attention and resources, which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

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

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

- the timing and cost of, and level of investment in, research and development activities relating to our product candidates, which may change from time to time;
- the cost of manufacturing our product candidates, which may vary depending on the quantity of production and the terms of our agreements with manufacturers;
- our ability to attract, hire and retain qualified personnel;
- the timing and success or failure of clinical trials for our product candidates or competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners;
- our ability to obtain regulatory approval for our product candidates, and the timing and scope of any such approvals we may receive;
- expenditures that we will or may incur to acquire or develop additional product candidates and technologies;
- the level of demand for our product candidates, should they receive approval, which may vary significantly;
- future accounting pronouncements or changes in our accounting policies;
- the risk/benefit profile, cost and reimbursement policies with respect to our products candidates, if approved, and existing and potential future drugs that compete with our product candidates;

and

the changing and volatile U.S., European and global economic environments.

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

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 pro forma book value per share of our tangible assets after subtracting our liabilities. As a result,

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investors purchasing shares of common stock in this offering will incur immediate dilution of $14.45 per share, based on the initial public offering price of $20.00 per share and our pro forma net tangible book value as of March 31, 2015.

Further, based on these assumptions, investors purchasing shares of common stock in this offering will contribute approximately 55% of the total amount invested by stockholders since our inception, but will own only approximately 22% of the shares of common stock outstanding. For information on how the foregoing amounts were calculated, see Dilution.

This dilution is due to the substantially lower price paid by our investors who purchased shares prior to this offering as compared to the price offered to the public in this offering, and the exercise price of stock options granted to our employees. In addition, as of March 31, 2015, options to purchase 1,190,051 shares of our common stock at a weighted average exercise price of $0.81 per share were outstanding. The exercise of any of these options or any outstanding options granted subsequent to March 31, 2015 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.

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

We will need additional capital in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

Pursuant to our 2015 Stock Option and Incentive Plan, or the 2015 Plan, which became effective upon the effectiveness of the registration statement of which this prospectus is a part, we are authorized to grant stock options and other equity-based awards to our employees, directors and consultants. The number of shares available for future grant under the 2015 Plan will automatically increase each year by up to 4% of all shares of our capital stock outstanding as of December 31 of the prior calendar year, subject to the ability of our board of directors or compensation committee to take action to reduce the size of the increase in any given year. In addition, 50,000 shares of our common stock are reserved for future issuance pursuant to our 2015 ESPP, which number of shares will automatically increase each year on January 1, from January 1, 2016 to January 1, 2025, by the lesser of (i) 3,000,000 shares of common stock, (ii) 1% of all shares of our capital stock outstanding as of December 31 of the prior calendar year, or (iii) such lesser number of shares as determined by the administrator of our 2015 ESPP. Currently, we plan to register the increased number of shares available for issuance under the 2015 Plan and the 2015 ESPP each year. If our board of directors elects to increase the number of shares available for future grant by the maximum amount each year, our stockholders may experience additional dilution, and our stock price may fall.

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

Sales of a substantial number of shares of our common stock in the public market could occur at any time. If our stockholders sell, or if the market perceives that our stockholders intend to sell, substantial amounts of our common stock in the public market following this offering, the price of our common stock could decline significantly. Based

upon the number of shares of common stock outstanding on an as-converted basis as of June 30, 2015, we will have outstanding a total of 29,429,554 shares of common stock after the completion of this offering, assuming no exercise of the underwriters option to purchase additional shares. Of these shares,

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approximately 5,794,942 shares of our common stock, plus any shares sold upon exercise of the underwriters option to purchase additional shares, will be freely tradable, without restriction, in the public market immediately following this offering.

The lock-up agreements pertaining to this offering will expire 180 days from the date of this prospectus (subject to extension upon the occurrence of specified events). Morgan Stanley & Co. LLC and Goldman, Sachs & Co., however, may, in their sole discretion, permit stockholders who are subject to these lock-up agreements to sell shares prior to the expiration of the lock-up agreements. Participants in the directed share program, which provides for the sale of up to 5% of the shares of common stock offered by this prospectus, have agreed to similar restrictions for 180 days following the date of this prospectus, which restrictions may be waived with the prior written consent of the representatives of the underwriters. See Underwriting Directed Share Program. After the lock-up agreements expire, based upon the number of shares of common stock outstanding on an as-converted basis as of June 30, 2015, up to an additional 23,334,612 shares of common stock will be eligible for sale in the public market, 19,433,039 of which shares are held by directors, executive officers and other affiliates and will be subject to Rule 144 under the Securities Act of 1933, as amended, or the Securities Act.

In addition, in connection with this offering, we intend to file one or more registration statements on Form S-8 registering the issuance of approximately 3.2 million shares of common stock subject to options or other equity awards issued or reserved for future issuance under our equity incentive plans. Shares registered under these registration statements on Form S-8 will be available for sale in the public market subject to vesting arrangements and exercise of options, the lock-up agreements described above and the restrictions of Rule 144 in the case of our affiliates.

Additionally, after this offering, the holders of an aggregate of 20,318,042 shares of our common stock, or their transferees, will have rights, subject to some conditions, to require us to file one or more registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. If we were to register the resale of these shares, they could be freely sold in the public market. If these additional shares are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

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

Our executive officers, directors, five percent stockholders and their affiliates beneficially own approximately 82.8% of our voting stock as of June 30, 2015 and, upon closing of this offering, that same group will beneficially own approximately 66% of our outstanding voting stock. Therefore, even after this offering, these stockholders will have the ability to influence us through their ownership positions. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders, acting together, may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may believe are in your best interest as one of our stockholders.

We will have broad discretion in the use of proceeds from this offering and may invest or spend the proceeds in ways with which you do not agree or in ways that ultimately may not increase the value of your investment.

We will have broad discretion over the use of proceeds from this offering. You may not agree with our decisions, and our use of the proceeds may not yield any return on your investment. We expect to use the net proceeds to us from this offering to continue the clinical development of GBT440, to fund the research and development of our other

programs, and for working capital and general corporate purposes. Our failure to apply the net proceeds from this offering effectively could compromise our ability to pursue our growth strategy and

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we might not be able to yield a significant return, if any, on our investment of these net proceeds. In addition, the net proceeds from this offering may not be sufficient for our anticipated uses, and we may need additional resources to progress our product candidates to the stage we expect. You will not have the opportunity to influence our decisions on how to use our net proceeds from this offering.

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

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

authorize blank check preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;

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

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

prohibit stockholder action by written consent;

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

provide that our directors may be removed only for cause;

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

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

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

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

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

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

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

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

We have incurred substantial losses during our history and do not expect to become profitable in the near future and we may never achieve profitability. To the extent that we continue to generate taxable losses, unused

losses will carry forward to offset future taxable income, if any, until such unused losses expire. Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an ownership change, generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation s ability to use its pre-change net operating loss carryforwards, or NOLs, and other pre-change tax attributes (such as research tax credits) to offset its post-change income or taxes may be limited. Our prior equity offerings and other changes in our stock ownership may have resulted in ownership changes. In addition, we may experience ownership changes in the future as a result of this offering or subsequent shifts in our stock ownership, some of which are outside of our control. As a result, if we earn net taxable income, our ability to use our pre-change net operating loss carryforwards to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

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

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

If we fail to maintain proper and effective internal controls, our ability to produce accurate and timely financial statements could be impaired, which could result in sanctions or other penalties that would harm our business.

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

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

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

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An active trading market for our common stock may not develop and you may not be able to resell your shares of our common stock at or above the initial offering price, if at all.

Prior to this offering, there has been no public market for our common stock. The initial public offering price for our common stock was determined through negotiations with the underwriters and may not be indicative of the price at which our common stock will trade upon the completion of this offering. Although our common stock has been approved for listing on The NASDAQ Global Select Market, an active trading market for our shares may never develop or be sustained following this offering. If an active market for our common stock does not develop or is not sustained, it may be difficult for you to sell shares you purchased in this offering at an attractive price, if at all.

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

As a public company, we will incur significant legal, accounting, and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act, as well as rules subsequently implemented by the SEC and The NASDAQ Global Select Market have imposed various requirements on public companies. In July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act, was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas such as say on pay and pay parity. Recent legislation permits smaller emerging growth companies to implement many of these requirements over a longer period and up to five years from the pricing of this offering. We intend to take advantage of this new legislation but cannot guarantee that we will not be required to implement these requirements sooner than budgeted or planned and thereby incur unexpected expenses. Stockholder activism, the current political environment, and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time consuming and costly. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain our current levels of such coverage.

The Sarbanes-Oxley Act requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. In particular, we will be required to perform system and process evaluation and testing of our internal controls over financial reporting to allow management to report, commencing in our annual report on Form 10-K for the year ending December 31, 2015, on the effectiveness of our internal controls over financial reporting, if then required by Section 404 of the Sarbanes-Oxley Act. Our testing may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses. Our compliance with Section 404 will require that we incur substantial accounting expense and expend significant management efforts. We currently do not have an internal audit group, and we will need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge. Moreover, if we are not able to comply with the requirements of Section 404 in a timely manner or if we identify or our independent registered public accounting firm identifies deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses, the market price of our stock could decline and we could be subject to sanctions or investigations by NASDAQ, the SEC, or other regulatory authorities, which would require additional financial and management resources.

Our ability to successfully implement our business plan and comply with Section 404 requires us to be able to prepare timely and accurate financial statements. We expect that we will need to continue to improve existing, and implement

new operational and financial systems, procedures and controls to manage our business effectively. Any delay in the implementation of, or disruption in the transition to, new or enhanced systems,

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procedures or controls, may cause our operations to suffer and we may be unable to conclude that our internal control over financial reporting is effective and, when we are no longer an emerging growth company, to obtain an unqualified report on internal controls from our auditors as required under Section 404 of the Sarbanes-Oxley Act. This, in turn, could have an adverse impact on trading prices for our common stock, and could adversely affect our ability to access the capital markets.

New laws and regulations as well as changes to existing laws and regulations affecting public companies, including the provisions of the Sarbanes-Oxley Act and rules adopted by the SEC and by NASDAQ, would likely result in increased costs to us as we respond to their requirements.

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

The trading market for our common stock will depend, in part, on the research and reports that securities or industry analysts publish about us or our business. Securities and industry analysts do not currently, and may never, publish research on our company. If no securities or industry analysts commence coverage of our company, the trading price for our stock would likely be negatively impacted. In the event that securities or industry analysts initiate coverage, if one or more of the analysts who cover us downgrade our stock or publish inaccurate or unfavorable research about our business, our stock price would likely decline. In addition, if our operating results fail to meet the forecast of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the sections entitled Prospectus Summary, Risk Factors, Management s Discussion and Analysis of Financial Condition and Results of Operations and Business, contains forward-looking statements that are based on our management s belief and assumptions and on information currently available to our management. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth, 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 in this prospectus include, but are not limited to, statements about:

- our expected uses of the net proceeds to us from this offering;
- the timing and the success of our ongoing Phase 1/2 clinical trial of GBT440 in healthy adult subjects and SCD patients;
- the timing and success of our planned additional clinical trials of GBT440 in pediatric patients and of any other product candidates we may develop;
- 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;
- our ability to obtain, including on an expedited basis, and maintain regulatory approval of GBT440 or any other product candidates we may develop;
- our expectation that our existing capital resources and the net proceeds from this offering will be sufficient to enable us to fund our planned development of GBT440 and any other product candidates we may identify and pursue;
- the benefits of the use of GBT440;
- 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 obtain orphan drug designation for GBT440 or any other product candidates we may identify and pursue in the United States, Europe or any other jurisdiction;

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

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

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;

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- our estimates of our expenses, ongoing losses, future revenue, capital requirements and our needs for or ability to obtain additional financing;
- our expectations regarding the time during which we will be an emerging growth company under the JOBS Act;
- our financial performance; and
- developments and projections relating to our competitors or our industry.

In some cases, you can identify forward-looking statements by terminology such as may, will, should, expects, intends, plans, anticipates, believes, estimates, predicts, potential, continue or the negative of these tern comparable terminology. These statements are only predictions. You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties and other factors, which are, in some cases, beyond our control and which could materially affect results. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under Risk Factors and elsewhere in this prospectus. If one or more of these risks or uncertainties occur, or if our underlying assumptions prove to be incorrect, actual events or results may vary significantly from those implied or projected by the forward-looking statements. No forward-looking statement is a guarantee of future performance. You should read this prospectus and the documents that we reference in this prospectus and have filed with the SEC as exhibits to the registration statement, of which this prospectus is a part, completely and with the understanding that our actual future results may be materially different from any future results expressed or implied by these forward-looking statements.

The forward-looking statements in this prospectus represent our views as of the date of this prospectus. 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 date of this prospectus.

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

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USE OF PROCEEDS

We estimate that our net proceeds from the sale of shares of our common stock in this offering will be approximately $109.4 million, or $126.1 million if the underwriters exercise in full their option to purchase additional shares, based upon the initial public offering price of $20.00 per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering and our cash and cash equivalents on hand as follows:

- approximately $50.0 million to fund our development of GBT440 for the treatment of SCD, including the completion of our ongoing Phase 1/2 clinical trial, planned clinical pharmacology studies and through the initiation of a pivotal clinical trial;
- approximately $15.0 million to conduct clinical trials of GBT440 or its analogs for the treatment of hypoxemic pulmonary disorders;
- approximately $15.0 million to complete and file an IND and begin a Phase 1/2 clinical trial of an oral kallikrein inhibitor for the treatment of HAE; and
- the remaining proceeds to fund new and ongoing research and development activities, working capital and other general corporate purposes, which may include funding for the hiring of additional personnel, capital expenditures and the costs of operating as a public company.

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 through early 2017.

We may also use a portion of the net proceeds to in-license, acquire or invest in new businesses, technology or assets. We are currently in active discussions with the Regents of the University of California, or the Regents, to obtain an exclusive license on commercially reasonable terms to the Regents interest in any GBT440 and GBT440 analog patent rights that we may jointly own with the Regents. Although we have no other specific agreements, commitments or understandings with respect to any in-license or acquisition, we evaluate such opportunities and engage in related discussions with other companies from time to time.

This expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions. As of the date of this prospectus, 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. 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 non-clinical studies and our ongoing clinical trial or any clinical trials we may commence in the future, our ability to take advantage of expedited programs or to obtain regulatory approval for GBT440 and any other product candidates we may identify and pursue, the timing and costs associated with the manufacture and supply of GBT440 and any other product candidates we may identify and pursue for clinical development or commercialization, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering.

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

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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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CAPITALIZATION

The following table sets forth our cash and cash equivalents and capitalization as of March 31, 2015:

- on an actual basis;
- on a pro forma basis to reflect (i) the conversion of all of the outstanding shares of our redeemable convertible preferred stock into an aggregate of 19,746,614 shares of common stock immediately prior to the completion of this offering and (ii) the filing and effectiveness of our restated certificate of incorporation following the conversion of all outstanding shares of our redeemable convertible preferred stock; and
- on a pro forma as adjusted basis to give further effect to the sale of shares of common stock in this offering at the initial public offering price of $20.00 per share, after deducting the underwriting discount and commissions and estimated offering expenses payable by us.

You should read this information together with our audited financial statements and related notes appearing elsewhere in this prospectus and the information set forth under the heading Selected Financial Data and Management s Discussion and Analysis of Financial Condition and Results of Operations.

	As of March 31, 2015		
	Actual	Pro Forma (unaudited)	Pro Forma As Adjusted
	(in thousands, except share and per share data)		
Cash and cash equivalents	$ 45,800	$ 45,800	$ 155,150
Redeemable convertible preferred stock, $0.001 par value per share 69,363,168 shares authorized; 69,113,168 shares issued and outstanding, actual; no shares issued and outstanding, pro forma and pro forma as adjusted	$ 103,396		
Stockholders (deficit) equity:			
Preferred stock, $0.001 par value; no shares authorized, issued and outstanding, actual; 5,000,000 shares authorized, no shares issued and outstanding, pro forma and pro forma as adjusted			
Common stock, $0.001 par value per share 94,000,000 shares authorized; 2,061,843 shares issued and outstanding, actual; 150,000,000 shares authorized, 21,808,457 shares issued and outstanding, pro forma and 27,808,457 shares issued and outstanding, pro forma as adjusted	2	22	28
Additional paid-in capital		103,376	212,720
Accumulated deficit	(57,652)	(57,652)	(57,652)

Total stockholders (deficit) equity	(57,650)	45,746	155,096
Total capitalization	$ 45,746	$ 45,746	$ 155,096

The number of shares of common stock issued and outstanding actual, pro forma and pro forma as adjusted in the table above excludes the following:

1,190,051 shares of our common stock issuable upon the exercise of stock options to purchase common stock that were outstanding as of March 31, 2015, with a weighted average exercise price of $0.81 per share;

985,338 shares of restricted common stock which were subject to our right of repurchase as of March 31, 2015;

882,557 shares of common stock issuable upon exercise of options granted subsequent to March 31, 2015 at a weighted-average exercise price of $4.21 per share and 607,853 shares of restricted common stock issued subsequent to March 31, 2015 at a purchase price of $3.40 per share;

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445,620 shares of common stock reserved for future issuance under our 2012 Stock Option and Grant Plan, or the 2012 Plan, as of March 31, 2015;

1,430,000 shares of common stock reserved for future issuance under our 2015 Stock Option and Incentive Plan, or the 2015 Plan, which became effective upon the effectiveness of the registration statement of which this prospectus is a part; and

50,000 shares of common stock reserved for future issuance under the 2015 ESPP, which became effective upon the effectiveness of the registration statement of which this prospectus is a part.

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DILUTION

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

Net tangible book value per share is determined by dividing our total tangible assets less our total liabilities by the number of shares of common stock outstanding. Our historical net tangible book value as of March 31, 2015 was $(58.3) million, or $(28.29) per share. Our pro forma net tangible book value as of March 31, 2015 was $45.1 million, or $2.07 per share, based on the total number of shares of our common stock outstanding as of March 31, 2015, after giving effect to the automatic conversion of all outstanding shares of our redeemable convertible preferred stock as of March 31, 2015 into an aggregate of 19,746,614 shares of common stock upon completion of this offering.

Net tangible book value dilution per share to new investors represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the pro forma as adjusted net tangible book value per share of common stock immediately after completion of this offering. After giving effect to our sale of shares of common stock in this offering at the initial public offering price of $20.00 per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of March 31, 2015 would have been $154.4 million, or $5.55 per share. This represents an immediate increase in net tangible book value of $3.48 per share to existing stockholders and an immediate dilution in net tangible book value of $14.45 per share to purchasers of common stock in this offering, as illustrated in the following table:

Initial public offering price per share		$ 20.00
Historical net tangible book value per share as of March 31, 2015	$ (28.29)	
Pro forma increase in net tangible book value per share as of March 31, 2015	30.36	
Pro forma net tangible book value per share as of March 31, 2015	2.07	
Increase in pro forma net tangible book value per share attributable to new investors	3.48	
Pro forma as adjusted net tangible book value per share after this offering		5.55
Dilution per share to investors participating in this offering		$ 14.45

If the underwriters option to purchase additional shares from us is exercised in full, the pro forma as adjusted net tangible book value per share after this offering would be $5.96 per share, the increase in pro forma as adjusted net tangible book value per share to existing stockholders would be $0.41 per share and the dilution to new investors purchasing shares in this offering would be $14.04 per share.

The following table shows, as of March 31, 2015, on a pro forma as adjusted basis described above, the differences between the existing stockholders and the purchasers of shares in this offering with respect to the number of shares purchased from us, the total consideration paid, which includes net proceeds received from the issuance of common and redeemable convertible preferred stock and cash received from the exercise of stock options, and the average price paid per share (in thousands, except shares, per share amounts and percentages):

	Shares Purchased		Total Consideration		Average Price
	Number	Percent	Amount	Percent	per Share
Existing stockholders	21,808,457	78%	$ 97,928	45%	$ 4.49
New investors	6,000,000	22	120,000	55	20.00
Totals	27,808,457	100%	$ 217,928	100%	$ 7.84

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The foregoing calculations exclude the following shares as of March 31, 2015:

- 1,190,051 shares of our common stock issuable upon the exercise of stock options to purchase common stock that were outstanding as of March 31, 2015, with a weighted average exercise price of $0.81 per share;
- 985,338 shares of restricted common stock which are subject to our right of repurchase;
- 882,557 shares of common stock issuable upon exercise of options granted subsequent to March 31, 2015 at a weighted average exercise price of $4.21 per share and 607,853 shares of restricted common stock issued subsequent to March 31, 2015 at a purchase price of $3.40 per share;
- 445,620 shares of our common stock issuable reserved for issuance pursuant to future awards under the 2012 Plan as of March 31, 2015;
- 1,430,000 shares of common stock reserved for issuance pursuant to future awards under the 2015 Plan, which became effective upon the effectiveness of the registration statement of which this prospectus is a part; and
- 50,000 shares of common stock reserved for future issuance under the 2015 ESPP, which became effective upon the effectiveness of the registration statement of which this prospectus is a part.

To the extent that any outstanding options are exercised, new options are issued under our stock-based compensation plans or we issue additional shares of common stock in the future, there will be further dilution to investors participating in this offering.

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SELECTED FINANCIAL DATA

The selected statement of operations data for the years ended December 31, 2013 and 2014 and the selected balance sheet data as of December 31, 2013 and 2014 are derived from our audited financial statements included elsewhere in this prospectus. The selected statements of operations data for the three months ended March 31, 2014 and 2015 and the selected balance sheet data as of March 31, 2015 are derived from our unaudited interim condensed financial statements included elsewhere in this prospectus. The unaudited interim condensed financial statements were prepared on a basis consistent with our audited financial statements and include, in management s opinion, all adjustments, consisting only of normal recurring adjustments that we consider necessary for a fair presentation of the financial information set forth in those statements.

Our historical results are not necessarily indicative of the results that may be expected in the future and our interim results are not necessarily indicative of the results to be expected for the full year or any other period. You should read the selected historical financial data below in conjunction with the section titled Management s Discussion and Analysis of Financial Condition and Results of Operations and the financial statements and related notes included elsewhere in this prospectus.

	Year Ended December 31,		Three Months Ended March 31,	
	2013	2014	2014	2015
			(unaudited)	
	(in thousands, except share and per share data)			
Summary of Operations Data:				
Operating expenses:				
Research and development	$ 12,855	$ 16,324	$ 3,877	$ 6,069
General and administrative	2,309	3,855	821	1,298
Related party expenses	499	332	171	53
Total operating expenses	15,663	20,511	4,869	7,420
Loss from operations	(15,663)	(20,511)	(4,869)	(7,420)
Change in fair value of Series A redeemable convertible preferred stock liability	(2,455)	(297)	(238)	
Interest income	2	1		3
Net loss	$ (18,116)	$ (20,807)	$ (5,107)	$ (7,417)
Net loss attributable to common stockholders	$ (19,851)	$ (23,772)	$ (5,695)	$ (8,657)
Net loss per share attributable to common stockholders, basic and diluted [1]	$ (16.14)	$ (14.20)	$ (3.81)	$ (4.22)
Weighted-average number of shares used in computing net loss per share attributable to common stockholders, basic and diluted [1]	1,230,241	1,673,919	1,496,607	2,052,874

Pro forma net loss per share, basic and diluted (unaudited) [1]	$ (1.51)	$ (0.34)
Weighted-average number of shares used in computing pro forma net loss per share, basic and diluted (unaudited) [1]	13,761,829	21,799,488

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	As of December 31, 2013	2014	As of March 31, 2015 (unaudited)
		(in thousands)	
Balance Sheet Data:			
Cash and cash equivalents	$ 3,278	$ 52,069	$ 45,800
Working capital (deficit)	(36)	51,056	43,634
Total assets	6,172	55,756	50,477
Series A redeemable convertible preferred stock liability	1,836		
Redeemable convertible preferred stock	28,225	102,161	103,396
Accumulated deficit	(28,047)	(49,328)	(57,652)
Total stockholders deficit	(25,974)	(49,326)	(57,650)

(1) See Notes 2 and 10 to our audited financial statements and Notes 2 and 7 to our unaudited interim condensed financial statements included elsewhere in this prospectus for an explanation of the calculations of our basic and diluted net loss per share attributable to common stockholders, pro forma net loss per share and the weighted-average number of shares used in the computation of the per share amounts.

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MANAGEMENT S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with the section entitled Selected Financial Data and our financial statements and related notes included elsewhere in this prospectus. This discussion and other parts of this prospectus contain forward-looking statements that involve risks and uncertainties, such as our plans, objectives, expectations, intentions and beliefs. Our actual results could differ materially from those discussed in these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those identified below and those discussed in the section entitled Risk Factors included elsewhere in this prospectus.

Overview

We are a biopharmaceutical company dedicated to discovering, developing and commercializing novel therapeutics to treat grievous blood-based disorders. We are developing our initial product candidate, GBT440, as a once-daily, oral prophylactic therapy for sickle cell disease, or SCD, and are currently evaluating GBT440 in both healthy subjects and SCD patients in a randomized, placebo-controlled, double-blind clinical trial that we characterize as a Phase 1/2 clinical trial. GBT440 targets the underlying mechanism of red blood cell sickling, which we believe provides the potential to treat SCD rather than only its associated symptoms. In addition to GBT440 for the treatment of SCD, we are leveraging our deep scientific expertise in the chemical and biological mechanisms of blood-based disorders to target hypoxemic pulmonary disorders and hereditary angioedema, or HAE. We own rights to our product candidate portfolio in the United States, Europe and other major markets.

In December 2014, we initiated our randomized, placebo-controlled, double-blind, single and multiple ascending dose Phase 1/2 clinical trial of GBT440 in healthy subjects and patients with SCD. In this trial, which is designed to enroll between 96 and 128 subjects across 12 cohorts, we are evaluating the safety, tolerability, pharmacokinetics, or PK, and pharmacodynamics, or PD, of GBT440, as well as exploratory markers of SCD activity, including anti-hemolytic effects and SCD-related clinical effects. Beyond SCD, we plan to develop GBT440 or one of its analogs as a potential therapeutic for acute and chronic hypoxemic pulmonary disorders, including acute respiratory distress syndrome, or ARDS, and idiopathic pulmonary fibrosis, or IPF, where hypoxia is believed to play a key role in disease pathogenesis and adverse patient outcomes. Additionally, we have identified several proprietary, small molecule kallikrein inhibitors in an effort to produce an orally administered therapy for the prevention of angioedema attacks.

Since our inception in 2011, we have devoted substantially all of our resources to identifying and developing our product candidates, including conducting clinical trials and preclinical studies and providing general and administrative support for these operations. We have funded our operations to date primarily from the issuance and sale of redeemable convertible preferred stock.

We have never been profitable and have incurred net losses in each year since inception. Our net losses were $18.1 million and $20.8 million for the years ended December 31, 2013 and 2014, respectively. Our net losses were $5.1 million and $7.4 million for the three months ended March 31, 2014 and 2015, respectively. As of March 31, 2015 we had an accumulated deficit of $57.7 million. To date, we have not generated any revenue. We do not expect to receive any revenue from any product candidates that we develop until we obtain regulatory approval and commercialize our products or enter into collaborative agreements with third parties. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations. As of June 30, 2015, we had $40.6 million of cash and cash equivalents.

Financial Operations Overview

Research and Development Expenses

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

employee-related expenses, which include salaries, benefits and stock-based compensation;

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expenses incurred under agreements with consultants, third-party contract organizations, and investigative clinical trial sites that conduct research and development activities on our behalf;

laboratory and vendor expenses related to the execution of preclinical studies and clinical trials;

the costs related to production of clinical supplies, including fees paid to contract manufacturers; and

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

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

The largest component of our total operating expenses has historically been our investment in research and development activities, including the clinical development of GBT440. We allocate research and development salaries, benefits, stock-based compensation and indirect costs to GBT440 and other product candidates that we may pursue on a program-specific basis, and we include these costs in the program-specific expenses.

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

	Year Ended December 31,		Three Months Ended March 31,	
	2013	2014	2014	2015
	(in thousands)			
Costs incurred by development program:				
GBT440 for the treatment of SCD	$ 7,555	$ 8,867	$ 2,042	$ 4,316
Oral treatment for HAE	4,261	5,069	1,278	1,481
Other preclinical programs	1,039	2,388	557	272
Total research and development expenses	$ 12,855	$ 16,324	$ 3,877	$ 6,069

To date, we have not incurred significant expenses for the development of GBT440 or its analogs in hypoxic pulmonary disorders. We expect our research and development expenses will increase in future periods as we continue to invest in research and development activities related to developing our product candidates, and as programs advance into later stages of development and we begin to conduct larger clinical trials. The process of conducting the necessary clinical research to obtain regulatory approval is costly and time-consuming, and the successful development of our product candidates is highly uncertain. As a result, we are unable to determine the duration and completion costs of our research and development projects or when and to what extent we will generate revenue from

the commercialization and sale of any of our product candidates.

General and Administrative Expenses

General and administrative expenses consist of personnel costs, allocated facilities costs and other expenses for outside professional services, including legal, patent, human resources, audit and accounting services. Personnel costs consist of salaries, benefits and stock-based compensation. Allocated expenses consist of expenses for rent and maintenance of facilities, depreciation and amortization expense and other supplies. We

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expect to incur additional expenses as a result of operating as a public company, including expenses related to compliance with the rules and regulations of the Securities and Exchange Commission, The NASDAQ Global Select Market, additional insurance expenses, investor relations activities and other administration and professional services.

Related party expenses

Related party expenses represent fees for management and advisory services provided by Third Rock Ventures, LLC, or TRV, a related party due to its significant ownership of our outstanding redeemable convertible preferred stock.

Critical Accounting Polices and Estimates

Our management s discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with United States generally accepted accounting principles, or U.S. GAAP. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. We believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management s judgments and estimates.

Accrued Research and Development Costs

We record accrued expenses for estimated costs of our research and development activities conducted by third-party service providers, which include the conduct of preclinical studies and clinical trials and contract manufacturing activities. We record the estimated costs of research and development activities based upon the estimated amount of services provided but not yet invoiced, and include these costs in accrued liabilities in the balance sheet and within research and development expense in the statement of operations and comprehensive loss. These costs are a significant component of our research and development expenses. We record accrued expenses for these costs based on the estimated amount of work completed and in accordance with agreements established with these third parties.

We estimate the amount of work completed through discussions with internal personnel and external service providers as to the progress or stage of completion of the services and the agreed-upon fee to be paid for such services. We make significant judgments and estimates in determining the accrued balance in each reporting period. As actual costs become known, we adjust our accrued estimates. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed, the number of patients enrolled and the rate of patient enrollment may vary from our estimates and could result in us reporting amounts that are too high or too low in any particular period. Our accrued expenses are dependent, in part, upon the receipt of timely and accurate reporting from clinical research organizations and other third-party service providers. To date, there have been no material differences from our accrued expenses to actual expenses.

Series A Redeemable Convertible Preferred Stock Liability

We recorded the redeemable convertible preferred stock liability incurred in connection with our Series A redeemable convertible preferred stock as a derivative financial instrument liability at the fair value on the date of issuance, and we remeasure it on each subsequent balance sheet date. The Series A preferred stock liability

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stems from our initial sale of Series A redeemable convertible preferred stock, in connection with which we were obligated to sell additional shares in subsequent closings contingent upon the achievement of certain development milestones. The subsequent closings were deemed to be freestanding financial instruments that were outside of our control. The changes in fair value are recognized as a gain or loss in the statements of operations and comprehensive loss. We estimated the fair value of this liability using Black Scholes option pricing models that include assumptions of probability of achievement of the development milestones, stock price per share, expected life, dividend yield and risk-free interest rate. All subsequent closings have occurred so there is no derivative liability as of December 31, 2014, and there will be no remeasurement through the statement of operations in future periods.

Stock-Based Compensation

We recognize compensation costs related to stock options granted to employees based on the estimated fair value of the awards on the date of grant, net of estimated forfeitures. We estimate the grant date fair value, and the resulting stock-based compensation expense, using the Black-Scholes option-pricing model. The grant date fair value of the stock-based awards is generally recognized on a straight-line basis over the requisite service period, which is generally the vesting period of the respective awards.

We account for stock-based compensation arrangements with non-employees using a fair value approach. The fair value of these options is measured using the Black-Scholes option pricing model reflecting the same assumptions as applied to employee options in each of the reported periods, other than the expected life, which is assumed to be the remaining contractual life of the option. The fair value of the unvested options under these arrangements is subject to remeasurement over the vesting terms as earned.

The Black-Scholes option-pricing model requires the use of highly subjective assumptions which determine the fair value of stock-based awards. These assumptions include:

Expected Term Our expected term represents the period that our stock-based awards are expected to be outstanding and is determined using the simplified method (based on the mid-point between the vesting date and the end of the contractual term).

Expected Volatility Since we are privately held and do not have any trading history for our common stock, the expected volatility was estimated based on the average volatility for comparable publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants. The comparable companies were chosen based on their similar size, stage in the life cycle, or area of specialty.

Risk-Free Interest Rate The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of option.

Expected Dividend We have never paid dividends on our common stock and have no plans to pay dividends on our common stock. Therefore, we used an expected dividend yield of zero.

In addition to the Black-Scholes assumptions, we estimate our forfeiture rate based on an analysis of our actual forfeitures and will continue to evaluate the adequacy of the forfeiture rate based on actual forfeiture experience, analysis of employee turnover behavior, and other factors. The impact from any forfeiture rate adjustment would be

recognized in full in the period of adjustment and if the actual number of future forfeitures materially differs from our estimates, we will be required to record adjustments to stock-based compensation in future periods.

For the years ended December 31, 2013 and 2014, stock-based compensation expense was $0.1 million and $0.4 million, respectively. For the three months ended March 31, 2014 and 2015, stock-based compensation expense was $38,000 and $0.3 million, respectively. As of March 31, 2015, we had $1.4 million of total unrecognized stock-based compensation costs, net of estimated forfeitures, which we expect to recognize over a weighted-average period of 3.6 years.

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Historically, for all periods prior to this initial public offering, the fair values of the shares of common stock underlying our share-based awards were estimated on each grant date by our board of directors. In order to determine the fair value of our common stock underlying option grants, our board of directors considered, among other things, contemporaneous valuations of our common stock prepared by an unrelated third-party valuation firm in accordance with the guidance provide by the American Institute of Certified Public Accountants Practice Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. Given the absence of a public trading market for our common stock, our board of directors exercised their judgment and considered a number of objective and subjective factors to determine the best estimate of the fair value of our common stock, including: our stage of development; progress of our research and development efforts; the rights, preferences and privileges of our preferred stock relative to those of our common stock; equity market conditions affecting comparable public companies and the lack of marketability of our common stock.

In January 2015, we granted options to purchase 119,427 shares of common stock at an exercise price per share of $1.61, and 21,428 shares of restricted stock with a purchase price of $1.61 per share.

In March 2015, we granted options to purchase 119,592 shares of common stock at an exercise price per share of $3.40, and 2,857 shares of restricted stock with a purchase price of $3.40 per share.

In April 2015, we granted options to purchase 637,848 shares of common stock at an exercise price of $3.40 per share, and 607,853 shares of restricted stock with a purchase price of $3.40 per share.

In June 2015, we granted options to purchase 244,709 shares of common stock at an exercise price of $6.34 per share.

In addition, in July and August 2015, our board of directors approved the issuance of options to purchase an aggregate of 317,205 shares of our common stock to board members and employees, which options will be issued in connection with this offering at an exercise price equal to the initial public offering price of our common stock.

In determining a fair value for our common stock, we estimated the enterprise value of our business using the option-pricing method backsolve, or OPM backsolve, a form of a market approach and a Probability Weighted Expected Return Method, or PWERM, approach. The OPM backsolve method derives the implied equity value for a company from a recent transaction involving the company s own securities based on an arms-length transaction. The market approach estimates the fair value of a company by including an estimated value of the business based on estimations surrounding future company values under initial public offering scenarios based on recent biopharmaceutical initial public offerings. The enterprise value is then allocated to the common stock using the Option Pricing Method, or OPM and the PWERM, or the hybrid method. The hybrid method applied the PWERM utilizing four going public scenarios, and the OPM was utilized to capture all scenarios in which we do not complete an initial public offering during 2015, factoring in dissolution.

For valuations after the completion of this offering, our board of directors will determine the fair value of each share of underlying common stock based on the closing price of our common stock as reported on the date of grant.

The intrinsic value of all outstanding options as of March 31, 2015 was $22.8 million based on the initial public offering price of our common stock of $20.00 per share.

Income Taxes

We use the liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on the differences between the financial reporting and the tax bases of assets and liabilities and are

measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. We assess the likelihood that the resulting deferred tax assets will be realized. A valuation allowance is provided when it is more likely than not that some portion or all of a deferred tax asset will not be realized.

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As of December 31, 2014, our total deferred tax assets, less our total deferred tax liabilities, were $19.5 million. Due to our lack of earnings history and uncertainties surrounding our ability to generate future taxable income, the net deferred tax assets have been fully offset by a valuation allowance. The deferred tax assets were primarily comprised of federal and state tax net operating losses and tax credit carryforwards.

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

We have not completed an analysis to assess whether an ownership change has occurred. If we have experienced an ownership change at any time since our formation, utilization of our net operating loss carryforwards would be subject to an annual limitation under Section 382 of the Code, which is determined by first multiplying the value of our stock at the time of the ownership change by the applicable long-term, tax-exempt rate, and then applying any additional adjustments that are required. Any limitation may result in expiration of a portion of the net operating loss carryforwards before utilization. Further, until a study is completed and any limitation known, no amounts are being considered as an uncertain tax position or disclosed as an unrecognized tax benefit. Due to the existence of the valuation allowance, future changes in our unrecognized tax benefits will not impact our effective tax rate. Any carryforwards that will expire prior to utilization as a result of such limitations will be removed from deferred tax assets, with a corresponding reduction of the valuation allowance.

Results of Operations

Comparison of the three months ended March 31, 2014 and 2015

	Three months ended March 31,		Increase/ (Decrease)
	2014	2015	
	(in thousands)		
Operating expenses:			
Research and development	$ 3,877	$ 6,069	$ 2,192
General and administrative	821	1,298	477
Related party expenses	171	53	(118)
Total operating expenses	4,869	7,420	2,551
Loss from operations	(4,869)	(7,420)	(2,551)
Change in fair value of Series A redeemable convertible preferred stock liability	(238)		238
Interest income		3	3

Net loss	$ (5,107)	$ (7,417)	$ (2,310)

Research and development

Research and development expenses increased by $2.2 million or 57%, from $3.9 million for the three months ended March 31, 2014 to $6.1 million for the three months ended March 31, 2015. The increase was

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primarily due to $2.3 million related to our SCD program for GBT440 as we initiated our Phase 1/2 clinical trial in early 2015. Expenses related to our HAE program and our other preclinical programs were relatively consistent for the three months ended March 31, 2014 compared to the three months ended March 31, 2015.

General and administrative

General and administrative expenses increased by $0.5 million or 58%, from $0.8 million for the three months ended March 31, 2014 to $1.3 million for the three months ended March 31, 2015. The increase was primarily due to a $0.4 million increase in salaries and benefits and recruiting expenses as we expanded our internal business management team and a $0.1 million net increase in other general and administrative expenses due to the growth of our operations.

Related party expenses

Related party expenses decreased by $0.1 million or 69%, from $0.2 million for the three months ended March 31, 2014 to $0.1 million for the three months ended March 31, 2015. The decrease was primarily due to a reduction in management services provided from TRV as we expanded our internal business management team.

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

The change in fair value of Series A redeemable convertible preferred stock liability was $0.2 million for the three months ended March 31, 2014 compared to zero for the three months ended March 31, 2015. The change in 2014 is for the increase in fair value of the Series A redeemable convertible preferred stock liability associated with our obligation to issue additional shares of Series A redeemable convertible preferred stock. We issued shares under our final obligation in October 2014, and accordingly, we no longer have an obligation to fair value as of that date.

Comparison of the years ended December 31, 2013 and 2014

	Year Ended December 31,		Increase/ (Decrease)
	2013	2014	
	(in thousands)		
Operating expenses:			
Research and development	$ 12,855	$ 16,324	$ 3,469
General and administrative	2,309	3,855	1,546
Related party expenses	499	332	(167)
Total operating expenses	15,663	20,511	4,848
Loss from operations	(15, 663)	(20,511)	(4,848)
Change in fair value of Series A redeemable convertible preferred stock liability	(2,455)	(297)	2,158
Interest income	2	1	(1)
Net loss	$ (18,116)	$ (20,807)	$ (2,691)

Research and development

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

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General and administrative

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

Related party expenses

Related party expenses decreased by $0.2 million or 33%, from $0.5 million for the year ended December 31, 2013 to $0.3 million for the year ended December 31, 2014. The decrease was primarily due to a reduction in management services provided from TRV as we expanded our internal business management team.

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

The change in fair value of Series A redeemable convertible preferred stock liability was $0.3 million for the year ended December 31, 2014, compared to a $2.5 million loss for the year ended December 31, 2013. The change in both periods represents the increase in fair value of the Series A redeemable convertible preferred stock liability associated with our obligation to issue additional shares of Series A redeemable convertible preferred stock. We issued the shares under our final obligation in October 2014, and accordingly, we no longer have an obligation as of that date.

Liquidity, Capital Resources and Plan of Operations

Since our inception in 2011 through March 31, 2015, our operations have been financed solely by net proceeds of $97.7 million from the sale of shares of our redeemable convertible preferred stock. As of March 31, 2015, we had $45.8 million in cash and cash equivalents and an accumulated deficit of $57.7 million.

Our primary use of cash is to fund operating expenses, which consist primarily of research and development expenditures. Cash used to fund operating expenses is impacted by the timing of when we pay these expenses, as reflected in the change in our outstanding accounts payable and accrued expenses.

We believe that our existing capital resources will be sufficient to meet our projected operating requirements at least through December 31, 2015. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. We will continue to require additional financing to advance GBT440 through clinical development, to develop other potential product candidates from our research programs and to fund operations for the foreseeable future. We will continue to seek funds through equity or debt financings, collaborative or other arrangements with corporate sources, or through other sources of financing. Adequate additional funding may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed could have a negative impact on our financial condition and our ability to pursue our business strategies. We anticipate that we will need to raise substantial additional capital, the requirements of which will depend on many factors, including:

- the time and cost necessary to complete our ongoing Phase 1/2 clinical trial of GBT440, to initiate and complete any pivotal clinical trials of GBT440 and to obtain regulatory approvals for GBT440, and the costs of post-marketing studies that could be required by regulatory authorities;

the progress and results of our Phase 1/2 clinical trial of GBT440;

the progress, timing, scope and costs of our nonclinical studies, clinical trials and other related activities, including the ability to enroll patients in a timely manner for our Phase 1/2 clinical trial of GBT440 and potential future clinical trials;

the costs of obtaining clinical and commercial supplies of GBT440 and any other product candidates we may develop;

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

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

the amount and timing of sales and other revenues from GBT440 and any other product candidates we may develop, including the sales price and the availability of adequate third-party reimbursement;

the cash requirements of any future acquisitions or discovery of product candidates;

the time and cost necessary to respond to technological and market developments;

the extent to which we may acquire or in-license other product candidates and technologies;

our ability to attract, hire and retain qualified personnel; and

the costs of maintaining, expanding and protecting our intellectual property portfolio.

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

If we need to raise additional capital to fund our operations, funding may not be available to us on acceptable terms, or at all. If we are unable to obtain adequate financing when needed, we may have to delay, reduce the scope of or suspend one or more of our clinical trials, research and development programs or commercialization efforts. We may seek to raise any necessary additional capital through a combination of public or private equity offerings, debt financings, and collaborations or licensing arrangements. If we do raise additional capital through public or private equity offerings, the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders rights. If we raise additional capital through debt financing, we may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If additional funding is required, there can be no assurance that additional funds will be available to us on acceptable terms on a timely basis, if at all. If we are unable to raise capital, we will need to curtail planned activities to reduce costs. Doing so will likely have an unfavorable effect on our ability to execute on our business plan.

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

	Year Ended December 31,		Three Months Ended March 31,	
	2013	2014	2014	2015
	(in thousands)		(unaudited, in thousands)	
Cash used in operating activities	$ (14,700)	$ (20,121)	$ (4,278)	$ (6,061)
Cash used in investing activities	(940)	(383)	(19)	(169)
Cash provided by (used in) financing activities	15,279	69,295	5,029	(39)
Net (decrease) increase in cash and cash equivalents	$ (361)	$ 48,791	$ 732	$ (6,269)

Cash flows from operating activities

Cash used in operating activities for the three months ended March 31, 2015 was $6.1 million, consisting of a net loss of $7.4 million, which was offset by non-cash charges of $0.2 million for depreciation and amortization expense and $0.3 million for stock-based compensation. The change in our net operating assets and liabilities was due primarily to a reduction of $0.4 million in our prepaid expenses for the advance payments made in connection with our Phase 1/2 clinical trial of GBT440 and deposits for the manufacturing of clinical trial materials, an increase of $0.3 million in accounts payable and an increase of $0.8 million in accrued expenses

related to our ongoing Phase 1/2 clinical trial of GBT440, which were partially offset by an increase of $0.4 million in other current assets related to our funding obligations for our Phase 1/2 clinical trial of GBT440 and by a decrease of $0.3 million in accrued compensation.

Cash used in operating activities for the three months ended March 31, 2014 was $4.3 million, consisting of a net loss of $5.1 million, which was offset primarily by non-cash charges of $0.2 million for depreciation and amortization expense and $0.2 million for remeasurement of our Series A redeemable convertible preferred stock liability. The change in our net operating assets and liabilities was due primarily to an increase of $0.5 million in accounts payable related to an increase in our research and development activities offset in part by a decrease of $0.2 million in accrued compensation.

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

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

Cash flows from investing activities

Cash used in investing activities for the three months ended March 31, 2014 and 2015 was related to our purchase of property and equipment for our office and laboratory facility.

Cash used in investing activities for the years ended December 31, 2013 and 2014 was related to our purchase of property and equipment of $0.9 million and $0.3 million, respectively. Purchases of property and equipment are primarily related to our office and laboratory facility. In addition, for the year ended December 31, 2014, restricted cash increased by $0.1 million related to an increase in collateral for the letter of credit under our facility lease.

Cash flows from financing activities

Cash provided by financing activities for the three months ended March 31, 2014 was primarily related to net proceeds from the issuance of redeemable convertible preferred stock of $5.0 million.

Cash used in financing activities for the three months ended March 31, 2015 was primarily related to deferred offering costs offset by proceeds from the issuance of restricted stock awards.

Cash provided by financing activities for the years ended December 31, 2013 and 2014 was primarily related to net proceeds from the issuance of redeemable convertible preferred stock of $15.2 million and $68.8 million, respectively. In addition, during the year ended December 31, 2014 we received net proceeds of $0.4 million in connection with the issuance of restricted stock awards.

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Internal Control over Financial Reporting

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

We are implementing measures designed to improve our internal control over financial reporting to remediate this material weakness, including the following:

- We are formalizing our internal control documentation and strengthening supervisory reviews by our management; and
- We are in the process of adding additional accounting personnel and segregating duties among accounting personnel.

These additional resources and procedures are designed to enable us to broaden the scope and quality of our internal review of underlying information related to financial reporting and to formalize and enhance our internal control procedures. With the oversight of senior management and our audit committee, we have begun taking steps and plan to take additional measures to remediate the underlying causes of the material weakness.

We, and our independent registered public accounting firm, were not required to perform an evaluation of our internal control over financial reporting as of December 31, 2014 in accordance with the provisions of the Sarbanes-Oxley Act. Accordingly, we cannot assure you that we have identified all, or that we will not in the future have additional, material weaknesses. Material weaknesses may still exist when we report on the effectiveness of our internal control over financial reporting as required by reporting requirements under Section 404 of the Sarbanes-Oxley Act after the completion of this offering.

Contractual Obligations and Other Commitments

The following table summarizes our contractual obligations as of December 31, 2014:

	Payments Due by Period				
Contractual Obligations:	**Less Than 1 Year**	**1 to 3 Years**	**4 to 5 Years**	**More Than 5 Years**	**Total**
			(in thousands)		
Operating lease obligations	$ 949	$ 2,128	$ 367	$	$ 3,444
Total contractual obligations	$ 949	$ 2,128	$ 367	$	$ 3,444

Off-Balance Sheet Arrangements

We have not entered into any off-balance sheet arrangements and do not have any holdings in variable interest entities.

Quantitative and Qualitative Disclosures about Market Risk

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities. We had cash and cash equivalents of $52.1 million and $45.8 million as of December 31, 2014 and March 31, 2015, respectively, which consist of bank deposits and money market funds. Such interest-earning instruments carry a degree of interest rate risk; however, historical fluctuations in interest income have not been significant. We had no outstanding debt as of December 31, 2014 and March 31, 2015.

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JOBS Act Accounting Election

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

Recent Accounting Pronouncements

In June 2014, the Financial Accounting Standards Board, or FASB, issued ASU 2014-10, *Development Stage Entities (Topic 915): Elimination of Certain Financial Reporting Requirements, Including an Amendment to Variable Interest Entities Guidance in Topic 810, Consolidation.* The ASU simplifies the accounting guidance by removing all incremental financial reporting requirements for development stage entities. The amendments related to the elimination of the inception-to-date information and other disclosure requirement of Topic 915 should be applied retrospectively, and are effective for annual reporting periods beginning after December 15, 2014, and interim periods therein. We early adopted this guidance and accordingly, there is no inception to date information presented in the financial statements included elsewhere is this prospectus.

In August 2014, the FASB issued ASU 2014-15, *Disclosure of Uncertainties about an Entity s Ability to Continue as a Going Concern.* ASU 2014-15 requires management to evaluate relevant conditions, events and certain management plans that are known or reasonably knowable that when, considered in the aggregate, raise substantial doubt about the entity s ability to continue as a going concern within one year after the date that the financial statements are issued, for both annual and interim periods. ASU 2014-15 also requires certain disclosures around management s plans and evaluation, as well as the plans, if any, that are intended to mitigate those conditions or events that will alleviate the substantial doubt. ASU 2014-15 is effective for fiscal years ending after December 15, 2016. We are currently evaluating the impact that the adoption of ASU 2014-15 will have on our financial statements and related disclosures.

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BUSINESS

Overview

We are a biopharmaceutical company dedicated to discovering, developing and commercializing novel therapeutics to treat grievous blood-based disorders. We are developing our initial product candidate, GBT440, as a once-daily, oral prophylactic therapy for sickle cell disease, or SCD, and are currently evaluating GBT440 in both healthy subjects and SCD patients in a randomized, placebo-controlled, double-blind clinical trial that we characterize as a Phase 1/2 clinical trial. SCD is a disease marked by severe pain crises, recurrent hospitalizations, multi-organ damage, and early mortality. GBT440 targets the underlying mechanism of red blood cell sickling, which we believe may provide the potential to treat SCD rather than only its associated symptoms. In addition to GBT440 for the treatment of SCD, we are leveraging our deep scientific expertise in the chemical and biological mechanisms of blood-based disorders to target hypoxemic pulmonary disorders and hereditary angioedema, or HAE. We own rights to our product candidate portfolio in the United States, Europe and other major markets. We own or co-own one issued U.S. patent that covers the composition of matter for GBT440, which is due to expire in 2032 (absent any applicable patent term extensions), and we own or co-own additional pending patent applications in the United States and selected foreign countries. Given the concentrated prescriber bases for our targeted indications, we intend to promote our products with a specialty sales force in the United States and Europe. We are also evaluating options for commercializing GBT440 in other significant markets, given the concentration of SCD in populations of African, Middle Eastern and South Asian descent.

SCD is a chronic, inherited blood disorder caused by a genetic mutation in the beta-chain of hemoglobin, which results in the formation of abnormal hemoglobin known as sickle hemoglobin, or HbS. Hemoglobin is contained within red blood cells, or RBCs. In its deoxygenated state, HbS has a propensity to polymerize, or bind together into long, rigid rods within an RBC, much like a sword within a balloon. Once HbS polymerizes, the RBC assumes a sickled shape and becomes inflexible, which can cause blockage in small blood vessels. Beginning in childhood, SCD patients suffer unpredictable and recurrent episodes or crises of severe pain due to blocked blood flow to organs, which often lead to psychosocial and physical disability. This blocked blood flow, combined with hemolytic anemia (the destruction of RBCs), can lead to multi-organ damage and early death. A 2014 publication noted that in the United States, SCD results in a decrease of approximately 25 to 30 years in life expectancy.

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

We believe there is a significant unmet need for an SCD therapy that:

- targets the underlying mechanism of RBC sickling, which has the potential to halt the progression of the disease;
- can be administered prophylactically in both children and adults;
- prevents or reduces the episodes or crises of severe pain associated with SCD;

prevents long-term complications of the disease;

has a more favorable side effect profile than currently available therapies; and

is available as a convenient, once-daily oral therapy.

GBT440 is a novel hemoglobin modifier that binds to hemoglobin, resulting in an increased affinity of hemoglobin for oxygen. In various studies of SCD, scientists have demonstrated that oxyhemoglobin, or hemoglobin in the oxygenated state, is a potent inhibitor of HbS polymerization. Therefore, we believe that increasing the proportion of oxyhemoglobin in blood could potentially delay the polymerization of HbS and prevent the sickling of RBCs, which may be able to ameliorate many, if not all, of the clinical manifestations of this disease.

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We believe that the natural activity of fetal hemoglobin, or HbF, as well as prior observations of the activity of other hemoglobin-modifying compounds, provide support for our approach to treating SCD with GBT440. HbF, which is present during fetal development and in early infancy until it is replaced with adult hemoglobin, has an inherently increased oxygen affinity that allows a fetus to extract oxygen from the mother s blood. Typically, newborns with SCD do not experience RBC sickling until approximately six to nine months of age, after which HbF is usually no longer expressed. Additionally, it has been observed that individuals who have inherited the HbS mutation and a gene deletion that allows them to continue to express 20% or more HbF in their RBCs into adulthood do not exhibit the clinical manifestations of SCD, despite expressing up to 80% HbS in their blood. Similarly, modification of hemoglobin by tucaresol, a drug that was developed in the 1990s, in the range of 10-24% demonstrated rapid anti-hemolytic and anti-sickling effects in SCD patients. However, the development of tucaresol was discontinued due to severe off-target immune-related side effects unrelated to its effects on hemoglobin modification. Based on these observations, we anticipate that to delay polymerization of HbS, GBT440 would need to bind to only approximately 20% of the total hemoglobin in a patient s blood. The results of our preclinical studies support our hypothesis that a modification of approximately 20% of HbS could prevent RBC sickling and may halt the progression of SCD without compromising oxygen delivery to the tissues.

In December 2014, we initiated our randomized, placebo-controlled, double-blind, single and multiple ascending dose Phase 1/2 clinical trial of GBT440 in healthy subjects and patients with SCD. In this trial, which is designed to enroll between 96 and 128 subjects across 12 cohorts, we are evaluating the safety, tolerability, pharmacokinetics, or PK, and pharmacodynamics, or PD, of GBT440, as well as exploratory markers of SCD activity, including anti-hemolytic effects and SCD-related clinical effects. As of July 31, 2015, we have dosed 48 subjects in six single dose cohorts, comprised of 40 healthy volunteers (30 of whom received GBT440 and ten of whom received placebo) and eight SCD patients (six of whom received GBT440 and two of whom received placebo). In the multiple dose arm of our trial, all 24 healthy volunteers have completed 15-day dosing, and eight SCD patients have completed 28-day dosing and are currently in the follow-up period. To date, there have been no serious adverse events among subjects treated with GBT440 in our Phase 1/2 clinical trial. One SCD patient who received placebo experienced an SCD-specific serious adverse event involving a sickle cell crisis. Among the six SCD patients who received multiple doses of GBT440, from baseline (Day -1) to Day 28, we have observed significant reductions in the number of sickled RBCs in all patients, which is the quintessential hallmark of the disease and the primary driver of disease pathology. We have also observed improvement in hemolysis markers as evidenced by declines in reticulocyte counts, unconjugated bilirubin and lactate dehydrogenase, or LDH, levels. Proof of concept was demonstrated within 15 days of once daily dosing with a rapid decline in hemolysis markers and improvement in anemia. We believe these initial data demonstrate the potential for GBT440 to serve as a disease-modifying therapy for SCD. Subject to data from one or more of the multiple dose cohorts of our Phase 1/2 clinical trial in SCD patients, we intend to engage in discussions with U.S. and European regulatory authorities to define the future development plan for GBT440.

Because available therapies in SCD are limited, the U.S. Food and Drug Administration, or the FDA, has suggested that the development of new therapies for SCD is an agency priority. As a result, we believe there may be an opportunity to accelerate the development of GBT440 through one or more of the FDA s expedited designation or approval programs. We believe that the data from SCD patients in our ongoing clinical trial, if positive, may provide an opportunity to demonstrate the beneficial effect of GBT440 on clinical parameters of hemolysis and resolution of anemia, which could potentially form the basis for qualification for expedited programs.

We believe there is a significant market opportunity in SCD. The U.S. Centers for Disease Control, or CDC, estimates the prevalence of SCD at 90,000 to 100,000 individuals in the United States, where newborn screening is mandatory. It is estimated that the prevalence of SCD in Europe is approximately 60,000. The global incidence of SCD is estimated to be 250,000 to 300,000 births annually. One study estimated that in the United States, the average annual cost for the care of an adult patient with the most common genotype of SCD exceeds $200,000, and the cumulative

lifetime costs exceed $8.0 million over an assumed 50-year lifespan, driven primarily by hospital admissions, physician fees, clinic and emergency department visits, and the costs of diagnostic procedures and outpatient consultations.

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Beyond SCD, we plan to develop GBT440 or one or more of its analogs as a potential therapeutic for acute and chronic hypoxemic pulmonary disorders, including acute respiratory distress syndrome, or ARDS, and idiopathic pulmonary fibrosis, or IPF, where hypoxia is believed to play a key role in disease pathogenesis and adverse patient outcomes. These are conditions in which the lungs cannot supply adequate oxygen to the blood. Additionally, we have identified several proprietary, small molecule kallikrein inhibitors in an effort to produce an orally administered therapy for the prevention of angioedema attacks. All currently marketed therapeutics for HAE must be administered intravenously or by subcutaneous injection. As a result, we believe that the availability of a safe and effective oral prophylactic agent would have the potential to transform the treatment paradigm for this disease.

To execute on this opportunity, we have assembled a team of employees, directors and scientific founders rich in scientific experience and capabilities in drug discovery, development and commercialization. Our management has a successful track record in developing and commercializing drug candidates. In aggregate, our team has contributed to 18 drug approvals, including Avastin, CellCept, Herceptin, INTEGRILIN, Kaletra, Kyprolis and Rituxan. We intend to leverage this expertise and experience to rapidly pursue the development of GBT440 and other product candidates that we may identify and develop.

Our Strategy

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

Rapidly advance GBT440 for the treatment of SCD. We have initiated a randomized, placebo-controlled, double-blind, single and multiple ascending dose Phase 1/2 clinical trial of GBT440 in healthy subjects and SCD patients. In this trial, we are evaluating safety as well as potential anti-sickling activity and clinical proof-of-concept. Subject to the successful completion of this clinical trial and the outcome of our discussions with regulatory authorities, we intend to advance GBT440 in clinical development for the treatment of SCD in adults, adolescents, children and infants.

Explore the development of GBT440 and other hemoglobin modifiers in hypoxemic pulmonary disorders with significant unmet medical need. Based on our preclinical and preliminary clinical observations demonstrating that GBT440 increases the oxygen affinity of hemoglobin, we also plan to develop GBT440 or one of its analogs as a potential therapeutic for acute and chronic hypoxemic pulmonary disorders. These are conditions in which the lungs cannot supply adequate oxygen to the blood. We are initially focusing our research and development activities on indications with significant unmet medical need, including ARDS and IPF, where hypoxia is believed to play a key role in disease pathogenesis and adverse patient outcomes.

Submit an Investigational New Drug application, or IND, and initiate clinical development for an oral kallikrein inhibitor in hereditary angioedema, or HAE. We have discovered several proprietary, small molecule kallikrein inhibitors in an effort to produce an orally administered therapy for the prevention of angioedema attacks. Plasma kallikrein s role in HAE is well established, and several clinical trials have demonstrated that kallikrein inhibition can reverse and/or prevent angioedema attacks. We are conducting research and development efforts directed to the selection of an IND candidate for clinical development of

an oral kallikrein inhibitor in HAE.

Retain development and commercialization rights to product candidates in our core disease areas in major markets. We plan to develop and commercialize our product candidates in major markets. We believe we can devise time and cost efficient strategies to develop and obtain regulatory approvals for new drugs. We have assembled an experienced team with a successful track record in pharmaceutical development, regulatory strategy and execution of global clinical trials. We intend to establish our own commercial organization in major markets and evaluate opportunities to establish distributor networks or strategic partnerships in smaller markets where third parties may have stronger

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local market knowledge. We believe the markets we currently intend to pursue can be served through a targeted commercial effort because the disease indications targeted by our product candidates are generally addressed by specialists.

Evaluate opportunities to expand the scope of our product offerings. We may also selectively form collaborative alliances to expand our capabilities and product offerings into new therapeutic areas and potentially accelerate commercialization in select geographic markets. Additionally, we may pursue acquisition or in-licensing of product candidates, particularly in our core disease area of blood-based disorders.

Our Approach

Our scientific focus and mission is to develop novel medicines that treat grievous blood-based disorders by arresting the underlying chemical and biological mechanisms of the disease. As one of the largest and most accessible organs, blood is a rich source of biologically and clinically validated targets. These targets can involve cellular components in the blood, including RBCs, platelets and white blood cells, as well as proteins, including proteases, circulating in plasma that are critical for homeostatic balance for a number of biological pathways, including the process of blood coagulation. Our current pipeline addresses SCD, a prototypic RBC disorder that results from a mutation in the beta-globin gene of hemoglobin, as well as HAE, a specific dysregulation of the coagulation cascade resulting from hereditary low blood levels of a protease, C1 esterase, that results in excess bradykinin and increased vascular permeability leading to angioedema attacks.

We possess deep scientific expertise in the chemical and biological mechanisms of blood-based disorders. We leverage our proprietary knowledge of protein structure and function, comprehensive biological assays and advanced drug discovery techniques to facilitate novel approaches for treating disorders of the blood. Our expertise includes the following specific capabilities:

conformational modulation, or changing the shape, of specific blood-based proteins;

the binding of molecules to protein targets to activate or inhibit these targets;

computational methods in protein structure, dynamics and ligand docking;

broad access to diverse libraries of compounds; and

comprehensive biological assays ranging from purified protein to whole blood and genetically-based animal models.

Our research efforts focus on blood-based targets that are well characterized and validated. Proteins present in various blood cells and plasma provide targets that are identified as relevant in disease pathology but to date, have not been successfully drugged. We apply our knowledge of structural biology-based drug design and medicinal chemistry to discover and optimize compounds for their activity against these targets, supported by strong clinical hypotheses and a clear path to clinical proof-of-concept. In parallel, we develop novel blood-based functional assays to provide

relevance to the target-drug interaction and use the results iteratively to further refine our potential drug candidates. For example, we approached the design of an oral inhibitor of the plasma enzyme kallikrein by first solving the crystal structure of an early inhibitor bound to the target human protein. Subsequently, this structure-based design in concert with plasma thrombin generation functional assays and dosing in rats, allowed us to carry out iterations to optimize highly selective kallikrein inhibitory activity while retaining positive pharmaceutical properties, including oral bioavailability.

Our clinical development strategy includes initial study designs that allow for the evaluation of each of our product candidates in well-defined patient populations. We believe this enables the potential for early proof-of-concept and a higher probability of technical success, as well as accelerated clinical development and regulatory approval. To date, our efforts have produced a pipeline of novel, mechanism-based small molecule therapeutics that we believe have the potential to address the underlying chemical and biological mechanisms of various non-malignant blood-based disorders. Using this approach, we advanced GBT440, our lead product candidate, from molecular modeling into clinical development in less than three years.

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Our Development Pipeline

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

(1) We intend to initiate clinical development of GBT440 in pediatric populations and in other genotypes of SCD following the demonstration of proof-of-concept in our ongoing Phase 1/2 clinical trial.
(2) GBT440 and GBT440 analogs include patent rights jointly owned with third parties.

GBT440 for the Treatment of Sickle Cell Disease

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

Sickle Cell Disease Overview

SCD is a grievous disease that can lead to hemolytic anemia (the destruction of RBCs within blood vessels), vaso-occlusion (blocked blood flow to tissues), progressive multi-organ damage and early death. Beginning in childhood, patients suffer unpredictable and recurrent episodes or crises of severe pain due to blocked blood flow to organs, which often lead to psychosocial and physical disability. In addition, the constant destruction of RBCs with the release of their contents into the blood often leads to damaged or diseased blood vessels, which further exacerbate blood flow obstruction and multi-organ damage. Consequences of SCD can manifest in early childhood and may include cognitive dysfunction, stroke, increased susceptibility to infections due to spleen failure, heart-lung complications, kidney dysfunction, leg ulcers, priapism (a medical emergency due to refractory penile erection) and premature death. A 2014 publication noted that in the United States SCD results in a decrease of approximately 25 to 30 years in life expectancy.

SCD is an inherited blood disorder caused by a genetic mutation in the beta-chain of hemoglobin, which results in mutant hemoglobin known as sickle hemoglobin, or HbS. Hemoglobin is a protein in RBCs that carries oxygen from the lungs to the body s tissues and returns carbon dioxide from the tissues back to the lungs. Hemoglobin accomplishes this diametric function by binding and then releasing oxygen through allosterism, a process by which the hemoglobin molecule changes its shape to be high affinity for oxygen in the lungs, where oxygen is abundant, and low affinity for oxygen in the tissues, where oxygen must be released. Oxyhemoglobin,

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the high oxygen affinity form of hemoglobin, is formed in the lungs during respiration, when oxygen binds to the hemoglobin molecule, while deoxygenated hemoglobin, the low oxygen affinity form of hemoglobin, is formed when oxygen molecules are removed from the binding site as blood flows from the lungs to the body. In patients with SCD, deoxygenated HbS molecules polymerize to form long, rigid rods within an RBC, much like a sword within a balloon. As a consequence, the normally round and flexible RBC becomes rigid and elongated into a sickled shape. Sickled RBCs do not flow properly in the bloodstream; they clog small blood vessels and reduce blood flow to the organs. This results in inadequate oxygen delivery, or hypoxia, to all body tissues, which can lead to multi-organ failure and premature death.

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

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

HbSS, or sickle cell anemia, where both genes are HbS;

HbSC, where one gene is HbS, and the other is HbC; and

HbS/ßthal, where one gene is HbS, and the other is Beta thalassemia.

The HbS mutation confers a change in the shape of hemoglobin in its deoxygenated state, which causes deoxygenated hemoglobin molecules to polymerize. This polymerization is the mechanism by which HbS causes RBC sickling in all SCD genotypes, leading to the clinical manifestations of the disease. The spectrum of presentation of these clinical manifestations, however, is heterogeneous among different age groups and SCD genotypes. For example, infancy to adolescence is often marked by failure of the spleen to function correctly (which puts patients at risk for serious infections), painful inflammation of the fingers and toes, and adverse effects on the central nervous system, including strokes. In adulthood, clinical manifestations of the disease include the death of bone tissue due to a lack of blood supply, leg ulcerations and end-organ damage (including kidney, lung, heart and cardiovascular disease). Published observations have also suggested that some patients exhibit a greater degree of hemolysis, or the destruction of RBCs in the blood, which is associated with

vasculopathy, or damage to the blood vessels, which can cause pulmonary hypertension, retinopathy, or damage to the retina of the eye, and leg ulcers, while others exhibit less hemolysis and present more predominantly with pain crises. While some patients may present with fewer pain crises or lower hemolysis (thus higher levels of hemoglobin), the consensus remains that treatment is needed to prevent the inevitable negative impact of chronic hemolysis on organ function.

Market Opportunity in SCD

The CDC estimates the prevalence of SCD at 90,000 to 100,000 individuals in the United States. The incidence of SCD is estimated at approximately 1 in 2,000 to 2,500 newborns in the United States. It is estimated that the prevalence of SCD in Europe is approximately 60,000. The global incidence of SCD is estimated to be 250,000 to 300,000 births annually. SCD is concentrated in populations of African, Middle Eastern and South Asian descent.

SCD is a standard part of mandatory newborn screening in the United States. Of SCD patients in the United States, approximately 45% are under the age of 18, and approximately 60% to 65% have the HbSS genotype, which is often referred to as sickle cell anemia, with the remaining 35% to 40% having other genotypes. In all genotypes of SCD, the mechanism that leads to the consequences of the disease involves the polymerization of HbS in its deoxygenated state, which results in RBC sickling. We believe that because of this common mechanism, GBT440 may show activity across all SCD genotypes, although all of the animal models studied to date have involved the HbSS genotype.

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

Current Treatment Options and Their Limitations

Management strategies for SCD have evolved slowly, and the prophylactic treatment of SCD remains a significant unmet medical need. HU, which was initially approved as a chemotherapy drug, was approved by the FDA in 1998 for the treatment of SCD in adults. HU is the only therapeutic approved for SCD, and there is no approved therapeutic for SCD in pediatric patients in the United States. The use of HU is significantly limited by its side effect profile, variable patient responses and concerns of long-term toxicity. HU s side effects include impairment of fertility and the suppression of white blood cells (neutropenia) and platelets (thrombocytopenia), which place patients at risk for infection and bleeding.

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

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

targets the underlying mechanism of RBC sickling, which has the potential to halt the progression of the disease;

can be administered prophylactically in both children and adults;

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prevents or reduces the episodes or crises of severe pain associated with SCD;

prevents long-term complications of the disease;

has a more favorable side effect profile than currently available therapies; and

is available as a convenient, once-daily oral therapy.

Overview of Hemoglobin Biology and GBT440 s Mechanism of Action

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

We have demonstrated in preclinical models that our novel hemoglobin modifiers, including GBT440, bind to hemoglobin, resulting in increased oxygen affinity. The effect of these compounds on the measured OEC is a shift of the curve to the left on the horizontal axis. In other words, at a given prevailing oxygen tension in the blood, we have observed a higher percentage of oxygen saturation, or a higher proportion of oxyhemoglobin in the blood, following the administration of GBT440.

In various studies of SCD, scientists have demonstrated that hemoglobin in the oxygenated state is a potent inhibitor of HbS polymerization. Therefore, we believe that increasing the proportion of oxyhemoglobin, or left-shifting the OEC, could potentially delay the polymerization of HbS and prevent the sickling of RBCs, which may be able to ameliorate many, if not all, of the clinical manifestations of this disease. Importantly, we are able to measure the proportion of hemoglobin modification (%HbMOD), which is expressed as the percentage of hemoglobin molecules occupied or bound by GBT440.

HbF, which is present during fetal development and persists for up to six to nine months in infants until it is replaced by adult hemoglobin, has an inherent high affinity for oxygen, which is critical for a developing fetus to capture oxygen from the mother s blood. Newborns with SCD do not experience RBC sickling until approximately six to nine months of age, after which HbF is no longer expressed. Additionally, it has been observed that individuals who have inherited the HbS mutation and a gene deletion that allows them to continue to express 20% or more HbF in their RBCs into adulthood do not exhibit the clinical manifestations of SCD, despite expressing up to 80% HbS in their blood. Similarly, modification of hemoglobin by tucaresol, a drug that was developed by Burroughs Wellcome Co. in the 1990s, in the range of 10-24% demonstrated rapid anti-hemolytic and anti-sickling effects in SCD patients. However, the development of tucaresol was discontinued due to severe off-target immune-related side effects unrelated to its effects on hemoglobin modification.

Based on these observations, we believe that to delay polymerization of HbS, GBT440 would need to bind to only approximately 20% of the total hemoglobin in a patient s blood. One potential concern with increasing the affinity of hemoglobin for oxygen, however, is that excessive oxygen affinity can prevent hemoglobin from releasing oxygen

into the tissues, thus causing hypoxia. We believe based on HbF data and our animal studies that 20% modification would likely not adversely compromise oxygen delivery to the tissues.

Preclinical Data for GBT440 in SCD

We have evaluated the pharmacological, PK and safety profile of GBT440 in *in vitro* and *in vivo* PD, safety pharmacology, pharmacokinetic, and single and repeat dose (up to 28 days) toxicology studies. The results of our preclinical studies support our hypothesis that a modification of approximately 20% of HbS is likely to prevent RBC sickling and could halt the progression of SCD without compromising oxygen delivery to the tissues. Based on these results, we decided to advance GBT440 into clinical development.

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In vitro studies demonstrated that GBT440 potently increases hemoglobin oxygen affinity of both normal and sickle hemoglobin. As shown in the OEC below, we observed that the addition of various concentrations of GBT440 (ranging from 300 micromolar (μM) to 1 millimolar (mM)) to whole blood (20% hematocrit, which is the fraction of RBCs in blood) from SCD patients resulted in a dose-dependent left shift of the OEC, or an increase in hemoglobin oxygen affinity. This implies that in low oxygen environments, as observed in hypoxic tissue capillaries, GBT440 is capable of increasing the concentration of oxyhemoglobin present in RBCs.

GBT440 dose-dependently left-shifts the OEC, indicating an increased hemoglobin oxygen affinity

We also observed that GBT440 maintains HbS in its oxygenated state and delays the polymerization of deoxygenated HbS. Polymerization delay times predict the probability of RBC sickling within hypoxic tissue capillaries in SCD. An increase in polymerization delay time is expected to prevent sickling of RBCs in hypoxic tissues, which may allow enough time for RBCs to recirculate to oxygen-rich areas in the body, such as the lungs, where hemoglobin polymerization does not occur. The figures below depict polymerization of deoxygenated HbS, as measured *in vitro* by an increase in turbidity or cloudiness based on optical density, or OD, at a wavelength of 700 nanometers (nm) on the y-axis, over time on the x-axis. As illustrated in the left panel of the graph below, we observed that GBT440 increased the polymerization delay time of deoxygenated HbS. In addition, the increase in polymerization delay time associated with GBT440 was observed to be similar to that of HbF, which is a natural inhibitor of deoxygenated HbS polymerization, as illustrated in the right panel of the graph below.

Inhibition of HbS polymerization by binding GBT440 to HbS (GBT440-HbS) is comparable to that of HbF

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We also evaluated the anti-sickling activity of GBT440 by *in vitro* addition to SCD patient blood and by dosing transgenic mice carrying the human HbS mutation (SS) in their hemoglobin. We evaluated blood samples from both SCD patients and the SS mice at various oxygen tensions (pO_2 = 3-150 mmHg) and measured the percentage of sickled RBCs.

In the SCD patient blood samples, the *in vitro* addition of GBT440 (300 μM to 1000 μM) prior to deoxygenation was observed to reduce the percentage of sickled RBCs at low oxygen tensions. The table below shows the percentage of sickled RBCs observed in SCD patient blood samples at 20 mmHg (3% O_2 saturation) at various concentrations of GBT440:

	No compound	**300 μM GBT440**	**600 μM GBT440**	**1000 μM GBT440**
% Sickled RBC	57 ± 17	38 ± 6	23 ± 4	7 ± 3

In transgenic mice orally dosed with GBT440 (100 mg/kg twice a day for ~10 days), RBC sickling was evaluated *ex vivo* at various oxygen tensions. The standard reference from many labs that measure pO_2 in arterial and venous blood from healthy individuals report an arterial pO_2 range of 80 to 100 mmHg and a venous pO_2 range of ~17 to 41 mmHg. The left panel of the graph below shows a representative GBT440-treated mouse with a notable decrease in RBC sickling (60%) at low oxygen tensions (pO_2 =10-25 mm Hg), as compared to a vehicle-treated control mouse.

Similar to SCD patients, the half-life of RBCs in SS mice is shorter than in healthy mice. SS mice exhibit increased RBC damage and RBC clearance. We conducted a study in which GBT440 and vehicle-treated SS mice were injected with biotin producing pulse labelled RBCs. The right panel of the graph below shows the levels of biotin-labeled RBCs (y-axis) over seven days (x-axis) for GBT440-treated and vehicle-treated SS mice, indicating a prolongation of RBC half-life (3.8 ± 0.1 days) in GBT440-treated versus vehicle-treated SS mice (2.4 ± 0.1 days).

GBT440 reduces *ex vivo* sickling and extends RBC half-life in a transgenic mouse model of SCD

In addition, the PK of GBT440 in four animal species showed preferential partitioning into the RBC compartment relative to blood plasma upon oral dosing, suggesting a high affinity and specificity for hemoglobin. Oral absorption and sustained blood exposure following single and repeat doses suggest that GBT440 may be suitable for daily oral dosing in patients.

Animal safety pharmacology studies of GBT440 have identified no adverse drug related effects and indicate low risk to humans for central nervous system, respiratory or cardiovascular function. Both *in vitro* and *in vivo* good laboratory practices, or GLP, studies demonstrate that GBT440 has a low risk of genotoxicity in humans.

GLP toxicology studies (28 day repeat dosing) identified expected pharmacologic effects in rats and a no adverse effect level in both rats and dogs that provided adequate safety factors for clinical investigation. Additionally, we observed an increase in hemoglobin levels and formation of new RBCs, consistent with the anticipated pharmacologic activity for a hemoglobin modifier with GBT440 s mechanism of action, at the no adverse effect level in rats. At the highest dose level tested in rats, which was approximately 40-fold higher than the target human dose, we observed gastrointestinal adverse events generally associated with the volume of compound dosed. Based on the results from our nonclinical studies, we elected to advance GBT440 into our first-in-human clinical trial in healthy subjects and SCD patients. In November 2014, the FDA cleared our IND, and the Medicines and Healthcare Products Regulatory Agency in the United Kingdom cleared our clinical trial authorization, or CTA, to proceed with this trial.

Ongoing Phase 1/2 Clinical Trial of GBT440

In December 2014, we initiated our first clinical trial of GBT440, a randomized, placebo-controlled, double-blind, single and multiple ascending dose study in which we are evaluating the safety, tolerability, PK and PD of GBT440 in both healthy subjects and patients with SCD. We refer to this trial as study GBT440-001. The trial is currently being conducted at Guy s Hospital in London, United Kingdom, and is designed to enroll between 96 and 128 subjects, randomized 6:2 (GBT440:placebo) in twelve cohorts. Subjects will receive daily oral dosing of GBT440 or placebo for one day (single dose) and up to 28 days (multiple ascending doses). We also intend to evaluate exploratory markers of SCD activity, including anti-hemolytic effects, and SCD-related clinical effects. We are evaluating GBT440 s ability to prevent the hemolysis or destruction of RBCs in SCD patients by measuring the blood levels of LDH and bilirubin, as well as reticulocyte counts. LDH and bilirubin are released when RBCs undergo hemolysis, and reticulocytes are young RBCs that are released by the bone marrow in response to the ongoing hemolysis; thus we believe that lower levels of LDH and bilirubin and reduced reticulocyte counts represent potential markers for decreased hemolysis. We also plan to gather *ex vivo* sickling data to evaluate whether GBT440 has the ability to prevent the sickling of RBCs when they are subjected to de-oxygenation in a test tube. We believe that findings of anti-sickling activity may translate into an improvement in anemia, as well as the prevention of the downstream effects such as pain episodes, leg ulcers and organ damage associated with RBC sickling in SCD patients. We anticipate that some of the data generated in this Phase 1/2 clinical trial could be used to support early proof-of-concept regarding the anti-sickling and clinical benefit of GBT440 in SCD patients. Subject to enrollment in accordance with our current plans, we anticipate completing this trial in the second quarter of 2016.

The following graphic illustrates the design of our Phase 1/2 clinical trial:

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As of July 31, 2015, we have dosed 48 subjects in six single dose cohorts, comprised of 40 healthy volunteers (30 of whom received GBT440 and ten of whom received placebo) and eight SCD patients (six of whom received GBT440 and two of whom received placebo) in study GBT440-001. Additionally, we have dosed 32 subjects in four multiple dose cohorts, comprised of 24 healthy volunteers (18 of whom received GBT440 and six of whom received placebo) and eight SCD patients (six of whom received GBT440 and two of whom received placebo). In the multiple dose arm of our trial, all 24 healthy volunteers have completed 15-day dosing and eight SCD patients have completed 28-day dosing and are currently in the follow-up period. All of the eight SCD patients who received multiple doses of GBT440 were evaluable for safety and efficacy at the 28-day time point.

To date, no drug-related serious adverse events have been reported. One serious adverse event involving a sickle cell crisis requiring hospitalization was reported in a placebo subject in the multiple dose cohort of SCD patients; the treatment assignment was unblinded by the principal investigator. Adverse events leading to dose modification in the multiple dose cohorts included a transient and mild generalized rash observed in one healthy volunteer, mild to moderate headache observed in one healthy volunteer, and mild to moderate abdominal pain observed in one SCD patient. We have observed no adverse events related to tissue hypoxia, renal, liver or immune functions. We observed a mild transient rash in a healthy subject in our recently initiated open-label, non-randomized clinical pharmacology study, which we refer to as study GBT440-002, studying the absorption, metabolism and elimination of GBT440. In this study, subjects receive a loading dose of 2000 mg of GBT440 (Day 1), followed by 400 mg daily for four days (Days 2-5, with radiolabelled dosing on Day 5). The healthy volunteer subject developed a mildly pruritic, papular rash on the neck and extremities on Day 2 of dosing, which was not associated with any systemic findings. Due to rapid improvement by the next day, the subject continued dosing. The rash has resolved, and the subject completed all doses of GBT440 in study GBT440-002.

Among the SCD patients who received multiple doses of GBT440 (700 mg once a day) in study GBT440-001, from baseline (Day -1) to Day 28, we have observed improvements in anemia as evidenced by an increase in hemoglobin (Hb) levels, improvement in hemolytic parameters and tissue oxygenation as evidenced by declines in reticulocyte counts, unconjugated bilirubin, LDH and erythropoietin levels (as shown in Table 1 below on page 91), as well as a marked reduction in sickled RBCs in the peripheral blood.

We are currently enrolling an additional eight SCD patients (six active, two placebo) in our once-daily, 28-day multidose study to corroborate our initial clinical findings. In addition, we plan to evaluate one additional cohort in eight SCD patients (six active, two placebo) to explore a lower dose regimen, to further understand the GBT440 dose effect. We expect to receive data from these additional patients in August and September 2015.

The following figures present data from the eight SCD patients (six active, two placebo) who have completed our once-daily, 28-day dosing regimen.

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The percentage declines in unconjugated bilirubin, LDH, reticulocyte counts and erythropoietin levels are indicated in Figures 1, 2, 3 and 4 below, respectively, and the improvement in mean Hb levels is shown in Figure 5 below.

Figure 1: Unconjugated Bilirubin Levels from Baseline to Day 28

SEM = standard error of the mean

Figure 2: Lactate Dehydrogenase Levels from Baseline to Day 28

SEM = standard error of the mean

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Figure 3: Reticulocyte Counts from Baseline to Day 28

SEM = standard error of the mean

Figure 4: Erythropoietin Levels from Baseline to Day 28

SEM = standard error of the mean

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Figure 5: Mean Hemoglobin Levels from Baseline to Day 28

SEM = standard error of the mean

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On average, GBT440-treated subjects demonstrated significant improvement in hemolytic anemia and reduction in sickle cells. We observed stabilization of the hemoglobin level as well as greater variability in the hemolytic parameters after Day 15. The amount of hemoglobin per cell (mean cell hemoglobin, or MCH) and RBC size (mean cell volume, or MCV) appeared to decline in some subjects following Day 15. Possible explanations for the decrease could be a decrease in iron available for erythropoiesis due to chronic inflammation, absolute or functional iron deficiency or some other cause. Further clinical studies will be required to determine whether the MCH and MCV values will increase over time and if they might be associated with further increases in hemoglobin levels. Nonetheless, after reviewing individual subject efficacy data together with individual subject PK profiles, as shown in Figure 6 below, we believe the exposure-response relationship over the 28 days of treatment provides a plausible explanation of the variability of the efficacy data after Day 15.

Figure 6: GBT440 Blood Levels During the 28-Day Dosing Period

The following figures present patient-by-patient data for the six SCD patients who received GBT440 and who have completed our once-daily, 28-day multidose study. We refer to these six SCD patients as GBT1 through GBT6.

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Subject GBT1 achieved relatively low GBT440 exposure; blood levels were less than 200 mM at all timepoints which measured trough concentrations. This subject demonstrated some improvement in hemolytic anemia, with hemoglobin showing a modest increase and reticulocytes, unconjugated bilirubin and LDH showing modest decreases; improvements in hemoglobin, reticulocytes and unconjugated bilirubin appeared to be greater on Day 15 than Day 28. The percentage of sickled cells in the subject s peripheral blood also decreased, although to a lesser extent than other subjects. We believe the lesser efficacy in GBT1 than in other subjects and lack of further improvement in hemolytic parameters from Day 15 to Day 28 are likely due to the low blood levels of GBT440 achieved in this subject. The reason for the low blood levels is not clear at this time; determining the factors that affect GBT440 exposure will require treatment of larger numbers of subjects. Subject GBT1 s hematology and hemolytic parameters after 28-day dosing are shown in Figure 7 below:

Figure 7: Hematology and Hemolytic Parameters for GBT1

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Subjects GBT2 and GBT3 achieved the highest exposures of GBT440, both maintaining blood levels above 200 mM beginning on Day 15 and maintained through 28 days. These subjects also demonstrated the most pronounced trends in improvement of hemolytic anemia. Both subjects showed progressive improvement in hemoglobin, reticulocyte and unconjugated bilirubin levels during the treatment period. The LDH level in subject GBT2 did not improve further from Day 15 to Day 28, but we believe this may be because this subject s LDH level on Day 15 was already near normal. The percentage of sickle cells in both subjects was nearly undetectable and showed continued and progressive improvement over 28 days. Subject GBT2 s and subject GBT3 s hematology and hemolytic parameters after 28-day dosing are shown in Figure 8 and Figure 9, respectively, below:

Figure 8: Hematology and Hemolytic Parameters for GBT2

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Figure 9: Hematology and Hemolytic Parameters for GBT3

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Subject GBT4 achieved drug exposures that were lower compared to subjects GBT2 and GBT3. While GBT4 showed improvement in hemoglobin, reticulocytes and LDH levels in the first 15 days, these values worsened after Day 15. The reason for this is unclear and may be due to intra-patient variability or potentially suboptimal drug exposure levels. Despite the changes in hematologic and hemolysis parameters after Day 15, the percentage of sickle cells in the subject s peripheral blood declined significantly on Day 15, and this reduced sickle cell count was maintained through Day 28. Subject GBT4 s hematology and hemolytic parameters after 28-day dosing are shown in Figure 10 below:

Figure 10: Hematology and Hemolytic Parameters for GBT4

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Subject GBT5 achieved high drug exposures through Day 12 (similar to the GBT440 exposure levels for subjects GBT2 and GBT3). This subject s dose was reduced on Day 11 from 700 mg to 400 mg, due to abdominal cramps, and drug levels were substantially lower (below 200 mM) after Day 12. While subject GBT5 showed initial improvements in unconjugated bilirubin, LDH, reticulocyte count and hemoglobin levels from baseline to Day 15, after Day 15, with the exception of hemoglobin, these values increased, which we believe may be related to the reduced drug levels after the dose reduction on Day 11. Subject GBT5 s hematology and hemolytic parameters after 28-day dosing are shown in Figure 11 below:

Figure 11: Hematology and Hemolytic Parameters for GBT5

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Subject GBT6 exhibited good drug exposure in the early dosing period while admitted in the clinical research unit, similar to subjects GBT2 and GBT3; however, on Day 15, GBT440 blood levels in this subject decreased by more than half and were low over the remainder of the dosing period. The PK profile is consistent with lack of adherence to the dosing regimen beginning at some time between Day 8 and 15, after the subject had left the clinical research unit. Subject GBT6 showed an initial significant improvement in all hematology and hemolytic parameters at Day 15, likely corresponding to favorable drug exposure during this early period. At Day 28, when trough drug exposures were near their lowest level, the improvements seen in hemoglobin, reticulocyte count and LDH were diminished. However, this subject s sickle cell count in the peripheral blood dramatically improved and remained very low throughout the treatment period despite what appears to be the re-emergence of hemolysis. We believe this may be due to sustained protection of the RBCs by GBT440 during the early treatment period, while newly emerging cells from the bone marrow are unprotected and undergo hemolysis.

Figure 12: Hematology and Hemolytic Parameters for GBT6

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Sickle-shaped RBCs constitute the basis of sickle cell disease and are the end-result of damage caused by numerous cycles of hemoglobin S polymerization, which results in abnormal, sticky and undeformable RBCs that cause pain crisis, vaso-occlusion and other clinical morbidity. As noted in the individual patient profiles above, five out of six patients treated with GBT440 exhibited profound reductions in sickle cell counts over the 28-day dosing period. A representative peripheral blood smear from a GBT-440 treated subject is shown in Figure 13 below.

Figure 13: Peripheral Blood Smear of a GBT440-Treated Subject at Baseline (Day -1) and Day 28

Overall, these data indicate that GBT440 was well tolerated in both healthy subjects and SCD patients. Proof of concept was demonstrated during this 28-day treatment period with a rapid decline in hemolytic parameters and improvement in anemia, which appear to correlate with drug exposure. We believe another possible explanation for the stability in the hemoglobin levels after Day 15 could be a decrease in iron available for erythropoiesis due to chronic inflammation, absolute or functional iron deficiency or some other cause. We believe this result is unlikely to be attributable to the loss of GBT440 drug effect, as this would be reflected by an overall decline in hemoglobin levels. Finally, treatment with GBT440 led to profound reductions in sickle cell counts in the peripheral blood, which we believe support the potential for GBT440 to serve as a disease-modifying therapy for SCD.

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Table 1: Summary of Hematology and Hemolytic Parameters

	Hb (g/dL)	Reticulocytes (%)	LDH (U/L)	Unconjugated Bilirubin (µmol/L)	Epo (U/L)	% Sickle Cell
GBT1						
Day -1	9.5	14.02	1239	26.0	132.0	19.4
Day 15	10.7	8.93	1381	17.7	40.1	10.8
Day 28	10.1	10.59	1146	19.6	45.4	11.2
GBT2						
Day -1	9.2	7.82	1009	102.3	64.2	15.1
Day 15	10.1	3.76	656	59.7	49.7	0.3
Day 28	10.5	2.25	669	56.7	43.8	0.15
GBT3						
Day -1	8.9	5.03	721	85.0	113.0	7.3
Day 15	8.9	2.36	643	44.0	67.6	2.9
Day 28	9.8	1.60	525	39.5	55.6	0.4
GBT4						
Day -1	8.2	5.18	696	11.5	68.5	5.3
Day 15	9.4	3.12	679	8.3	42.0	0.2
Day 28	9.0	3.42	758	12.5	54.0	0.4
GBT5						
Day -1	9.6	5.62	884	15.2	173.0	2.1
Day 15	10.3	5.22	750	8.4	123.0	0.3
Day 28	11.0	5.76	820	14.8	152.0	0.6
GBT6						
Day -1	9.8	8.19	825	58.2	39.4	8.3
Day 15	10.4	5.64	642	44.6	38.8	1.7
Day 28	9.6	8.96	766	39.3	65.3	0.4
PLA1						
Day -1	8.2	15.84	1650	244.4	70.9	14.0
Day 15	8.3	16.04	1713	186.2	82.0	21.2
Day 28	7.4	18.19	1495	181.1	125.0	17.1
PLA2						
Day -1	7.7	7.73	1310	18.0	116.0	12.7
Day 15	7.6	5.72	1094	17.8	101.0	13.0
Day 28	7.6	6.92	1200	19.2	104.0	14.6

Hb = hemoglobin, Epo = erythropoietin, GBT = GBT treated subject, PLA = placebo subject

Subsequent Clinical and Regulatory Path for GBT440

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

populations in the first half of 2016.

We believe GBT440 may hold significant potential for SCD patients and could become the first mechanism-based and disease-modifying therapeutic for this grievous disease. Based on nonclinical data and the size of the SCD patient population in the United States and Europe, we believe GBT440 may meet the FDA s requirements

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for an Orphan Drug Designation, or ODD, and could be eligible for the ODD designation in Europe. Subject to the availability of data from SCD patients in our ongoing clinical trial, we intend to submit ODD applications in the United States and Europe for GBT440 in SCD. Additionally, because available therapies in SCD are limited, the FDA has suggested that the development of new therapies for SCD is an agency priority. As a result, we believe there may be an opportunity to accelerate the development of GBT440 through one or more of the FDA s expedited designation or approval programs, such as Fast Track, Breakthrough Therapy, Accelerated Approval and Priority Review. In particular, we believe that if positive, the data from SCD patients receiving multiple doses in our ongoing clinical trial, such as reduction in LDH, bilirubin, reticulocyte counts and improvement in anemia, may demonstrate the beneficial effect of GBT440 on clinical parameters of hemolysis and resolution of anemia, which could potentially form the basis for qualification for expedited designation or approval programs.

Evaluation of GBT440 and Analogs in Hypoxemic Pulmonary Disorders

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

We are evaluating our proprietary compounds in a variety of disorders in which hypoxia is believed to play a key role in disease progression and adverse patient outcomes, including IPF and ARDS.

IPF is a disease characterized by progressive scarring of the lungs, which leads to their deterioration. The prognosis is poor for patients with IPF, which occurs primarily in people 40 to 70 years old, with a median survival time from diagnosis of two to three years.

ARDS occurs when fluid builds up in the alveoli, or air sacs within the lungs, commonly as a result of diffuse alveolar injury, pulmonary edema and profound hypoxemia caused by sepsis, aspiration, trauma or massive transfusion. Nearly all ARDS patients require endotracheal intubation, mechanical ventilation and high fraction of inspired oxygen, or FiO_2, to maintain adequate oxygenation. While much of the mortality is caused by the underlying disease, complications associated with the current standard of care, including ventilator-associated pneumonia or tissue damage as a result of unequalized air pressure between the ventilator and the surrounding environment in the case of mechanical ventilation, or exposure to toxic oxygen concentrations ($FiO_2 > 50\%$), are a major cause of morbidity, mortality and healthcare costs. This highlights the need for a therapy that reduces the duration and intensity of mechanical ventilation and the exposure to toxic levels of oxygen concentration in ARDS patients.

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

Study 1: Tolerance of animals to 5% O_2 hypoxia

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

In the acute lung injury model (Study 2), lipopolysaccharide, or LPS (a potent pro-inflammatory bacterial endotoxin), was used to induce lung injury. Additionally, animals were exposed to 5% O_2 producing hypoxemia. In the chronic lung injury model (Study 3), bleomycin was used to induce lung injury, resulting in increased fibrosis and hypoxemia over a period of two weeks. The animals were then treated with a GBT440 analog or control. The results of these studies are shown in the graphs below, which suggest that a hemoglobin-modifying agent such as GBT440 may improve oxygen uptake in a lung with diffuse injury characterized by acute inflammation or fibrosis.

Study 2: Tolerance of LPS-treated animals to 5% O_2 hypoxia

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

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

Oral Kallikrein Inhibitor in Hereditary Angioedema

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

All currently marketed therapeutics for HAE must be administered intravenously or by subcutaneous injection. As a result, we believe that the availability of a safe and effective oral prophylactic agent would have the potential to transform the treatment paradigm for this disease. We are currently conducting preclinical research to develop an orally available therapeutic that could potently and selectively inhibit plasma kallikrein for the treatment of HAE. We believe that increased selectivity for the target will result in fewer off-target effects as compared to currently available therapeutics for HAE. Subject to the results of our ongoing preclinical research, we intend to select a product candidate for clinical investigation with the goal of initiating a Phase 1 clinical trial of an oral kallikrein inhibitor for HAE in the second half of 2016.

Manufacturing

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

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We believe the synthesis of the drug substance for GBT440 is reliable and reproducible from readily available starting materials, and the synthetic routes are amenable to large-scale production and do not require unusual equipment or handling in the manufacturing process. We have obtained an adequate supply of the drug substance for GBT440 from our first CMO to satisfy our immediate clinical and nonclinical demands. We have engaged a second drug substance CMO to ensure continuity of supply, to increase overall production capacity and to conduct additional research and development work to refine our current manufacturing process. We are implementing improvements to our drug substance manufacturing process to further ensure production capacity adequate to meet future development and commercial demands. We have also contracted with a third drug substance CMO with sufficient production capacity for larger scale production, which we anticipate will be required to support late stage development and commercialization.

Drug product formulation development work for GBT440 is in progress. We have contracted with a third-party manufacturer capable of both formulation development and drug product manufacturing through early commercialization. We may identify a second drug product manufacturer in the future to add further capacity and redundancy to our supply chain. In our ongoing clinical trial of GBT440, we are utilizing a powder in capsule formulation. For future development and commercialization, we intend to develop both capsule and liquid/solution formulations for the adult/adolescent and children/infant SCD populations, respectively.

Intellectual Property

We strive to protect the proprietary technology that we believe is important to our business, including seeking and maintaining patents and patent applications intended to cover our product candidates and compositions, their methods of use and processes for their manufacture, and any other aspects of inventions that are commercially important to the development of our business. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

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

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

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

States Patent and Trademark Office, or USPTO, to determine priority of invention.

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Patents

Our patent portfolio includes three issued U.S. patents, two allowed U.S. patent applications, and several U.S. and foreign patent applications in the early stages of prosecution. The issued patent (U.S. Patent No. 9,018,210) covering the composition of matter for GBT440 and analogs, which we may own jointly with the Regents of the University of California, or the Regents, was granted on April 28, 2015 and is currently expected to expire in 2032 absent any applicable patent term extensions. The issued U.S. patents (U.S. Patent Nos. 8,952,171 and 9,012,450), covering the composition of matter for GBT440 analogs, were granted on February 10, 2015 and April 21, 2015, respectively, and are currently expected to expire in 2033 and 2032, respectively, absent any applicable patent term extensions. We also own U.S. Patent No. 9,012,450 jointly with the Regents. The risks associated with joint ownership of patent rights are more fully discussed under Risk Factors Risks Related to Our Intellectual Property. The foreign patent applications covering the composition of matter for GBT440 and analogs, if issued, would in each case be expected to expire between 2032 and 2035, absent any applicable patent term extensions. Our patent applications fall into three major categories: (i) GBT440; (ii) GBT440 analogs and (iii) kallikrein modulators.

GBT440 patent portfolio. Our patent portfolio relating to GBT440 is comprised of seven patent families and includes patent applications covering certain compositions of matter, methods of use and certain polymorphs related to GBT440 pending in a variety of jurisdictions, including the United States, jurisdictions under the Patent Cooperation Treaty, or PCT, Argentina, and Taiwan. The issued U.S. patent (U.S. Patent No. 9,018,210) covering the composition of matter for GBT440 was granted on April 28, 2015 and is currently expected to expire in 2032, absent any applicable patent term extensions. Any patents that may issue from our other patent applications relating to GBT440 in the United States, if issued, would be expected to expire between 2032 and 2035, absent any applicable patent term extensions. Any patents that may issue from corresponding PCT and foreign patent applications, if issued, would also be expected to expire between 2032 and 2035, absent any applicable patent term extensions. Some of these pending patent applications are jointly owned by us and the Regents.

GBT440 analogs patent portfolio. Our patent portfolio relating to GBT440 analogs is comprised of ten patent families and includes patent applications covering certain compositions of matter and methods of use for GBT440 analogs pending in a variety of jurisdictions, including the United States, jurisdictions under the PCT, Argentina and Taiwan. The two issued U.S. patents (U.S. Patent No. 8,952,171 and U.S. Patent No. 9,012,450, respectively) covering the composition of matter for GBT440 analogs are currently expected to expire in 2033 and 2032, respectively, absent any applicable patent term extensions. Any patents that may issue from the other patent applications relating to GBT440 analogs in the United States, if issued, would be expected to expire between 2032 and 2036, absent any applicable patent term extensions. Any patents that may issue from corresponding PCT and foreign patent applications, if issued, would be expected to expire between 2032 and 2036, absent any applicable patent term extensions. Some of these pending patent applications are jointly owned by us and the Regents.

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

Patent term

The base term of a U.S. patent is 20 years from the filing date of the earliest-filed non-provisional patent application from which the patent claims priority assuming that all maintenance fees are paid. The term of a U.S. patent can be lengthened by patent term adjustment, which compensates the owner of the patent for administrative delays at the USPTO the extent of which is offset by delays by the patent owner before the USPTO in obtaining the patent. In some

cases, the term of a U.S. patent is shortened by a terminal disclaimer that reduces its term to that of an earlier-expiring patent. The term of a U.S. patent may be eligible for patent term extension under the Drug Price

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Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act, to account for at least some of the time the drug is under development and regulatory review after the patent is granted. With regard to a drug for which FDA approval is the first permitted marketing of the active ingredient, the Hatch-Waxman Act allows for extension of the term of one U.S. patent that includes at least one claim covering the composition of matter of an FDA-approved drug, an FDA-approved method of treatment using the drug and/or a method of manufacturing the FDA-approved drug. The extended patent term cannot exceed the shorter of five years beyond the non-extended expiration of the patent or 14 years from the date of the FDA approval of the drug. Some foreign jurisdictions, including Europe and Japan, have analogous patent term extension provisions, which allow for extension of the term of a patent that covers a drug approved by the applicable foreign regulatory agency. In the future, if our product candidates receive FDA approval, we expect to apply for patent term extension on patents, if issued, covering those products, their methods of use and/or methods of manufacture.

Trade secrets

In addition to patents, we rely on trade secrets and know-how to develop and maintain our competitive position. We typically rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. We protect trade secrets and know-how by establishing confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors and contractors. These agreements generally provide that all confidential information developed or made known during the course of an individual or entities relationship with us must be kept confidential during and after the relationship. These agreements also typically provide that all inventions resulting from work performed for us or relating to our business and conceived or completed during the period of employment or assignment, as applicable, shall be our exclusive property. In addition, we take other appropriate precautions, such as physical and technological security measures, to guard against misappropriation of our proprietary information by third parties.

Sales and Marketing

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

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

Competition

The biopharmaceutical industry is highly competitive. There are many public and private biopharmaceutical companies, universities, governmental agencies and other research organizations actively engaged in the research and

development of products that may be similar to our product candidates or address similar markets. In addition, the number of companies seeking to develop and commercialize products and therapies similar to our product candidates is likely to increase.

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In the area of SCD, we expect to face competition from HU (marketed as DROXIA or Hydrea by Bristol-Myers Squibb Company as well as in generic form), which is currently the only approved therapeutic for the treatment of SCD. Several companies are also developing product candidates for chronic treatment in SCD, including Selexys Pharmaceuticals Corporation (in collaboration with Novartis AG), which is engaged in the clinical development of SelG1, an anti-P-selectin monoclonal antibody, and Baxter International Inc., which is conducting a Phase 2 clinical trial of Aes-103, an orally available small molecule compound that is also intended to work by increasing hemoglobin oxygen affinity. We also expect to face competition from one-time therapies for SCD, including hematopoietic stem cell transplantation, gene therapy and gene editing. In particular, Bellicum Pharmaceuticals, Inc. is conducting a Phase 1/2 clinical trial of BPX-501 as an adjunct T-cell therapy administered after allogeneic hematopoietic stem cell transplant in pediatric patients with orphan inherited blood disorders, and bluebird bio, Inc. is currently engaged in the clinical development of LentiGlobin BB305, which aims to treat SCD by inserting a functional human beta-globin gene into the patient s own hematopoietic stem cells, or HSCs, *ex vivo* and then transplanting the modified HSCs into the patient s bloodstream.

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

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

Government Regulation

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

U.S. drug development

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. Drugs are also subject to other federal, state and local statutes and regulations. The process

of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

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Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the FDA s refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, product recalls or withdrawals from the market, product seizures, total or partial suspension of production or distribution injunctions, fines, refusals of government contracts, restitution, disgorgement, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

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

- completion of extensive non-clinical studies in accordance with applicable regulations, including the FDA s GLP regulations;
- submission to the FDA of an IND application, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, or ethics committee at each clinical trial site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with applicable IND regulations, good clinical practices, or GCPs, and other clinical-trial related regulations to establish the safety and efficacy of the investigational drug for each proposed indication;
- submission to the FDA of an NDA, for a new drug;
- a determination by the FDA within 60 days of its receipt of an NDA to accept it for filing;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities where the drug is produced to assess compliance with current good manufacturing practices, or cGMPs, to assure that the facilities, methods and controls are adequate to preserve the drug s identity, strength, quality and purity;
- potential FDA audit of the non-clinical and/or clinical trial sites that generated the data in support of the NDA; and
- FDA review and approval of the NDA, including consideration of the views of any FDA advisory committee, prior to any commercial marketing or sale of the drug in the United States.

The non-clinical and clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for our product candidates will be granted on a timely basis, or at all. The data required to support an NDA is generated in two distinct development stages: non-clinical and clinical. The non-clinical development stage generally involves synthesizing the active component, developing the formulation and determining the manufacturing process, as well as carrying out non-human toxicology, pharmacology and drug metabolism studies in the laboratory, which support subsequent clinical testing in humans. The sponsor must submit the results of the non-clinical studies, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational drug product to humans, and must become effective before human clinical trials may begin.

The clinical stage of development involves the administration of the drug candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor s control, in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and

any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Further, each clinical trial must be reviewed and approved by an independent IRB for each institution at which the clinical trial will be conducted to ensure that the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries.

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

Clinical trials

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

Phase 1 clinical trials generally involve a small number of healthy volunteers who are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action, side effect tolerability and safety of the drug.

Phase 2 clinical trials typically involve studies in disease-affected patients to determine the dose required to produce the desired benefits. At the same time, safety and further pharmacokinetic and pharmacodynamic information is collected, possible adverse effects and safety risks are identified and a preliminary evaluation of efficacy is conducted.

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

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

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

clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB s requirements or if the drug has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access to certain data from the trial. Concurrent with clinical trials, companies usually

complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, must include methods for testing the identity, strength, quality and purity of the final drug product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

NDA and FDA review process

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

Under the Prescription Drug User Fee Act, or PDUFA, as amended, each NDA must be accompanied by a user fee. The FDA adjusts the PDUFA user fees on an annual basis. According to the FDA s fee schedule, effective through September 30, 2015, the user fee for an application requiring clinical data, such as an NDA, is approximately $2.3 million. PDUFA also imposes an annual product fee for human drugs (approximately $0.1 million) and an annual establishment fee (approximately $0.6 million) on facilities used to manufacture prescription drugs. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on NDAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

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

Before approving an NDA, the FDA will conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether they comply with cGMPs. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The FDA may also audit data from clinical trials to ensure compliance with GCP requirements. Additionally, the FDA may refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. The FDA will likely re-analyze the clinical trial data, which could result in extensive discussions between the FDA and the applicant during the review process. The review and evaluation of an NDA by the FDA is extensive and time consuming and may take longer than originally planned to complete, and we may not receive a timely approval, if at all.

After the FDA evaluates an NDA, it will issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the

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application will not be approved in its present form. A Complete Response Letter usually describes all of the specific deficiencies in the NDA identified by the FDA. The Complete Response Letter may require additional clinical data and/or an additional pivotal Phase 3 clinical trial(s), and/or other significant and time-consuming requirements related to clinical trials, non-clinical studies or manufacturing. If a Complete Response Letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data.

Orphan drug designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug product intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for this type of disease or condition will be recovered from sales of the product. Orphan product designation must be requested before submitting an NDA. After the FDA grants orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication for seven years from the date of such approval, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity by means of greater effectiveness, greater safety, or by providing a major contribution to patient care. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication than that for which the orphan product has exclusivity. Orphan product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same product as defined by the FDA for the same indication we are seeking, or if our product candidate is determined to be contained within the competitor s product for the same indication or disease. If a drug designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity. Orphan drug status in the European Union, or EU, has similar, but not identical, requirements and benefits.

Expedited development and review programs

The FDA has a Fast Track program that is intended to expedite or facilitate the process for reviewing new drugs that meet certain criteria. Specifically, new drugs are eligible for Fast Track designation if they are intended to treat a serious or life threatening condition and non-clinical or clinical data demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to both the product and the specific indication for which it is being studied. The sponsor of a new drug may request the FDA to designate the drug as a Fast Track product at any time during the clinical development of the product prior to receiving NDA approval.

Any product submitted to the FDA for marketing, including under a Fast Track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. Any product is eligible for priority review if it treats a serious or life-threatening condition and, if approved, would provide a significant improvement in safety and effectiveness compared to available therapies.

The FDA will attempt to direct additional resources to the evaluation of an application for a new drug designated for priority review in an effort to facilitate the review. A product may also be eligible for accelerated approval. An investigational drug may obtain accelerated approval if it treats a serious or life-threatening

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

Additionally, a drug may be eligible for designation as a breakthrough therapy if the drug is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. The benefits of breakthrough therapy designation include the same benefits as fast track designation, plus intensive guidance from FDA to ensure an efficient drug development program. Fast Track designation, priority review, accelerated approval and breakthrough designation do not change the standards for approval but may expedite the development or approval process.

Pediatric information

Under the Pediatric Research Equity Act, an NDA or supplement to an NDA must contain data to assess the safety and efficacy of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of pediatric data or full or partial waivers. The Food and Drug Administration Safety and Innovation Act, which was signed into law on July 9, 2012, amended the FDCA to require that a sponsor who is planning to submit a marketing application for a drug that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan, or PSP, within sixty days of an end-of-Phase 2 meeting or, if there is no end-of-Phase 2 meeting as early as practicable before the initiation of the Phase 3 or Phase 2/3 study. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from non-clinical studies, early phase clinical trials, and/or other clinical development programs.

Post-marketing requirements

Following approval of a new product, a pharmaceutical company and the approved product are subject to continuing regulation by the FDA, including, monitoring and recordkeeping activities, reporting of adverse experiences and complying with promotion and advertising requirements, which include restrictions on promoting drugs for uses or for patient populations for which the drug was not approved (known as off-label use), and limitations on industry-sponsored scientific and educational activities. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such off-label uses. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use. Further, if there are any modifications to the drug, including changes in indications, labeling, or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA or NDA supplement, which may require the applicant to develop additional data or conduct additional non-clinical studies and clinical trials.

The FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMP. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products in accordance with cGMP regulations. These manufacturers must comply with cGMP regulations that require among other things, quality control and quality assurance, the maintenance of

records and documentation, and the obligation to investigate and correct any deviations from cGMP. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. The discovery of violative conditions, including failure to conform to cGMP, could result in enforcement actions, and the discovery of problems with a product after approval may result in restrictions on a product, manufacturer or holder of an approved NDA, including recall.

Other regulatory matters

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

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

Moreover, although we would not submit claims directly to payors, drug manufacturers can be held liable under the federal False Claims Act, which prohibits anyone from knowingly presenting, or causing to be presented, for payment to federal programs (including Medicare and Medicaid) claims for items or services, including drugs, that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services. The government may deem manufacturers to have caused the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label. In addition, our future activities relating to the reporting of wholesaler or estimated retail prices for our products, the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state, and third-party reimbursement for our products, and the sale and marketing of our products, are subject to scrutiny under this law. Penalties for a False Claims Act violation include three times the actual damages sustained by the government, plus mandatory civil penalties of between $5,500 and $11,000 for each separate false claim, the potential for exclusion from participation in federal healthcare programs, and the potential implication of various federal criminal statutes.

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

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

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

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

U.S. patent term restoration and marketing exclusivity

Depending upon the timing, duration and specifics of the FDA approval of our drug candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product s approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA plus the time between the submission date of an NDA and the approval of that application, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we intend to apply for restoration of patent term for one of our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA. The request for patent term extension must be filed within a very short time frame after approval of the drug by the FDA. Failure to meet this time frame negates any patent term extension available.

Marketing exclusivity provisions under the FDCA can also delay the submission or the approval of certain marketing applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovator drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder. The FDCA also provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA for a drug

product that contains an active moiety that has been previously approved if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example for new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not

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prohibit the FDA from approving ANDAs for drugs containing the active agent for the original indication or condition of use. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the non-clinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and efficacy. Orphan drug exclusivity, as described above, may offer a seven-year period of marketing exclusivity, except in certain circumstances. Pediatric exclusivity is another type of regulatory market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued Written Request for such a trial. The FDA issues a written request for pediatric clinical trials prior to approval of a NDA only where it determines that information relating to the use of a drug in a pediatric population, or part of the pediatric population, may produce health benefits in that population.

European Union drug development

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

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

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

European Union drug review and approval

In the European Economic Area, or EEA, (which is comprised of the 27 Member States of the EU plus Norway, Iceland and Liechtenstein), medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of marketing authorizations:

The Community MA is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the European Medicines Agency, or EMA, and is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, advanced-therapy medicines such as gene-therapy, somatic cell-therapy or tissue-engineered medicines, and medicinal products containing a new active substance indicated for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions, and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member States through the Mutual Recognition Procedure.

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If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. Under the Decentralized Procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member State, or RMS. The competent authority of the RMS prepares a draft assessment report, a draft summary of the product characteristics, or SPC, and a draft of the labeling and package leaflet, which are sent to the other Member States (referred to as the Member States Concerned) for their approval. If the Member States Concerned raise no objections, based on a potential serious risk to public health, to the assessment, SPC, labeling, or packaging proposed by the RMS, the product is subsequently granted a national MA in all the Member States (i.e., in the RMS and the Member States Concerned).

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

European Union new chemical entity exclusivity

In the EU, new chemical entities, sometimes referred to as new active substances, qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. The data exclusivity, if granted, prevents regulatory authorities in the EU from referencing the innovator s data to assess a generic application for eight years, after which generic marketing authorization can be submitted, and the innovator s data may be referenced, but not approved for two years. The overall ten-year period will be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are determined to bring a significant clinical benefit in comparison with existing therapies.

European Union orphan designation and exclusivity

In the EU, the EMA s Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than 5 in 10,000 persons in the EU Community (or where it is unlikely that the development of the medicine would generate sufficient return to justify the investment) and for which no satisfactory method of diagnosis, prevention, or treatment has been authorized (or, if a method exists, the product would be a significant benefit to those affected).

In the EU, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity is granted following medicinal product approval. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. Orphan drug designation must be requested before submitting an application for marketing approval. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

Rest of the world regulation

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

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

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Reimbursement

Sales of our products will depend, in part, on the extent to which our products will be covered by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. In the United States, no uniform policy of coverage and reimbursement for drug products exists. Accordingly, decisions regarding the extent of coverage and amount of reimbursement to be provided for any of our products will be made on a payor by payor basis. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained.

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

The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the Department of Health and Human Services as a condition for states to receive federal matching funds for the manufacturer s outpatient drugs furnished to Medicaid patients. Effective in 2010, the ACA made several changes to the Medicaid Drug Rebate Program, including increasing pharmaceutical manufacturers rebate liability by raising the minimum basic Medicaid rebate on most branded prescription drugs from 15.1% of average manufacturer price, or AMP, to 23.1% of average manufacturer price, or AMP, and adding a new rebate calculation for line extensions (i.e., new formulations, such as extended release formulations) of solid oral dosage forms of branded products, as well as potentially impacting their rebate liability by modifying the statutory definition of AMP. The ACA also expanded the universe of Medicaid utilization subject to drug rebates by requiring pharmaceutical manufacturers to pay rebates on Medicaid managed care utilization as of 2010 and by expanding the population potentially eligible for Medicaid drug benefits, to be phased-in by 2014. The CMS have proposed to expand Medicaid rebate liability to the territories of the United States as well.

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

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

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

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

Employees

As of June 30, 2015, we employed 47 full-time employees, including 37 in research and development and ten general and administrative and no part-time employees, in the United States. We have never had a work stoppage, and none of our employees is represented by a labor organization or under any collective-bargaining arrangements. We consider our employee relations to be good.

Facilities

We lease our office and laboratory space, which consists of 28,000 square feet located in South San Francisco, California. Our leases for this facility expire on April 30, 2018. We believe our current office and laboratory space is sufficient to meet our needs until the expiration of our lease.

Legal Proceedings

As of the date of this prospectus, we were not party to any material legal matters or claims. In the future, we may become party to legal matters and claims arising in the ordinary course of business, the resolution of which we do not anticipate would have a material adverse impact on our financial position, results of operations or cash flows.

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MANAGEMENT

Executive Officers and Directors

The following table sets forth certain information about our executive officers and directors, including their ages as of July 30, 2015.

Name	Age	Position(s)
Executive Officers:		
Ted W. Love, M.D.	56	President, Chief Executive Officer and Director
Eleanor L. Ramos, M.D.	59	Chief Medical Officer
Jung Choi	46	Chief Business and Strategy Officer
Peter Radovich	37	Vice President, Program Leadership and Business Strategy
John Schembri	53	Vice President, Finance and Administration
Hing Sham	63	Senior Vice President, Chemistry
Directors:		
Willie L. Brown, Jr. (3)	81	Director
Charles Homcy, M.D. (2)(3)	67	Director
Deval L. Patrick (1)(2)	58	Director
Mark L. Perry (1)(2)	59	Director
Kevin P. Starr (1)	52	Director

(1) Member of the Audit Committee.
(2) Member of the Compensation Committee.
(3) Member of the Nominating and Corporate Governance Committee.

The following paragraphs provide information as of the date of this prospectus about our executive officers and directors. The information presented includes information about each of our directors specific experience, qualifications, attributes and skills that led our board of directors to the conclusion that he should serve as a director.

Ted W. Love, M.D. Dr. Love has served as our Chief Executive Officer and President since June 2014, and as a member of our board of directors since September 2013. From February 2010 to August 2012, Dr. Love served as executive vice president, research and development and technical operations of Onyx Pharmaceuticals, Inc. Prior to that, from 2001 to January 2009, he served as president, chief executive officer and chairman of Nuvelo, Inc., and previously served as senior vice president, development of Theravance, Inc., from 1998 to 2001. Previously, he spent six years at Genentech, Inc., where he held a number of senior management positions in medical affairs and product development and served as chairman of Genentech s Product Development Committee. Dr. Love currently serves on the board of directors of Amicus Therapeutics, Inc., Oncothyreon Inc. and KaloBios Pharmaceuticals, Inc. Dr. Love holds a B.A. from Haverford College and an M.D. from Yale Medical School. He completed a residency in internal medicine and fellowship in cardiology at the Massachusetts General Hospital. Dr. Love s qualifications to serve on our board of directors include his role as our principal executive officer and more than 20 years of broad leadership and management experience in the pharmaceutical industry.

Eleanor L. Ramos, M.D. Dr. Ramos has served as our Chief Medical Officer since May 2014. Prior to joining us, since September 2011, she served as chief medical officer of Theraclone Sciences, Inc., where she led the

development of monoclonal antibody therapies for viral diseases. From May 2009 to June 2011, Dr. Ramos served as the senior vice president and chief medical officer at ZymoGenetics Inc. (acquired by Bristol-Myers Squibb Company in 2010), where she was responsible for the oversight of the company s clinical portfolio in the therapeutic areas of inflammation, oncology, viral hepatitis and hemostasis. Earlier in her career, she also led significant clinical research and development initiatives while at Bristol-Myers Squibb and Roche Global Development in the area of solid organ transplantation, and leading the Clinical Trials Group at the Immune

Tolerance Network while at the University of California, San Francisco. Previously, Dr. Ramos held faculty appointments at Harvard Medical School, the University of Florida, Yale University and the University of California, San Francisco. Dr. Ramos holds an M.D. from Tufts University School of Medicine and completed her training in transplant nephrology at the Brigham and Women s Hospital.

Jung E. Choi. Ms. Choi has served as our Chief Business and Strategy Officer since April 2015. From April 2014 to March 2015, Ms. Choi served as senior vice president, corporate development for InterMune, Inc. (acquired by Roche Holding AG in 2014), and served as an advisor on strategy and business development to InterMune from March 2013 to April 2014. Prior to joining InterMune, from February 2011 to March 2013, Ms. Choi led corporate and business development for Chimerix, Inc. as a consultant and senior vice president, corporate development. Prior to that, from August 2001 to August 2010, Ms. Choi held various management positions at Gilead Sciences, Inc., including leadership of business development, licensing, and mergers and acquisition activities. During her tenure at Gilead Sciences, Ms. Choi built and oversaw the corporate development group, and led the U.S. commercial launch of Hepsera® for the treatment of the hepatitis B virus. Ms. Choi holds a B.A. in human biology and an M.B.A. from Stanford University.

Peter Radovich. Mr. Radovich has served as our Vice President, Program Leadership and Business Strategy since November 2014. Prior to that, in September 2006, he joined Onyx Pharmaceuticals, Inc. (acquired by Amgen, Inc.) and served as vice president, program leadership from February 2014 to November 2014 and as senior director from August 2011 to February 2014, during which time he led the company s global, cross-functional product team responsible for the development and commercialization of Kyprolis®. Prior to joining Onyx, from 2004 to 2006, Mr. Radovich was at Chiron Corporation (now Novartis AG) in product marketing supporting Proleukin® (interleukin-2) in multiple oncology indications. Mr. Radovich holds a B.A. in biology and chemistry from Texas Christian University and an M.B.A. from Washington University in St. Louis.

John Schembri. Mr. Schembri has served as our Vice President, Finance and Administration since January 2014. Prior to joining us, since June 2011, Mr. Schembri served as vice president and chief financial officer at StemPar Sciences, Inc. From July 2009 to May 2011, he was a consulting chief financial officer to early-stage companies. Prior to that, Mr. Schembri served as chief financial officer of BiPar Sciences, Inc., from January 2007 until it was acquired by sanofi-aventis S.A. in 2009. Prior to joining BiPar Sciences, Mr. Schembri led the finance team at Sirna Therapeutics, Inc., from January 2006 until it was acquired by Merck & Co., Inc. in December 2006. He also served a key role in the $2 billion sale and integration of COR Therapeutics Inc. to Millennium Pharmaceuticals, Inc. in 2001. Mr. Schembri holds a B.S. in business administration from California State Polytechnic University, San Luis Obispo.

Hing Sham, Ph.D. Dr. Sham has served as our Senior Vice President, Chemistry since July 2014. Most recently, from January 2013 to July 2014, Dr. Sham served as head of research and development at iOneWorldHealth/Path.org (PATH), a non-profit pharmaceutical development organization. Prior to that, from September 2006 to November 2012, he served as senior vice president of research and head of chemical sciences at Elan Pharmaceuticals, Inc., where he led the chemistry team in the discovery of two clinical candidates for the treatment of Alzheimer s disease. From July 1983 to August 2006, Dr. Sham worked at Abbott Laboratories Inc., where he and his team discovered and advanced 10 clinical candidates spanning cardiovascular disease, HIV, oncology and diabetes. His 24-year tenure at Abbott Laboratories culminated in his appointment as a distinguished research fellow in global pharmaceutical discovery. Dr. Sham is the co-inventor of Norvir® and the primary inventor of Kaletra®, Abbott Laboratories first and second-generation HIV protease inhibitors approved for the treatment of HIV. Dr. Sham has published more than 180 scientific articles in peer-reviewed journals and is a named inventor on 81 issued U.S. patents. Dr. Sham was named Hero of Chemistry by the American Chemical Society in 2003. Dr. Sham holds a Ph.D. in synthetic organic chemistry from the University of Hawaii and completed his post-doctoral training in the department of chemistry at Indiana University.

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Willie L. Brown, Jr. Mr. Brown has served as a member of our board of directors since January 2015. Since January 2004, Mr. Brown has served as an attorney at law representing clients before state and local governments. Prior to that, from January 1996 to January 2004, Mr. Brown served as the 41st mayor of San Francisco. Mr. Brown is a practicing attorney, community leader and well-respected public official who served over 31 years in the California State Assembly, spending more than 14 years as its Speaker, from 1980 to 1995. He currently serves as chairman and chief executive officer of The Willie L. Brown, Jr. Institute on Politics and Public Service, an independent, non-profit organization providing a forum for non-partisan education, debate and discussion of public policy issues. Mr. Brown holds a degree in political science from San Francisco State University and a J.D. from University of California, Hastings College of the Law. He has received over 17 honorary degrees from prestigious institutions throughout his life. Mr. Brown s qualifications to serve on our board of directors include more than 50 years of political, business and non-profit experience.

Charles Homcy, M.D. Dr. Homcy has served as a member of our board of directors since February 2011. In 2010, Dr. Homcy joined Third Rock Ventures, a venture capital firm, as a venture partner. He served as president and chief executive officer of Portola Pharmaceuticals, Inc. since co-founding the company in 2003 until 2010. Prior to that, Dr. Homcy served as the president of research and development at Millennium Pharmaceuticals, Inc., following its acquisition of COR Therapeutics Inc. in 2002. He joined COR in 1995 as executive vice president of research and development, and he served as a director of the company from 1998 to 2002. Dr. Homcy has been a clinical professor of medicine at the University of California, San Francisco Medical School, and attending physician at the San Francisco Veterans Affairs Hospital since 1997. He was previously president of the medical research division of American Cyanamid-Lederle Laboratories, a division of Wyeth-Ayest Laboratories. He currently serves as co-chairman of the board of directors of Portola and on the board of directors of Geron Corporation, Cephalon, Inc., MyoKardia, Inc. and TOPICA Pharmaceuticals, Inc. Dr. Homcy holds a B.A. and an M.D. from Johns Hopkins University. Dr. Homcy s qualifications to serve on our board of directors include his significant experience building and leading successful biotechnology companies and his scientific expertise.

Deval. L. Patrick. Mr. Patrick has served as a member of our board of directors since April 2015. In April 2015, Mr. Patrick joined Bain Capital, LLC, where he serves as managing director. From January 2007 to January 2015, Mr. Patrick served as the governor of Massachusetts. Prior to his tenure in government, from 2000 to 2004, Mr. Patrick served as the executive vice president and general counsel at The Coca-Cola Company. Prior to that, he served as general counsel at ChevronTexaco Corp. (previously Texaco Inc.), from 1998 to 1999. Mr. Patrick received an A.B. in English and American Literature from Harvard College and a J.D. from Harvard Law School. Mr. Patrick s qualifications to serve on our board of directors include his significant experience as a business and government leader with a record of success in solving complex problems, making strategic investments, managing crises and building teams locally, nationally and internationally.

Mark L. Perry. Mr. Perry has served as a member of our board of directors since April 2015. From October 2012 to October 2013, Mr. Perry served as an entrepreneur-in-residence at Third Rock Ventures. Since August 2011, he has served on various boards of companies and non-profit organizations. In October 2004, Mr. Perry joined Aerovance, Inc. as a director, and he served as president and chief executive officer of Aerovance from February 2007 to October 2011. Prior to that, Mr. Perry served as the senior business advisor of Gilead Sciences, Inc. from April 2004 to February 2007 and as an executive officer from May 1994 to April 2004, during which time he served in a variety of capacities, including general counsel, chief financial officer and executive vice president of operations. Earlier in his career, from 1981 to 1994, Mr. Perry served as an attorney at Cooley LLP, and was a partner of the firm from 1987 to 1994. Mr. Perry currently serves on the board of directors of Nvidia Corporation and MyoKardia, Inc. Mr. Perry received a B.A. in history from the University of California, Berkeley and a J.D. from the University of California, Davis. Mr. Perry s qualifications to serve on our board of directors include more than 30 years of experience serving in professional and management positions in the biotechnology industry.

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Kevin P. Starr. Mr. Starr has served as a member of our board of directors since May 2012. In April 2007, Mr. Starr co-founded Third Rock Ventures, where he remains a partner. From January 2003 to March 2007, Mr. Starr undertook a number of entrepreneurial endeavors in the life science and entertainment industries. From December 2001 to December 2002, Mr. Starr served as chief operating officer of Millennium Pharmaceuticals, Inc. He also served as Millennium s chief financial officer from December 1998 to December 2002. Mr. Starr currently serves on the board of directors of Sage Therapeutics, Inc., Agios Pharmaceuticals, Inc., Alnylam Pharmaceuticals, Inc., PanOptica, Inc., MyoKardia, Inc., Afferent Pharmaceuticals, Inc. and Zafgen, Inc. Mr. Starr received an M.S. in corporate finance from Boston College and a B.S./B.A. in mathematics and business from Colby College. Mr. Starr s qualifications to serve on our board of directors include his executive management roles with responsibility over key financial and business planning functions and experience in the formation, development and business strategy of multiple start-up companies in the life sciences sector.

Composition of our Board of Directors

As of July 30, 2015, our board of directors consisted of six members, each of whom are members pursuant to the board composition provisions of our certificate of incorporation and our stockholders agreement, which agreement is described under Certain Relationships and Related Party Transactions in this prospectus. These board composition provisions will terminate upon the completion of this offering. Upon the termination of these provisions, there will be no further contractual obligations regarding the election of our directors. Effective upon the completion of this offering, we intend to form a nominating and corporate governance committee. Our nominating and corporate governance committee and our board of directors may consider a broad range of factors relating to the qualifications and background of director nominees, which may include diversity, which is not only limited to race, gender or national origin, although we currently have no formal policy regarding board diversity. Our nominating and corporate governance committee s and our board of directors priority in selecting board members is identification of persons who will further the interests of our stockholders through his or her established record of professional accomplishment, the ability to contribute positively to the collaborative culture among board members, knowledge of our business, understanding of the competitive landscape and professional and personal experiences and expertise relevant to our growth strategy. Our directors hold office until their successors have been elected and qualified or until the earlier of their resignation or removal. Our amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the completion of this offering also provide that our directors may be removed only for cause by the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in an annual election of directors, and that any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office.

Director Independence. Our board of directors has determined that Willie L. Brown, Jr., Deval L. Patrick and Mark L. Perry are independent directors, including for purposes of the rules of NASDAQ Stock Market and relevant federal securities laws and regulations. There are no family relationships among any of our directors or executive officers.

Staggered Board. In accordance with the terms of our amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the completion of this offering, our board of directors will be divided into three classes, Class I, Class II and Class III, with each class serving staggered three-year terms. Upon the expiration of the term of a class of directors, directors in that class will be eligible to be elected for a new three-year term at the annual meeting of stockholders in the year in which their term expires.

Our Class I directors will be Ted W. Love and Charles Homcy;

Our Class II directors will be Willie L. Brown, Jr. and Kevin Starr; and

Our Class III directors will be Deval L. Patrick and Mark L. Perry.

Our amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the completion of this offering provide that the number of directors may be changed only by resolution of our board of directors.

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The division of our board of directors into three classes with staggered three-year terms may delay or prevent stockholder efforts to effect a change of our management or a change in control.

Committees of our Board of Directors

Our board of directors has established an audit committee, a compensation committee and a nominating and corporate governance committee, each of which will operate pursuant to a charter adopted by our board of directors and will be effective upon the effectiveness of the registration statement of which this prospectus is a part. Following the completion of this offering, copies of each committee s charter will be posted on the Corporate Governance section of our website, at *www.globalbloodtx.com*. The inclusion of our website address in this prospectus does not incorporate by reference the information on or accessible through our website into this prospectus.

Audit Committee. Effective upon the effectiveness of the registration statement of which this prospectus is a part, Kevin Starr, Deval L. Patrick and Mark L. Perry will serve on the audit committee, which will be chaired by Kevin Starr. Our board of directors has determined that Deval L. Patrick and Mark L. Perry are independent for audit committee purposes as that term is defined in the rules of the SEC and the applicable NASDAQ Stock Market rules, and that each member of the audit committee has sufficient knowledge in financial and auditing matters to serve on the audit committee. Our board of directors has designated each of Kevin Starr and Mark L. Perry as an audit committee financial expert, as defined under the applicable rules of the SEC. While Mr. Starr does not satisfy the independence requirements under applicable NASDAQ Stock Market rules or the independence requirements of the SEC applicable to members of audit committees, the transition rules of the SEC provide that up to two members of the audit committee may be exempt from these more stringent independence requirements for 90 days after the effectiveness of this registration statement, and one member may be exempt for one year after the effectiveness of this registration statement. Our board of directors intends to cause our audit committee to comply with the transition rules within the applicable time periods. The audit committee s responsibilities include:

- appointing, approving the compensation of, and assessing the independence of our independent registered public accounting firm;
- pre-approving auditing and permissible non-audit services, and the terms of such services, to be provided by our independent registered public accounting firm;
- reviewing the overall audit plan with our independent registered public accounting firm and members of management responsible for preparing our financial statements;
- reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly financial statements and related disclosures as well as critical accounting policies and practices used by us;
- coordinating the oversight and reviewing the adequacy of our internal control over financial reporting;

establishing policies and procedures for the receipt and retention of accounting-related complaints and concerns;

recommending based upon the audit committee s review and discussions with management and our independent registered public accounting firm whether our audited financial statements shall be included in our Annual Report on Form 10-K;

monitoring the integrity of our financial statements and our compliance with legal and regulatory requirements as they relate to our financial statements and accounting matters;

preparing the audit committee report required by SEC rules to be included in our annual proxy statement;

reviewing all related person transactions for potential conflict of interest situations and approving all such transactions; and

reviewing quarterly earnings releases and scripts.

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Compensation Committee. Effective upon the effectiveness of the registration statement of which this prospectus is a part, Mark L. Perry, Charles Homcy and Deval L. Patrick will serve on the compensation committee, which will be chaired by Mark L. Perry. Our board of directors has determined that Mark L. Perry and Deval L. Patrick are independent as defined in the applicable NASDAQ Stock Market rules. The compensation committee s responsibilities include:

- annually reviewing and approving corporate goals and objectives relevant to the compensation of our Chief Executive Officer;
- evaluating the performance of our Chief Executive Officer in light of such corporate goals and objectives and determining the compensation of our Chief Executive Officer;
- reviewing and approving the compensation of our other executive officers;
- reviewing and establishing our overall management compensation, philosophy and policy;
- overseeing and administering our compensation and similar plans;
- evaluating and assessing potential and current compensation advisors in accordance with the independence standards identified in the applicable NASDAQ Stock Market rules;
- retaining and approving the compensation of any compensation advisors;
- reviewing and approving our policies and procedures for the grant of equity-based awards;
- reviewing and making recommendations to the board of directors with respect to director compensation; and
- reviewing and discussing with management the compensation discussion and analysis to be included in our annual proxy statement or Annual Report on Form 10-K.

Nominating and Corporate Governance Committee. Effective upon the effectiveness of the registration statement of which this prospectus is a part, Willie L. Brown, Jr. and Charles Homcy will serve on the nominating and corporate governance committee, which will be chaired by Willie L. Brown, Jr. Our board of directors has determined that Willie L. Brown, Jr. is independent as defined in the applicable NASDAQ Stock Market rules. The nominating and corporate governance committee s responsibilities include:

developing and recommending to the board of directors criteria for board and committee membership;

establishing procedures for identifying and evaluating board of director candidates, including nominees recommended by stockholders;

reviewing the size and composition of the board of directors to ensure that it is composed of members containing the appropriate skills and expertise to advise us;

identifying individuals qualified to become members of the board of directors;

recommending to the board of directors the persons to be nominated for election as directors and to each of the board s committees;

developing and recommending to the board of directors a code of business conduct and ethics and a set of corporate governance guidelines;

developing a mechanism by which violations of the code of business conduct and ethics can be reported in a confidential manner;

overseeing the evaluation of the board of directors and its committees; and

reviewing and discussing with the board of directors the corporate succession plans for the Chief Executive Officer and other executive officers.

Our board of directors may from time to time establish other committees.

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Compensation Committee Interlocks and Insider Participation

None of the members of our compensation committee has at any time during the prior three years been one of our officers or employees. None of our executive officers currently serves, or in the past fiscal year has served, as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving on our board of directors or compensation committee.

Corporate Governance

We have adopted a code of business conduct and ethics that applies to all of our employees, officers and directors, including those officers responsible for financial reporting, which will be effective upon completion of this offering. Upon the completion of this offering, our code of business conduct and ethics will be available on our website at *www.globalbloodtx.com*. The inclusion of our website address in this prospectus does not incorporate by reference the information on or accessible through our website into this prospectus. We intend to disclose any substantive amendments to the code, or any waivers of its requirements, on our website or in a Current Report on Form 8-K.

Board Leadership Structure and Board s Role in Risk Oversight

We do not currently have a chairman of the board, but have appointed Mark L. Perry to serve as our lead independent director upon the completion of this offering. We believe that the appointment of a lead independent director allows our Chief Executive Officer to focus on our day-to-day business, while allowing the lead independent director to lead the board of directors in its fundamental role of providing advice to and independent oversight of management. Our board of directors recognizes the time, effort and energy that the Chief Executive Officer is required to devote to his position in the current business environment, as well as the commitment required to serve as our lead independent director, particularly as the board of directors oversight responsibilities continue to grow. While our amended and restated bylaws and corporate governance guidelines do not require that we appoint a separate chairman and Chief Executive Officer, our board of directors believes that having separate positions is the appropriate leadership structure for us at this time and demonstrates our commitment to good corporate governance.

Risk is inherent with every business, and how well a business manages risk can ultimately determine its success. We face a number of risks, including risks relating to our operations, strategic direction and intellectual property as more fully discussed under Risk Factors in this prospectus. Management is responsible for the day-to-day management of risks we face, while our board of directors, as a whole and through its committees, has responsibility for the oversight of risk management. In its risk oversight role, our board of directors has the responsibility to satisfy itself that the risk management processes designed and implemented by management are adequate and functioning as designed.

The role of the board of directors in overseeing the management of our risks is conducted primarily through committees of the board of directors, as disclosed in the descriptions of each of the committees above and in the charters of each of the committees. The full board of directors (or the appropriate board committee in the case of risks that are under the purview of a particular committee) discusses with management our major risk exposures, their potential impact on us, and the steps we take to manage them. When a board committee is responsible for evaluating and overseeing the management of a particular risk or risks, the chairman of the relevant committee reports on the discussion to the full board of directors during the committee reports portion of the next board meeting. This enables the board of directors and its committees to coordinate the risk oversight role, particularly with respect to risk interrelationships.

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EXECUTIVE AND DIRECTOR COMPENSATION

Summary Compensation Table

The following table presents information regarding the total compensation earned by each individual who served as our chief executive officer, or CEO, at any time during the fiscal year ended December 31, 2014 and our two other most highly compensated executive officers who were serving as executive officers as of December 31, 2014. We refer to these officers as our named executive officers.

Name and Principal Position	Year	Salary ($)	Bonus ($)	Stock Awards ($) [1]	Option Awards ($) [1]	Non-Equity Incentive Plan Compensation ($) [2]	All Other Compensation ($) [3]	Total ($)
Ted W. Love, M.D. [4] *President and CEO*	2014	255,673[4]	20,000[5]	350,000		56,500	2,207	684,380
Mark A. Goldsmith, M.D., Ph.D. [6] *Former President and CEO*	2014						[6]	
Uma Sinha, Ph.D. [7] *Former Chief Scientific Officer*	2014	321,547		21,000		57,500	3,201	403,248
Eleanor L. Ramos, M.D. [8] *Chief Medical Officer*	2014	224,135	25,000[9]		49,723	47,500	11,653	358,011

(1) In accordance with SEC rules, these columns reflect the aggregate grant date fair value of the option awards and stock awards granted during 2014 computed in accordance with Financial Accounting Standard Board ASC Topic 718 for stock-based compensation transactions, or ASC 718. Assumptions used in the calculation of these amounts are included in Note 7 to our financial statements included elsewhere in this prospectus. These amounts do not reflect the actual economic value that will be realized by the named executive officer upon the vesting of stock options, the exercise of stock options, the lapse of our repurchase option on shares of restricted stock or the sale of shares of our common stock.

(2) The amounts reported reflect the discretionary cash bonus determined by our board of directors based on the achievement of certain performance goals and metrics as specified by our board of directors.

(3) The amounts reported in this column include contributions by us in connection with (i) group term life insurance, (ii) long term disability, (iii) 401(k) plan benefits and (iv) relocation benefits.

(4) Dr. Love was appointed as our President and CEO in June 2014. The amounts reported under the caption Salary include fees in the amount of $17,292 paid in cash during 2014 for Dr. Love s service as a non-employee director prior to his appointment as our President and CEO.

(5) This amount reflects a one-time bonus in recognition of Dr. Love s individual performance during 2014.

(6) Dr. Goldsmith served as our President and CEO from May 2012 to June 2014. Dr. Goldsmith did not receive any cash compensation from the Company for his services in this capacity, as his consulting services were provided to the Company through Third Rock Ventures LLC, or TRV. As described below under Narrative to Summary Compensation Table Consulting Arrangement for Services of Named Executive Officer and Certain Relationships and Related Party Transactions, we incurred management fees totaling $332,000 during 2014 for the services TRV

provides, which include, among other things, the services of Dr. Goldsmith and Dr. Homcy, one of our directors, as well as other personnel who are not required to be included in the table above. Of the total fees we incurred with TRV in 2014, $216,800 related to the services provided by Dr. Goldsmith.

(7) Dr. Sinha was appointed as our Chief Scientific Officer in July 2014. Prior to that, she served as our Senior Vice President, Research from January 2013. Dr. Sinha s employment with us ended in June 2015.

(8) Dr. Ramos was appointed as our Chief Medical Officer in May 2014.

(9) This amount reflects a one-time signing bonus of $25,000 in connection with Dr. Ramos s appointment as our Chief Medical Officer.

Narrative to Summary Compensation Table

Employment Arrangements with Our Named Executive Officers

We have entered into an employment agreement or letter agreement with each of our named executive officers in connection with their employment with us, with the exception of our former President and CEO, Dr. Goldsmith, as described below under Consulting Arrangement for Services of Named Executive Officer. Except as noted below, these employment agreements and offer letters provide for at will employment.

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Ted W. Love, M.D.

We entered into an employment offer letter agreement with Dr. Love in May 2014, pursuant to which he began serving as our President and CEO in June 2014. The letter agreement entitles Dr. Love to an initial annual base salary of $425,000, subject to adjustment pursuant to our employee compensation policies in effect from time to time. Pursuant to the terms of his letter agreement, Dr. Love is considered annually for a bonus target of up to 35% of his annual base salary, as determined by our board of directors based on a combination of our achievement of certain performance goals and Dr. Love s achievement of individual goals. In connection with his appointment as President and CEO, we issued Dr. Love 714,285 shares of our common stock pursuant to a restricted stock award agreement dated June 11, 2014.

Pursuant to his employment offer letter agreement, in the event that we terminate Dr. Love s employment without cause, we will provide certain termination benefits, including (i) continuation of base salary for a period of nine months after the effective date of termination and (ii) continuation of group health plan benefits to the extent authorized by and consistent with COBRA, with the cost of the regular premium for such benefits shared in the same relative proportion by us and Dr. Love as in effect on the effective date of termination until the earlier of (x) the date that is nine months after the effective date of termination and (y) the date Dr. Love becomes eligible for health benefits through another employer or otherwise becomes ineligible for COBRA, in each case, subject to Dr. Love s execution and non-revocation of a separation agreement and release, resignation from all positions with us and compliance with our instructions regarding Company property.

Under Dr. Love s letter agreement, the term cause is generally defined as follows: (i) dishonest statements or acts with respect to us or any of our affiliates, or any current or prospective customers, suppliers vendors or other third parties with which such entity does business; (ii) commission of (A) a felony or (B) any misdemeanor involving moral turpitude, deceit, dishonesty or fraud; (iii) failure to perform assigned duties and responsibilities to our reasonable satisfaction, which failure continues, in our reasonable judgment, after written notice by us; (iv) gross negligence, willful misconduct or insubordination with respect to us or any of our affiliates; or (v) material violation of any provision of any agreement(s) between Dr. Love and us relating to noncompetition, nonsolicitation, nondisclosure and/or assignment of inventions.

Prior to Dr. Love s appointment as our President and CEO in June 2014, he served as a member of our board of directors beginning in September 2013 and continues to serve on our board of directors. Dr. Love s compensation as a director for the period in 2014 prior to his appointment as our President and CEO is described below under Director Compensation.

Uma Sinha, Ph.D.

We entered into an employment offer letter agreement with Dr. Sinha in November 2012, pursuant to which she served as Senior Vice President, Research from January 2013 through July 2014. She was appointed as our Chief Scientific Officer in July 2014. In connection with the commencement of Dr. Sinha s employment in 2012, we paid her a signing bonus of $100,000. The letter agreement entitles Dr. Sinha to an initial annual base salary of $300,000, subject to adjustment pursuant to our employee compensation policies in effect from time to time, which was later increased by our board of directors to $335,000 per year in connection with Dr. Sinha s promotion to Chief Scientific Officer. Pursuant to the terms of her agreement, Dr. Sinha was issued an option to purchase 85,714 shares of our common stock on March 14, 2013. In connection with her promotion to the position of Chief Scientific Officer, we issued Dr. Sinha 42,857 shares of our common stock pursuant to a restricted stock award agreement dated September 10, 2014. Dr. Sinha s employment with us ended in June 2015.

Eleanor L. Ramos, M.D.

We entered into an employment offer letter agreement with Dr. Ramos, pursuant to which she assumed the role of Chief Medical Officer in May 2014. The agreement entitles Dr. Ramos to an initial annual base salary of $350,000, subject to adjustment pursuant to our employee compensation policies in effect from time to time. Pursuant to the terms of her agreement, Dr. Ramos is considered annually for a bonus target of 25% of her annual

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base salary, as determined by the board of directors based on a combination of our achievement of certain performance goals and Dr. Ramos achievement of individual performance goals. Pursuant to the terms of her agreement, Dr. Ramos was issued an option to purchase 142,857 shares of our common stock on June 11, 2014 pursuant to an incentive stock option agreement. In connection with commencement of her employment, we granted Dr. Ramos a signing bonus of $25,000 and a relocation assistance payment of $10,000.

Benefits Provided upon a Change in Control

In July 2015, our board of directors adopted a change in control policy. Pursuant to the policy, in the event the employment of any of our named executive officers is terminated by us or our acquirer or successor without cause within one year after the consummation of a sale event, he or she will be entitled to receive the following payments and benefits, subject to his or her timely execution of a severance agreement, including a general release of claims:

- a lump sum cash payment equal to nine months (or 12 months in the case of Dr. Love as our CEO) of the named executive officer s then-current base salary;
- payment of the named executive officer s target annual incentive compensation;
- if the named executive officer elects to continue his or her group healthcare benefits, payment of an amount equal to the monthly employer contribution we would have made to provide the named executive officer with health insurance if he or she had remained employed by us until the earlier of (i) nine months (or 12 months in the case of Dr. Love as our CEO) following the date of termination or (ii) the end of the named executive officer s COBRA health continuation period; and
- all stock options and other stock-based awards granted to the named executive officer will become fully exercisable and non-forfeitable as of the date of the named executive officer s termination.

In addition, upon a sale event, to the extent Section 280G of the Internal Revenue Code of 1986, as amended, is applicable, each named executive officer who is then employed with us will be entitled to receive the better treatment of: (i) payment of the full amounts set forth above to which the named executive officer is entitled or (ii) payment of such lesser amount that does not trigger excise taxes under Section 280G.

Employee Confidentiality and Assignment Agreements

Each of our named executive officers has entered into a standard form agreement with respect to confidential information and assignment of inventions. Among other things, this agreement obligates each named executive officer to refrain from disclosing any of our proprietary information received during the course of employment and to assign to us any inventions conceived or developed during the course of employment.

Consulting Arrangement for Services of Named Executive Officer

Since our inception in 2011, we have received consulting and management services from TRV pursuant to an unwritten agreement with TRV, or the TRV Agreement. Dr. Goldsmith, our former President and CEO, provided consulting services to us through TRV pursuant to the TRV Agreement. Of the $332,000 in total fees we incurred with

TRV in 2014, $216,800 related to the services provided by Dr. Goldsmith. In connection with his role as our President and CEO, we issued Dr. Goldsmith 85,714 shares of our common stock pursuant to a restricted stock purchase agreement dated May 7, 2012. There are no other agreements or arrangements between us and Dr. Goldsmith with respect to his services as our former President and CEO.

See Certain Relationships and Related Party Transactions for additional information regarding our relationship with TRV and the TRV Agreement.

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Outstanding Equity Awards at Fiscal Year End

The following table presents the outstanding equity awards held by each of our named executive officers as of December 31, 2014:

	Option Awards				Stock Awards	
Name	Number of Securities underlying Unexercised Options Exercisable (#)	Number of Securities underlying Unexercised Options Unexercisable (#)	Option Exercise Price ($)	Option Expiration Date	Number of Shares that Have Not Vested (#)	Market Value of Shares that Have Not Vested ($) [1]
Ted W. Love, M.D.			N/A	N/A	14,732[2]	23,719
			N/A	N/A	714,285[3]	1,150,000
Mark A. Goldsmith, M.D., Ph.D.			N/A	N/A	[4]	
Uma Sinha, Ph.D.	16,071[5]	48,214[5]	$ 0.32	3/14/2023		
			N/A	N/A	40,178[6]	64,688
Eleanor L. Ramos, M.D.	[7]	142,857[7]	$ 0.49	6/10/2024		

(1) There was no public market for our common stock as of December 31, 2014. The fair value of our common stock as of December 31, 2014 was $1.61 per share.

(2) In connection with his service as a director prior to his appointment as our President and CEO, Dr. Love was issued 21,428 shares of common stock under a restricted stock purchase agreement dated December 9, 2013, pursuant to which all of the shares were initially subject to our repurchase option, which lapsed with respect to 5,357 of the shares on September 4, 2014, and which lapses with respect to the remaining 16,071 shares in equal quarterly installments over the following three years through September 4, 2017.

(3) In connection with his service as our President and CEO, Dr. Love was issued 714,285 shares of common stock under a restricted stock purchase agreement dated June 26, 2014, pursuant to which all of the shares are initially subject to our repurchase option, which lapses with respect to 178,571 of the shares on June 9, 2015, and which lapses with respect to the remaining 535,714 shares in equal quarterly installments over the following three years through June 9, 2018.

(4) In September 2014, in connection with Dr. Goldsmith s resignation from our board of directors, the vesting of all of his shares of common stock, which were subject to our repurchase option, was accelerated such that all shares were vested in full as of December 31, 2014.

(5) Represents shares underlying an option to purchase an aggregate of 85,714 shares of our common stock granted to Dr. Sinha in March 2013. 21,428 of the shares underlying the option vested on January 3, 2014, and the remaining 64,286 shares vest in equal quarterly installments over the following three years through January 3, 2017. On January 22, 2014, Dr. Sinha exercised the option with respect to 21,428 vested shares.

(6) Dr. Sinha was issued 42,857 shares of common stock under a restricted stock purchase agreement dated October 6, 2014, pursuant to which all of the shares were initially subject to our repurchase option, which lapses in 16 equal quarterly installments over a period of four years from July 1, 2014.

(7)

Represents shares underlying an option to purchase an aggregate of 142,857 shares of our common stock granted to Dr. Ramos in June 2014. 35,714 of the shares underlying the option will vest on May 12, 2015, and the remaining 107,143 shares vest in equal quarterly installments over the following three years through May 12, 2018.

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Director Compensation

The following table provides certain information concerning compensation earned by the directors who were not named executive officers during the year ended December 31, 2014. Compensation earned during 2014 by Dr. Love for his service as a director prior to his appointment as our President and CEO is reported above in the Summary Compensation Table. Directors Willie L. Brown, Jr., Deval L. Patrick and Mark L. Perry each joined our board of directors in 2015, and accordingly, did not receive any compensation from us during the year ended December 31, 2014.

Name	Fees Earned or Paid in Cash ($)	All Other Compensation ($)	Total ($)
Charles Homcy, M.D. (1)		(1)	
Kevin P. Starr			

(1) Dr. Homcy provides consulting services to us under our consulting and management services arrangement with TRV. Of the total fees we incurred with TRV in 2014, $39,000 related to the services provided by Dr. Homcy. See Certain Relationships and Related Party Transactions for additional information regarding our consulting relationship with TRV.

Prior to his appointment as our President and CEO in June 2014, Dr. Love served as a non-employee director from September 2013 to June 2014. During the year ended December 31, 2014, we paid Dr. Love an aggregate of $17,292 in cash for his services to us as a non-employee director, which is reported above in the Summary Compensation Table. After Dr. Love was appointed as our President and CEO, he did not receive any compensation from us for his services as a director. In connection with his appointment as a non-employee director, we granted Dr. Love a restricted stock award of 21,428 shares of our common stock in September 2013 pursuant to a restricted stock agreement. All of the shares were initially subject to our repurchase right, which lapsed with respect to 25% of the shares on the first anniversary of the commencement of Dr. Love s service on our board of directors, and which lapses with respect to the remaining 75% of the shares in equal quarterly installments over the next three years.

Pursuant to our current policy on compensation of non-employee directors, each individual who joins our board of directors as a non-employee director is entitled to receive a cash retainer of $25,000 per year, payable quarterly in arrears and pro-rated for any partial year served. In addition, each non-employee director is entitled to be granted, at his or her election, an option to purchase 21,428 shares of our common stock or a restricted stock award of 21,428 shares of our common stock, subject to vesting (or the lapsing of our repurchase right, in the case of restricted stock) of 25% of the shares on the first anniversary of the commencement of the director s service on our board of directors and of the remaining 75% of the shares in equal quarterly installments over the next three years.

In July 2015, our board of directors adopted a non-employee director compensation policy, to be effective as of the completion of this offering, that is designed to provide a total compensation package that enables us to attract and retain, on a long-term basis, high-caliber non-employee directors. Under this policy, all non-employee directors will be paid cash compensation as set forth below, prorated based on days of service during a calendar year:

Board of Directors

	Annual Retainer
All non-employee members	$ 35,000
Audit Committee:	
Chairperson	$ 15,000
Non-Chairperson members	$ 7,500
Compensation Committee:	
Chairperson	$ 10,000
Non-Chairperson members	$ 5,000
Nominating and Corporate Governance Committee:	
Chairperson	$ 8,000
Non-Chairperson members	$ 4,000

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In addition, under the policy, each new non-employee director who is initially appointed or elected to our board of directors after effectiveness of the policy will receive an option grant to purchase up to 30,000 shares of common stock, which will vest in equal monthly installments over a period of three years following the grant date, subject to the director s continued service on our board of directors. In addition, on the date of each annual meeting of our stockholders, each continuing non-employee director will be eligible to receive an annual option grant to purchase 15,000 shares of common stock, which will vest in equal monthly installments during the 12 months following the grant date, subject to the director s continued service on our board of directors. All stock options granted to our non-employee directors pursuant to this policy are subject to full acceleration of vesting upon the consummation of a sale event. Our non-employee directors may also be granted such additional stock options in such amounts and on such dates as our board of directors may recommend. All of the foregoing options will be granted at fair market value on the date of grant and will be exercisable (to the extent vested) for up to one year following cessation of the director s service on our board of directors, so long as the director was not removed for cause.

We have also agreed to reimburse all reasonable out-of-pocket expenses incurred by non-employee directors in attending Board and committee meetings.

Compensation Risk Assessment

We believe that although a portion of the compensation provided to our executive officers and other employees is performance-based, our executive compensation program does not encourage excessive or unnecessary risk taking. This is primarily due to the fact that our compensation programs are designed to encourage our executive officers and other employees to remain focused on both short-term and long-term strategic goals, in particular in connection with our pay-for-performance compensation philosophy. As a result, we do not believe that our compensation programs are reasonably likely to have a material adverse effect on our company.

Equity Compensation Plans

2012 Stock Option and Grant Plan

The 2012 Stock Option and Grant Plan, or the 2012 Plan, was approved by our board of directors and our stockholders on May 30, 2012. Under the 2012 Plan, 3,785,713 shares of common stock have been reserved for issuance in the form of incentive stock options, non-qualified stock options, restricted stock, unrestricted stock or any combination of the foregoing. The shares issuable pursuant to awards granted under the 2012 Plan are authorized but unissued shares.

The 2012 Plan is administered by our board or at the discretion of the board, a committee of the board comprised of not less than two (2) directors, which has full power to select the individuals to whom awards will be granted and to determine the specific terms and conditions of each award, subject to the provisions of the 2012 Plan. Pursuant to the 2012 Plan and subject to applicable law, the committee may, in its discretion, delegate to the CEO the power to designate non-officer employees as recipients of options and to determine the number of options to be granted to such employees; provided, however, the committee must specify the total number of options to be awarded by the CEO and shall not delegate the authority to set the exercise price or vesting terms of such options, other than as specifically authorized by the committee.

The option exercise price of each option granted under the 2012 Plan is determined by our board and may not be less than the fair market value of a share of common stock on the date of grant. The term of each option is fixed by the board and may not exceed 10 years from the date of grant. The board determines at what time or times each option may be exercised when granting the option.

The 2012 Plan provides that, upon the consummation of a sale event, unless provision is made in connection with the sale event for the assumption or continuation of the awards by the successor entity or substitution of the awards with new awards of the successor entity, with appropriate adjustment, the 2012 Plan and all outstanding

and unexercised options issued thereunder will terminate upon the effective time of the sale event. We may make or provide for cash payment to holders of options equal to the difference between (i) the per share cash consideration in the sale event multiplied by the number of shares subject to outstanding options being cancelled, and (ii) the aggregate exercise price to the holders of all vested and exercisable options.

Our board may amend the 2012 Plan but no such action may adversely affect the rights of an award holder without such holder s consent. Approval by our stockholders of amendments to the 2012 Plan must be obtained if required by law.

As of August 5, 2015, options to purchase 1,703,049 shares of common stock were outstanding under the 2012 Plan. Our board has determined not to make any further awards under the 2012 Plan following the completion of this offering.

2015 Stock Option and Incentive Plan

In July 2015, our board of directors adopted, and our stockholders approved, our 2015 Stock Option and Incentive Plan, or the 2015 Plan. Our 2015 Plan became effective upon the effectiveness of the registration statement of which this prospectus is a part and is not expected to be utilized until after the completion of this offering except with respect to the grant of options to purchase 317,205 shares of common stock, which will become effective immediately following the effectiveness of the registration statement of which this prospectus is a part. Our 2015 Plan will provide for the grant of incentive stock options, within the meaning of Section 422 of the Code, to our employees and any of our parent and subsidiary corporations employees, and for the grant of nonstatutory stock options, restricted stock, restricted stock units, stock appreciation rights, performance units and performance shares to our employees, directors and consultants, and our parent and subsidiary corporations employees and consultants.

We have initially reserved 1,430,000 shares of our common stock, or the Initial Limit, for the issuance of awards under the 2015 Plan. The 2015 Plan provides that the number of shares reserved and available for issuance under the plan will automatically increase each January 1, beginning on January 1, 2016, by 4% of the outstanding number of shares of our common stock on the immediately preceding December 31 or such lesser number of shares as determined by our compensation committee, or the Annual Increase. This number is subject to adjustment in the event of a stock split, stock dividend or other change in our capitalization.

The shares we issue under the 2015 Plan will be authorized but unissued shares or shares that we reacquire. The shares of common stock underlying any awards that are forfeited, cancelled, held back upon exercise or settlement of an award to satisfy the exercise price or tax withholding, reacquired by us prior to vesting, satisfied without any issuance of stock, expire or are otherwise terminated (other than by exercise) under the 2015 Plan and the 2012 Plan will be added back to the shares of common stock available for issuance under the 2015 Plan.

Stock options and stock appreciation rights with respect to no more than 1,750,000 shares of stock may be granted to any one individual in any one calendar year and the maximum performance-based award payable to any one individual under the 2015 Plan is 1,750,000 shares of stock or $2,000,000 in the case of cash-based awards. The maximum aggregate number of shares that may be issued in the form of incentive stock options shall not exceed the Initial Limit cumulatively increased on January 1, 2016 and on each January 1 thereafter by the lesser of the Annual Increase for such year or 2,857,000 shares of common stock.

The 2015 Plan will be administered by our compensation committee. Our compensation committee has full power to select, from among the individuals eligible for awards, the individuals to whom awards will be granted, to make any combination of awards to participants, and to determine the specific terms and conditions of each award, subject to the

provisions of the 2015 Plan. Persons eligible to participate in the 2015 Plan will be those full or part-time officers, employees, non-employee directors and other key persons (including consultants) as selected from time to time by our compensation committee in its discretion.

The 2015 Plan permits the granting of both options to purchase common stock intended to qualify as incentive stock options under Section 422 of the Code and options that do not so qualify. The option exercise price of each option will be determined by our compensation committee but may not be less than 100% of the fair market value of our common stock on the date of grant. The term of each option will be fixed by our compensation committee and may not exceed 10 years from the date of grant. Our compensation committee will determine at what time or times each option may be exercised.

Our compensation committee may award stock appreciation rights subject to such conditions and restrictions as we may determine. Stock appreciation rights entitle the recipient to shares of common stock, or cash, equal to the value of the appreciation in our stock price over the exercise price. The exercise price of each stock appreciation right may not be less than 100% of the fair market value of our common stock on the date of grant.

Our compensation committee may award shares of restricted common stock and restricted stock units to participants subject to such conditions and restrictions as it may determine. These conditions and restrictions may include the achievement of certain performance goals and continued employment with us through a specified vesting period. Our compensation committee may also grant shares of common stock that are free from any restrictions under the 2015 Plan. Unrestricted stock may be granted to participants in recognition of past services or other valid consideration and may be issued in lieu of cash compensation due to such participant.

Our compensation committee may grant performance share awards to participants that entitle the recipient to receive shares of common stock upon the achievement of certain performance goals and such other conditions as our compensation committee shall determine.

Our compensation committee may grant cash bonuses under the 2015 Plan to participants, subject to the achievement of certain performance goals.

Our compensation committee may grant awards of restricted stock, restricted stock units, performance shares or cash-based awards under the 2015 Plan that are intended to qualify as performance-based compensation under Section 162(m) of the Code. Those awards would only vest or become payable upon the attainment of performance goals that are established by our compensation committee and related to one or more performance criteria. The performance criteria that would be used with respect to any such awards include: earnings before interest, taxes, depreciation and amortization, net income (loss) (either before or after interest, taxes, depreciation and amortization), changes in the market price of our common stock, economic value-added, funds from operations or similar measure, sales or revenue, acquisitions or strategic transactions, operating income (loss), cash flow (including, but not limited to, operating cash flow and free cash flow), return on capital, assets, equity, or investment, stockholder returns, return on sales, gross or net profit levels, productivity, expense, margins, operating efficiency, customer satisfaction, working capital, earnings (loss) per share of stock, sales or market shares and number of customers, any of which may be measured either in absolute terms or as compared to any incremental increase or as compared to results of a peer group. From and after the time that we become subject to Section 162(m) of the Code, the maximum award that is intended to qualify as performance-based compensation under Section 162(m) of the Code that may be made to any one employee during any one calendar year period is shares of common stock with respect to a stock-based award and $2,000,000 with respect to a cash-based award.

The 2015 Plan provides that in the case of, and subject to, the consummation of a sale event as defined in the 2015 Plan, all outstanding awards may be assumed, substituted or otherwise continued by the successor entity. To the extent that the successor entity does not assume, substitute or otherwise continue such awards, then upon the effectiveness of the sale event, all stock options and stock appreciation rights will automatically terminate. In the event of such termination, individuals holding options and stock appreciation rights will be permitted to exercise such options and

stock appreciation rights prior to the sale event. In addition, in connection

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with a sale event, we may make or provide for a cash payment to participants holding options and stock appreciation rights equal to the difference between the per share cash consideration payable to stockholders in the sale event and the exercise price of the options or stock appreciation rights.

The 2015 Plan also provides that, in the event an individual s service relationship is terminated without cause, as defined in the 2015 Plan, within one year following the consummation of a sale event, any awards assumed or substituted in such sale event will become fully vested and nonforfeitable, in each case as of the date of termination of the service relationship, with any awards with conditions and restrictions relating to the attainment of performance goals deemed achieved at 100% of target levels.

Our board of directors may amend or discontinue the 2015 Plan and our compensation committee may amend or cancel outstanding awards for purposes of satisfying changes in law or any other lawful purpose, but no such action may adversely affect rights under an award without the holder s consent. Certain amendments to the 2015 Plan require the approval of our stockholders.

No awards may be granted under the 2015 Plan after the date that is ten years from the date of stockholder approval. No awards under the 2015 Plan have been made prior to the date of this prospectus.

2015 Employee Stock Purchase Plan

In July 2015, our board of directors adopted, and our stockholders approved, our 2015 Employee Stock Purchase Plan, or the 2015 ESPP. The 2015 ESPP became effective upon the effectiveness of the registration statement of which this prospectus forms a part.

The 2015 ESPP authorizes the initial issuance of up to 50,000 shares of our common stock to participating employees. The 2015 ESPP provides that the number of shares reserved and available for purchase under the plan will automatically increase each January 1, from January 1, 2016 until January 1, 2025, by the lesser of (i) 3,000,000 shares of common stock, (ii) 1% of the outstanding number of shares of our common stock on the immediately preceding December 31 or (iii) such lesser number of shares as determined by the administrator of the 2015 ESPP. This number is subject to adjustment in the event of a stock split, stock dividend or other change in our capitalization.

All employees who are employed by us or our designated subsidiaries and whose customary employment is for more than 20 hours a week are eligible to participate in the 2015 ESPP. Any employee who owns, or would own upon such purchase under the 2015 ESPP, 5% or more of the voting power or value of our stock is not eligible to purchase shares under our the 2015 ESPP.

We may make one or more offerings to our employees to purchase stock under the 2015 ESPP consisting of one or more purchase periods. The initial offering will commence as of the effective date of this offering and end on January 31, 2016. Unless otherwise determined by the administrator of the 2015 ESPP, each subsequent offering will begin on each January 31 and July 31 and end on the January 31 and July 31, respectively, that is the date six months after the first day of the applicable offering period. The administrator may designate different offering periods in its discretion but no offering shall exceed 27 months in duration.

Each employee who is a participant in the 2015 ESPP may purchase shares by authorizing payroll deductions at a minimum of 1% and up to 15% of his or her eligible compensation for each pay period. Unless the participating employee has previously withdrawn from the offering, his or her accumulated payroll deductions will be used to purchase common stock on the last business day of the purchase period at a price equal to 85% of the fair market value of the common stock on either the first or the last day of the purchase period, whichever is lower, provided that

no more than 2,500 shares of common stock or such other lesser maximum number established by the plan administrator may be purchased by any one employee during each offering period. Under applicable tax rules, an employee may purchase no more than $25,000 worth of common stock, valued at the start of the purchase period, under the 2015 ESPP in any calendar year.

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The accumulated payroll deductions of any employee who is not a participant on the last day of an offering period will be refunded. An employee s rights under the 2015 ESPP terminate upon voluntary withdrawal from the plan or when the employee ceases employment for any reason.

The 2015 ESPP may be terminated or amended by our board of directors at any time. Amendments that increase the number of shares of our common stock authorized under the 2015 ESPP and certain other amendments require the approval of our stockholders.

401(k) Plan and Other Benefits

We maintain a tax-qualified retirement plan, or the 401(k) Plan, that provides eligible U.S. employees with an opportunity to save for retirement on a tax advantaged basis. Eligible employees are able to defer eligible compensation subject to applicable annual Code limits. Employees pre-tax or Roth contributions are allocated to each participant s individual account and are then invested in selected investment alternatives according to the participants directions. Employees are immediately and fully vested in their contributions. Our 401(k) Plan is intended to be qualified under Section 401(a) of the Code with our 401(k) Plan s related trust intended to be tax exempt under Section 501(a) of the Code. As a tax-qualified retirement plan, contributions to our 401(k) Plan and earnings on those contributions are not taxable to the employees until distributed from our 401(k) Plan. We may, but are not required to, make matching contributions. We also pay, on behalf of our employees, the premiums for health, life and disability insurance.

Pension Benefits, Non-Qualified Contribution Plans and other Non-Qualified Defined Compensation Plans

We do not provide a pension plan or non-qualified defined contribution plans for any of our employees, and none of our named executive officers participated in a non-qualified defined compensation plan during the fiscal year ended December 31, 2014 and during the three months ended March 31, 2015.

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CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

Other than compensation arrangements, we describe below the transactions, and series of similar transactions, since January 1, 2012, to which we were a party or will be a party, in which:

- the amounts involved exceeded or will exceed $120,000; and
- any of our directors, executive officers or holders of more than 5% of our capital stock, or any member of the immediate family of the foregoing persons, had or will have a direct or indirect material interest.

Prior to this offering, we did not have a formal policy concerning transactions with related persons. In connection with this offering, we have adopted a written policy, effective upon completion of this offering, that requires all future transactions between us and any director, executive officer, holder of 5% or more of any class of our capital stock or any member of the immediate family of, or entities affiliated with, any of them, or any other related persons (as defined in Item 404 of Regulation S-K) or their affiliates, in which the amount involved is equal to or greater than $120,000, be approved in advance by our audit committee. Any request for such a transaction must first be presented to our audit committee for review, consideration and approval. In approving or rejecting any such proposal, our audit committee is to consider the relevant facts and circumstances available and deemed relevant to the audit committee, including, but not limited to, the extent of the related party s interest in the transaction, and whether the transaction is on terms no less favorable to us than terms we could have generally obtained from an unaffiliated third party under the same or similar circumstances.

Private Placements of Securities

Common Stock Issuances

In April 2012, we entered into a restricted stock purchase agreement with Charles Homcy, M.D., a member of our board of directors, pursuant to which we issued to Dr. Homcy an aggregate of 214,285 shares of our common stock at a price of $0.0035 per share, for an aggregate purchase price of $750.

In May 2012, we entered into a securities purchase agreement with Third Rock Ventures II, L.P., or TRV II, pursuant to which we issued to TRV II an aggregate of 568,571 shares of our common stock at a price of $0.0035 per share, for an aggregate purchase price of $1,990.

Series A Preferred Stock Financing

In May 2012, we entered into a securities purchase agreement with TRV II pursuant to which we issued, in a series of closings, an aggregate of 40,663,168 shares of our Series A redeemable convertible preferred stock at a purchase price of $1.00 per share. In April 2014, we entered into a joinder agreement and an amendment to the securities purchase agreement, pursuant to which Third Rock Ventures III, L.P., or TRV III, was added as a purchaser under the securities purchase agreement and we increased the aggregate number of shares of Series A redeemable convertible preferred stock issuable under such agreement to 50,163,168.

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The following table summarizes the participation in the Series A redeemable convertible preferred stock financing by any of our directors, executive officers, holders of more than 5% of our voting securities, or any member of the immediate family of the foregoing persons:

Name	Shares of Series A Preferred	Aggregate Purchase Price Paid	Date Purchased
Third Rock Ventures II, L.P.	13,663,168	$ 13,663,168[(1)]	5/31/2012
Third Rock Ventures II, L.P.	5,000,000	$ 5,000,000	2/28/2013
Third Rock Ventures II, L.P.	5,000,000	$ 5,000,000	7/12/2013
Third Rock Ventures II, L.P.	5,000,000	$ 5,000,000	10/31/2013
Third Rock Ventures II, L.P.	5,000,000	$ 5,000,000	1/31/2014
Third Rock Ventures II, L.P.	5,000,000	$ 5,000,000	4/29/2014
Third Rock Ventures III, L.P.	5,000,000	$ 5,000,000	4/29/2014
Third Rock Ventures II, L.P.	3,000,000	$ 3,000,000	10/1/2014
Third Rock Ventures III, L.P.	3,000,000	$ 3,000,000	10/1/2014

(1) Includes 3,663,168 shares of Series A redeemable convertible preferred stock issued at a price of $1.00 per share upon the conversion of principal and accrued interest under convertible promissory notes previously issued by us to TRV II.

Series B Preferred Stock Financing

In December 2014, we entered into a securities purchase agreement with various investors, pursuant to which we agreed to issue, in a single closing, an aggregate of 19,200,000 shares of our Series B redeemable convertible preferred stock at a price of $2.50 per share.

The following table summarizes the participation in the Series B redeemable convertible preferred stock financing by any of our directors, executive officers, holders of more than 5% of our voting securities, or any member of the immediate family of the foregoing persons:

Name	Shares of Series B Preferred	Aggregate Purchase Price Paid	Date Purchased
Fidelity Select Portfolios: Biotechnology Portfolio	8,985,915	$ 22,464,787.50	12/22/2014
	1,814,085	$ 4,535,212.50	12/22/2014

Fidelity Advisors Series VII: Fidelity Advisor
Biotechnology Fund

Agreements with Stockholders

In connection with the Series B redeemable convertible preferred stock financing, we entered into the Amended and Restated Investors Rights Agreement, dated as of December 22, 2014, with certain of our stockholders, including our principal stockholders and their affiliates and the Amended and Restated Stockholders Agreement, dated as of December 22, 2014, with certain of our stockholders, including our principal stockholders and their affiliates. All of the material provisions of these agreements will terminate immediately prior to the completion of this offering, other than the provisions relating to registration rights, which will continue in effect following the completion of this offering and entitle the holders of such rights to have us register their shares of our common stock for sale in the United States. See Description of Capital Stock Registration Rights.

Since our inception in 2011, we have received consulting and management services from TRV, pursuant to the TRV Agreement, which through its affiliates, has a controlling interest in us. During the year ended December 31, 2014 and the six months ended June 30, 2015, we incurred expenses from TRV of an aggregate of $332,000 and $65,000, respectively, for these services, which included, among other things, the services of Drs. Goldsmith and Homcy, as well as other personnel who are not required to be included in the disclosure herein.

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We have incurred expenses from TRV of an aggregate of $1,860,000 for these services from our inception through June 30, 2015 pursuant to the TRV Agreement. As described above under Executive and Director Compensation, our former President and CEO provided us with consulting services pursuant to the TRV Agreement, and our director, Dr. Homcy, currently provides us with consulting services pursuant to the TRV Agreement. Dr. Homcy and Mr. Starr, another member of our board of directors, are affiliated with TRV. Drs. Goldsmith and Homcy did not receive any cash compensation from us, as their consulting services were provided to us through TRV.

Executive Officer and Director Compensation

See Executive and Director Compensation for information regarding compensation of directors and executive officers.

Employment Agreements

We have entered into offer letters or employment agreements with each of our executive officers. For more information regarding our agreements with our named executive officers for the fiscal year ended December 31, 2014, see Executive and Director Compensation Narrative to Summary Compensation Table Employment Arrangements with Our Named Executive Officers.

Director Agreements

We have entered into a director letter agreement with Willie L. Brown, Jr., who was appointed as one of our directors as of January 1, 2015, pursuant to which Mr. Brown is entitled to an annual cash retainer of $25,000. In addition, Mr. Brown was issued 21,428 shares of common stock under a restricted stock purchase agreement dated February 3, 2015, pursuant to which all of the shares were initially subject to our repurchase option, which lapses with respect to 5,357 of the shares on January 1, 2016, and which lapses with respect to the remaining 16,071 shares in equal quarterly installments over the following three years through January 1, 2019, in connection with his service as a director.

We have entered into a director letter agreement with Deval L. Patrick, who was appointed as one of our directors as of April 8, 2015, pursuant to which Mr. Patrick is entitled to an annual cash retainer of $25,000. In addition, Mr. Patrick was issued an option to purchase 21,428 shares of common stock under a non-qualified stock option agreement dated April 9, 2015. All of the shares underlying the option were initially unvested and unexercisable, and will vest and become exercisable with respect to 5,357 of the shares on April 8, 2016, and with respect to the remaining 16,071 shares in equal quarterly installments over the following three years through April 8, 2019, in connection with his service as a director.

We have entered into a director letter agreement with Mark L. Perry, who was appointed as one of our directors as of April 8, 2015, pursuant to which Mr. Perry is entitled to an annual cash retainer of $25,000. In addition, Mr. Perry was issued 21,428 shares of common stock under a restricted stock purchase agreement dated April 27, 2015, pursuant to which all of the shares were initially subject to our repurchase option, which lapses with respect to 5,357 of the shares on April 8, 2016, and which lapses with respect to the remaining 16,071 shares in equal quarterly installments over the following three years through April 8, 2019, in connection with his service as a director.

Indemnification Agreements

We have entered into or plan to enter into indemnification agreements with each of our directors and executive officers, the form of which is attached as an exhibit to the registration statement of which this prospectus is a part. The indemnification agreements and our restated certificate of incorporation and amended and restated bylaws require us

to indemnify our directors and officers to the fullest extent permitted by Delaware law.

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PRINCIPAL STOCKHOLDERS

The following table presents information concerning the beneficial ownership of the shares of our common stock as of June 30, 2015, by:

- each person we know to be the beneficial owner of 5% or more of our outstanding shares of our capital stock;
- each of our directors;
- each of our named executive officers; and
- all of our executive officers and directors as a group.

The following table does not reflect any shares of common stock that may be purchased pursuant to our directed share program described under Underwriters Directed Share Program.

We have determined beneficial ownership in accordance with SEC rules. The information does not necessarily indicate beneficial ownership for any other purpose. Under these rules, a person is deemed to be a beneficial owner of our common stock if that person has a right to acquire ownership within 60 days by the exercise of options or the conversion of our redeemable convertible preferred stock. A person is also deemed to be a beneficial owner of our common stock if that person has or shares voting power, which includes the power to vote or direct the voting of our common stock, or investment power, which includes the power to dispose of or to direct the disposition of such capital stock. Except in cases where community property laws apply or as indicated in the footnotes to this table, we believe that each stockholder identified in the table possesses sole voting and investment power over all shares of common stock shown as beneficially owned by the stockholder.

Percentage of beneficial ownership in the table below is based on 23,429,554 shares of common stock deemed to be outstanding as of June 30, 2015, assuming the conversion of all outstanding shares of redeemable convertible preferred stock into common stock, and 29,429,554 shares of common stock outstanding after the completion of this offering. The table below assumes that the underwriters do not exercise their option to purchase additional shares. If the underwriters exercise their option to purchase additional shares in full, we will sell an aggregate of 900,000 additional shares of common stock. Shares of common stock subject to options that are currently exercisable or exercisable within 60 days of June 30, 2015 are considered outstanding and beneficially owned by the person holding the options for the purpose of computing the percentage ownership of that person but are not treated as outstanding for the purpose of computing the percentage ownership of any other person. Unless otherwise indicated below, the address of each individual listed below is c/o Global Blood Therapeutics, Inc., 400 East Jamie Court, Suite 101, South San Francisco, CA 94080.

Name and Address of Beneficial Owner	Number of Shares Beneficially	Number of Shares Beneficially	Percentage of Shares	Percentage of Shares

	Owned before Offering	Owned after Offering	Beneficially Owned before Offering	Beneficially Owned after Offering
5% or Greater Stockholders:				
Entities affiliated with Third Rock Ventures [1]	14,760,904	14,760,904	63.0%	50.2%
Entities affiliated with Fidelity [2]	3,085,714	3,085,714	13.2%	10.5%
Executive Officers and Directors:				
Ted W. Love, M.D. [3].	1,135,711	1,135,711	4.9%	3.9%
Eleanor L. Ramos, M.D. [4]	49,463	49,463	*%	*%
Willie L. Brown, Jr. [5].	21,428	21,428	*%	*%
Charles Homcy, M.D. [6]	214,285	214,285	*%	*%
Kevin Starr [1][7]	14,760,904	14,760,904	63.0%	50.2%
Mark Perry [8]	21,428	21,428	*%	*%
Deval Patrick [9]			*%	*%
All executive officers and directors as a group (11 persons) [10]	16,412,368	16,412,368	69.7%	55.6%

* Represents beneficial ownership of less than one percent.

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(1) Consists of an aggregate of 14,760,904 shares of common stock, including: (i) 571,428 shares of common stock held by Third Rock Ventures II, L.P. (TRV II LP), (ii) 11,903,762 shares of common stock issuable upon conversion of 41,663,168 shares of Series A redeemable convertible preferred stock held by TRV II and (iii) 2,285,714 shares of common stock issuable upon conversion of 8,000,000 shares of Series A redeemable convertible preferred stock held by Third Rock Ventures III, L.P. (TRV III LP). Each of Third Rock Ventures II GP, LP (TRV II GP), the general partner of TRV II LP, and Third Rock Ventures GP II, LLC (TRV II LLC), the general partner of TRV II GP, and Mark Levin, Kevin Starr and Robert Tepper, the managers of TRV II LLC, may be deemed to have voting and investment power over the shares held of record by TRV II LP, and each of Third Rock Ventures III GP, LP (TRV III GP), the general partner of TRV III LP, and Third Rock Ventures GP III, LLC (TRV III LLC), the general partner of TRV III GP, and Mark Levin, Kevin Starr and Robert Tepper, the managers of TRV III LLC, may be deemed to have voting and investment power over the shares held of record by TRV III LP. The address for each of TRV II LP and TRV III LP is 29 Newbury Street, Suite 401, Boston, MA 02116.

(2) Consists of an aggregate of 3,085,714 shares of common stock issuable upon conversion of: (i) 8,985,915 shares of Series B redeemable convertible preferred stock held by Fidelity Select Portfolios: Biotechnology Portfolio and (ii) 1,814,085 shares of Series B redeemable convertible preferred stock held by Fidelity Advisor Series VII: Fidelity Advisor Biotechnology Fund. These accounts are managed by direct or indirect subsidiaries of FMR LLC. Edward C. Johnson 3d is a Director and the Chairman of FMR LLC and Abigail P. Johnson is a Director, the Vice Chairman and the President of FMR LLC. Members of the family of Edward C. Johnson 3d, including Abigail P. Johnson, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC. Neither FMR LLC nor Edward C. Johnson 3d nor Abigail P. Johnson has the sole power to vote or direct the voting of the shares owned directly by the various investment companies registered under the Investment Company Act (Fidelity Funds) advised by Fidelity Management & Research Company (FMR Co), a wholly owned subsidiary of FMR LLC, which power resides with the Fidelity Funds Boards of Trustees. Fidelity Management & Research Company carries out the voting of the shares under written guidelines established by the Fidelity Funds Boards of Trustees. The address for Fidelity Select Portfolios: Biotechnology Portfolio is Brown Brothers Harriman & Co., 525 Washington Blvd., Jersey City, NJ 07310, Attn: Michael Lerman, 15th Floor, Corporate Actions, and the address for Fidelity Advisor Series VII: Fidelity Advisor Biotechnology Fund is State Street Bank & Trust, PO Box 5756, Boston, Massachusetts 02206, Attn: Bangle & Co fbo Fidelity Advisor Series VII: Fidelity Advisor Biotechnology Fund.

(3) Consists of: 1,135,711 shares of common stock, of which 749,195 shares are subject to our right of repurchase as of June 30, 2015, held by Dr. Love.

(4) Consists of: options to purchase 49,463 shares of common stock that are exercisable within 60 days of June 30, 2015, held by Dr. Ramos.

(5) Consists of: 21,428 shares of common stock, all of which are subject to our right of repurchase as of June 30, 2015, held by Mr. Brown.

(6) Consists of: 214,285 shares of common stock held by Dr. Homcy.

(7) Mr. Starr is affiliated with TRV II LP and TRV III LP. Each of TRV II GP, the general partner of TRV II LP, and TRV II LLC, the general partner of TRV II GP, and Mark Levin, Kevin Starr and Robert Tepper, the managers of TRV II LLC, may be deemed to have voting and investment power over the shares held of record by TRV II LP, and each of TRV III GP, the general partner of TRV III LP, and TRV III LLC, the general partner of TRV III GP, and Mark Levin, Kevin Starr and Robert Tepper, the managers of TRV III LLC, may be deemed to have voting and investment power over the shares held of record by TRV III LP. No stockholder, director, officer, manager,

member or employee of TRV II GP, TRV III GP, TRV II LLC or TRV III LLC has beneficial ownership (within the meaning of Rule 13d-3 promulgated under the Exchange Act) of any shares held by TRV II LP or TRV III LP.

(8) Consists of 21,428 shares of common stock, all of which are subject to our right of repurchase as of June 30, 2015, held by Mr. Perry.

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(9) Mr. Patrick does not beneficially own any shares of common stock or hold any options to purchase shares of common stock that are exercisable within 60 days of June 30, 2015.

(10) Includes the number of shares beneficially owned by the named executive officers and directors listed in the above table, as well as (i) options to purchase 29,196 shares of common stock that are exercisable within 60 days of June 30, 2015, held by John Schembri, (ii) options to purchase 2,321 shares of common stock that are exercisable within 60 days of June 30, 2015, held by Peter Radovich, (iii) 9,285 shares of common stock, all of which are subject to our right of repurchase as of June 30, 2015, and options to purchase 25,490 shares of common stock that are exercisable within 60 days of June 30, 2015, held by Hing Sham, and (iv) 142,857 shares of common stock, all of which are subject to our right of repurchase as of June 30, 2015, held by Jung Choi.

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DESCRIPTION OF CAPITAL STOCK

Upon the completion of this offering and after giving effect to the conversion into common stock and retirement of all outstanding shares of our redeemable convertible preferred stock, our authorized capital stock will consist 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 will be undesignated, and there will be 29,429,554 shares of common stock outstanding and no shares of preferred stock outstanding. As of June 30, 2015, we had approximately 61 record holders of our capital stock. All of our outstanding shares of redeemable convertible preferred stock will convert into shares of our common stock upon the completion of this offering. In addition, upon the completion of this offering, options to purchase 1,703,049 shares of our common stock will be outstanding (not including options to purchase an aggregate of 317,205 shares of common stock that will be granted effective immediately after the effectiveness of the registration statement of which this prospectus is a part) and 1,480,000 shares of our common stock will be reserved for future grants under our equity incentive plans (including the options to purchase an aggregate of 317,205 shares of common stock that will be granted immediately after the effectiveness of the registration statement of which this prospectus is a part).

The following description of our capital stock and provisions of our restated certificate of incorporation and amended and restated bylaws are summaries of material terms and provisions and are qualified by reference to our restated certificate of incorporation and amended and restated bylaws, copies of which have been filed with the SEC as exhibits to the registration statement of which this prospectus is a part. The descriptions of our common stock and preferred stock reflect amendments to our amended and restated certificate of incorporation and bylaws that will become effective upon the completion of this offering.

Common Stock

Upon the completion of this offering, we will be authorized to issue one class of common stock. Holders of our common stock are entitled to one vote for each share of common stock held of record for the election of directors and on all matters submitted to a vote of stockholders. Holders of our common stock are entitled to receive dividends ratably, if any, as may be declared by our board of directors out of legally available funds, subject to any preferential dividend rights of any preferred stock then outstanding. Upon our dissolution, liquidation or winding up, holders of our common stock are entitled to share ratably in our net assets legally available after the payment of all our debts and other liabilities, subject to the preferential rights of any preferred stock then outstanding. Holders of our common stock have no preemptive, subscription, redemption or conversion rights and no sinking fund provisions are applicable to our common stock. The rights, preferences and privileges of holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future. Except as described under Antitakeover Effects of Delaware Law and Provisions of our Restated Certificate of Incorporation and Amended and Restated Bylaws below, a majority vote of the holders of common stock is generally required to take action under our restated certificate of incorporation and amended and restated bylaws.

Preferred Stock

Upon the completion of this offering, our board of directors will be authorized, without action by the stockholders, to designate and issue up to an aggregate of 5,000,000 shares of preferred stock in one or more series. Our board of directors can designate the rights, preferences and privileges of the shares of each series and any of its qualifications, limitations or restrictions. Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of common stock. The issuance of preferred stock, while providing flexibility in connection with possible future financings and acquisitions

and other corporate purposes could, under certain circumstances, have the effect of restricting dividends on our common stock, diluting the voting power of our common stock, impairing the liquidation rights of our common stock, or delaying, deferring or preventing a change in control of our company, which might harm the market price of our common stock. See also Antitakeover Effects of Delaware Law and

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Provisions of our Restated Certificate of Incorporation and Amended and Restated Bylaws Provisions of our Restated Certificate of Incorporation and Amended and Restated Bylaws Undesignated preferred stock below.

Our board of directors will make any determination to issue such shares based on its judgment as to our company s best interests and the best interests of our stockholders. Upon the completion of this offering, we will have no shares of preferred stock outstanding and we have no current plans to issue any shares of preferred stock following completion of this offering.

Registration Rights

Upon the completion of this offering, the holders of 20,318,042 shares of our common stock, including shares issuable upon the conversion of our convertible preferred 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

Upon the completion of this offering, 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. A demand for registration may not be made until six months after the effective date of the registration statement for this offering.

Short Form Registration Rights

Upon the completion of this offering, 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) a deemed liquidation event, as defined in our amended and restated certificate of incorporation (as in effect prior to the completion of this offering) or certain other events constituting a sale of the company, (ii) at such time after our initial public offering 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 initial public offering.

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 that will become effective upon the completion of this offering 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

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

- before the stockholder became interested, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;

- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or

at or after the time the stockholder became interested, the business combination was approved by our board of directors and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

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

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

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

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

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

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

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

Our restated certificate of incorporation and amended and restated bylaws to be in effect upon completion of this offering will 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

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by a majority of the outstanding shares entitled to vote on the amendment, and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, directors, limitation of liability and the amendment of our restated certificate of incorporation must be approved by not less than 75% of the outstanding shares entitled to vote on the amendment, and not less than 75% of the outstanding shares of each class entitled to vote thereon as a class. Our bylaws may be amended by the affirmative vote of a majority vote of the directors then in office, subject to any limitations set forth in the bylaws; and may also be amended by the affirmative vote of at least 75% of the outstanding shares entitled to 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.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC. The transfer agent and registrar s address is 6201 15th Avenue, Brooklyn, NY 11219.

Listing

Our common stock has been approved for listing on The NASDAQ Global Select Market under the symbol GBT.

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SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our common stock. Future sales of our common stock in the public market, or the availability of such shares for sale in the public market, could adversely affect market prices prevailing from time to time. As described below, only a limited number of shares will be available for sale shortly after this offering due to contractual and legal restrictions on resale. Nevertheless, sales of our common stock in the public market after such restrictions lapse, or the perception that those sales may occur, could adversely affect the prevailing market price at such time and our ability to raise equity capital in the future.

Based on the number of shares of common stock outstanding as of June 30, 2015, upon completion of this offering, 29,429,554 shares of common stock will be outstanding, assuming no exercise by the underwriters of their option to purchase additional shares and no exercise of options. All of the shares sold in this offering (other than any shares sold pursuant to our directed share program that are subject lock up restrictions as described under Underwriters Directed Share Program) will be freely tradable. The remaining shares of common stock outstanding after this offering will be restricted as a result of securities laws or lock-up agreements as described below. Following the expiration of the lock-up period, all shares will be eligible for resale in compliance with Rule 144 or Rule 701 under the Securities Act. Restricted securities as defined under Rule 144 of the Securities Act were issued and sold by us in reliance on exemptions from the registration requirements of the Securities Act. These shares may be sold in the public market only if registered or qualified for an exemption from registration, such as under Rule 144 or Rule 701 under the Securities Act.

Rule 144

In general, a person who has beneficially owned restricted stock for at least six months would be entitled to sell their securities provided that (i) such person is not deemed to have been one of our affiliates at the time of, or at any time during the 90 days preceding, a sale and (ii) we are subject to the Exchange Act periodic reporting requirements for at least 90 days before the sale. Persons who have beneficially owned restricted shares for at least six months but who are our affiliates at the time of, or any time during the 90 days preceding, a sale, would be subject to additional restrictions, by which such person would be entitled to sell within any three-month period only a number of securities that does not exceed the greater of either of the following:

- 1% of the number of shares then outstanding, which will equal approximately 294,295 shares immediately after this offering assuming no exercise of the underwriters option to purchase additional shares, based on the number of shares outstanding as of June 30, 2015; or
- the average weekly trading volume of our common stock on The NASDAQ Global Select Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale;

provided, in each case, that we have been subject to the Exchange Act periodic reporting requirements for at least 90 days before the sale. Such sales both by affiliates and by non-affiliates must also comply with the manner of sale, current public information and notice provisions of Rule 144.

Rule 701

Rule 701 under the Securities Act, or Rule 701, as in effect on the date of this prospectus, permits resales of shares in reliance upon Rule 144 but without compliance with certain restrictions of Rule 144, including the holding period

requirement. Most of our employees, executive officers or directors who purchased shares under a written compensatory plan or contract may be entitled to rely on the resale provisions of Rule 701, but all holders of Rule 701 shares are required to wait until 90 days after the date of this prospectus before selling their shares. However, substantially all Rule 701 shares are subject to lock-up agreements as described below and under Underwriting included elsewhere in this prospectus and will become eligible for sale upon the expiration of the restrictions set forth in those agreements.

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Lock-up Agreements

In connection with this offering, we, each of our directors and executive officers, and holders of approximately 23,334,612 shares of our outstanding stock have agreed with the underwriters that for a period of 180 days following the date of this prospectus, subject to certain exceptions, we will not offer, sell, assign, transfer, pledge, contract to sell or otherwise dispose of or hedge any shares of our common stock (including any shares acquired pursuant to our directed share program) or any securities convertible into or exchangeable for shares of our common stock. Morgan Stanley & Co. LLC and Goldman, Sachs & Co. may, in their sole discretion, at any time, release all or any portion of the shares from the restrictions in this agreement.

Rule 10b5-1 Trading Plans

Following the completion of this offering, certain of our officers and directors may adopt written plans, known as Rule 10b5-1 trading plans, in which they will contract with a broker to buy or sell shares of our common stock on a periodic basis to diversify their assets and investments. Under these 10b5-1 trading plans, a broker may execute trades pursuant to parameters established by the officer or director when entering into the plan, without further direction from such officer or director. Such sales would not commence until the expiration of the applicable lock-up agreements entered into by such officer or director in connection with this offering.

Registration Rights

We are party to an investor rights agreement which provides that holders holding 20,318,042 shares of our common stock, including shares issuable upon the conversion of our convertible preferred stock, have the right to demand that we file a registration statement or request that their shares of our common stock be covered by a registration statement that we are otherwise filing. See Description of Capital Stock Registration Rights in this prospectus. Except for shares purchased by affiliates, registration of their shares under the Securities Act would result in these shares becoming freely tradable without restriction under the Securities Act immediately upon effectiveness of the registration, subject to the expiration of the lock-up period described above and under Underwriting in this prospectus, and to the extent such shares have been released from any repurchase option that we may hold.

Equity Incentive Plans

As soon as practicable after the effectiveness of the registration statement of which this prospectus forms a part, we intend to file a Form S-8 registration statement under the Securities Act to register shares of our common stock subject to options outstanding or reserved for issuance under our equity incentive plans. This registration statement will become effective immediately upon filing, and shares covered by this registration statement will thereupon be eligible for sale in the public markets, subject to Rule 144 limitations applicable to affiliates and any lock-up agreements. For a more complete discussion of our equity incentive plans, see Executive and Director Compensation Equity Compensation Plans.

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

The following is a general discussion of certain material U.S. federal income and estate tax considerations relating to ownership and disposition of our common stock by a non-U.S. holder. For purposes of this discussion, the term non-U.S. holder means a beneficial owner of our common stock that is not, for U.S. federal income tax purposes a partnership or:

- an individual who is a citizen or resident of the United States;
- a corporation, or other entity treated as a corporation for U.S. federal income tax purposes, created or organized in or under the laws of the United States or of any political subdivision of the United States;
- an estate the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust, if a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons (as defined in the Code) have authority to control all substantial decisions of the trust or if the trust has a valid election in effect to be treated as a U.S. person under applicable U.S. Treasury Regulations.

A modified definition of non-U.S. holder applies for U.S. federal estate tax purposes (as discussed below).

This discussion is based on current provisions of the Code, existing and proposed U.S. Treasury Regulations promulgated thereunder, current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus and all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any change could alter the tax consequences to non-U.S. holders described in this prospectus. In addition, the Internal Revenue Service, or the IRS, could challenge one or more of the tax consequences described in this prospectus.

We assume in this discussion that each non-U.S. holder holds shares of our common stock as a capital asset (generally, property held for investment) within the meaning of Section 1221 of the Code. This discussion does not address all aspects of U.S. federal income and estate taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder s individual circumstances nor does it address any aspects of state, local or non-U.S. taxes, or U.S. federal taxes other than income and estate taxes. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

- insurance companies;
- tax-exempt organizations;

financial institutions;

brokers or dealers in securities;

pension plans;

controlled foreign corporations;

passive foreign investment companies;

owners that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment;

certain U.S. expatriates;

persons who have elected to mark securities to market;

persons subject to the unearned income Medicare contribution tax;

persons subject to the alternative minimum tax; or

persons that acquire our common stock as compensation for services.

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In addition, this discussion does not address the tax treatment of partnerships (including any entity or arrangement treated as a partnership for U.S. federal income tax purposes) or other entities that are transparent for U.S. federal income tax purposes or persons who hold their common stock through partnerships or other entities that are transparent for U.S. federal income tax purposes. In the case of a holder that is classified as a partnership for U.S. federal income tax purposes, the tax treatment of a person treated as a partner in such partnership for U.S. federal income tax purposes generally will depend on the status of the partner and the activities of the partner and the partnership. A person treated as a partner in a partnership or who holds their stock through another transparent entity should consult his, her or its own tax advisor regarding the tax consequences of the ownership and disposition of our common stock through a partnership or other transparent entity, as applicable.

Prospective investors should consult their own tax advisors regarding the U.S. federal, state, local and non-U.S. income and other tax considerations of acquiring, holding and disposing of our common stock.

Distributions on our Common Stock

We do not currently expect to pay dividends. See Dividend Policy above in this prospectus. However, in the event that we do pay distributions of cash or property on our common stock, those distributions 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. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder s investment, up to such holder s tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below under the heading Gain on Sale, Exchange or Other Taxable Disposition of Common Stock.

Subject also to the discussions below under the headings Information Reporting and Backup Withholding Tax and Foreign Account Tax Compliance Act, dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder s country of residence. If we determine, at a time reasonably close to the date of payment of a distribution on our common stock, that the distribution will not constitute a dividend because we do not anticipate having current or accumulated earnings and profits, we intend not to withhold any U.S. federal income tax on the distribution as permitted by U.S. Treasury Regulations. If we or another withholding agent apply over-withholding, a non-U.S. holder may be entitled to a refund or credit of any excess tax withheld by timely filing an appropriate claim with the IRS.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States, and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements. To obtain this exemption, a non-U.S. holder must generally provide us with a properly executed original and unexpired IRS Form W-8ECI properly certifying such exemption. However, such U.S. effectively connected income, net of specified deductions and credits, is taxed at the same graduated U.S. federal income tax rates applicable to U.S. persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is a corporation may also, under certain circumstances, be subject to an additional branch profits tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder s country of residence.

A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder s country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or applicable successor form) and satisfy applicable certification and other requirements. Non-U.S. holders are urged to consult their own tax advisors regarding their entitlement to benefits under a relevant

income tax treaty.

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A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim with the IRS.

Any documentation provided to an applicable withholding agent may need to be updated in certain circumstances. The certification requirements described above also may require a non-U.S. holder to provide its U.S. taxpayer identification number.

Gain on Sale, Exchange or Other Taxable Disposition of Common Stock

Subject to the discussions below under the headings Information Reporting and Backup Withholding Tax and Foreign Account Tax Compliance Act, a non-U.S. holder generally will not be subject to U.S. federal income tax or withholding tax on gain recognized on a sale, exchange or other taxable disposition of our common stock unless:

- the gain is effectively connected with the non-U.S. holder s conduct of a trade or business in the United States, and, if an applicable income tax treaty so provides, the gain is attributable to a permanent establishment or fixed base maintained by the non-U.S. holder in the United States; in these cases, the non-U.S. holder will be taxed on a net income basis at the regular graduated rates and in the manner applicable to U.S. persons, and, if the non-U.S. holder is a foreign corporation, an additional branch profits tax at a rate of 30%, or a lower rate as may be specified by an applicable income tax treaty, may also apply;

- the non-U.S. holder is an individual present in the United States for 183 days or more in the taxable year of the disposition and certain other conditions are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty) on the amount by which the non-U.S. holder s capital gains allocable to U.S. sources exceed capital losses allocable to U.S. sources during the taxable year of the disposition ; or

- we are or were a U.S. real property holding corporation during a certain look-back period, unless our common stock is regularly traded on an established securities market and the non-U.S. holder held no more than five percent of our outstanding common stock, directly or indirectly, during the shorter of the five-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. Generally, a corporation is a U.S. real property holding corporation if the fair market value of its U.S. real property interests equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we believe that we have not been and are not currently, and we do not anticipate becoming, a U.S. real property holding corporation for U.S. federal income tax purposes.

Information Reporting and Backup Withholding Tax

We (or the applicable paying agent) must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. Non-U.S. holders may have to comply with specific certification procedures to establish that the holder is not a U.S. person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to dividends on our common stock. Generally, a holder will comply with such procedures if it provides a properly executed IRS Form W-8BEN or W-8BEN-E or otherwise meets documentary evidence requirements for establishing that it is a non-U.S. holder, or otherwise establishes an exemption.

Information reporting and backup withholding generally will apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a

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non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement. Any documentation provided to an applicable withholding agent may need to be updated in certain circumstances.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder may be refunded or credited against the non-U.S. holder s U.S. federal income tax liability, if any, provided that an appropriate claim is timely filed with the IRS.

Foreign Account Tax Compliance Act

Legislation commonly referred to as the Foreign Account Tax Compliance Act and associated guidance, or collectively, FATCA, will generally impose a 30% withholding tax on any withholdable payment (as defined below) to a foreign financial institution, unless such institution enters into an agreement with the U.S. government to collect and provide to the U.S. tax authorities substantial information regarding U.S. account holders of such institution (which would include certain equity and debt holders of such institution, as well as certain account holders that are foreign entities with United States owners) or another applicable exception applies or such institution is compliant with applicable foreign law enacted in connection with an applicable intergovernmental agreement between the United States and a foreign jurisdiction. FATCA will also generally impose a 30% withholding tax on any withholdable payment (as defined below) to a foreign entity that is not a financial institution, unless such entity provides the withholding agent with a certification identifying the substantial U.S. owners of the entity (which generally includes any U.S. person who directly or indirectly owns more than 10% of the entity), if any, or another applicable exception applies or such entity is compliant with applicable foreign law enacted in connection with an applicable intergovernmental agreement between the United States and a foreign jurisdiction. Under certain circumstances, a non-U.S. holder might be eligible for refunds or credits of such taxes.

Under final regulations and other current guidance, withholdable payments will generally include dividends on our common stock, as well as the gross proceeds of a disposition of our common stock on or after January 1, 2017. The FATCA withholding tax will apply regardless of whether a payment would otherwise be exempt from or not subject to U.S. nonresident withholding tax (e.g., as capital gain).

Federal Estate Tax

Common stock owned or treated as owned by an individual who is a non-U.S. holder (as specially defined for U.S. federal estate tax purposes) at the time of death will be included in the individual s gross estate for U.S. federal estate tax purposes and, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax or other treaty provides otherwise.

The preceding discussion of material U.S. federal tax considerations is for general information only. It is not tax advice. Prospective investors should consult their own tax advisors regarding the particular U.S. federal, state, local and non-U.S. tax consequences of purchasing, holding and disposing of our common stock, including the consequences of any proposed changes in applicable laws.

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UNDERWRITING

Under the terms and subject to the conditions in an underwriting agreement dated the date of this prospectus, the underwriters named below, for whom Morgan Stanley & Co. LLC and Goldman, Sachs & Co. are acting as representatives, have severally agreed to purchase, and we have agreed to sell to them the number of shares indicated below:

Name	Number of Shares
Morgan Stanley & Co. LLC	2,250,000
Goldman, Sachs & Co.	2,250,000
Cowen and Company, LLC	1,050,000
Wedbush Securities Inc.	450,000
Total:	6,000,000

The underwriters and the representatives are collectively referred to as the underwriters and the representatives, respectively. The underwriters are offering the shares of common stock subject to their acceptance of the shares from us and subject to prior sale. The underwriting agreement provides that the obligations of the several underwriters to pay for and accept delivery of the shares of common stock offered by this prospectus are subject to the approval of certain legal matters by their counsel and to certain other conditions. The underwriters are obligated to take and pay for all of the shares of common stock offered by this prospectus if any such shares are taken. However, the underwriters are not required to take or pay for the shares covered by the underwriters option to purchase additional shares described below. The offering of the shares by the underwriters is subject to receipt and acceptance and subject to the underwriters right to reject any order in whole or in part.

The underwriters initially propose to offer part of the shares of common stock directly to the public at the offering price listed on the cover page of this prospectus and part to certain dealers. After the initial offering of the shares of common stock, the offering price and other selling terms may from time to time be varied by the representatives.

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase up to 900,000 additional shares of common stock at the public offering price listed on the cover page of this prospectus, less underwriting discounts and commissions. The underwriters may exercise this option solely for the purpose of covering the option to purchase additional shares, if any, made in connection with the offering of the shares of common stock offered by this prospectus. To the extent the option is exercised, each underwriter will become obligated, subject to certain conditions, to purchase about the same percentage of the additional shares of common stock as the number listed next to the underwriter s name in the preceding table bears to the total number of shares of common stock listed next to the names of all underwriters in the preceding table.

The following table shows the per share and total public offering price, underwriting discounts and commissions, and proceeds before expenses to us. These amounts are shown assuming both no exercise and full exercise of the underwriters option to purchase up to an additional 900,000 shares of our common stock.

		Total	
	No Exercise		

	Per Share		Full Exercise
Public offering price	$ 20.00	$ 120,000,000	$ 138,000,000
Underwriting discounts and commissions to be paid by us	1.40	8,400,000	9,660,000
Proceeds, before expenses, to us	$ 18.60	$ 111,600,000	$ 128,340,000

The estimated offering expenses payable by us, exclusive of the underwriting discounts and commissions, are approximately $2.25 million. We have agreed to reimburse the underwriters up to $40,000 for expenses relating to the clearance of this offering with the Financial Industry Regulatory Authority, Inc.

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The underwriters have informed us that they do not intend sales to discretionary accounts to exceed 5% of the total number of shares of common stock offered by them.

Our common stock has been approved for listing on The NASDAQ Global Select Market under the trading symbol GBT.

We and all directors and officers and the holders of substantially all of our outstanding stock and stock options have agreed that, without the prior written consent of Morgan Stanley & Co. LLC and Goldman, Sachs & Co. on behalf of the underwriters, we and they will not, during the period ending 180 days after the date of this prospectus (the restricted period):

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

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

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

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

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

- the sale of shares to the underwriters;

- our issuance common stock upon the exercise of an option or a warrant or the conversion of a security outstanding on the date of this prospectus of which the underwriters have been advised in writing;

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

the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares of common stock, provided that (i) such plan does not provide for the transfer of common stock during the restricted period and (ii) to the extent a public announcement or filing under the Exchange Act, if any, is required or voluntarily made regarding the establishment of such plan, such announcement or filing shall include a statement to the effect that no transfer of common stock may be made under such plan during the restricted period.

The above restrictions apply to any shares purchased pursuant to our directed share program.

Morgan Stanley & Co. LLC and Goldman, Sachs & Co., in their sole discretion, may release our common stock and other securities subject to the lock-up agreements described above in whole or in part at any time with or without notice.

In order to facilitate the offering of our common stock, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of our common stock. Specifically, the underwriters may sell

more shares than they are obligated to purchase under the underwriting agreement, creating a short position. A short sale is covered if the short position is no greater than the number of shares available for purchase by the underwriters under the option to purchase additional shares. The underwriters can close out a covered short sale by exercising the option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to close out a covered short sale, the underwriters will consider, among other things, the open market price of shares compared to the price available under the option to purchase additional shares. The underwriters may also sell shares in excess of the option to purchase additional shares, creating a naked short position. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are 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 this offering. As an additional means of facilitating this offering, the underwriters may bid for, and purchase, shares of common stock in the open market to stabilize the price of our common stock. The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions. These activities may raise or maintain the market price of the common stock above independent market levels or prevent or retard a decline in the market price of our common stock. The underwriters are not required to engage in these activities and may end any of these activities at any time.

We and the several underwriters have agreed to indemnify each other against certain liabilities, including liabilities under the Securities Act and liabilities incurred in connection with the directed share program referred to below.

A prospectus in electronic format may be made available on websites maintained by one or more underwriters, or selling group members, if any, participating in this offering. The representatives may agree to allocate a number of shares of common stock to underwriters for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters that may make Internet distributions on the same basis as other allocations.

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. Certain of the underwriters and their respective affiliates have, from time to time, performed, and may in the future perform, various financial advisory and investment banking services for us, for which they received or will receive customary fees and expenses.

In addition, in the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities), currencies, commodities, and credit default swaps and other financial instruments (including bank loans) for their own account and for the accounts of their customers and may at any time hold long and short positions in such securities and instruments. Such investment and securities activities may involve our securities and instruments. The underwriters and their respective affiliates may also make investment recommendations or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long or short positions in such securities and instruments.

Pricing of the Offering

Prior to this offering, there has been no public market for our common stock. The initial public offering price was determined by negotiations between us and the representatives. Among the factors considered in determining the initial public offering price were our future prospects and those of our industry in general, our sales, earnings and

certain other financial and operating information in recent periods, and the price-earnings ratios, price-sales ratios, market prices of securities, and certain financial and operating information of companies engaged in activities similar to ours.

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Directed Share Program

At our request, the underwriters have reserved 5% of the shares of common stock to be issued by us and offered by this prospectus for sale, at the initial public offering price, to directors, officers, employees, business associates and related persons of Global Blood Therapeutics, Inc. The number of shares of common stock available for sale to the general public will be reduced to the extent these individuals purchase such reserved shares. Any reserved shares that are not so purchased will be offered by the underwriters to the general public on the same basis as the other shares offered by this prospectus.

Selling Restrictions

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State) an offer to the public of any shares of our common stock may not be made in that Relevant Member State, except that an offer to the public in that Relevant Member State of any shares of our 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:

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

(b) to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives for any such offer; or

(c) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of shares of our common stock shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an offer to the public in relation to any shares of our 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 any shares of our common stock to be offered so as to enable an investor to decide to purchase any shares of our common stock, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, the expression Prospectus Directive means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State, and the expression 2010 PD Amending Directive means Directive 2010/73/EU.

Japan

No registration pursuant to Article 4, paragraph 1 of the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948, as amended) (the FIEL) has been made or will be made with respect to the solicitation of the application for the acquisition of the shares of common stock.

Accordingly, the shares of common stock have not been, directly or indirectly, offered or sold and will not be, directly or indirectly, offered or sold in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan) or to others for re-offering or re-sale, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan except pursuant to an exemption from the registration requirements, and otherwise in compliance with, the FIEL and the other applicable laws and regulations of Japan.

For Qualified Institutional Investors (QII)

Please note that the solicitation for newly-issued or secondary securities (each as described in Paragraph 2, Article 4 of the FIEL) in relation to the shares of common stock constitutes either a QII only private placement

or a QII only secondary distribution (each as described in Paragraph 1, Article 23-13 of the FIEL). Disclosure regarding any such solicitation, as is otherwise prescribed in Paragraph 1, Article 4 of the FIEL, has not been made in relation to the shares of common stock. The shares of common stock may only be transferred to QIIs.

For Non-QII Investors

Please note that the solicitation for newly-issued or secondary securities (each as described in Paragraph 2, Article 4 of the FIEL) in relation to the shares of common stock constitutes either a small number private placement or a small number private secondary distribution (each as is described in Paragraph 4, Article 23-13 of the FIEL). Disclosure regarding any such solicitation, as is otherwise prescribed in Paragraph 1, Article 4 of the FIEL, has not been made in relation to the shares of common stock. The shares of common stock may only be transferred en bloc without subdivision to a single investor.

Hong Kong

The shares may not be offered or sold by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap.32, Laws of Hong Kong), or (ii) to professional investors within the meaning of the Securities and Futures Ordinance (Cap.571, Laws of Hong Kong) and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a prospectus within the meaning of the Companies Ordinance (Cap.32, Laws of Hong Kong), and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the SFA), (ii) to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased under Section 275 by a relevant person which is: (a) a corporation (which is not an accredited investor) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries rights and interest in that trust shall not be transferable for 6 months after that corporation or that trust has acquired the shares under Section 275 except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA; (2) where no consideration is given for the transfer; or (3) by operation of law.

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United Kingdom

Each underwriter has represented and agreed that:

(a) 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 (the FSMA) received by it in connection with the issue or sale of the shares of our common stock in circumstances in which Section 21(1) of the FSMA does not apply to us; and

(b) 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 our common stock in, from or otherwise involving the United Kingdom.

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LEGAL MATTERS

The validity of the common stock offered hereby will be passed upon for us by Goodwin Procter LLP, San Francisco, California and for the underwriters by Davis Polk & Wardwell LLP, Menlo Park, California.

EXPERTS

The financial statements of Global Blood Therapeutics, Inc. as of December 31, 2013 and 2014 and for each of the years in the two-year period ended December 31, 2014 are included herein in reliance upon the report of KPMG LLP, independent registered public accounting firm, appearing elsewhere 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-1 under the Securities Act that registers the shares of our common stock to be sold in this offering. This prospectus does not contain all of the information set forth in the registration statement and the exhibits and schedules filed as part of the registration statement. For further information with respect to us and our common stock, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. Statements contained in this 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 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. Copies of these materials can be obtained at prescribed rates from the Public Reference Section of the SEC at the principal offices of the SEC, 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.

Upon completion of this offering, we will become subject to the reporting and information requirements of the Exchange Act and, as a result, will 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.

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GLOBAL BLOOD THERAPEUTICS, INC.

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Report of Independent Registered Public Accounting Firm

The Board of Directors

Global Blood Therapeutics, Inc.:

We have audited the accompanying balance sheets of Global Blood Therapeutics, Inc. (the Company) as of December 31, 2013 and 2014, and the related statements of operations and comprehensive loss, redeemable convertible preferred stock and stockholders deficit, and cash flows for each of the years in the two-year period ended December 31, 2014. These financial statements are the responsibility of the Company s management. Our responsibility is to express an opinion on these financial statements based on our audits.

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

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Global Blood Therapeutics, Inc. as of December 31, 2013 and 2014, and the results of its operations and its cash flows for each of the years in the two-year period ended December 31, 2014, in conformity with U.S. generally accepted accounting principles.

/s/ KPMG LLP

San Francisco, California

March 18, 2015, except for note 12, as to which the date is July 30, 2015

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GLOBAL BLOOD THERAPEUTICS, INC.

Balance Sheets

(In thousands, except share and per share amounts)

	December 31, 2013	December 31, 2014
Assets		
Current assets:		
Cash and cash equivalents	$ 3,278	$ 52,069
Prepaid expenses	382	1,135
Other current assets	66	389
Total current assets	3,726	53,593
Property and equipment, net	2,366	2,023
Restricted cash	80	140
Total assets	$ 6,172	$ 55,756
Liabilities, Redeemable Convertible Preferred Stock and Stockholders Equity (Deficit)		
Current liabilities:		
Accounts payable	$ 845	$ 541
Payable due to related party	129	14
Accrued expenses	349	948
Accrued compensation	576	847
Series A redeemable convertible preferred stock liability	1,836	
Other current liabilities	27	187
Total current liabilities	3,762	2,537
Other liabilities	159	384
Total liabilities	3,921	2,921
Commitments and contingencies (Note 9)		
Redeemable convertible preferred stock, $0.001 par value: 41,163,168 and 69,363,168 shares authorized as of December 31, 2013 and 2014; 28,913,168 and 69,113,168 shares issued and outstanding as of December 31, 2013 and 2014; redemption value of $103,289 as of December 31, 2014	28,225	102,161
Stockholders equity (deficit):		

Common stock, $0.001 par value, 60,000,000 and 94,000,000 shares authorized as of December 31, 2013 and 2014; 1,388,089 and 1,954,488 shares issued and outstanding as of December 31, 2013 and 2014	1	2
Additional paid-in capital	2,072	
Accumulated deficit	(28,047)	(49,328)
Total stockholders equity (deficit)	(25,974)	(49,326)
Total liabilities, redeemable convertible preferred stock and stockholders equity (deficit)	$ 6,172	$ 55,756

See accompanying notes.

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GLOBAL BLOOD THERAPEUTICS, INC.

Statements of Operations and Comprehensive Loss

(In thousands, except share and per share amounts)

	Year Ended December 31,	
	2013	**2014**
Operating expenses:		
Research and development	$ 12,855	$ 16,324
General and administrative	2,309	3,855
Related party expenses	499	332
Total operating expenses	15,663	20,511
Loss from operations	(15,663)	(20,511)
Change in fair value of Series A redeemable convertible preferred stock liability	(2,455)	(297)
Interest income	2	1
Net loss and comprehensive loss	$ (18,116)	$ (20,807)
Net loss attributable to common stockholders	$ (19,851)	$ (23,772)
Net loss per share attributable to common stockholders, basic and diluted	$ (16.14)	$ (14.20)
Weighted-average number of shares used in computing net loss per share attributable to common stockholders, basic and diluted	1,230,241	1,673,919
Pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)		$ (1.51)
Weighted-average number of shares used in computing pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)		13,761,829

See accompanying notes.

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GLOBAL BLOOD THERAPEUTICS, INC.

Statements of Redeemable Convertible Preferred Stock and Stockholders Deficit

(In thousands, except share amounts)

	Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders Deficit
	Shares	Amount	Shares	Amount			
Balance at December 31, 2012	13,663,168	$ 9,451	971,418	$ 1	$ 444	$ (9,794)	$ (9,349)
Issuance of Series A redeemable convertible preferred stock, net of $15 in issuance costs	15,250,000	15,235					
Remeasurement of fair value and settlement of Series A redeemable convertible preferred stock liability		1,804			3,081		3,081
Accretion of redeemable convertible preferred stock to redemption value		1,735			(1,598)	(137)	(1,735)
Vesting of founders shares and restricted stock awards			412,386		6		6
Common stock issued on exercise of stock options			4,285		1		1
Stock-based compensation expense					138		138
Net loss						(18,116)	(18,116)
Balance at December 31, 2013	28,913,168	28,225	1,388,089	1	2,072	(28,047)	(25,974)
Issuance of Series A redeemable convertible preferred stock, net of $393 derivative liability and $16 in issuance costs	21,000,000	20,591					
Issuance of Series B redeemable convertible preferred stock, net of $146 in issuance costs	19,200,000	47,854					
Settlement of fair value of Series A redeemable convertible preferred stock		2,526					

liability							
Accretion of redeemable convertible preferred stock to redemption value		2,965			(2,491)	(474)	(2,965)
Vesting of founders shares and restricted stock awards			411,333	1	20		21
Common stock issued on exercise of stock options			155,066		49		49
Stock-based compensation expense					350		350
Net loss						(20,807)	(20,807)
Balance at December 31, 2014	69,113,168	$ 102,161	1,954,488	$ 2	$	$ (49,328)	$ (49,326)

See accompanying notes.

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GLOBAL BLOOD THERAPEUTICS, INC.

Statements of Cash Flows

(In thousands)

	Year Ended December 31,	
	2013	**2014**
CASH FLOWS FROM OPERATING ACTIVITIES		
Net loss	$ (18,116)	$ (20,807)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	534	666
Remeasurement of Series A redeemable convertible preferred stock liability	2,455	297
Stock-based compensation	138	350
Changes in operating assets and liabilities:		
Prepaid expenses	(73)	(753)
Other current assets	149	(323)
Accounts payable	(465)	(304)
Payable due to related party	(68)	(115)
Accrued expenses	183	599
Accrued compensation	494	271
Other current liabilities	38	17
Other noncurrent liabilities	31	(19)
Net cash used in operating activities	(14,700)	(20,121)
CASH FLOWS FROM INVESTING ACTIVITIES		
Purchase of property and equipment	(940)	(323)
Increase in restricted cash		(60)
Net cash used in investing activities	(940)	(383)
CASH FLOWS FROM FINANCING ACTIVITIES		
Proceeds from issuance of redeemable convertible preferred stock, net of issuance costs	15,235	68,838
Proceeds from issuance of restricted stock awards	43	408
Proceeds from the exercise of common stock options	1	49
Net cash provided by financing activities	15,279	69,295
Net (decrease) increase in cash and cash equivalents	(361)	48,791
Cash and cash equivalents at beginning of period	3,639	3,278
Cash and cash equivalents at end of period	$ 3,278	$ 52,069

SUPPLEMENTAL DISCLOSURES OF NON-CASH FINANCING INFORMATION:		
Remeasurement and settlement of fair value of Series A redeemable convertible preferred stock liability	$ 4,885	$ 2,526
Accretion of Series A redeemable convertible preferred stock	$ 1,735	$ 2,965

See accompanying notes.

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GLOBAL BLOOD THERAPEUTICS, INC.

Notes to Financial Statements

1. Organization and Basis of Presentation

Global Blood Therapeutics Inc. (the Company) was incorporated in Delaware in February 2011 and commenced operations in May 2012. The Company is a biopharmaceutical company dedicated to discovering, developing and commercializing novel therapeutics to treat grievous blood-based disorders. The Company s primary activities have been establishing its facilities, recruiting personnel, conducting development of its product candidates, including clinical studies, and raising capital. The Company s principal operations are based in South San Francisco, California, and it operates in one segment.

Need for Additional Capital

In the course of its development activities, the Company has sustained operating losses and expects such losses to continue over the next several years. The Company s ultimate success depends on the outcome of its research and development activities. Since inception through December 31, 2014, the Company has incurred cumulative net losses of $49.3 million. Management expects to incur additional losses in the future to conduct product research and development and recognizes the need to raise additional capital to fully implement its business plan. The Company intends to raise such capital through the issuance of additional equity, and potentially through borrowings, and strategic alliances with partner companies. However, if such financing is not available at adequate levels, the Company will need to reevaluate its operating plans. Management believes that its existing cash and cash equivalents will be sufficient to fund the Company s cash requirements through at least December 31, 2015.

2. Summary of Significant Accounting Policies

Use of Estimates

The accompanying financial statements have been prepared in accordance with U.S. generally accepted accounting principles (GAAP). The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities as of the date of the financial statements and the reported amounts of expenses during the reporting period. On an ongoing basis, management evaluates its estimates, including those related to the valuation of derivatives, accruals for research and development activities, common stock, stock-based compensation; and income taxes. Management bases its estimates on historical experience and on various other market-specific and relevant assumptions that management believes to be reasonable under the circumstances. Actual results could differ from those estimates.

Cash and Cash Equivalents

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

Restricted Cash

Restricted cash consists of money market funds held by the Company s financial institution as collateral for the Company s letter of credit under its facility lease.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to a concentration of credit risk consist of cash and cash equivalents. The Company s cash and cash equivalents are held by a financial institution in the United States. Amounts on deposit may at times exceed federally insured limits. Management believes that the financial institution is financially sound, and accordingly, minimal credit risk exists with respect to the financial institution.

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GLOBAL BLOOD THERAPEUTICS, INC.

Notes to Financial Statements

Property and Equipment

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

Impairment of Long-Lived Assets

The Company evaluates its long-lived assets, including property and equipment, for impairment whenever events or changes in circumstances indicate that the carrying value of these assets may not be recoverable. Recoverability of these assets is measured by comparison of the carrying amount of each asset to the future undiscounted cash flows the asset is expected to generate over its remaining life. If the asset is considered to be impaired, the amount of any impairment is measured as the difference between the carrying value and the fair value of the impaired asset. There have been no impairments of the Company s long-lived assets for the periods presented.

Deferred Rent

Rent expense is recognized on a straight-line basis over the noncancelable term of the Company s operating lease and, accordingly, the Company records the difference between cash rent payments and the recognition of rent expense as a deferred rent liability, which is included within other liabilities on the balance sheet.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development costs consist of expenses associated with clinical trials, outside research consultants, contract manufacturing expenses, salaries, employee benefits and allocated facility costs.

Preclinical study and clinical trial expenditures are a component of research and development expenses and are charged to operations as incurred. The expenses related to preclinical studies and clinical trials are based on estimates of the services received and efforts expended pursuant to contracts with research institutions and clinical research organizations that conduct and manage the studies on behalf of the Company. The financial terms of these agreements are subject to negotiation and vary from contract to contract and may result in uneven payment flows. Payments under the contracts depend on factors such as the achievement of certain events and the completion of portions of the study or similar conditions. Expenses related to preclinical studies and clinical trials are accrued based on the estimated level of activity incurred under each contract. Payments made to third parties under these arrangements in advance of the receipt of the related services are deferred as prepaid assets, depending on the terms of the agreement, until the services are rendered.

Stock-Based Compensation

The Company measures and recognizes stock-based compensation expense, including employee and non-employee equity awards, based on fair value at the grant date. The Company uses the Black-Scholes option-pricing model to calculate fair value. Stock-based compensation expense recognized in the statements of operations is based on options ultimately expected to vest, taking into consideration estimated forfeitures. Stock-based compensation expense is revised in subsequent periods, if necessary, if actual forfeitures differ from these estimates. When estimating forfeitures, the Company considers historic voluntary termination behaviors as well

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GLOBAL BLOOD THERAPEUTICS, INC.

Notes to Financial Statements

as trends of actual option forfeitures. For options granted to nonemployees, the Company revalues the unearned portion of the stock-based compensation and the resulting change in fair value is recognized in the statements of operations over the period the related services are rendered.

Income Taxes

Income taxes are accounted for under the asset and liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date. The Company recognizes the effect of income tax positions only if those positions are more likely than not of being sustained. Recognized income tax positions are measured at the largest amount that is greater than 50% likely of being realized. Changes in recognition or measurement are reflected in the period in which the change in judgment occurs. Valuation allowances are established when necessary to reduce deferred tax assets to the amounts more likely than not will be realized. Interest and penalties related to unrecognized tax benefits are recognized as a component of income tax expense.

Net Loss per Share Attributable to Common Stockholders

Basic net loss per share attributable to common stockholders is calculated by dividing the net loss attributable to common stockholders by the weighted average number of shares of common stock outstanding during the period, without consideration for common stock equivalents. The net loss attributable to common stockholders is calculated by adjusting the net loss of the Company for the accretion on the redeemable convertible preferred stock. Diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders, since the effects of potentially dilutive securities are antidilutive given the net loss of the Company.

Unaudited Pro Forma Net Loss per Share Attributable to Common Stockholders

Pro forma basic and diluted net loss per share attributable to common stockholders has been computed to give effect to the conversion of the redeemable convertible preferred stock into common stock in connection with the Company s initial public offering. The unaudited pro forma net loss per share attributable to common stockholders does not include the shares expected to be sold and related proceeds to be received from the initial public offering.

Recent Accounting Pronouncements

In June 2014, the Financial Accounting Standards Board (FASB) issued Accounting Standards Update (ASU) 2014-10, *Development Stage Entities (Topic 915): Elimination of Certain Financial Reporting Requirements, Including an Amendment to Variable Interest Entities Guidance in Topic 810, Consolidation.* ASU 2014-10 simplifies the accounting guidance by removing all incremental financial reporting requirements for development stage entities. The amendments related to the elimination of the inception-to-date information and other

disclosure requirement of Topic 915 should be applied retrospectively, and are effective for annual reporting periods beginning after December 15, 2014, and interim periods therein. The Company early adopted this guidance and accordingly, there is no inception to date information presented in these financial statements.

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In August 2014, the FASB issued ASU 2014-15, *Disclosure of Uncertainties about an Entity s Ability to Continue as a Going Concern*. ASU 2014-15 requires management to evaluate relevant conditions, events and certain management plans that are known or reasonably knowable that when, considered in the aggregate, raise substantial doubt about the entity s ability to continue as a going concern within one year after the date that the financial statements are issued, for both annual and interim periods. ASU 2014-15 also requires certain disclosures around management s plans and evaluation, as well as the plans, if any, that are intended to mitigate those conditions or events that will alleviate the substantial doubt. ASU 2014-15 is effective for fiscal years ending after December 15, 2016. The Company is currently evaluating the impact that the adoption of ASU 2014-15 will have on its financial statements and related disclosures.

3. Fair Value Measurements

Fair value accounting is applied for all financial assets and liabilities that are recognized or disclosed at fair value in the financial statements on a recurring basis (at least annually). Financial instruments include cash and cash equivalents, restricted cash, accounts payable and accrued liabilities that approximate fair value due to their relatively short maturities.

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

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

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

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

The Company s financial instruments consist of Level 1 assets and Level 3 liabilities. Where quoted prices for identical assets are available in an active market, securities are classified as Level 1. Level 1 assets consist of highly liquid money market funds, which include $80,000 and $140,000 of funds that are collateral for the Company s facility lease that are included within restricted cash. There were no unrealized gains and losses in the Company s investments in these money market funds.

In certain cases where there is limited activity or less transparency around inputs to valuation, securities are classified as Level 3. Level 3 liabilities consist of the Series A redeemable convertible preferred stock liability (see Note 6).

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Financial assets and liabilities subject to fair value measurements on a recurring basis and the level of inputs used in such measurements are as follows (in thousands):

	December 31, 2013			
	Total	Level 1	Level 2	Level 3
Financial Assets:				
Money market funds	$ 3,358	$ 3,358	$	$
Total financial assets	$ 3,358	$ 3,358	$	$
Financial Liabilities:				
Series A redeemable convertible preferred stock liability	$ 1,836	$	$	$ 1,836
Total financial liabilities	$ 1,836	$	$	$ 1,836

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

The Series A redeemable convertible preferred stock liability stems from the initial sale of Series A redeemable convertible preferred stock wherein the Company was obligated to sell additional shares in subsequent closings contingent upon the achievement of certain development milestones. The subsequent closings were deemed to be freestanding financial instruments that were outside the control of the Company. The Company estimates the fair value of this liability using Black-Scholes Option Pricing models that include the assumptions of probability of the financing occurring, stock price per share, expected term, and discount rate. The change in fair value is recognized as a gain or loss in the statements of operations and comprehensive loss. See Note 6 for further discussion on the Series A redeemable convertible preferred stock liability and related valuations.

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The following table sets forth a summary of the changes in the fair value of the Company s Level 3 financial instruments as follows (in thousands):

	Series A Redeemable Convertible Preferred Stock Liability
Balance at January 1, 2013	$ 4,266
Net increase in fair value upon revaluation	2,455
Settlement of liability due to issuance of Series A redeemable convertible preferred shares	(1,804)
Change in fair value due to amendments to the Series A Stock Purchase Agreement	(3,081)
Balance at December 31, 2013	1,836
Net increase in fair value upon revaluation	297
Recognition of fair value of liability due to new obligation for Series A financing in April 2014	393
Settlement of tranche liability due to issue of Series A redeemable convertible preferred shares	(2,526)
Balance at December 31, 2014	$

4. Balance Sheet Components

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

	December 31,	
	2013	2014
Laboratory equipment	$ 2,493	$ 2,611
Computer equipment	272	472
Leasehold improvements	240	245
Total property and equipment	3,005	3,328
Less: accumulated depreciation and amortization	(639)	(1,305)
Property and equipment, net	$ 2,366	$ 2,023

Depreciation and amortization expense for the years ended December 31, 2013 and 2014 was $534,000 and $666,000, respectively.

Accrued Expenses

Accrued expenses consist of the following (in thousands):

	December 31,	
	2013	**2014**
Accrued clinical and manufacturing expenses	$ 293	$ 749
Accrued professional and consulting services	6	153
Other	49	46
Total accrued expenses	$ 349	$ 948

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5. Redeemable Convertible Preferred Stock and Stockholders Deficit

Redeemable Convertible Preferred Stock

As of December 31, 2013 redeemable convertible preferred stock consisted of the following (in thousands, except share amounts):

	Shares Authorized	Shares Issued and Outstanding	Net Carrying Value	Aggregate Liquidation Preference
Series A	41,163,168	28,913,168	$ 28,225	$ 31,321
Total redeemable convertible preferred stock	41,163,168	28,913,168	$ 28,225	$ 31,321

As of December 31, 2014 redeemable convertible preferred stock consisted of the following (in thousands, except share amounts):

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

Significant provisions of the redeemable convertible preferred stock are as follows:

Liquidation

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

but unpaid thereon, whether or not declared, together with any other dividends declared but unpaid thereon. The original issue price is $2.50 for the Series B and $1.00 for the Series A redeemable convertible preferred stock. After payments of the full liquidation preferences of the Series A and B redeemable convertible preferred stock described above, the remaining assets of the Company would have been available for distribution to stockholders.

However if, the aggregate amount which the holders of Series A and Series B redeemable convertible preferred stock are entitled to receive under the above-described provisions should exceed $2.50 and $6.25 per share, respectively, (the Maximum Participation Amount), each holder of Series A and Series B redeemable convertible preferred stock shall be entitled to receive upon such liquidation, dissolution or winding up of the Company or Deemed Liquidation Event the greater of:

(i) The Maximum Participation Amount and

(ii) The amount such holder would have received if all shares of Series A and Series B redeemable convertible preferred stock had been converted into common stock immediately prior to such liquidation, dissolution or winding up of the Company or Deemed Liquidation Event.

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Each of the following events shall be considered a Deemed Liquidation Event unless the holders of at least majority of the then outstanding shares of Series A and B redeemable convertible preferred stock elect otherwise by written notice sent to the Company:

(i) a merger or consolidation in which the Company is a constituent party or a subsidiary of the Company is a constituent party;

(ii) the sale, lease, transfer, exclusive license or other disposition, all or substantially all the assets of the Company.

Voting

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

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

Conversion

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

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

(ii) *Mandatory Conversion Rights:* Upon either (a) for each of Series A and Series B redeemable convertible preferred stock the date and time, or the occurrence of an event, specified by vote or written consent of holders of at least a majority of the then outstanding shares of Series A redeemable convertible preferred stock or Series B redeemable convertible preferred stock or (b) the closing of the sale of shares of common stock to the public in a qualified initial public offering, all outstanding shares of redeemable convertible preferred stock shall automatically be converted into shares of common stock, at the then effective conversion rate. A qualified initial public offering is the closing of a firm commitment underwritten public offering with aggregate gross proceeds of not less than $35.0 million.

Dividends

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

Redemption

The Series A redeemable convertible preferred stock is redeemable, at the election of majority of the holders of Series A redeemable convertible preferred stock, on or after the later to occur of the redemption in full of all

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outstanding shares of Series B redeemable convertible preferred stock and the seventh anniversary of the Series A preferred stock issue date (or May 2019), in three annual installments at the original issue price of $1.00 per share, plus any unpaid accruing dividends (whether or not declared).

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

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

Common Stock

As of December 31, 2014, the Company had reserved the following shares of common stock for issuance as follows:

Series A redeemable convertible preferred stock outstanding, as converted	14,260,904
Series B redeemable convertible preferred stock outstanding, as converted	5,485,710
Restricted shares subject to future vesting	1,121,979
Options issued and outstanding	954,567
Options available for future grants	651,816
Total	22,474,976

Restricted Stock

In May 2012 the Company issued 1,345,709 shares of restricted common stock to founders at $0.0035 per share of which 1,249,282 were subject to future vesting. Under the related stock purchase agreements, the Company has the right to repurchase the common stock which right lapses according to individual vesting schedules. In order to vest, the holders are required to provide continued service to the Company. Upon vesting, the appropriate amounts are

transferred from liabilities to additional paid-in capital. If the holder of any unvested restricted common stock is terminated for any reason, the Company has the right to repurchase the unvested shares at the stockholder s original purchase price. As such, the shares subject to future vesting are not deemed outstanding for accounting purposes until the shares vest. As of December 31, 2013 and 2014, 545,083 and 174,150 of these shares remained subject to repurchase and $2,000 and $1,000, respectively, were recorded as liabilities pertaining to the restricted common stock.

The Company has issued stock awards to employees under the 2012 Stock Option and Grant Plan. Under the related stock purchase agreements, the Company has the right to repurchase the common stock at the lower of fair value and the stockholders original purchase price which right lapses according to individual vesting

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schedules. In order to vest, the holders are required to provide continued service to the Company. Upon vesting, the appropriate amounts are transferred from liabilities to additional paid in capital. If the holder of any unvested restricted common stock is terminated for any reason, the Company has the right to repurchase the unvested shares at the stockholder s original purchase price. As such, the shares subject to future vesting are not deemed outstanding for accounting purposes until the shares vest. As of December 31, 2013 and 2014, 146,034 and 947,829 of these shares remained subject to repurchase and $46,000 and $435,000, respectively, were recorded as liabilities pertaining to the unvested restricted stock awards.

6. Series A Redeemable Convertible Preferred Stock Liability

The Company recorded the redeemable convertible preferred stock liability incurred in connection with its Series A redeemable convertible preferred stock as a derivative financial instrument liability at the fair value on the date of issuance, and remeasures it on each subsequent balance sheet date. The Series A preferred stock liability stems from the initial sale of Series A redeemable convertible preferred stock wherein the Company was obligated to sell additional shares in subsequent closings contingent upon the achievement of certain development milestones. The subsequent closings were deemed to be freestanding financial instruments that were outside the control of the Company. The changes in fair value are recognized as a gain or loss in the statements of operations and comprehensive loss and liability is remeasured at each reporting period and settlement of the related Series A tranche closings. The Company estimated the fair value of this liability using the Black Scholes option pricing model that include assumptions of probability of achievement of the development milestones or funding of the financing, stock price per share, expected term and risk-free interest rate.

In May 2012, the Company entered into a Series A Preferred Stock Purchase Agreement (the Agreement) for the issuance of up to approximately 41,000,000 shares of Series A redeemable convertible preferred stock at a price of $1.00 per share, in multiple closings. The initial closing occurred on May 31, 2012 whereby 10,000,000 shares of Series A redeemable convertible preferred stock were issued for gross cash proceeds of $10.0 million and 3,663,168 shares were issued upon conversion of outstanding convertible promissory notes payable with a carrying value of $3.7 million. According to the initial terms of the Agreement, the Company would issue 10,000,000 and 17,000,000 shares, respectively, under the same terms as the initial closing, in two subsequent closings (Tranche 1 and Tranche 2) contingent upon the achievement of certain development milestones.

On the date of the initial closing, the Company recorded a Series A redeemable convertible preferred stock liability of $3.8 million as the obligation/right to complete Tranche 1 and Tranche 2 were deemed to be freestanding financial instruments that were outside the control of the Company. The fair value of the redeemable convertible preferred stock liability on the date of the initial closing was determined using the option pricing method based on the following assumptions: 70 90% probability of achievement of the development milestones, stock price of $1.00 per share, a term of 0.59 1.34 years, and discount rate of 20%.

The terms of the Agreement were amended twice during 2013. In February 2013, the number of shares to be issued in Tranche 1 was changed (Amendment No. 1) from one tranche of 10,000,000 shares to two tranches of 5,000,000 shares each (Tranche 1(a) and Tranche 1(b)) and the issuance of the 17,000,000 shares in Tranche 2 was revised to be part of a third closing. In October 2013, Tranche 2 was changed from one closing of 17,000,000 shares into two

closings (Amendment No. 2), one for 5,000,000 shares and one for the remaining 12,000,000 shares (Tranche 3) to be issued in one or more subsequent closings as mutually agreed upon by the Company and 75% of the outstanding Series A redeemable convertible preferred stockholders. Changes in the fair value of the preferred stock liability arising from the amendments that reduce the liability are deemed to be capital contributions as they were initiated and agreed upon by the investor, who is deemed to be a related party and controlling shareholder due to stock ownership.

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In February 2013, the Company completed the closing of Tranche 1(a) and issued 5,000,000 shares of Series A redeemable convertible preferred stock for gross cash proceeds of $5.0 million. In addition, the Company issued 250,000 shares to a new investor for gross cash proceeds of $250,000. At this time the redeemable convertible preferred stock liability was remeasured using the option pricing method based on the following assumptions: 70%-90% probability of achievement of the development milestones, stock price of $1.00 per share, a term of 0.33 0.59 years, and discount rate of 20%.

In July 2013, the Company completed the closing of Tranche 1(b) and issued 5,000,000 shares of Series A redeemable convertible preferred stock for gross cash proceeds of $5.0 million. At this time the redeemable convertible preferred stock liability was remeasured using the option pricing method based on the following assumptions: 90% probability of achievement of the development milestones, stock price of $1.00 per share, a term of 0.22 years, and discount rate of 20%.

In October 2013, the Company completed the closing of Tranche 2 and issued 5,000,000 shares of Series A redeemable convertible preferred stock for gross cash proceeds of $5.0 million. In conjunction with Tranche 2 closing, the Company entered into Amendment No. 2 to increase the number of permitted subsequent closings for the remaining 12,000,000 shares with no change in total commitment of funds. At this time the preferred stock liability was remeasured using the option pricing method based on the following assumptions: 90% probability of achievement of the development milestones, stock price of $1.00 per share, a term of 0.25 0.49 years, and discount rate of 20%.

At December 31, 2013, the redeemable convertible preferred stock liability, which related solely to Tranche 3, was remeasured at $1.8 million using the option pricing method based on the following assumptions: 90% probability of achievement of the development milestones, stock price of $1.00 per share, a term of 0.08 0.33 years, and discount rate of 20%.

In January 2014, the Company completed the first closing of Tranche 3 and issued 5,000,000 shares of Series A redeemable convertible preferred stock for gross cash proceeds of $5.0 million (Tranche 3(a)). The Company had a remaining obligation to issue up to an aggregate of 7,000,000 shares (Tranche 3(b)) of its Series A redeemable convertible preferred stock in one or more subsequent closings. At this time the redeemable convertible preferred stock liability was remeasured using the option pricing method based on the following assumptions: 90% probability of achievement of the development milestones, stock price of $1.00 per share, a term of 0.24 years, and discount rate of 20%.

In April 2014, the Company completed the Tranche 3(b) closing of its Series A Series A redeemable preferred stock. At this time the Company issued 7,000,000 shares of its Series A Series A redeemable preferred stock for $7.0 million in cash. This satisfied the Company s remaining obligation/right under the Tranche 3 discussed above. At this time the preferred stock liability was remeasured using the option pricing method based on the following assumptions: 100% probability of achievement of the development milestones, stock price of $1.00 per share, a term of 0.42 years, and discount rate of 20%.

In conjunction with Tranche 3(b) above, the Company issued an additional 3,000,000 shares of its Series A redeemable convertible preferred stock for $3.0 million in cash in April 2014. In addition, the Company amended and

restated the Agreement (Amendment No. 3) to allow for an additional subsequent close of its Series A redeemable convertible preferred stock for up to an aggregate of 6,000,000 shares (Tranche 4) in a subsequent closing to occur on or before October 1, 2014, based on the approval of a majority of the Company s Board of Directors. At this time the preferred stock liability was remeasured using the option pricing method based on the following assumptions: 100% probability of achievement of the development milestones, stock price of $1.00 per share, a term of 0.42 years, and discount rate of 20%.

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In October 2014 the Company completed the Tranche 4 closing and issued 6,000,000 shares of Series A redeemable convertible preferred stock for gross cash proceeds of $6.0 million. This satisfied the Company s tranche obligation that was outstanding under Amendment No. 3.

At December 31, 2014, there was no outstanding obligations related to the Series A redeemable convertible preferred stock liability as all obligations were settled in the Tranche 4 closing of the issuance of Series A redeemable convertible preferred stock. For the years ended December 31, 2013 and 2014, the Company recorded a total charge of $2.5 million and $297,000, respectively, for the changes in the fair value of the Series A redeemable convertible preferred stock liability in the statement of operations and comprehensive loss. For the year ended December 31, 2013, the Company recorded $3.1 million in additional paid-in capital from the modification of the terms of the Agreement in 2013. There were no such modifications in 2014. For the years ended December 31, 2013 and 2014, the Company recorded $1.8 million and $2.5 million as the settlement of the outstanding obligation/right of the Series A redeemable convertible preferred stock liability in redeemable convertible preferred stock.

7. Stock Option and Grant Plan

In 2012, the Company adopted the 2012 Stock Option and Grant Plan (the 2012 Plan) under which the Company s board of directors may grant incentive stock options to employees, including officers and members of the Board of Directors who are also employees of the Company, and non-statutory stock options (options that do not qualify as incentive options) and/or restricted stock of the Company to employees, officers, directors, or consultants of the Company. The Company has reserved 2,785,713 shares of common stock for issuance under the 2012 Plan. Awards granted under the 2012 Plan expire no later than 10 years from the date of grant. For incentive stock options and nonstatutory stock options, the option price shall not be less than 100% of the fair market value on the day of grant. If at the time the Company grants an option and the optionee directly or by attribution owns stock possessing more than 10% of the total combined voting power of all classes of stock of the Company, the option price is required to be at least 110% of the of the fair market value on the day of grant. Options granted typically vest over a four-year period but may be granted with different vesting terms.

As of December 31, 2013 and 2014, there were 576,150 shares and 651,816 shares, respectively, available for the Company to grant under the 2012 Plan.

The following summarizes option activity under the 2012 Plan:

	Number of Options	Weighted-Average Exercise Price	Weighted-Average remaining contractual term (years)	Aggregate Intrinsic Value (in thousands)
Balance, January 1, 2013	230,425	$ 0.32	9.8	

Options granted	398,497		0.32			
Options exercised	(4,285)		0.32			
Options canceled	(5,714)		0.32			
Balance, December 31, 2013	618,923		0.32	9.2		
Options granted	544,423		0.44			
Options exercised	(155,066)		0.32			
Options canceled	(53,713)		0.32			
Balance Outstanding, December 31, 2014	954,567	$	0.38	9.0	$	1,170
Exercisable, December 31, 2014	88,213	$	0.33	8.4	$	113
Vested and expected to vest, December 31, 2014	948,860	$	0.38	9.0	$	1,163

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The aggregate intrinsic values of options outstanding, exercisable, vested and expected to vest were calculated as the difference between the exercise price of the options and the estimated fair value of the Company s common stock, as determined by the Board of Directors, as of December 31, 2014. The intrinsic value of options exercised for the years ended December 31, 2013 and 2014 was zero and $35,000, respectively.

During the years ended December 31, 2013 and 2014, the estimated weighted-average grant-date fair value of the options vested was $0.21 and $0.35 per share, respectively and the estimated weighted-average grant-date fair value of common stock underlying options granted was $0.31 and $0.34 per share, respectively.

Employee Stock Options Valuation

The fair value of employee and director stock option awards was estimated at the date of grant using a Black-Scholes option-pricing model with the following assumptions:

	Year Ended December 31,	
	2013	2014
Expected term (in years)	6.0-6.1	6.0-6.1
Volatility	79.8%-86.6%	80.7%-93.0%
Risk-free interest rate	1.12%-1.31%	1.89%-2.10%
Dividend yield		

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

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

Expected Term The Company s expected term represents the period that the Company s options granted are expected to be outstanding and is determined using the simplified method (based on the mid-point between the vesting date and the end of the contractual term). The Company has very limited historical information to develop reasonable expectations about future exercise patterns and post-vesting employment termination behavior for its stock option grants.

Expected Volatility Since the Company is privately held and does not have any trading history for its common stock, the expected volatility was estimated based on the average volatility for comparable publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants. The comparable companies were chosen based on their similar size, stage in the life cycle or area of specialty.

Risk-Free Interest Rate The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of option.

Expected Dividend The Company has never paid dividends on its common stock and has no plans to pay dividends on its common stock. Therefore, the Company used an expected dividend yield of zero.

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Stock Options Granted to Non-employees

Stock-based compensation related to stock options granted to non-employees is recognized as the stock options are earned. The fair value of the stock options granted is calculated at each reporting date using the Black-Scholes option-pricing model with the following assumptions:

	Year Ended December 31,	
	2013	2014
Expected term (in years)	5.0-9.4	5.0-9.9
Volatility	79.7%-88.1%	77.6%-82.3%
Risk-free interest rate	0.88%-2.63%	1.49%-2.68%
Dividend yield		

During the years ended December 31, 2013, and 2014, the Company granted 202,142 and 31,999 shares, respectively, to non-employee consultants and recorded stock-based compensation expense of $2,000 and $17,000, respectively.

Restricted Stock Awards

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

A summary of the Company s non-vested restricted stock for the periods is as follows:

	Number of Shares
Balance, January 1, 2013	965,719
Granted	137,784
Vested	(412,386)
Balance, December 31, 2013	691,117
Granted	902,710
Vested	(411,333)
Repurchased by company	(60,515)
Balance, December 31, 2014	1,121,979

RSAs granted during the years ended December 31, 2013 and 2014 vest over four years, subject to the continued service relationship with the Company. During the years ended December 31, 2013 and 2014, the estimated weighted-average grant date fair value of restricted stock issued was $0.23 and $0.33 per share, respectively. During the year December 31, 2013 and 2014, $112,000 and $289,000, respectively, of stock-based compensation expense was recognized related to these RSAs. The Company recognizes the expense using a straight-line basis over the requisite service period of the award. As of December 31, 2014, there was $427,000 of total unrecognized compensation cost related to unvested RSAs with service-based vesting conditions. These costs are expected to be recognized over a weighted average period of 2.3 years.

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

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GLOBAL BLOOD THERAPEUTICS, INC.

Notes to Financial Statements

Stock-Based Compensation Expense

Total stock-based compensation recognized for both employees and non-employee was as follows (in thousands):

	Year Ended December 31,	
	2013	2014
Research and development	$ 113	$ 248
General and administrative	25	102
Total stock-based compensation expense	$ 138	$ 350

As of December 31, 2014, unrecognized stock-based compensation cost related to outstanding unvested stock options that are expected to vest was $458,000. This unrecognized stock-based compensation cost is expected to be recognized over a weighted-average period of 3.8 years.

8. Income Taxes

No provision for income taxes was recorded for the years ended December 31, 2013 and 2014. The Company has incurred net operating losses for all the periods presented. The Company has not reflected any benefit of such net operating loss carryforwards in the accompanying financial statements. The Company has established a full valuation allowance against its deferred tax assets due to the uncertainty surrounding the realization of such assets.

The effective tax rate of the provision for income taxes differs from the federal statutory rate as follows:

	Year Ended December 31,	
	2013	2014
Federal statutory income tax rate	34.0%	34.0%
Non-deductible changes in fair value	(4.9)	(0.6)
Federal and state tax credits	2.1	2.4
Change in valuation allowance	(31.4)	(35.8)
Other	0.2	
	0.0%	0.0%

The components of the deferred tax assets and liabilities are as follows (in thousands):

	December 31, 2013	2014
Deferred tax assets:		
Net operating loss carryforwards	$ 9,752	$ 17,651
Tax credits	904	1,630
Accruals and reserves	271	374
Stock based compensation		122
Gross deferred tax assets	10,927	19,777
Valuation allowance	(10,577)	(19,495)
Net deferred tax assets	350	282
Deferred tax liabilities:		
Property and equipment	(350)	(282)
Net deferred tax	$	$

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GLOBAL BLOOD THERAPEUTICS, INC.

Notes to Financial Statements

Realization of the deferred tax assets is dependent upon future taxable income, if any, the amount and timing of which are uncertain. The Company has established a valuation allowance to offset deferred tax assets as of December 31, 2013 and 2014 due to the uncertainty of realizing future tax benefits from its net operating loss carryforwards and other deferred tax assets. The valuation allowance increased by approximately $6.8 million and $8.9 million during the year ended December 31, 2013 and 2014, respectively. The increase in the valuation allowance is mainly related to the increase in net operating loss carryforwards incurred during the respective taxable years.

At December 31, 2014, the Company has net operating loss carryforwards for Federal income tax purposes of approximately $44.6 million which are available to offset future taxable income, if any, through 2034 and net operating loss carryforwards for state income tax purposes of approximately $42.4 million which are available to offset future taxable income, if any, through 2034. The net deferred tax asset above does not include any amounts attributable to excess stock option deductions. As of December 31, 2014, the Company had research and development tax credit carryforwards of approximately $1.5 million and $1.1 million available to reduce future taxable income, if any, for federal and state income tax purposes, respectively. If not utilized, the federal credit carryforwards will begin expiring in 2031, and the state credits carry forward indefinitely.

Federal and state laws impose substantial restrictions on the utilization of net operating loss and tax credit carryforwards in the event of an ownership change for tax purposes, as defined in Section 382 of the Internal Revenue Code. As a result of such ownership changes, the Company s ability to realize the potential future benefit of tax losses and tax credits that existed at the time of the ownership change may be significantly reduced. The Company s deferred tax asset and related valuation allowance would be reduced as a result. The Company has not yet performed a Section 382 study to determine the amount of reduction, if any.

No liability related to uncertain tax positions is recorded on the financial statements related to uncertain tax positions. It is the Company s policy to include penalties and interest expense related to income taxes as a component of other expense and interest expense, respectively, as necessary.

A reconciliation of the beginning and ending amount of unrecognized tax benefits is as follows (in thousands):

	December 31,	
	2013	2014
Balance at beginning of year	$ 122	$ 352
Additions based on tax positions related to current year	230	282
Balance at end of year	$ 352	$ 634

The Company does not expect that its uncertain tax positions will materially change in the next twelve months. The reversal of the uncertain tax benefits would not impact the Company s effective tax rate as the Company continues to maintain a full valuation allowance against its deferred tax assets.

The Company files income tax returns in the United States and California. The Company is not currently under examination by income tax authorities in federal, state or other jurisdictions. All tax returns remain open for examination by federal and state authorities for three and four years, respectively, from the date of utilization of any net operating loss or credits.

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GLOBAL BLOOD THERAPEUTICS, INC.

Notes to Financial Statements

9. Commitments and Contingencies

Facilities

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

In October 2014, the Company assumed the noncancelable operating lease from a neighboring tenant for approximately 12,000 square feet of adjacent laboratory and office space on substantially the same economic terms as the Company s primary facility operating lease. The Company anticipates that related lease payments will commence in March 2015 and expire in April 2018.

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

Year ending December 31,	Amount
2015	$ 949
2016	1,050
2017	1,078
2018	367
Total	$ 3,444

Through February 2015, the Company was a party to a Space Sharing Agreement and a Shared Services Agreement with a biotechnology company that is also majority-owned by Third Rock Ventures. Under these agreements, specified expenses were shared equally between the two companies at cost and not subject to any markup or markdown. For the year ended December 31, 2013 and 2014, the Company recorded reimbursements of $107,000 and $234,000, respectively, under these agreements. The Company has a receivable of $64,000 and $24,000, respectively, from these reimbursements which are included within other current assets on the balance sheets as of December 31, 2013 and 2014.

Rent expense for the facility operating lease consisted of the following (in thousands):

	Year ended December 31,	
	2013	2014
Minimum rental	$ 554	$ 554
Net reimbursement under Space Sharing Agreement	(52)	(54)

Facility rental expense, net	$ 502	$ 500

Other

Liabilities for loss contingencies arising from claims, assessments, litigation, fines, and penalties and other sources are recorded when it is probable that a liability has been incurred and the amount can be reasonably estimated. Legal costs incurred in connection with loss contingencies are expensed as incurred. The Company enters into contracts in the normal course of business with contract research organizations for preclinical studies and clinical trials and contract manufacturing organizations for the manufacture of clinical trial materials.

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Notes to Financial Statements

10. Net Loss and Unaudited Pro Forma Net Loss per Share Attributable to Common Stockholders

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

	Year Ended December 31,	
	2013	2014
Numerator:		
Net loss	$ (18,116)	$ (20,807)
Accretion and dividends on redeemable convertible preferred stock	(1,735)	(2,965)
Net loss attributable to common stockholders	$ (19,851)	$ (23,772)
Denominator:		
Weighted average common shares outstanding	1,230,241	1,673,919
Net loss per share attributable to common stockholders, basic and diluted	$ (16.14)	$ (14.20)

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

	December 31,	
	2013	2014
Redeemable convertible preferred stock as converted	8,260,906	19,746,614
Options to purchase common stock	618,923	954,567
Restricted stock subject to future vesting	691,117	1,121,979
Total	9,570,946	21,823,160

Unaudited Pro Forma Net Loss Per Share

The following table sets forth the computation of the Company s unaudited pro forma basic and diluted net loss per share attributable to common stockholders during the year ended December 31, 2014 (in thousands, except for share and per share amounts):

	Year Ended December 31, 2014 (Unaudited)
Net loss, basic and diluted	$ (20,807)
Shares used in computing net loss per share attributable to common stockholders, basic and diluted	1,673,919
Pro forma adjustment to reflect assumed conversion of redeemable convertible preferred stock	12,087,910
Shares used in computing pro forma net loss per share attributable to common stockholders, basic and diluted	13,761,829
Pro forma net loss per share attributable to common stockholders, basic and diluted	$ (1.51)

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GLOBAL BLOOD THERAPEUTICS, INC.

Notes to Financial Statements

11. Related Party Transactions

The majority investor in the Company is an investment fund controlled by Third Rock Ventures, LLC (TRV). As of December 31, 2013 and 2014, three and two members of the Company s Board of Directors were partners in TRV, respectively. For the years ended December 31, 2013 and 2014, the Company incurred $499,000 and $332,000 for management and advisory services provided by TRV to the Company of which $129,000 and $14,000 was payable as of December 31, 2013 and 2014. The Company is party to a Series A Preferred Stock Purchase Agreement with TRV which allowed for the future sale to TRV of Series A redeemable convertible preferred stock at stated terms (see Note 6). As of December 31, 2014, all closings of the Series A redeemable convertible preferred stock financing had been completed.

12. Subsequent Events

Reverse Stock Split

In July 2015, the Company s board of directors approved an amendment to the Company s amended and restated certificate of incorporation to effect a reverse split of the Company s issued and outstanding common stock at a 1-for-3.5 ratio, which was effected on July 30, 2015. The par value and authorized shares of common stock and convertible preferred stock were not adjusted as a result of the reverse split. All issued and outstanding common stock, options to purchase common stock and per share amounts contained in the financial statements have been retroactively adjusted to reflect the reverse stock split for all periods presented. The financial statements have also been retroactively adjusted to reflect a proportional adjustment to the conversion ratio for each series of preferred stock that will be effected in connection with the reverse stock split.

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GLOBAL BLOOD THERAPEUTICS, INC.

Condensed Balance Sheets

(In thousands, except share and per share amounts)

	December 31, 2014	March 31, 2015 (Unaudited)	Pro forma Stockholders Equity as of March 31, 2015 (Unaudited)
Assets			
Current assets:			
Cash and cash equivalents	$ 52,069	$ 45,800	
Prepaid expenses	1,135	757	
Other current assets	389	1,437	
Total current assets	53,593	47,994	
Property and equipment, net	2,023	2,343	
Restricted cash	140	140	
Total assets	$ 55,756	$ 50,477	
Liabilities, Redeemable Convertible Preferred Stock and Stockholders Equity (Deficit)			
Current liabilities:			
Accounts payable	$ 541	$ 1,616	
Payable due to related party	14	53	
Accrued expenses	948	1,937	
Accrued compensation	847	542	
Other current liabilities	187	212	
Total current liabilities	2,537	4,360	
Other liabilities	384	371	
Total liabilities	2,921	4,731	
Commitments and contingencies			
Redeemable convertible preferred stock, $0.001 par value: 69,363,168 shares authorized as of December 31, 2014 and March 31, 2015 (unaudited); 69,113,168 shares issued and outstanding as of December 31, 2014 and March 31, 2015 (unaudited); redemption value of $104,529 as of March 31, 2015 (unaudited)	102,161	103,396	$
Stockholders equity (deficit):			

Common stock, $0.001 par value, 94,000,000 shares authorized as of December 31, 2014 and March 31, 2015 (unaudited); 1,954,488 and 2,061,843 shares issued and outstanding as of December 31, 2014 and March 31, 2015 (unaudited), respectively; 150,000,000 shares authorized, 21,808,457 shares issued and outstanding, pro forma (unaudited)	2	2	22
Additional paid-in capital			103,376
Accumulated deficit	(49,328)	(57,652)	(57,652)
Total stockholders equity (deficit)	(49,326)	(57,650)	$ 45,746
Total liabilities, redeemable convertible preferred stock and stockholders equity (deficit)	$ 55,756	$ 50,477	

See accompanying notes to unaudited interim condensed financial statements.

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GLOBAL BLOOD THERAPEUTICS, INC.

Condensed Statements of Operations and Comprehensive Loss

(Unaudited)

(In thousands, except share and per share amounts)

	Three Months Ended March 31,	
	2014	**2015**
Operating expenses:		
Research and development	$ 3,877	$ 6,069
General and administrative	821	1,298
Related party expenses	171	53
Total operating expenses	4,869	7,420
Loss from operations	(4,869)	(7,420)
Change in fair value of Series A redeemable convertible preferred stock liability	(238)	
Interest income		3
Net loss and comprehensive loss	$ (5,107)	$ (7,417)
Net loss attributable to common stockholders	$ (5,695)	$ (8,657)
Net loss per share attributable to common stockholders, basic and diluted	$ (3.81)	$ (4.22)
Weighted-average number of shares used in computing net loss per share attributable to common stockholders, basic and diluted	1,496,607	2,052,874
Pro forma net loss per share, basic and diluted		$ (0.34)
Weighted-average number of shares used in computing pro forma net loss per share, basic and diluted		21,799,488

See accompanying notes to unaudited interim condensed financial statements.

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GLOBAL BLOOD THERAPEUTICS, INC.

Condensed Statements of Cash Flows

(Unaudited)

(In thousands)

	Three Months Ended March 31,	
	2014	**2015**
CASH FLOWS FROM OPERATING ACTIVITIES		
Net loss	$ (5,107)	$ (7,417)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	158	183
Loss on sale of fixed assets		18
Remeasurement of Series A redeemable convertible preferred stock liability	238	
Stock-based compensation	38	322
Changes in operating assets and liabilities:		
Prepaid expenses	73	378
Other current assets	66	(362)
Accounts payable	493	334
Payable due to related party	42	39
Accrued expenses	(82)	754
Accrued compensation	(204)	(305)
Other current liabilities	11	
Other noncurrent liabilities	(4)	(5)
Net cash used in operating activities	(4,278)	(6,061)
CASH FLOWS FROM INVESTING ACTIVITIES		
Purchase of property and equipment	(19)	(169)
Net cash used in investing activities	(19)	(169)
CASH FLOWS FROM FINANCING ACTIVITIES		
Proceeds from issuance of redeemable convertible preferred stock, net of issuance costs	4,991	(5)
Payments of deferred offering costs		(62)
Proceeds from issuance of restricted stock awards	36	45
Repurchase of unvested restricted stock awards	(5)	(17)
Proceeds from the exercise of common stock options	7	
Net cash provided by (used in) financing activities	5,029	(39)
Net increase (decrease) in cash and cash equivalents	732	(6,269)

Cash and cash equivalents at beginning of period	3,278	52,069
Cash and cash equivalents at end of period	$ 4,010	$ 45,800
SUPPLEMENTAL DISCLOSURES OF NON-CASH INVESTING AND FINANCING INFORMATION:		
Remeasurement and settlement of fair value of Series A redeemable convertible preferred stock liability	$ 409	$
Accretion of Series A and Series B redeemable convertible preferred stock	$ 588	$ 1,240
Accrued purchase of property and equipment	$ 21	$ 356
Accrued deferred offering costs	$	$ 620

See accompanying notes to unaudited interim condensed financial statements.

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GLOBAL BLOOD THERAPEUTICS, INC.

Notes to Unaudited Interim Condensed Financial Statements

1. Organization and Basis of Presentation

Global Blood Therapeutics Inc. (the Company) was incorporated in Delaware in February 2011 and commenced operations in May 2012. The Company is a biopharmaceutical company dedicated to discovering, developing and commercializing novel therapeutics to treat grievous blood-based disorders. The Company s primary activities have been establishing its facilities, recruiting personnel, conducting development of its product candidates, including clinical studies, and raising capital. The Company s principal operations are based in South San Francisco, California, and it operates in one segment.

Need for Additional Capital

In the course of its development activities, the Company has sustained operating losses and expects such losses to continue over the next several years. The Company s ultimate success depends on the outcome of its research and development activities. Since inception through March 31, 2015, the Company has incurred cumulative net losses of $57.7 million. Management expects to incur additional losses in the future to conduct product research and development and recognizes the need to raise additional capital to fully implement its business plan. The Company intends to raise such capital through the issuance of additional equity, and potentially through borrowings, and strategic alliances with partner companies. However, if such financing is not available at adequate levels, the Company will need to reevaluate its operating plans. Management believes that its existing cash and cash equivalents will be sufficient to fund the Company s cash requirements through at least December 31, 2015.

2. Summary of Significant Accounting Policies

Unaudited Interim Financial Statements

The interim condensed balance sheet as of March 31, 2015, and the statements of operations and comprehensive loss, and cash flows for the three months ended March 31, 2014 and 2015 are unaudited. The unaudited interim financial statements have been prepared on the same basis as the annual financial statements and reflect, in the opinion of management, all adjustments of a normal and recurring nature that are necessary for the fair presentation of the Company s financial position as of March 31, 2015 and its results of operations and cash flows for the three months ended March 31, 2014 and 2015. The financial data and the other financial information disclosed in these notes to the financial statements related to the three-month periods are also unaudited. The results of operations for the three months ended March 31, 2015 are not necessarily indicative of the results to be expected for the year ending December 31, 2015 or for any other future annual or interim period. The balance sheet as of December 31, 2014 included herein was derived from the audited financial statements as of that date. These financial statements should be read in conjunction with the Company s audited financial statements included elsewhere in this prospectus.

Unaudited Pro Forma Stockholders Equity

The pro forma stockholders equity as of March 31, 2015 presents the Company s stockholders equity as though all of the Company s outstanding redeemable convertible preferred stock had automatically converted into shares of common stock upon the completion of an initial public offering (IPO) of the Company s common stock. The shares of common stock issuable and the proceeds expected to be received in the initial public offering are excluded from such pro forma financial information.

Use of Estimates

The accompanying financial statements have been prepared in accordance with U.S. generally accepted accounting principles (GAAP). The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and

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Notes to Financial Statements

disclosure of contingent assets and liabilities as of the date of the financial statements and the reported amounts of expenses during the reporting period. On an ongoing basis, management evaluates its estimates, including those related to the valuation of derivatives, accruals for research and development activities, common stock, stock-based compensation; and income taxes. Management bases its estimates on historical experience and on various other market-specific and relevant assumptions that management believes to be reasonable under the circumstances. Actual results could differ from those estimates.

Cash and Cash Equivalents

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

Restricted Cash

Restricted cash consists of money market funds held by the Company s financial institution as collateral for the Company s letter of credit under its facility lease.

Deferred Offering Costs

Deferred offering costs, consisting of legal, accounting, printer and filing fees related to the IPO are capitalized. The deferred offering costs will be offset against proceeds from the IPO upon the effectiveness of the offering. In the event the offering is terminated, all capitalized deferred offering costs will be expensed. As of March 31, 2015, $682,000 of deferred offering costs were capitalized, which are included in other current assets in the accompanying condensed balance sheet. There were no such costs capitalized as of December 31, 2014.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development costs consist of expenses associated with clinical trials, outside research consultants, contract manufacturing expenses, salaries, employee benefits and allocated facility costs.

Preclinical study and clinical trial expenditures are a component of research and development expenses and are charged to operations as incurred. The expenses related to preclinical studies and clinical trials are based on estimates of the services received and efforts expended pursuant to contracts with research institutions and clinical research organizations that conduct and manage the studies on behalf of the Company. The financial terms of these agreements are subject to negotiation and vary from contract to contract and may result in uneven payment flows. Payments under the contracts depend on factors such as the achievement of certain events and the completion of portions of the study or similar conditions. Expenses related to preclinical studies and clinical trials are accrued based on the estimated level of activity incurred under each contract. Payments made to third parties under these arrangements in advance of the receipt of the related services are deferred as prepaid assets, depending on the terms of the agreement, until the services are rendered.

Net Loss per Share Attributable to Common Stockholders

Basic net loss per share attributable to common stockholders is calculated by dividing the net loss attributable to common stockholders by the weighted average number of shares of common stock outstanding during the period, without consideration for common stock equivalents. The net loss attributable to common stockholders is calculated by adjusting the net loss of the Company for the accretion on the redeemable

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Notes to Financial Statements

convertible preferred stock. Diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders, since the effects of potentially dilutive securities are antidilutive given the net loss of the Company.

Unaudited Pro Forma Net Loss per Share

Pro forma basic and diluted net loss per share has been computed to give effect to the conversion of the redeemable convertible preferred stock into common stock in connection with the Company s initial public offering. The unaudited pro forma net loss per share does not include the shares expected to be sold and related proceeds to be received from the initial public offering.

3. Fair Value Measurements

Fair value accounting is applied for all financial assets and liabilities that are recognized or disclosed at fair value in the financial statements on a recurring basis (at least annually). Financial instruments include cash and cash equivalents, restricted cash, accounts payable and accrued liabilities that approximate fair value due to their relatively short maturities.

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

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

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

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

The Company s financial instruments consist of Level 1 assets. Where quoted prices for identical assets are available in an active market, securities are classified as Level 1. Level 1 assets consist of highly liquid money market funds, which as of December 31, 2014 and March 31, 2015 includes $140,000 of funds that are collateral for the Company s facility lease that are included within restricted cash. There were no unrealized gains and losses in the Company s investments in these money market funds.

Financial assets subject to fair value measurements on a recurring basis and the level of inputs used in such measurements are as follows (in thousands):

	December 31, 2014			
	Total	**Level 1**	**Level 2**	**Level 3**
Financial Assets:				
Money market funds	$ 52,209	$ 52,209	$	$
Total financial assets	$ 52,209	$ 52,209	$	$

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Notes to Financial Statements

	March 31, 2015			
	Total	**Level 1**	**Level 2**	**Level 3**
Financial Assets:				
Money market funds	$ 45,940	$ 45,940	$	$
Total financial assets	$ 45,940	$ 45,940	$	$

4. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	December 31, 2014	**March 31, 2015**
Accrued clinical and manufacturing expenses	$ 749	$ 1,505
Accrued professional and consulting services	153	430
Other	46	2
Total accrued expenses	$ 948	$ 1,937

5. Redeemable Convertible Preferred Stock and Stockholders Deficit

Redeemable Convertible Preferred Stock

As of December 31, 2014 redeemable convertible preferred stock consisted of the following (in thousands, except share amounts):

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

As of March 31, 2015 redeemable convertible preferred stock consisted of the following (in thousands, except share amounts):

	Shares Authorized	Shares Issued and Outstanding	Net Carrying Value	Aggregate Liquidation Preference
Series A	50,163,168	49,913,168	$ 55,160	$ 56,142
Series B	19,200,000	19,200,000	48,236	48,387
Total redeemable convertible preferred stock	69,363,168	69,113,168	$ 103,396	$ 104,529

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GLOBAL BLOOD THERAPEUTICS, INC.

Notes to Financial Statements

Common Stock

As of March 31, 2015, the Company had reserved the following shares of common stock for issuance as follows:

Series A redeemable convertible preferred stock outstanding, as converted	14,260,904
Series B redeemable convertible preferred stock outstanding, as converted	5,485,710
Restricted shares subject to future vesting	985,338
Options issued and outstanding	1,190,051
Options available for future grants	445,620
Total	22,367,623

Restricted Stock

As of December 31, 2014 and March 31, 2015, 174,150 and 96,475 shares of common stock issued to founders remained subject to repurchase and $1,000 and less than $1,000, respectively, were recorded as liabilities pertaining to the restricted common stock.

As of December 31, 2014 and March 31, 2015, 947,829 and 888,863 shares of common stock issued to employees remained subject to repurchase and $435,000 and $453,000 respectively, were recorded as liabilities pertaining to the unvested restricted stock awards.

6. Stock Option and Grant Plan

As of March 31, 2015, there were 445,620 shares available for the Company to grant under the 2012 Plan.

The following summarizes option activity under the 2012 Plan:

	Number of Options	Weighted-Average Exercise Price	Weighted-Average remaining contractual term (years)	Aggregate Intrinsic Value (in thousands)
Balance, December 31, 2014	954,567	$ 0.38	9.0	
Options granted	239,019	$ 2.50		

Options exercised					
Options canceled	(3,535)	$ 0.32			
Balance Outstanding, March 31, 2015	1,190,051	$ 0.81	9.0	$	3,077
Exercisable, March 31, 2015	149,081	$ 0.33	8.3	$	457
Vested and expected to vest, March 31, 2015	1,175,899	$ 0.80	8.9	$	3,053

The aggregate intrinsic values of options outstanding, exercisable, vested and expected to vest were calculated as the difference between the exercise price of the options and the estimated fair value of the Company s common stock, as determined by the Board of Directors, as of March 31, 2015.

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GLOBAL BLOOD THERAPEUTICS, INC.

Notes to Financial Statements

During the three months ended March 31, 2014 and 2015, the estimated weighted-average grant-date fair value of the options vested was $0.25 and $0.34 per share, respectively, and the estimated weighted-average grant-date fair value of common stock underlying options granted was $0.26 and $1.68 per share, respectively.

Employee Stock Options Valuation

The fair value of employee and director stock option awards was estimated at the date of grant using a Black-Scholes option-pricing model with the following assumptions:

	Three Months Ended March 31,	
	2014	**2015**
Expected term (in years)	6.0-6.1	6.0-6.1
Volatility	87.8%-88.1%	75.9%-77.0%
Risk-free interest rate	1.9%-2.1%	1.5%-1.7%
Dividend yield		

Stock Options Granted to Non-employees

Stock-based compensation related to stock options granted to non-employees is recognized as the stock options are earned. The fair value of the stock options granted is calculated at each reporting date using the Black-Scholes option-pricing model with the following assumptions:

	Three Months Ended March 31,	
	2014	**2015**
Expected term (in years)	5.0-9.9	5.0-9.9
Volatility	77.6%-82.3%	77.6%-88.1%
Risk-free interest rate	1.5%-2.7%	0.9%-2.7%
Dividend yield		

During the three months ended March 31, 2014 the Company granted 11,428 stock options to non-employee consultants. The Company did not grant any stock options to non-employee consultants during the three months ended March 31, 2015. The Company recorded stock-based compensation expense related to these awards of $3,000 and $29,000 for the three months ended March 31, 2014 and 2015, respectively.

Restricted Stock Awards

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

A summary of the Company s non-vested restricted stock for the periods is as follows:

	Number of Shares
Balance, December 31, 2014	1,121,979
Granted	24,285
Vested	(107,355)
Repurchased by company	(53,571)
Balance, March 31, 2015	985,338

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RSAs granted during the three months ended March 31, 2015 vest over four years, subject to the continued service relationship with the Company. During the three months ended March 31, 2014 and 2015, the estimated weighted-average grant date fair value of restricted stock issued was $0.23 and $1.02 per share, respectively. During the three months ended March 31, 2014 and 2015, $29,000 and $266,000, respectively, of stock-based compensation expense was recognized related to these RSAs. The Company recognizes the expense using a straight-line basis over the requisite service period of the award. As of March 31, 2015, there was $287,000 of total unrecognized compensation cost related to unvested RSAs with service-based vesting conditions. These costs are expected to be recognized over a weighted average period of 2.6 years.

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

Stock-Based Compensation Expense

Total stock-based compensation recognized for both employees and non-employee was as follows (in thousands):

	Three Months Ended March 31,	
	2014	**2015**
Research and development	$ 30,000	$ 265,000
General and administrative	8,000	57,000
Total stock-based compensation expense	$ 38,000	$ 322,000

As of March 31, 2015 unrecognized stock-based compensation cost related to outstanding unvested stock options that are expected to vest was $1.1 million. This unrecognized stock-based compensation cost is expected to be recognized over a weighted average period of 3.9 years.

7. Net Loss per Share Attributable to Common Stockholders and Pro Forma Net Loss per Share

The following table sets forth the computation of the basic and diluted net loss per share attributable to common stockholders during the three months ended March 31, 2014 and 2015 (in thousands, except share and per share data):

	Three Months Ended March 31,	
	2014	**2015**

Numerator:		
Net loss	$ (5,107)	$ (7,417)
Accretion and dividends on redeemable convertible preferred stock	(588)	(1,240)
Net loss attributable to common stockholders	$ (5,695)	$ (8,657)
Denominator:		
Weighted average common shares outstanding	1,496,607	2,052,874
Net loss per share attributable to common stockholders, basic and diluted	$ (3.81)	$ (4.22)

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Notes to Financial Statements

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

	March 31,	
	2014	**2015**
Redeemable convertible preferred stock as converted	9,689,477	19,746,614
Options to purchase common stock	683,351	1,190,051
Restricted stock subject to future vesting	672,962	985,338
Total	11,045,790	21,922,003

Unaudited Pro Forma Net Loss Per Share

The following table sets forth the computation of the Company s unaudited pro forma basic and diluted net loss per share during the three months ended March 31, 2015 (in thousands, except for share and per share amounts):

	Three Months Ended March 31, 2015
Net loss, basic and diluted	$ (7,417)
Weighted average shares used in computing net loss per share, basic and diluted	2,052,874
Pro forma adjustment to reflect assumed conversion of redeemable convertible preferred stock	19,746,614
Weighted average shares used in computing pro forma net loss per share, basic and diluted	21,799,488
Pro forma net loss per share, basic and diluted	$ (0.34)

8. Related Party Transactions

The majority investor in the Company is an investment fund controlled by Third Rock Ventures, LLC (TRV). As of March 31, 2015, two members of the Company s Board of Directors were also partners in TRV. For the three months ended March 31, 2014 and 2015, the Company incurred $171,000 and $53,000, respectively, for management and

advisory services provided by TRV to the Company. As of December 31, 2014 and March 31, 2015, the Company had an outstanding payable to TRV of $14,000 and $53,000 respectively.

9. Subsequent Events

Stock Plan Activity

On April 9, 2015 the Company increased the number of shares available under the 2012 Stock Option and Grant Plan by 1,000,000 to a total of 3,785,713 shares. On that date the Company also issued 1,245,700 stock awards, including options to purchase 637,848 shares of common stock, at an exercise price of $3.40 per share and 607,853 shares of restricted common stock with a purchase price of $3.40 per share. 819,992 of the awards are subject to quarterly vesting on a ratable basis over four years and 425,709 of the awards vest upon the achievement of various scientific, clinical and business milestone objectives.

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In June 2015, the Company granted options to purchase 244,709 shares of common stock at an exercise price of $6.34 per share.

Reverse Stock Split

In July 2015, the Company s board of directors approved an amendment to the Company s amended and restated certificate of incorporation to effect a reverse split of the Company s issued and outstanding common stock at a 1-for-3.5 ratio, which was effected on July 30, 2015. The par value and authorized shares of common stock and convertible preferred stock were not adjusted as a result of the reverse split. All issued and outstanding common stock, options to purchase common stock and per share amounts contained in the financial statements have been retroactively adjusted to reflect the reverse stock split for all periods presented. The financial statements have also been retroactively adjusted to reflect a proportional adjustment to the conversion ratio for each series of preferred stock that will be effected in connection with the reverse stock split.

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6,000,000 Shares

Common Stock

Prospectus

Morgan Stanley **Goldman, Sachs & Co.**

Cowen and Company **Wedbush PacGrow**