

Global Blood Therapeutics, Inc.  
Form 10-Q  
August 07, 2017  
Table of Contents

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

**FORM 10-Q**

(Mark One)

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

**For the quarterly period ended June 30, 2017**

**OR**

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

**For the transition period from \_\_\_\_\_ to \_\_\_\_\_**

**Commission file number: 001-37539**

**Global Blood Therapeutics, Inc.**

**(Exact name of registrant as specified in its charter)**

**Delaware**  
**(State or other jurisdiction of**  
**incorporation or organization)**  
**400 East Jamie Court, Suite 101, South San Francisco**  
**South San Francisco, CA 94080**  
**(Address of principal executive offices)**  
**(650) 741-7700**  
**(Registrant's telephone number, including area code)**

**27-4825712**  
**(I.R.S. Employer**  
**Identification No.)**

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes No

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes No

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of large accelerated filer, accelerated filer, smaller reporting company, and emerging growth company in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer

Accelerated filer

Non-accelerated filer (Do not check if a smaller reporting company)

Smaller reporting company

Emerging growth company

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes No

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

As of July 31, 2017, there were 43,676,804 shares of the registrant's Common Stock, par value \$0.001 per share, outstanding.



Table of Contents

## TABLE OF CONTENTS

	<b>Page</b>
<u>PART I. FINANCIAL INFORMATION</u>	3
<u>Item 1. Financial Statements (Unaudited)</u>	3
<u>Condensed Consolidated Balance Sheets as of June 30, 2017 (Unaudited) and December 31, 2016</u>	3
<u>Condensed Consolidated Statements of Operations and Comprehensive Loss for the Three and Six</u>	
<u>Months Ended June 30, 2017 and 2016 (Unaudited)</u>	4
<u>Condensed Consolidated Statements of Cash Flows for the Six Months Ended June 30, 2017 and</u>	
<u>2016 (Unaudited)</u>	5
<u>Notes to Unaudited Interim Condensed Consolidated Financial Statements</u>	6
<u>Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations</u>	13
<u>Item 3. Quantitative and Qualitative Disclosures About Market Risk</u>	20
<u>Item 4. Controls and Procedures</u>	21
<u>PART II. OTHER INFORMATION</u>	21
<u>Item 1. Legal Proceedings</u>	21
<u>Item 1A. Risk Factors</u>	21
<u>Item 2. Unregistered Sales of Equity Securities and Use of Proceeds</u>	54
<u>Item 3. Defaults Upon Senior Securities</u>	54
<u>Item 4. Mine Safety Disclosures</u>	54
<u>Item 5. Other Information</u>	54
<u>Item 6. Exhibits</u>	54
<u>SIGNATURES</u>	55

**Table of Contents****PART I. FINANCIAL INFORMATION****Item 1. Financial Statements****GLOBAL BLOOD THERAPEUTICS, INC.****Condensed Consolidated Balance Sheets****(In thousands, except share and per share amounts)**

	<b>June 30, 2017</b>	<b>December 31, 2016</b>
	<b>(Unaudited)</b>	
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 93,741	\$ 92,072
Short-term marketable securities	136,075	55,202
Prepaid expenses and other current assets	5,036	2,495
Total current assets	234,852	149,769
Property and equipment, net	5,200	2,420
Long-term marketable securities	60,779	50,058
Restricted cash	1,046	140
Total assets	\$ 301,877	\$ 202,387
<b>Liabilities and Stockholders Equity</b>		
Current liabilities:		
Accounts payable	\$ 4,966	\$ 4,320
Accrued liabilities	6,586	5,319
Accrued compensation	4,492	4,967
Other liabilities, current	1,104	909
Total current liabilities	17,148	15,515
Other liabilities, noncurrent	3,019	563
Total liabilities	20,167	16,078
Commitments and contingencies (Note 8)		
Stockholders equity:		
Preferred stock, \$0.001 par value, 5,000,000 shares authorized as of June 30, 2017 and December 31, 2016		
Common stock, \$0.001 par value, 150,000,000 shares authorized as of June 30, 2017 (unaudited) and December 31, 2016, respectively; 43,115,738 and 36,638,156 shares issued and outstanding as of June 30, 2017 (unaudited) and December 31, 2016, respectively	43	37

Edgar Filing: Global Blood Therapeutics, Inc. - Form 10-Q

Additional paid-in capital	510,083	367,371
Accumulated other comprehensive loss	(268)	(166)
Accumulated deficit	(228,148)	(180,933)
Total stockholders' equity	281,710	186,309
Total liabilities and stockholders' equity	\$ 301,877	\$ 202,387

*See accompanying notes to unaudited interim condensed consolidated financial statements.*

Table of Contents**GLOBAL BLOOD THERAPEUTICS, INC.****Condensed Consolidated Statements of Operations and Comprehensive Loss****(Unaudited)****(In thousands, except share and per share amounts)**

	<b>Three Months Ended June 30,</b>		<b>Six Months Ended June 30,</b>	
	<b>2017</b>	<b>2016</b>	<b>2017</b>	<b>2016</b>
Operating expenses:				
Research and development	\$ 18,278	\$ 13,427	\$ 35,561	\$ 25,842
General and administrative	6,152	4,379	12,590	8,681
Total operating expenses	24,430	17,806	48,151	34,523
Loss from operations	(24,430)	(17,806)	(48,151)	(34,523)
Other income (expense):				
Interest income, net	689	131	1,130	248
Other expenses, net	(142)		(194)	
Total other income, net	547	131	936	248
Net loss	(23,883)	(17,675)	(47,215)	(34,275)
Other comprehensive loss:				
Net unrealized loss on marketable securities, net of tax	(89)		(102)	
Comprehensive loss	\$ (23,972)	\$ (17,675)	\$ (47,317)	\$ (34,275)
Basic and diluted net loss per common share	\$ (0.55)	\$ (0.58)	\$ (1.15)	\$ (1.15)
Weighted-average number of shares used in computing basic and diluted net loss per common share	43,063,996	30,381,948	41,112,266	29,911,678

*See accompanying notes to unaudited interim condensed consolidated financial statements.*

**Table of Contents****GLOBAL BLOOD THERAPEUTICS, INC.****Condensed Consolidated Statements of Cash Flows****(Unaudited)****(In thousands)**

	<b>Six Months Ended June 30,</b>	
	<b>2017</b>	<b>2016</b>
<b>CASH FLOWS FROM OPERATING ACTIVITIES:</b>		
Net loss	\$ (47,215)	\$ (34,275)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	608	520
Amortization of premium on marketable securities	380	
Stock-based compensation	5,234	2,732
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(2,550)	(427)
Accounts payable	623	1,189
Accrued liabilities	1,375	796
Accrued compensation	(475)	614
Other liabilities	(33)	(12)
Net cash used in operating activities	(42,053)	(28,863)
<b>CASH FLOWS FROM INVESTING ACTIVITIES:</b>		
Purchase of property and equipment	(575)	(955)
Purchase of marketable securities	(124,861)	
Maturities of marketable securities	32,785	
Increase in restricted cash	(906)	
Net cash used in investing activities	(93,557)	(955)
<b>CASH FLOWS FROM FINANCING ACTIVITIES:</b>		
Proceeds from issuance of common stock in public offering, net	135,625	112,728
Proceeds from issuance of common stock in settlement of employee stock purchase plan and exercise of stock options	1,654	498
Net cash provided by financing activities	137,279	113,226
Net increase in cash and cash equivalents	1,669	83,408
Cash and cash equivalents at beginning of period	92,072	148,502
Cash and cash equivalents at end of period	\$ 93,741	\$ 231,910



**SUPPLEMENTAL DISCLOSURES OF NON-CASH INVESTING AND FINANCING INFORMATION:**

Acquired property and equipment	\$	2,897	\$	
Accrued purchase of property and equipment	\$	30	\$	13
Accrued offering costs	\$		\$	449

*See accompanying notes to unaudited interim condensed consolidated financial statements.*

**Table of Contents**

**GLOBAL BLOOD THERAPEUTICS, INC.**

**Notes to Unaudited Interim Condensed Consolidated Financial Statements**

**1. Organization and Basis of Presentation**

Global Blood Therapeutics, Inc. (the Company, we, us, and our) was incorporated in Delaware in February 2011 and commenced operations in May 2012. We are a clinical-stage biopharmaceutical company dedicated to discovering, developing and commercializing novel therapeutics to treat grievous blood-based disorders with significant unmet needs. Our primary activities have been establishing our facilities, recruiting personnel, conducting development of our product candidates, including clinical trials, and raising capital. Our principal operations are based in South San Francisco, California, and we operate in one segment.

***Follow-on Offering***

In February 2017, we completed a follow-on offering and issued an aggregate of 5,867,347 shares of our common stock at a price of \$24.50 per share, including 765,306 shares of our common stock sold directly to the underwriters when they exercised their over-allotment option at the price of \$24.50 per share. We received total proceeds of \$135.6 million from the offering, net of underwriting discounts and commissions and offering expenses.

***Need for Additional Capital***

In the course of our development activities, we have sustained operating losses and we expect such losses to continue over the next several years. Our ultimate success depends on the outcome of our research and development activities. Since inception through June 30, 2017, we have incurred cumulative net losses of \$228.1 million. We expect to incur additional losses in the future to conduct product research and development and we recognize the need to raise additional capital to fully implement our business plan. We intend to raise such capital through the issuance of additional equity, and potentially through borrowings, and strategic alliances with partner companies. However, if such financing is not available at adequate levels, we will need to re-evaluate our operating plans. We believe that our existing cash and cash equivalents and marketable securities will be sufficient to fund our cash requirements for at least the next twelve months.

**2. Summary of Significant Accounting Policies**

***Basis of Preparation***

The accompanying unaudited interim condensed consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ( U.S. GAAP ) and applicable rules and regulations of the Securities and Exchange Commission ( SEC ) regarding interim financial reporting. As permitted under those rules, certain footnotes or other financial information that are normally required by U.S. GAAP have been condensed or omitted, and accordingly the balance sheet as of December 31, 2016 has been derived from audited consolidated financial statements at that date but does not include all of the information required by U.S. GAAP for complete financial statements. These unaudited interim condensed consolidated financial statements have been prepared on the same basis as our annual consolidated financial statements and, in the opinion of management, reflect all adjustments (consisting only of normal recurring adjustments) that are necessary for a fair presentation of our financial information. The results of operations for the three and six months ended June 30, 2017 are not necessarily indicative of the results to be expected for the year ending December 31, 2017 or for any other interim period or for any other future year.

The accompanying unaudited interim condensed consolidated financial statements and related financial information should be read in conjunction with the audited financial statements and the related notes thereto for the year ended December 31, 2016 included in our Annual Report on Form 10-K, filed with the SEC on March 13, 2017.

***Reclassification***

Certain prior year amounts in the condensed consolidated statements of operations and comprehensive loss have been reclassified to conform to the current year's presentation. This reclassification did not have an impact on our results of operations or financial condition as of June 30, 2016.

***Use of Estimates***

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

## **Table of Contents**

### ***Principles of Consolidation***

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

### ***Significant Accounting Policies***

Except as noted below, there have been no material revisions in our significant accounting policies described in Note 2 to the consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2016.

### ***Stock-based Compensation***

We measure and recognize stock-based compensation expense, including employee and non-employee equity awards, based on fair value at the grant date. We use the Black-Scholes option-pricing model to calculate fair value. Stock-based compensation expense recognized in the condensed consolidated statements of operations is based on stock awards ultimately vested, taking into consideration actual forfeitures. For options granted to non-employees, we revalue the unearned portion of the stock-based compensation and the resulting change in fair value is recognized in the condensed consolidated statements of operations over the period the related services are rendered.

### ***Recent Accounting Pronouncements***

In May 2017, the FASB issued ASU No. 2017-09, *Compensation – Stock Compensation (Topic 718)*, which is intended to clarify and reduce the diversity in practice and cost and complexity when applying the guidance in Topic 718, Compensation – Stock Compensation, to a change to the terms or conditions of a share-based payment award. The new standard is effective for annual periods, and interim periods within those annual periods, beginning after December 15, 2017. Early adoption is permitted. We believe that the adoption of this new standard will have no impact on our financial position or result of operations and have not elected to early adopt the amendment.

### ***Accounting Pronouncements Adopted***

In March 2016, the FASB issued ASU No. 2016-09, *Improvements to Employee Share-Based Payment Accounting* (ASU 2016-09), which is intended to simplify several aspects of the accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities, and classification on the statement of cash flows. ASU 2016-09 is effective for annual periods beginning after December 15, 2016, and interim periods within those annual periods. We adopted ASU 2016-09 in the first quarter of 2017.

The impact of adopting ASU 2016-09 resulted in the following:

Classification of excess income tax benefits from stock-based compensation arrangement as a discrete item within income tax expense, rather than recognizing such excess income tax benefits in additional paid-in capital. The adoption of this guidance resulted in an increase of approximately \$1.1 million of net operating losses, which has an impact of \$0.4 million on our deferred tax assets before our full valuation allowance established against the related deferred tax assets.

Recognition of forfeitures as they occur. The cumulative effect adjustment as a result of the adoption of ASU 2016-09 on a modified retrospective basis was insignificant.

A change in classification of cash flows resulting from excess tax benefits and cash paid by us when directly withholding shares for tax-withholding purposes on a retrospective basis. The adoption of these provisions did not result in changes in our condensed consolidated statements of cash flow.

There were no other material impacts to our condensed consolidated financial statements as a result of adopting this updated standard.

### **3. Fair Value Measurements**

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

**Table of Contents**

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

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

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

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

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

	<b>June 30, 2017</b>			
	<b>Total</b>	<b>Level 1</b>	<b>Level 2</b>	<b>Level 3</b>
<b>Financial Assets:</b>				
Money market funds	\$ 88,659	\$ 88,659	\$	\$
Corporate debt securities	60,631		60,631	
U.S. government agency securities	76,287		76,287	
Certificates of deposits	14,919		14,919	
U.S. government securities	50,015		50,015	
<b>Total financial assets</b>	<b>\$ 290,511</b>	<b>\$ 88,659</b>	<b>\$ 201,852</b>	<b>\$</b>

	<b>December 31, 2016</b>			
	<b>Total</b>	<b>Level 1</b>	<b>Level 2</b>	<b>Level 3</b>
<b>Financial Assets:</b>				
Money market funds	\$ 72,597	\$ 72,597	\$	\$
Corporate debt securities	48,531		48,531	
U.S. government agency securities	39,712		39,712	
Certificates of deposits	19,117		19,117	
U.S. government securities	7,999		7,999	
<b>Total financial assets</b>	<b>\$ 187,956</b>	<b>\$ 72,597</b>	<b>\$ 115,359</b>	<b>\$</b>

We estimate the fair values of our investments in corporate debt securities, government and government related securities and certificates of deposits by taking into consideration valuations obtained from third-party pricing services. The fair value of our marketable securities classified within Level 2 is based upon observable inputs that may

include benchmark yields, reported trades, broker/dealer quotes, issuer spreads, two-sided markets, benchmark securities, bids, offers and reference data including market research publications. At June 30, 2017 and December 31, 2016, the weighted average remaining contractual maturities of our Level 2 investments was less than one year and all of these investments are rated A-1/P-1/F1 or A/A2, or higher by Moody's, S&P and Fitch. There were no transfers between Level 1 and Level 2 during the periods presented.

**Table of Contents****4. Available-for-Sale Securities**

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

	June 30, 2017				December 31, 2016			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Estimated Fair Value	Amortized Cost	Unrealized Gains	Unrealized Losses	Estimated Fair Value
<b>Financial Assets:</b>								
Money market funds	\$ 88,659	\$	\$	\$ 88,659	\$ 72,597	\$	\$	\$ 72,597
Corporate debt securities	60,730		(99)	60,631	48,594	2	(65)	48,531
U.S. government agency securities	76,402	2	(117)	76,287	39,763	1	(52)	39,712
Certificates of deposits	14,942	2	(25)	14,919	19,169		(52)	19,117
U.S. government securities	50,046		(31)	50,015	7,999			7,999
<b>Total</b>	<b>\$ 290,779</b>	<b>\$ 4</b>	<b>\$ (272)</b>	<b>\$ 290,511</b>	<b>\$ 188,122</b>	<b>\$ 3</b>	<b>\$ (169)</b>	<b>\$ 187,956</b>

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

	June 30, 2017	December 31, 2016
Cash and cash equivalents	\$ 93,657	\$ 82,696
Short-term marketable securities	136,075	55,202
Long-term marketable securities	60,779	50,058
<b>Total</b>	<b>\$ 290,511</b>	<b>\$ 187,956</b>

Gross unrealized gains or losses were not significant at either June 30, 2017 or December 31, 2016. We do not intend to sell the investments that are in an unrealized loss position, and it is unlikely that we will be required to sell the investments before recovery of their amortized cost basis, which may be maturity. We have determined that the gross unrealized losses on our marketable securities were temporary in nature during the periods presented. All marketable securities with unrealized losses have been in a loss position for less than twelve months and the loss is not material as of June 30, 2017 and December 31, 2016.

**5. Balance Sheet Components*****Property and Equipment***

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



Edgar Filing: Global Blood Therapeutics, Inc. - Form 10-Q

	<b>June 30, 2017</b>	<b>December 31, 2016</b>
Laboratory equipment	\$ 4,202	\$ 3,895
Computer equipment	995	972
Leasehold improvements	685	678
Construction-in-progress	3,188	137
<b>Total property and equipment</b>	<b>9,070</b>	<b>5,682</b>
Less: accumulated depreciation and amortization	(3,870)	(3,262)
<b>Property and equipment, net</b>	<b>\$ 5,200</b>	<b>\$ 2,420</b>

**Table of Contents*****Accrued liabilities***

Accrued liabilities consist of the following (in thousands):

	<b>June 30, 2017</b>	<b>December 31, 2016</b>
Accrued clinical and manufacturing expenses	\$ 5,856	\$ 4,759
Accrued professional and consulting services	520	507
Other	210	53
<b>Total accrued liabilities</b>	<b>\$ 6,586</b>	<b>\$ 5,319</b>

***Other liabilities, current and noncurrent***

Other liabilities consist of the following (in thousands):

	<b>June 30, 2017</b>	<b>December 31, 2016</b>
Restricted shares subject to repurchase, current	\$ 841	\$ 846
Deferred rent, current	263	61
Other taxes payable		2
<b>Total other liabilities, current</b>	<b>\$ 1,104</b>	<b>\$ 909</b>
Restricted shares subject to repurchase, noncurrent	\$ 326	\$ 534
Deferred rent, noncurrent	2,693	29
<b>Total other liabilities, noncurrent</b>	<b>\$ 3,019</b>	<b>\$ 563</b>

**6. Stock Based Compensation**

In January 2017, we adopted the 2017 Inducement Equity Plan (the 2017 Inducement Plan). Under the 2017 Inducement Plan, 300,000 shares of our common stock were initially reserved for the issuance of non-qualified stock options and other equity-based awards to induce highly-qualified prospective officers and employees who are not currently employed by us or our subsidiaries to become employed with our company. The number of shares initially reserved for grant is subject to adjustment for reorganization, recapitalization, stock dividend, stock split, or similar changes in our capital stock. As of June 30, 2017, there were no stock awards granted under the 2017 Plan.

We have two additional stock-based compensation plans the 2015 Stock Option and Incentive Plan (the 2015 Plan) and the 2012 Stock Option and Grant Plan (the 2012 Plan). As of June 30, 2017, there were 1,766,036 shares reserved for the future issuance of equity awards under the 2015 Plan. Upon adoption of the 2015 Plan in July 2015, no new awards or grants are permitted under the 2012 Plan. See Note 7 to the Consolidated Financial Statements included in our Annual Report on Form 10-K for the year ended December 31, 2016 for additional information related to these stock-based compensation plans.

**Stock Options**

The following summarizes option activity under the 2012 Plan and 2015 Plan:

		<b>Number of Options</b>	<b>Weighted-Average Exercise Price</b>
Outstanding	December 31, 2016	2,769,702	\$ 11.99
Options granted		803,615	22.94
Options exercised		(415,665)	2.71
Options canceled		(79,273)	20.45
Outstanding	June 30, 2017	3,078,379	\$ 15.89

**Table of Contents**

The fair values of stock options granted to employees were calculated using the following assumptions:

	Three Months Ended		Six Months Ended	
	June 30,		June 30,	
	2017	2016	2017	2016
Expected term (in years)	5.3-6.1	5.3-6.1	5.3-6.1	5.3-6.1
Volatility	70.9%-75.6%	80.5%-82.3%	70.9%-75.6%	79.4%-82.3%
Risk-free interest rate	1.8%-2.3%	1.1%-1.5%	1.8%-2.3%	1.1%-1.9%
Dividend yield				

**Restricted Stock Units**

In January 2017, the Compensation Committee of our Board of Directors approved the commencement of granting restricted stock units ( RSUs ) to our employees. RSUs are share awards that entitle the holder to receive freely tradable shares of our common stock upon the completion of a specific period of continued service. RSUs are generally subject to forfeiture if employment terminates prior to the release of vesting restrictions. RSUs granted are valued at the market price of our common stock on the date of grant. We recognize noncash compensation expense for the fair value of RSUs on a straight-line basis over the requisite service period of these awards.

The following summarizes RSU activity under the 2015 Plan and related information (in thousands, except share, per share amounts and vesting period):

	Number of RSUs	Weighted-Average Grant Date Fair Value	Weighted-Average Remaining Vesting Period (years)	Aggregate Intrinsic Value
Non-vested units December 31, 2016		\$		
RSUs granted	404,485	22.44		
RSUs vested				
RSUs forfeited	(1,710)	29.75		
Non-vested units June 30, 2017	402,775	\$ 22.40	1.90	\$ 11,016

**Stock-Based Compensation Expense**

Total stock-based compensation recognized by function was as follows (in thousands):

	Three Months Ended		Six Months Ended	
	June 30,		June 30,	
	2017	2016	2017	2016
Research and development	\$ 1,440	\$ 602	\$ 2,513	\$ 1,147
General and administrative	1,220	863	2,721	1,585

Total stock-based compensation expense	\$ 2,660	\$ 1,465	\$ 5,234	\$ 2,732
----------------------------------------	----------	----------	----------	----------

## 7. Net Loss per Share

Basic net loss per share is computed by dividing net loss by the weighted-average number of common shares outstanding for the period. Since we were in a loss position for all periods presented, diluted net loss per share is the same as basic net loss per share for all periods as the inclusion of all potential common shares outstanding would have been anti-dilutive.

**Table of Contents**

The following securities were not included in the diluted net loss per share calculations because their effect was anti-dilutive:

	Three Months Ended		Six Months Ended	
	June 30,		June 30,	
	2017	2016	2017	2016
Options to purchase common stock	3,078,379	2,662,841	3,078,379	2,662,841
Restricted stock subject to future vesting	515,469	881,617	515,469	881,617
Restricted stock units	402,775		402,775	
Employee stock purchase plan	21,020	44,890	21,020	44,890
<b>Total</b>	<b>4,017,643</b>	<b>3,589,348</b>	<b>4,017,643</b>	<b>3,589,348</b>

**8. Commitments and Contingencies****Facilities**

In March 2017, we entered into a noncancelable operating lease (the Lease) for approximately 67,185 square feet of space in South San Francisco, California (the New Facility). The date on which we will become responsible for paying rent under the Lease (the Rent Commencement Date) will be the earlier of December 15, 2017 or the date the New Facility is ready for occupancy. The Lease expires 10 years after the Rent Commencement Date. The Lease grants us an option to extend the Lease for an additional 10-year period. Future minimum rental payments under the Lease during the 10-year term are \$45.8 million in the aggregate. The Lease further provides that we are obligated to pay to the landlord certain costs, including taxes and operating expenses. As of June 30, 2017, the Lease term has not commenced as we did not have the right to use or control physical access to the New Facility. We have capitalized \$2.9 million of costs in construction-in-progress within property and equipment, net for construction of leasehold improvement at the New Facility as of June 30, 2017 acquired with the tenant inducement provided under the Lease.

We provided a standby letter of credit of \$0.9 million as security for our obligations under the Lease which was issued in March 2017. This standby letter of credit is classified as restricted cash.

We currently lease approximately 36,740 square feet of office and lab space located in South San Francisco, California (the Existing Facility). All of our lease agreements associated with the Existing Facility expire on or before April 2018. We do not plan to cancel the existing lease agreements for our Existing Facility prior to their respective expiration dates.

Future annual minimum lease payments due under the new and existing operating leases at December 31 of each year are as follows (in thousands):

Year ending December 31,	Amount <sup>1</sup>
2017 (six months)	\$ 860
2018	3,462
2019	4,134
2020	4,279

Edgar Filing: Global Blood Therapeutics, Inc. - Form 10-Q

2021	4,428
Thereafter	29,787
Total	\$ 46,950

*(1) The table above is prepared under the assumption that the Rent Commencement Date at the New Facility starts on December 15, 2017.*

Rent expense for the three months ended June 30, 2017 and 2016 was \$0.4 million and \$0.3 million, respectively, and for the six months ended June 30, 2017 and 2016 was \$0.8 million and \$0.6 million, respectively. The operating leases require us to share in prorated operating expenses and property taxes based upon actual amounts incurred; those amounts are not fixed for future periods and, therefore, are not included in the future commitments listed above.

---

**Table of Contents**

**Item 2. 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 in conjunction with our unaudited condensed consolidated financial statements and related notes included in Part I, Item 1 of this Quarterly Report on Form 10-Q and with our audited consolidated financial statements and related notes thereto for the year ended December 31, 2016, included in our Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 13, 2017, or our Annual Report.*

*This discussion and other parts of this Quarterly Report on Form 10-Q contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended and Section 21E of the Securities Exchange Act of 1934, as amended, that involve risks and uncertainties, such as statements of our plans, objectives, expectations and intentions. In some cases you can identify forward-looking statements by terms such as may, will, expect, anticipate, estimate, intend, plan, predict, potential, believe, should and similar expressions. 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 discussed in the section of this Quarterly Report on Form 10-Q titled Risk Factors. We caution readers not to place undue reliance on any forward-looking statements made by us, which speak only as of the date they are made. Except as may be required by law, we assume no obligation to update these forward-looking statements or the reasons that results could differ from these forward-looking statements.*

**Overview**

We are a clinical-stage biopharmaceutical company dedicated to discovering, developing and commercializing novel therapeutics to treat grievous blood-based disorders with significant unmet need. Our lead product candidate is GBT440, an oral, once-daily therapy that modulates hemoglobin's affinity for oxygen, which we believe inhibits hemoglobin polymerization in sickle cell disease, or SCD, and improves hypoxemia in idiopathic pulmonary fibrosis, or IPF. We are developing GBT440 for SCD and IPF.

We are currently evaluating GBT440 in SCD in a Phase 3 clinical trial of GBT440 in adult and adolescent patients with SCD. In addition, we are evaluating the safety and pharmacokinetics of single and multiple doses of GBT440 in a Phase 2a clinical trial of adolescent and pediatric patients with SCD, and in July 2017 we announced that we have expanded this open-label trial to include a new single-dose cohort in children aged 6-11. In December 2015, the Food and Drug Administration, or FDA, granted Fast Track Designation and Orphan Drug Designation for GBT440 for the treatment of SCD and in November 2016 GBT440 was granted Orphan Drug Designation in Europe for the treatment of SCD. In June 2017, the European Medicines Agency, or EMA, granted PRIME designation for GBT440 for the treatment of SCD. The PRIME program is a new regulatory mechanism that provides for early and proactive EMA support to medicine developers to help patients benefit as early as possible from innovative new products that have demonstrated the potential to significantly address an unmet medical need.

In addition, we are conducting two Phase 2a clinical trials of GBT440 for the potential treatment of IPF, which is a hypoxemic pulmonary disorder. We are also conducting a Phase 1 study called Basecamp in healthy volunteers, which is intended to support our understanding of GBT440's effects on hypoxemia and complement our ongoing Phase 2a program in IPF. We are also engaged in other pre-clinical research and development activities.

SCD is marked by red blood cell, or RBC, destruction and occluded blood flow and hypoxia, leading to anemia, stroke, multi-organ failure, severe pain crises, and shortened patient life span. GBT440 inhibits abnormal hemoglobin polymerization, the underlying mechanism that causes sickling of RBCs. In our clinical trials to date of GBT440 in SCD patients, we observed reduced markers of red blood cell destruction, improvements in anemia, improvements in



markers of tissue oxygenation, and reduced numbers of sickled RBCs.

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

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

## **Table of Contents**

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

Prior to our initial public offering, or IPO, we had funded our operations primarily from the issuance and sale of redeemable convertible preferred stock. In August 2015, we completed our IPO pursuant to which we issued 6,900,000 shares of our common stock at a price of \$20.00 per share. We received \$126.2 million from the IPO, net of underwriting discounts and commissions and offering expenses. In July 2016, we completed a follow-on offering pursuant to which we issued an aggregate of 6,667,228 shares of our common stock at a price of \$18.75 per share, including 6,400,000 shares sold at the initial closing in June 2016 and 267,228 shares sold pursuant to the exercise of the underwriters' over-allotment option to purchase additional shares in July 2016. We received aggregate proceeds of \$117.0 million from the offering, net of underwriting discounts and commissions and offering expenses. In October 2016, we filed our shelf registration statement on Form S-3 for the potential offering, issuance and sale by us of up to a maximum aggregate offering price of \$250 million of our common stock, preferred stock, debt securities, warrants, and/or units. In February 2017, we completed a follow-on offering under the shelf registration pursuant to which we issued an aggregate of 5,867,347 shares of our common stock at a price of \$24.50 per share. We received aggregate proceeds of \$135.6 million from the offering, net of underwriting discounts and commissions and offering expenses. After the completion of this follow-on offering in February 2017, up to a maximum aggregate offering price of \$106.2 million of our common stock, preferred stock, debt securities, warrants and/or units remain available for issuance pursuant to our shelf registration statement on Form S-3.

We have never been profitable and have incurred net losses in each year since inception. Our net losses were \$47.2 million and \$34.3 million for the six months ended June 30, 2017 and 2016, respectively. As of June 30, 2017, we had an accumulated deficit of \$228.1 million. To date, we have not generated any revenue. We do not expect to receive any revenue from any product candidates that we develop until we obtain regulatory approval and commercialize our products or enter into collaborative agreements with third parties. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations. As of June 30, 2017, we had \$93.7 million in cash and cash equivalents and \$196.9 million in marketable securities.

## **Critical Accounting Policies 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.

Other than the below, there have been no material changes to our critical accounting policies from those described in Management's Discussion and Analysis of Financial Condition and Results of Operations included in our Annual Report.

## ***Stock-Based Compensation***

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

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

**Table of Contents**

Stock-based compensation expense was calculated based on awards at the time of grant, and is reduced for actual forfeitures at the time that the forfeitures occur.

The estimated fair value of stock options, RSPs and RSUs is expensed on a straight-line basis over the service period of the grant and the estimated fair value of performance-contingent options and RSPs is expensed using an accelerated method over the term of the award once we determine that it is probable that those performance milestones will be achieved. Compensation expense for RSPs that contain performance conditions is based on the grant date fair value of the award. Compensation expense is recorded over the requisite service period based on management's best estimate as to whether it is probable that the shares awarded are expected to vest. We assess the probability of the performance indicators being met on a continuous basis.

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

**Results of Operations****Comparison of the Three Months Ended June 30, 2017 and 2016**

	<b>Three Months Ended</b>		<b>\$ Change</b>	<b>% Change</b>
	<b>2017</b>	<b>2016</b>		
	<b>June 30,</b>			
	<b>(in thousands, except percentages)</b>			
Operating expenses:				
Research and development	\$ 18,278	\$ 13,427	\$ 4,851	36%
General and administrative	6,152	4,379	1,773	40%
Total operating expenses	24,430	17,806	6,624	37%
Loss from operations	(24,430)	(17,806)	(6,624)	37%
Interest income, net	689	131	558	426%
Other expenses, net	(142)		(142)	*
Net loss	\$ (23,883)	\$ (17,675)	\$ (6,208)	35%

\* *Change is not meaningful*  
*Research and development*

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

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

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

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

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

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

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

The largest component of our total operating expenses is our investment in research and development activities, including the clinical development of 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.

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.

**Table of Contents**

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

	<b>Three Months Ended June 30,</b>			
	<b>2017</b>	<b>2016</b>	<b>\$ Change</b>	<b>% Change</b>
<b>Costs incurred by development program:</b>				
GBT440 for the treatment of SCD	\$ 12,823	\$ 7,534	\$ 5,289	70%
GBT440 for the treatment of hypoxemic pulmonary disorders	2,197	1,507	690	46%
Other preclinical programs	3,258	4,386	(1,128)	(26)%
<b>Total research and development expenses</b>	<b>\$ 18,278</b>	<b>\$ 13,427</b>	<b>\$ 4,851</b>	<b>36%</b>

Research and development expenses increased by \$4.9 million or 36%, to \$18.3 million for the three months ended June 30, 2017 from \$13.4 million for the three months ended June 30, 2016. The increase was primarily due to increased internal and external expenses related to our SCD program for GBT440 of \$5.3 million as we advanced this program, including expansion of our Phase 2a clinical trial of adolescent and pediatric patients in the quarter ended June 30, 2016 and incurred costs related to our Phase 3 study in 2017. In addition, there was \$0.7 million in increased internal and external costs associated with conducting our two Phase 2a clinical trials of GBT440 in IPF and our Phase 1 study in healthy volunteers that we refer to as our Basecamp study initiated in 2017. These increases were partially offset by a \$1.1 million decrease in expenses related to preclinical efforts for our other research-stage programs, which is primarily due to our former hereditary angioedema program that was discontinued in September 2016.

*General and administrative*

General and administrative expenses increased by \$1.8 million or 40%, to \$6.2 million for the three months ended June 30, 2017 from \$4.4 million for the three months ended June 30, 2016. The increase was primarily due to an increase of \$1.1 million in salaries and benefits, including \$0.4 million of related stock-based compensation expense, as a result of our hiring additional personnel and an increase of \$0.8 million in other general and administrative expenses, such as professional and consulting services, due to the growth of our operations.

*Comparison of the Six Months Ended June 30, 2017 and 2016*

	<b>Six Months Ended</b>			
	<b>June 30,</b>			
	<b>2017</b>	<b>2016</b>	<b>\$ Change</b>	<b>% Change</b>
	<b>(in thousands, except percentages)</b>			
<b>Operating expenses:</b>				
Research and development	\$ 35,561	\$ 25,842	\$ 9,719	38%
General and administrative	12,590	8,681	3,909	45%
<b>Total operating expenses</b>	<b>48,151</b>	<b>34,523</b>	<b>13,628</b>	<b>39%</b>
<b>Loss from operations</b>	<b>(48,151)</b>	<b>(34,523)</b>	<b>(13,628)</b>	<b>39%</b>

Edgar Filing: Global Blood Therapeutics, Inc. - Form 10-Q

Interest income, net	1,130	248	882	356%
Other expenses, net	(194)		(194)	*
Net loss	\$ (47,215)	\$ (34,275)	\$ (12,940)	38%

\* *Change is not meaningful*

**Table of Contents***Research and development*

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

	<b>Six Months Ended June 30,</b>			
	<b>2017</b>	<b>2016</b>	<b>\$ Change</b>	<b>% Change</b>
<b>Costs incurred by development program:</b>				
GBT440 for the treatment of SCD	\$ 24,604	\$ 14,702	\$ 9,902	67%
GBT440 for the treatment of hypoxemic pulmonary disorders	4,859	2,371	2,488	105%
Other preclinical programs	6,098	8,769	(2,671)	(30)%
<b>Total research and development expenses</b>	<b>\$ 35,561</b>	<b>\$ 25,842</b>	<b>\$ 9,719</b>	<b>38%</b>

Research and development expenses increased by \$9.7 million or 38%, to \$35.6 million for the six months ended June 30, 2017 from \$25.8 million for the six months ended June 30, 2016. The increase was primarily due to increased internal and external expenses related to our SCD program for GBT440 of \$9.9 million as we advanced this program, including expansion of our Phase 2a clinical trial of adolescent and pediatric patients in the quarter ended June 30, 2016 and incurred costs related to our Phase 3 study in 2017. In addition, there was \$2.5 million in increased internal and external costs associated with conducting our two Phase 2a clinical trials of GBT440 in IPF as well as initiation of our Phase 1 study in healthy volunteers that we refer to as our Basecamp study in 2017. These increases were partially offset by a \$2.7 million decrease in expenses related to preclinical efforts for our other research-stage programs, which is primarily due to our former hereditary angioedema program that was discontinued in September 2016.

*General and administrative*

General and administrative expenses increased by \$3.9 million or 45%, to \$12.6 million for the six months ended June 30, 2017 from \$8.7 million for the six months ended June 30, 2016. The increase was primarily due to an increase of \$2.9 million in salaries and benefits, including \$1.1 million of related stock-based compensation expense, as a result of our hiring additional personnel and an increase of \$1.2 million in other general and administrative expenses, such as professional and consulting services, due to the growth of our operations.

**Liquidity, Capital Resources and Plan of Operations**

We are not profitable and have incurred losses and negative cash flows from operations each year since our inception. Prior to our IPO, our operations were financed primarily by net proceeds from the sale and issuance of convertible preferred stock. In August 2015, we completed our IPO pursuant to which we issued 6,900,000 shares of our common stock at a price to the public of \$20.00 per share and received proceeds of \$126.2 million, net of underwriting discounts and commissions and offering expenses. In July 2016, we completed a follow-on offering pursuant to which we issued an aggregate of 6,667,228 shares of our common stock at a price of \$18.75 per share, including 6,400,000 shares sold at the initial closing in June 2016 and 267,228 shares sold pursuant to the exercise of the underwriters over-allotment option to purchase additional shares in July 2016. We received aggregate proceeds of \$117.0 million from the offering, net of underwriting discounts and commissions and offering expenses. In October 2016, we filed our shelf registration statement on Form S-3 for the potential offering, issuance and sale by us of up to a maximum aggregate offering price of \$250 million of our common stock, preferred stock, debt securities, warrants, and/or units. In February 2017, we completed a follow-on offering under the shelf registration pursuant to which we issued an



aggregate of 5,867,347 shares of our common stock at a price of \$24.50 per share. We received aggregate proceeds of \$135.6 million from the offering, net of underwriting discounts and commissions and offering expenses. After the completion of this follow-on offering in February 2017, up to a maximum aggregate offering price of \$106.2 million of our common stock, preferred stock, debt securities, warrants and/or units remain available under our shelf registration statement on Form S-3. As of June 30, 2017, we had \$93.7 million in cash and cash equivalents and \$196.9 million in marketable securities.

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

**Table of Contents**

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

the time and cost necessary to complete our Phase 3 HOPE study of GBT440 for the potential treatment of SCD, as well as to complete our ongoing Phase 2a clinical trial in adolescent and pediatric patients in this development program;

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

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

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

the progress, timing, scope and costs of our nonclinical studies, our clinical trials and other related activities, including our ability to enroll subjects in a timely manner for our Phase 3 HOPE study as well as our other multiple Phase 1 and 2a clinical trials of GBT440 for SCD or hypoxemia in IPF patients, and our potential future clinical trials;

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

our ability to advance our development programs, including our program for the clinical investigation of GBT440 in SCD patients and in hypoxemia in IPF patients through nonclinical and clinical development, as well as any other potential product candidate programs we may identify and pursue, and the timing and scope of these development activities;

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

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

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

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

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

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

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

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

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

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

**Table of Contents**

The following table summarizes our cash flows for the periods indicated (in thousands):

	<b>Six Months Ended</b>	
	<b>June 30,</b>	
	<b>2017</b>	<b>2016</b>
Cash used in operating activities	\$ (42,053)	\$ (28,863)
Cash used in investing activities	(93,557)	(955)
Cash provided by financing activities	137,279	113,226
Net increase in cash and cash equivalents	\$ 1,669	\$ 83,408

***Cash flows from operating activities***

Cash used in operating activities for the six months ended June 30, 2017 was \$42.1 million, consisting of a net loss of \$47.2 million, which was partially offset by non-cash charges of \$5.2 million for stock-based compensation and \$1.0 million for depreciation and amortization expense. The change in our net operating assets and liabilities was due primarily to an increase of \$2.6 million of prepaid expenses and other current assets due to advance payments made in connection with our Phase 3 HOPE study and an increase of \$1.4 million in our accrued liabilities related to an increase in our research and development activities and an increase in professional and consulting services due to the growth of our operations.

Cash used in operating activities for the six months ended June 30, 2016 was \$28.9 million, consisting of a net loss of \$34.3 million, which was partially offset by non-cash charges of \$2.7 million for stock-based compensation and \$0.5 million for depreciation and amortization expense. The change in our net operating assets and liabilities was due primarily to an increase of \$1.2 million in accounts payable due to timing of payments, an increase of \$0.8 million in our accrued liabilities related to increased clinical and development activities and expenses for our follow-on offering in June 2016, an increase of \$0.6 million in accrued compensation for estimated annual incentive payments and a decrease of \$0.4 million in our prepaid expenses related to a decrease in advance payments made in connection with our Phase 1/2 clinical trial of GBT440 for SCD and deposits for the manufacturing of clinical trial materials.

***Cash flows from investing activities***

Cash used in investing activities for the six months ended June 30, 2017 was \$93.6 million, consisting of the purchase of marketable securities of \$124.9 million, an increase in restricted cash of \$0.9 million related to the signing of the facility lease in March 2017, and purchase of property and equipment for our office and laboratory facility of \$0.6 million, which are partially offset by maturities of marketable securities of \$32.8 million.

Cash used in investing activities for the six months ended June 30, 2016 was related to our purchase of property and equipment for our office and laboratory facility.

***Cash flows from financing activities***

Cash provided by financing activities for the six months ended June 30, 2017 was \$137.3 million, primarily from net proceeds of \$135.6 million from the issuance of common stock in connection with our follow-on offering completed in February 2017 and to a lesser extent, proceeds of \$1.7 million from the issuance of common stock to participants in the employee stock purchase plan and exercise of stock option.

Cash provided by financing activities for the six months ended June 30, 2016 was \$113.2 million, primarily from net proceeds of \$112.3 million from the issuance of common stock in connection with our follow-on offering in June 2016 and to a lesser extent, proceeds of \$0.5 million from the issuance of common stock to participants in the employee stock purchase plan.

**Off-Balance Sheet Arrangements**

As of June 30, 2017, we had no off-balance sheet arrangements as defined in Item 303(a)(4) of Regulation S-K as promulgated by the SEC.

**Table of Contents****Contractual Obligations and Other Commitments**

In March 2017, we entered into a noncancelable operating lease (the Lease) for approximately 67,185 square feet of space in South San Francisco, California (the New Facility). The date on which we will become responsible for paying rent under the Lease (the Rent Commencement Date) will be earlier of December 15, 2017 or the date the New Facility is ready for occupancy. The Lease expires 10 years after the Rent Commencement Date. The Lease grants us an option to extend the Lease for an additional 10-year period.

The following table summarizes our contractual obligations under the new and existing operating leases as of June 30, 2017 (in thousands):

	<b>Total</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>	<b>2020</b>	<b>2021</b>	<b>Thereafter</b>
Operating lease obligations <sup>1</sup>	\$ 46,950	\$ 860	\$ 3,462	\$ 4,134	\$ 4,279	\$ 4,428	\$ 29,787
Total contractual obligations	\$ 46,950	\$ 860	\$ 3,462	\$ 4,134	\$ 4,279	\$ 4,428	\$ 29,787

<sup>(1)</sup> The table above is prepared under the assumption that the Rent Commencement Date at the New Facility starts on December 15, 2017.

**Recent Accounting Pronouncements**

In May 2017, the FASB issued ASU No. 2017-09, *Compensation – Stock Compensation (Topic 718)*, which is intended to clarify and reduce the diversity in practice and cost and complexity when applying the guidance in Topic 718, Compensation – Stock Compensation, to a change to the terms or conditions of a share-based payment award. The new standard is effective for annual periods, and interim periods within those annual periods, beginning after December 15, 2017. Early adoption is permitted. We believe that the adoption of this new standard will have no impact on our financial position or result of operations and have not elected to early adopt the amendment.

**Accounting Pronouncements Adopted**

In March 2016, the FASB issued ASU No. 2016-09, *Improvements to Employee Share-Based Payment Accounting* (ASU 2016-09), which is intended to simplify several aspects of the accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities, and classification on the statement of cash flows. ASU 2016-09 is effective for annual periods beginning after December 15, 2016, and interim periods within those annual periods. We adopted ASU 2016-09 in the first quarter of 2017.

The impact of adoption ASU 2016-09 resulted in the following:

Classification of excess income tax benefits from stock-based compensation arrangement as a discrete item within income tax expense, rather than recognizing such excess income tax benefits in additional paid-in capital. The adoption of this guidance resulted in an increase of approximately \$1.1 million of net operating losses, which has an impact of \$0.4 million on our deferred tax assets before our full valuation allowance established against the related deferred tax assets.

Recognition of forfeitures as they occur. The cumulative effect adjustment as a result of the adoption of ASU 2016-09 on a modified retrospective basis was insignificant.

A change in classification of cash flows resulting from excess tax benefits and cash paid by us when directly withholding shares for tax-withholding purposes on a retrospective basis. The adoption of these provisions did not result in changes in our condensed consolidated statements of cash flow.

There were no other material impacts to our condensed consolidated financial statements as a result of adopting this updated standard.

**Item 3. Quantitative and Qualitative Disclosures about Market Risk**

Our market risks as of June 30, 2017 have not changed materially from those discussed in Item 7A of our Annual Report on Form 10-K for the year ended December 31, 2016, filed with the SEC on March 13, 2017.

## **Table of Contents**

### **Item 4. Controls and Procedures**

#### *Evaluation of Disclosure Controls and Procedures*

As required by Rule 13a-15(b) under the Securities Exchange Act of 1934, as amended (the Exchange Act), our management, under the supervision and with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of the design and operation of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of June 30, 2017. Based on the evaluation of our disclosure controls and procedures as of June 30, 2017, our Chief Executive Officer and Chief Financial Officer have concluded that, as of June 30, 2017, our disclosure controls and procedures were effective at the reasonable assurance level.

#### *Changes in Internal Control over Financial Reporting*

There have been no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the quarter ended June 30, 2017 that have materially affected, or are reasonably likely to materially affect, our internal controls over financial reporting.

## **PART II. OTHER INFORMATION**

### **Item 1. Legal Proceedings**

We are not currently a party to any material litigation or other material legal proceedings.

### **Item 1A. Risk Factors.**

*This Quarterly Report on Form 10-Q contains forward-looking information based on our current expectations. Because our business is subject to many risks and our actual results may differ materially from any forward-looking statements made by or on behalf of us, this section includes a discussion of important factors that could affect our business, operating results, financial condition and the trading price of our common stock. This discussion should be read in conjunction with our condensed consolidated financial statements as of June 30, 2017 and December 31, 2016 and the notes accompanying those consolidated financial statements.*

### **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 six months ended June 30, 2017 and 2016 were \$47.2 million and \$34.3 million, respectively. As of June 30, 2017, we had an accumulated deficit of \$228.1 million. We have not generated any revenue since our inception, and have financed our operations primarily through the sale of equity securities. We continue to incur significant research and development and other expenses related to our ongoing operations and expect to incur losses for the foreseeable future. We anticipate these losses will increase as we:

continue to advance GBT440 in clinical development, for which we have initiated the Phase 3 HOPE study of GBT440 for the potential treatment of patients with SCD, have initiated a Phase 2a clinical trial of GBT440 for the potential treatment of low oxygen levels, also known as hypoxemia, in patients with idiopathic pulmonary fibrosis, or IPF, have initiated a Phase 1 clinical study to evaluate the physiologic effects of GBT440 in healthy volunteers under hypoxic conditions and exercise conditions that maximally stress heart and lung function, and have additional Phase 1/2a clinical trials ongoing in SCD and IPF patients;

establish and maintain manufacturing and supply relationships with third parties that can provide adequate supplies (in amount and quality) of GBT440 to support further clinical development and, if approved, commercialization;

seek and obtain regulatory and marketing approvals for GBT440 for any indication;

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

advance our other programs through nonclinical and clinical development and commence development activities for any additional product candidates we may identify; and

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

## Table of Contents

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

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

We are currently advancing GBT440 through clinical development, including in a multi-national Phase 3 clinical trial of GBT440 that will enroll up to 400 patients with SCD. We are also evaluating the safety and pharmacokinetics of single and multiple doses of GBT440 in a Phase 2a clinical trial of adolescent and pediatric patients with SCD, which we recently expanded to include a new single-dose cohort in children aged 6-11. We are also conducting two Phase 2 studies of GBT440 for the potential treatment of hypoxemia in patients with IPF, as well as a complementary Phase 1 study of GBT440 in healthy volunteers to evaluate the physiologic effects of GBT440 under hypoxic conditions and exercise conditions that maximally stress heart and lung function. GBT440 is currently our only product candidate in clinical development, although we are conducting nonclinical research activities in other programs.

Developing biopharmaceutical products is expensive and time-consuming, and we expect our research and development expenses to increase substantially in connection with our ongoing activities, particularly as we advance GBT440 and other product candidates that we may identify and pursue in clinical trials. As of June 30, 2017 and December 31, 2016, we had working capital of \$217.7 million and \$134.3 million, respectively and capital resources consisting of cash and cash equivalents and short and long-term marketable securities totaling \$290.6 million and \$197.3 million, respectively. Because the outcome of any clinical development and regulatory approval process is highly uncertain, we cannot reasonably estimate the actual capital amounts necessary to successfully complete the development, regulatory approval process and commercialization of GBT440 or any other future product candidates.

In August 2015, we sold 6,900,000 shares of common stock in our initial public offering, the net proceeds of which totaled \$126.2 million, after deducting underwriting discounts and commissions and offering expenses incurred by us. In July 2016 we completed the sale of 6,667,228 shares of common stock in a follow-on offering, the net proceeds of which totaled \$117.0 million, after deducting underwriting discounts and commissions and offering expenses. In October 2016, we filed our shelf registration statement on Form S-3 for the potential offering, issuance and sale by us of up to a maximum aggregate offering price of \$250 million of our common stock, preferred stock, debt securities, warrants, and/or units. In February 2017, we completed the sale of 5,867,347 shares of common stock in a follow-on offering under the shelf registration, the net proceeds of which totaled \$135.6 million, after deducting underwriting discounts and commissions and offering expenses. After the completion of this follow-on offering in February 2017, up to a maximum aggregate offering price of \$106.2 million of our common stock, preferred stock, debt securities, warrants and/or units remain available under our shelf registration statement on Form S-3. We expect that our existing capital resources consisting of cash and cash equivalents and marketable securities, will be sufficient to fund our operations for at least the next twelve months.

However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings or other sources, such as strategic collaborations or license and development agreements. Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize GBT440 or any other product candidates that we may identify and pursue. Moreover, such financing may result in dilution to stockholders, imposition of debt covenants and repayment obligations, or other restrictions that may affect our business. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans.

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

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

**Table of Contents**

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

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

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

the progress, timing, scope and costs of our nonclinical studies, our clinical trials and other related activities, including our ability to enroll subjects in a timely manner for our Phase 3 HOPE study as well as our other multiple Phase 1 and 2a clinical trials of GBT440 for SCD or hypoxemia in IPF patients, and our potential future clinical trials;

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

our ability to advance our development programs, including our program for the clinical investigation of GBT440 in SCD patients and in hypoxemia in IPF patients through nonclinical and clinical development, as well as any other potential product candidate programs we may identify and pursue, and the timing and scope of these development activities;

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

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

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

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

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

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

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

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

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

Additional funds may not be available when we need them, on terms that are acceptable to us, or at all. If adequate funds are not available to us on a timely basis, we may be required to delay, limit or terminate our lead product candidate GBT440 in one or more of our research or development programs or the commercialization of any product candidates or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially and adversely affect our business, prospects, financial condition and results of operations.

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

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

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

**Table of Contents**

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

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

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

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

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

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

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

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

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

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

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

***We are heavily dependent on the success of our lead product candidate, GBT440, and all of our other programs are still in the nonclinical development stage. If we are unable to successfully complete clinical development, obtain regulatory approval for, and commercialize GBT440, or experience delays in doing so, our business will be materially harmed.***

To date, we have invested a majority of our efforts and financial resources in the nonclinical and clinical development of our lead and initial product candidate GBT440, including conducting nonclinical studies and clinical trials and providing general and administrative support for these operations. We do not have any other clinical product candidates. Our future success is highly dependent on our ability to successfully develop, obtain regulatory approval for, and commercialize GBT440 for one or more potential indications. Before we can generate any revenues from sales of GBT440, we must conduct substantial additional clinical development (including, among others, multiple ongoing clinical studies and toxicology studies, and possibly additional future nonclinical studies and clinical trials to demonstrate safety and efficacy of GBT440 for any potential indication). In addition, we will need to seek and obtain regulatory approval for any potential indication, secure an adequate manufacturing supply to support larger clinical trials and commercial sales and build a commercial organization. Further, the success of GBT440 as a potential commercial product will also depend on patent and trade secret protection, acceptance of GBT440 by patients, the medical community and third-party payors, its ability to compete with other therapies, the status and availability of healthcare coverage and adequate reimbursement, and maintenance of an acceptable safety and efficacy profile following approval, among other factors. If we do not achieve all of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize GBT440, which would materially harm our business.

GBT440 is currently our only product candidate to have advanced into clinical trials. We are developing GBT440 as an oral, once-daily therapy for the potential treatment of SCD, and are currently evaluating GBT440 in SCD patients in ongoing Phase 1/2a clinical trials and in the HOPE study, which is a Phase 3 clinical trial in adult and adolescent SCD patients. In addition, we are conducting a Phase 1/2 program evaluating GBT440 for the potential treatment of hypoxemia in IPF. Conducting clinical trials in parallel in different patient populations with different conditions is riskier than conducting serial testing, in part because negative findings in one program could impact both programs, or be perceived as being negative for both programs even if data and results suggest otherwise.

---

**Table of Contents**

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

We are also very dependent on the data and results that we obtain over time from our most advanced clinical trial of GBT440. In late 2016, we initiated the Phase 3 HOPE study, which is designed to enroll up to 400 SCD patients, age 12 years and older, who have had at least one episode of vaso-occlusive crisis in the previous year. The primary endpoint of the HOPE study relates to the proportion of patients who achieve an increase in hemoglobin levels (compared to baseline) as pre-specified in the study protocol. We have not previously conducted any clinical study of GBT440 in SCD patients using this primary endpoint, and we do not believe this measure has been used as a primary endpoint for any registration studies for any other SCD therapies. In addition, the HOPE study also uses a new patient reported outcomes, or PRO, instrument that we recently developed, and that has not been utilized before in any clinical studies, to generate data for a secondary endpoint in the HOPE study.

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

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

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

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



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

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

We may not achieve our pre-specified endpoints in the HOPE study, or in other clinical trials where there is limited or no regulatory guidance regarding appropriate clinical endpoints, which would decrease the probability of obtaining marketing approval for GBT440 or any other product candidate we may develop. Any inability to design clinical trials with protocols and endpoints acceptable to applicable regulatory authorities, and to obtain regulatory approvals for GBT440 and any other product candidates that we may pursue, would have an adverse impact on our business, prospects, financial condition and results of operations.

---

**Table of Contents**

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

The results of nonclinical studies and clinical trials of GBT440, our other product candidates and future product candidates that we may pursue may not be predictive of the results of later-stage clinical trials, and interim results of a clinical trial may not necessarily predict final results. For example, our nonclinical studies and clinical trials to date of GBT440 in SCD have involved mostly one genotype of SCD, known as HbSS, and the results of these studies may not be replicated in other genotypes of SCD or in subsequent clinical trials. The HOPE study of GBT440 in SCD is not limited to only the HbSS genotype. Additionally, any positive results generated in our Phase 1/2 clinical trial of GBT440 in SCD in adults do not ensure that we will achieve similar results in the HOPE study, which will enroll both adult and adolescent populations, or our ongoing Phase 2a clinical trial of GBT440 in adolescents and pediatric patients with SCD, which we expanded in July 2017 to include an additional single-dose cohort in children aged 6-11, or in any other potential indications for GBT440, such as IPF and other hypoxemic pulmonary disorders. Our later stage clinical trials, such as the HOPE study, may involve significantly broader patient populations than those in earlier clinical trials.

Product candidates in later stages of clinical trials, such as our HOPE study, may fail to demonstrate the desired safety and efficacy despite having progressed through nonclinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier studies, and we cannot be certain that we will not face similar setbacks.

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

Our failure to demonstrate the required characteristics to support marketing approval for GBT440 or any other product candidate we may choose to develop in any ongoing or future clinical trials would substantially harm our business, prospects, financial condition and results of operations.

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

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

Based on our discussions with the FDA regarding the design of the HOPE study of GBT440 in SCD patients, we believe that if the HOPE study meets the primary endpoint and at least one key secondary endpoint, the data and results from this Phase 3 clinical trial could form the basis for regulatory approval of GBT440 for SCD treatment in the United States. However, before being able to seek or to obtain full or even conditional approval of GBT440 for the

treatment of SCD, we may be required to conduct additional clinical trials or nonclinical studies of GBT440, including one or more additional Phase 3 clinical trials or other studies. The FDA may also require a longer follow-up period for subjects treated with GBT440 prior to accepting an NDA submission. We do not have a special protocol assessment agreement in place with the FDA. We are in the process of seeking input from various European regulatory authorities regarding a pathway to approval of GBT440 for the potential treatment of SCD patients based on the HOPE study.

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

**Table of Contents**

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

Before obtaining marketing approval from regulatory authorities for the sale of any our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates in humans. Clinical testing is expensive, time-consuming and uncertain as to outcome. We expect to conduct the HOPE study, which will enroll up to 400 SCD patients, at multiple clinical sites located in the United States, Europe, Africa and the Middle East, with top line data and results expected in the first half of 2019. In addition, we have multiple ongoing Phase 1/2 clinical studies of GBT440 for the potential treatment of SCD patients or hypoxemia in IPF patients. We cannot guarantee that the HOPE study or any other clinical trials for GBT440 or any other product candidates we may pursue will be conducted as planned or completed on schedule, if at all. A failure of one or more clinical trials can occur at any stage of testing. Events that may prevent successful or timely completion of clinical development include:

delays or failures in reaching a consensus with regulatory agencies on study design, including clinical endpoints sufficient to support an approval decision;

delays or failures to receive approval for conduct of clinical studies in one or more geographies which could result in delays in enrollment and availability of data and results;

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

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

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

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

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

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

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

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

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

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

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

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

changes in regulatory requirements and guidance that require amending or submitting new clinical protocols or obtaining additional IRB or other approvals to conduct or complete clinical studies of our product candidates. We could also encounter delays if a clinical trial is suspended or terminated for any reason (which could occur as a result of termination by us, by the IRBs or ethics committees of the institutions in which such trials are being conducted, by an independent Safety Review Board for such trial, or by the FDA or other regulatory authorities). A clinical trial can be suspended or terminated for a wide variety of reasons, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by us, or the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, or failure to demonstrate a benefit from using a drug candidate. In addition, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional studies to bridge the development program from the data and results for the earlier product candidate to the modified product candidate.

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

---

**Table of Contents**

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

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

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

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

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

Clinical trials by their nature utilize only a small sample of the potential patient population. Our Phase 1/2 clinical program of GBT440 in SCD patients and IPF patients are providing only very limited experience of GBT440 in SCD patients and IPF patients. For example, our Phase 1/2a clinical trials of GBT440 in SCD are designed to enroll between 96 and 128 subjects, and our ongoing Phase 2a clinical trials of hypoxemia in IPF patients are designed to enroll only up to 49 subjects. In contrast, the Phase 3 HOPE study is designed to enroll up to 400 adult and adolescent SCD patients. However, even this larger trial design will enroll only a very small fraction of all patients with SCD. Any rare and severe side effects of GBT440 may be uncovered only in later stages of our ongoing clinical trials (such as our larger HOPE study), or only in trials involving different patient populations (such as pediatric patients or IPF patients), or only during post-approval studies or safety reporting. Many product candidates that initially showed promise in early stage testing have later been found to cause side effects that prevented their further development. Moreover, a nonclinical toxicology study with GBT440 in non-humans and clinical trials involving other hemoglobin modifiers (other than GBT440) have shown a decrease in oxygen delivery to tissue when a significant percentage of hemoglobin is modified. Hemoglobin modifiers, by increasing HbS's affinity for oxygen, can cause a shift in oxygen

levels, potentially resulting in tissue hypoxia. To date, clinical studies of GBT440 have not shown evidence of tissue hypoxia. However, if GBT440 or any other product candidates that we may develop are associated with tissue hypoxia or any other undesirable side effects or unexpected undesirable characteristics in clinical trials or nonclinical studies, we may need to abandon their development or limit their development to more narrow uses or subpopulations, which could adversely affect our business, prospects, financial condition and results of operations.

---

**Table of Contents**

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

We believe there may be an opportunity to accelerate the development of our lead product candidate GBT440 through one or more of the FDA's expedited programs, such as fast track, breakthrough therapy, accelerated approval or priority review, or through EMA's new PRIME program, and we have pursued and intend to pursue one or more of these expedited programs for GBT440. However, we cannot be assured that GBT440 or any other product candidates that we may develop will qualify for or benefit from any such programs in the United States or any foreign regulatory jurisdictions.

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

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

In June 2017, EMA granted PRIME designation for GBT440 for the treatment of SCD. The PRIME program is a new regulatory mechanism that provides for early and proactive EMA support to medicine developers to help patients benefit as early as possible from innovative new products that have demonstrated the potential to significantly address an unmet medical need. Although breakthrough designation or access to any other expedited program, including EMA's new PRIME program, may expedite the development or approval process, it does not change the standards for approval. Even if we are successful in obtaining a fast-track or breakthrough therapy designation or access to any other expedited program through the FDA or any other regulatory authority, such as the PRIME program, we may not experience faster development timelines or achieve faster review or approval compared to conventional FDA or foreign regulatory procedures.

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

***Although the FDA and the European Commission have each granted orphan drug designation to our lead product candidate GBT440 for the potential treatment of SCD, we may not receive orphan drug designation for any other product candidates for which we may submit new applications for orphan drug designation, and any orphan drug designations that we have received or may receive in the future may not confer marketing exclusivity or other expected commercial benefits.***

Our business strategy focuses on the development of product candidates for the treatment of rare, chronic blood disorders that may be eligible for FDA or European Union, or EU, orphan drug designation. Regulatory authorities in some jurisdictions, including the United States and the EU, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is



intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States. In the EU, the Committee for Orphan Medicinal Products of the EMA recommends orphan drug designation to promote the development of medical products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the EU and for which no satisfactory method of diagnosis, prevention, or treatment is authorized (or in other very limited circumstances). In 2015 and 2016, respectively, the FDA and the European Commission (acting on a positive recommendation by the EMA) each granted orphan drug designation for GBT440 for the treatment of patients with SCD.

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

Although the FDA and the EMA have each granted orphan drug designation to GBT440 for the treatment of SCD, we may apply for orphan drug designation for GBT440 in other jurisdictions or for other indications, or for other product candidates we may develop and pursue in the future. Applicable regulatory authorities may not grant us these additional designations. In addition, the exclusivity granted under any orphan drug designations that we have received or may receive may not effectively protect the product candidate from competition because different drugs can be approved for the same condition. For example, in the United States, even after an orphan drug is approved, the FDA can subsequently approve another drug for the same condition if the FDA concludes that the later drug is clinically superior, or the FDA can approve a competitor application for the same drug for a different indication than the orphan drug designation. Any inability to secure or maintain orphan drug designation or the exclusivity benefits of this designation would have an adverse impact on our ability to develop and commercialize our product candidates.

**Table of Contents**

***Even if we receive regulatory approval for our lead product candidate GBT440 or any other product candidate that we may develop and pursue, we will be subject to ongoing regulatory obligations and scrutiny and may be subject to significant restrictions relating to product labeling, distribution or other post-marketing requirements.***

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

In addition, manufacturers and manufacturers facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to current Good Manufacturing Practices, or cGMP s. For our lead product candidate GBT440 and any other product candidates we may pursue, we are wholly reliant on third party contract manufacturers for clinical as well as any commercial supplies of product candidates and products. As such, we and our contract manufacturers are subject to continual review and periodic inspections to assess compliance with cGMP requirements and must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, and quality control. We will also be required to report certain adverse reactions and production problems, if any, to the FDA and comparable foreign regulatory authorities, and to comply with requirements concerning advertising and promotion for our products. In addition, we are subject to very rapid reporting obligations relating to any adverse events or serious adverse events relating to our product candidates and any approved products, if any. Our failure to report adverse events we become aware of within the prescribed timeframes could have serious negative consequences for our development programs, business and operations. In addition, any promotional communications or materials for prescription drugs are subject to a variety of complex legal and regulatory restrictions, including but not limited to consistency with the approved product s approved label. Failure to obey these standard marketing requirements for any approved product (if any) could have serious negative consequences for our commercialization activities (if any), business and operations.

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

issue untitled or warning letters;

impose civil or criminal penalties;

impose injunctions;

impose fines;

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

suspend regulatory approval;

suspend ongoing clinical trials;

seek voluntary product recalls and impose publicity requirements;

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

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

seize or detain products.

## **Table of Contents**

As a company, we have no experience with obtaining approval for, launching or commercializing any product candidates or products, or with complying with most of these complex ongoing regulatory requirements. It will take significant effort and management attention to address how to comply with these requirements in any jurisdiction for which we seek any product approval. Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity even if significant liabilities do not result. Any failure to comply with these complex ongoing regulatory requirements may significantly and adversely affect our ability to obtain approval for, launch, commercialize and generate revenues from GBT440 or any future product candidates. If we are subject to regulatory sanctions or if regulatory approval for our product candidates is withdrawn or limited, our business, prospects, financial condition and results of operations would be significantly harmed.

### **Risks Related to Our Reliance on Third Parties**

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

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

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

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

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

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

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

**Table of Contents**

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

reliance on the third party for regulatory compliance and quality assurance;

the possible breach or termination of the manufacturing agreement by the third party or by us, including at a time that is costly or inconvenient for us;

the inability of the third party to satisfy our ordering requirements as to quality, quantity and/or price;

the possible misappropriation of our proprietary information, including our trade secrets and know-how; and

the unwillingness of the third party to extend or renew terms with us when desired.

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

Our lead product candidate GBT440 and any future product candidates that we may develop may compete with other product candidates and marketed drugs for access to manufacturing facilities. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. Although we currently have adequate supplies to conduct our ongoing clinical trials, if we are unable to enter into relationships with additional contract manufacturers, or our current or future contract manufacturers cannot perform as agreed, we may experience delays and incur additional costs in our clinical development and potential commercialization activities. Our current and anticipated future dependence upon others for the manufacturing of our product candidates and any marketed drugs may adversely affect our future profit margins and our ability to commercialize any product candidates that receive marketing approval on a timely and competitive basis.

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

All entities involved in the preparation of therapeutics for clinical trials or commercial sale, including our existing contract manufacturers for our lead product candidate GBT440, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical trials must be manufactured in

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

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

## **Table of Contents**

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

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

These factors could cause us to incur higher costs and could cause the delay or termination of clinical trials, regulatory submissions, required approvals, or commercialization of our product candidates. Furthermore, if our suppliers fail to meet contractual requirements and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials may be delayed or we could lose potential revenue.

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

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

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

## **Risks Related to Our Intellectual Property**



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

## **Table of Contents**

As is the case with other biopharmaceutical companies, our success depends in large part on our ability to obtain and maintain protection of the intellectual property, particularly patents, that we may exclusively license or own solely and jointly with others in the United States and other countries with respect to our product candidates and technology, including our lead product candidate GBT440. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our product candidates.

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

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal, technological and factual questions and has in recent years been the subject of much litigation. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States, or vice versa. Further, we may not be aware of all third-party intellectual property rights potentially relating to our product candidates. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing or, in some cases, not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are and will remain highly uncertain. The patent examination process may require us or our licensors, licensees or collaboration partners to narrow the scope of the claims of our or our licensors, licensees or collaboration partners pending and future patent applications, which may limit the scope of patent protection that may be obtained. Our pending and future patent applications may not result in patents being issued that protect our lead product candidate GBT440 or any future product candidates, in whole or in part, or which effectively prevent others from commercializing competitive product candidates. Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our patents by developing similar or alternative product candidates in a non-infringing manner, or by successfully seeking to narrow or invalidate our patents or render them unenforceable. Our and our licensors, licensees or collaboration partners' patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications, and then only to the extent the issued claims cover the technology.

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

patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize GBT440 or any future product candidates.

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

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

---

**Table of Contents**

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 AIA, enacted in 2011, the United States has moved to a first to file system similar to other countries' systems. The AIA also includes a number of significant changes that affect the way patent applications are prosecuted, and may also affect patent litigation. The effects of these changes are currently unclear as the USPTO must still implement various regulations, the courts have yet to address certain of these provisions and the applicability of the AIA and new regulations remain to be issued. Accordingly, it is not clear what, if any, impact the AIA will have on the operation of our business. However, the AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of patents that may issue from such patent applications, all of which could have a material adverse effect on our business and financial condition. Any further changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents and patent applications or narrow the scope of our potential patent protection.

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

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

We may in the future become party to, or be threatened with, adversarial proceedings or litigation against us regarding third party intellectual property rights with respect to GBT440 or our future product candidates, that would cause us to incur substantial expenses and, if successful against us, could cause us to pay substantial damages, including treble damages and attorneys' fees if we are found to be willfully infringing a third party's patents. We may also be required to indemnify parties with whom we have contractual relationships against such claims. If a patent infringement suit were brought against us, we could be forced to stop or delay research, development, manufacturing or sales of the product or product candidate that is the subject of the suit. As a result of patent infringement claims, or in order to avoid potential claims, we may choose to seek, or be required to seek, a license from the third party to continue developing, manufacturing and marketing our product candidates and would most likely be required to pay license fees or royalties or both, that could be significant. These licenses may not be available on acceptable terms, or at all. Even if we were able to obtain a license, the rights may be nonexclusive, which would give our competitors access to the same intellectual property licensed to us. Ultimately, we could be prevented from commercializing a product, or forced to redesign it, or to cease some aspect of our business operations if, as a result of actual or threatened patent infringement claims, we are unable to enter into licenses on acceptable terms. Even if we are successful in defending against such claims, such litigation can be expensive, uncertain, and time consuming to litigate, and would divert management's attention from our core business. Any of these events could harm our business significantly.

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

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

Competitors or other parties may infringe our patents or other intellectual property. Although we are not currently involved in any litigation, if we were to initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are multiple potential grounds for a validity challenge or an unenforceability assertion. The outcome following legal assertions of invalidity and unenforceability is often highly unpredictable.

## **Table of Contents**

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

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

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

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

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

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

We jointly own certain patents and patent applications with third parties. In the absence of an agreement with each co-owner of jointly owned patent rights, we will be subject to default rules pertaining to joint ownership. Some countries require the consent of all joint owners to exploit, license or assign jointly owned patents, and if we are unable to obtain that consent from the joint owners, we may be unable to exploit the invention or to license or assign our rights under these patents and patent applications in those countries. For example, in 2015 we secured exclusive rights from the Regents of the University of California, or the Regents, for certain patents and patent applications that they jointly own with us related to our lead product candidate GBT440 and GBT440 analogs. Additionally, in the United States, each co-owner may be required to be joined as a party to any claim or action we may wish to bring to enforce these patent rights, which may limit our ability to pursue third party infringement claims.

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

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

**Table of Contents**

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

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

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

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

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

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

Filing, prosecuting and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries worldwide, or from selling or importing products



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

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

## **Table of Contents**

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

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

An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned to a first-to-file system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. A third party that files a patent application in the USPTO after that date but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by the third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application, but circumstances could prevent us from promptly filing patent applications on our inventions.

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

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

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

## **Risks Related to Commercialization**

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

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

the efficacy and potential advantages of our drugs compared to alternative treatments;

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

the convenience and ease of administration of our drugs compared to alternative current and future treatments;

**Table of Contents**

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

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

the strength of marketing and distribution support;

the availability of third-party coverage and adequate reimbursement;

the clinical indications and approved labeling for which the drug is approved;

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

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

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

Although some of our employees have experience with commercializing products while employed at other companies, as a company we have no experience selling and marketing our product candidates, as a management team we have not commercialized any product candidates, and we currently have no marketing or sales organization. To successfully commercialize any products that may result from our development programs, we will need to develop these capabilities, either on our own or with others. If our product candidates receive regulatory approval, we intend to establish a sales and marketing organization with technical expertise and supporting distribution capabilities to commercialize our product candidates in major markets, which will be expensive, difficult, risky and time consuming. Any failure or delay in the development of our internal sales, marketing, and distribution capabilities would adversely impact the commercialization of our products, if any are approved.

Further, given our lack of prior experience in marketing and selling biopharmaceutical products, our initial estimate of the size of the required sales force may be materially more or less than the size of the sales force actually required to effectively commercialize our product candidates. As such, we may be required to hire substantially more sales representatives to adequately support the commercialization of our product candidates or we may incur excess costs as a result of hiring more sales representatives than necessary. With respect to certain geographical markets, we may enter into collaborations with other entities to utilize their local marketing and distribution capabilities, but we may be unable to enter into such agreements on favorable terms, if at all. If our future collaborators do not commit sufficient resources to commercialize our future products, if any, and we are unable to develop the necessary marketing capabilities on our own, we will be unable to generate sufficient product revenue to sustain our business. We may be competing with companies that currently have extensive and well-funded marketing and sales operations. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against more established companies.

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

Our target patient populations are small, and accordingly the pricing, coverage and reimbursement of our product candidates, if approved, must be adequate to support our commercial infrastructure. Our per-patient prices must be sufficient to recover our development and manufacturing costs and potentially achieve profitability. Accordingly, the availability of government funded or private insurance coverage for our product candidates for any approved indications, and the extent of reimbursement by governmental and private payors, will be essential for most patients to be able to afford expensive treatments, such as we expect ours to be assuming approval. Sales of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by third party payors, like private health insurers, including health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, and government health administration authorities, like Medicare and Medicaid. If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved drug products. The process for determining whether a third-party payor will provide coverage for a product may be separate from the process for setting the reimbursement rate that the payor will pay for the product. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the FDA-approved products for a particular indication. Moreover, a third-party payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. For example, the payor's reimbursement payment rate may not be adequate or may require co-payments that patients find unacceptably high. Additionally, coverage and reimbursement for products can differ significantly from payor to payor.

---

**Table of Contents**

In the United States, significant decisions about reimbursement for new medicines are made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, as CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare and enters into contracts with drug manufacturers for discounted drug prices for Medicaid under the Medicaid Drug Rebate Program. The practices and requirements relating to the payment of rebates by drug manufacturers for Medicaid purchases are determined by each state, and in some cases, if a company does not enter into a rebate agreement, its Medicaid sales will be subjected to a prior authorization procedure that requires state agency approval to qualify a doctor's prescription for reimbursement.

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

Moreover, increasing efforts by governmental and third-party payors, in the United States and abroad, to cap or reduce healthcare costs may cause such organizations to limit both coverage and levels of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of any of our product candidates, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative and political changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, drug prices are under significant scrutiny in the markets in which our products may be sold, and drug pricing and other healthcare costs continue to be subject to intense political and social pressures which we anticipate will continue and escalate on a global basis. As a result, our business and reputation may be harmed, our stock price may be adversely impacted and experience periods of volatility, we may have difficulty raising funds and our results of operations may be adversely impacted.

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

In some countries, particularly in the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. To obtain coverage and reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies, or to meet other criteria for pricing approval. If reimbursement of our product candidates is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business and operations could be harmed, possibly materially, based on the large population of patients with SCD who reside in foreign countries.

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

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

the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or paying any remuneration (including any kickback, bribe, or certain rebates), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under U.S. federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

**Table of Contents**

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

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

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

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

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

analogous state laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including, but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and



entities; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts; and

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

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

**Table of Contents**

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

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

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

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

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

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

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

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

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

new requirements under the federal Physician Payments Sunshine Act for drug manufacturers to report information related to payments and other transfers of value made to physicians and teaching hospitals as

well as ownership or investment interests held by physicians and their immediate family members;

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

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

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

Since its enactment, there have been judicial and Congressional challenges to numerous aspects of the ACA, and the federal executive and legislative branches are actively seeking to replace the ACA with new federal legislation. There may also be federal and state regulatory changes that impact or repeal the ACA or healthcare programs, insurance coverage or reimbursement generally. These efforts have significantly increased uncertainty regarding the availability of healthcare programs, insurance coverage and reimbursement as a general matter as well as for our product candidates, and we cannot predict how these events will impact our business or operations.

In addition, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which have resulted in several recent Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, reduce the price of drugs under Medicare and reform government program reimbursement methodologies for products. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

## **Table of Contents**

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

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. We are currently aware of various existing therapies and development candidates that may compete with our lead product candidate GBT440 for the potential treatment of SCD or IPF. We have competitors both in the United States and internationally, including major multinational pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies. Many of our competitors have substantially greater financial, technical, and other resources, such as larger research and development, marketing and manufacturing organizations. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. As a result, these companies may obtain regulatory approval more rapidly than we are able to and may be more effective in selling and marketing their products as well. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or licensing on an exclusive basis, products that are more effective or less costly than any product candidate that we may develop, or achieve earlier patent protection, regulatory approval, product commercialization and market penetration than we do. Additionally, technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing our product candidates against competitors.

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

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

## **Risks Related to Our Business and Industry**

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

We are highly dependent on the management, research and development, clinical, financial and business development expertise of our executive officers, as well as the other members of our scientific and clinical teams. Although we have employment offer letters with each of our executive officers, each of them may terminate their employment with

us at any time. We do not maintain key person insurance for any of our executives or employees.

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

**Table of Contents**

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

As our development progresses, we expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of research, drug development, regulatory affairs and, if any of our product candidates are filed for or receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

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

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

the research methodology used may not be successful in identifying potential product candidates;

competitors may develop alternatives that render our product candidates obsolete or less attractive;

product candidates we develop may nevertheless be covered by third parties' patents or other exclusive rights;

the market for a product candidate may change during our program so that such a product may become unreasonable to continue to develop;

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

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

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

If we fail to develop and successfully commercialize other product candidates, our business and future prospects may be harmed and our business will be more vulnerable to any problems that we encounter in developing and commercializing our lead product candidate GBT440.

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

The use of our product candidates, including our lead product candidate GBT440, in clinical trials and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. There is a risk that our product candidates may induce adverse events. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

impairment of our business reputation;

withdrawal of clinical trial participants;

**Table of Contents**

costs due to related litigation;

distraction of management's attention from our primary business;

substantial monetary awards to patients or other claimants;

increased warnings on product labels or additional restrictions imposed by regulatory authorities;

the recall of our product candidates;

the inability to commercialize our product candidates; and

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

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

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

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

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



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

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

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

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

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

**Table of Contents**

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

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

Any future collaborations that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of us and our collaborators. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations. Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable product candidate and, in some cases, costly and time-consuming disputes or termination of the collaboration arrangement. These disagreements can be difficult to resolve successfully, and any such termination or expiration would adversely affect us financially and could harm our business reputation. Many collaborations in the pharmaceutical and biotechnology industries do not result in successful outcomes, for a wide variety of reasons.

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

Our business strategy currently incorporates potential international expansion as we conduct our multi-national Phase 3 HOPE study of our lead product candidate GBT440 for the potential treatment of SCD inside and outside the United States, and plan to seek to obtain regulatory approval to and commercialize GBT440 in patient populations inside and outside the United States. If GBT440 is approved, we may hire sales representatives and conduct physician and patient association outreach activities outside of the United States. Doing business internationally involves a number of risks, including but not limited to:

multiple, conflicting, and changing laws and regulations such as privacy regulations, tax laws, export and import restrictions, employment laws, regulatory requirements, and any requirements to obtain other governmental approvals, permits, and licenses;

failure by us to obtain and maintain regulatory approvals for the sale or use of our products in various countries;

additional potentially relevant third-party patent rights;

complexities and difficulties in obtaining protection for and enforcing our intellectual property;

difficulties in staffing and managing foreign operations;

complexities associated with managing multiple payor reimbursement regimes, government payors, or patient self-pay systems;

limits in our ability to penetrate international markets;

financial risks, such as longer payment cycles, difficulty collecting accounts receivable, the impact of local and regional financial crises on demand and payment for our products, and exposure to foreign currency exchange rate fluctuations;

natural disasters, political and economic instability, including wars, terrorism, and political unrest, outbreak of disease, boycotts, curtailment of trade, and other business restrictions;

certain expenses including, among others, expenses for travel, translation, and insurance; and

regulatory and compliance risks that relate to maintaining accurate information and control over sales and activities that may fall within the purview of the U.S. Foreign Corrupt Practices Act, its books and records provisions, or its anti-bribery provisions.

**Table of Contents**

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

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

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

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

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

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

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

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

Earthquakes or other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

## **Table of Contents**

***Our internal computer systems, or those of our third party vendors, may fail or suffer security breaches, which could result in a material disruption of our drug development programs.***

Despite the implementation of security measures, our internal computer systems and those of our third party vendors are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our drug development programs. For example, the loss of data from completed or ongoing clinical trials or nonclinical studies for any of our product candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of our product candidates could be delayed.

## **Risks Related to Our Equity Securities**

***If we fail to maintain proper and effective systems of disclosure controls and internal controls over financial reporting to the extent required under applicable regulations, the accuracy and timeliness of our financial reporting may be adversely affected, and we could be subject to sanctions or other penalties that would harm our business.***

As a public company, we are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, Section 404, or Section 404, of the Sarbanes-Oxley Act of 2002, or Sarbanes Oxley, and the rules and regulations of The NASDAQ Stock Market. Section 404 generally requires our management and independent registered public accounting firm to report on the effectiveness of our internal control over financial reporting. Company responsibilities required by Sarbanes Oxley include establishing and maintaining corporate oversight and adequate internal control over financial reporting and disclosure controls and procedures. Effective internal controls are necessary for us to produce reliable financial reports and are important to help prevent financial fraud.

Beginning with the annual report on Form 10-K for the fiscal year ending December 31, 2016, Section 404 requires an annual management assessment of the effectiveness of our internal control over financial reporting. Once we are no longer an emerging growth company under the Jumpstart Our Business Startups Act of 2012, as amended, or the JOBS Act or, if prior to such date, we opt to no longer take advantage of the applicable exemption, we will be required to include an opinion from our independent registered public accounting firm on the effectiveness of our internal control over financial reporting. We expect to incur additional professional fees and internal costs to expand our accounting and finance functions and to expend significant management efforts in order to comply with these requirements. Previously we have never been required to test our internal controls within a specified period and, as a result, we may experience difficulty in meeting these reporting requirements in a timely manner.

We carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and our Chief Financial Officer, of the effectiveness of our internal control over financial reporting for the purpose of providing the reports required by Section 404. Based on our assessment and using the Committee of Sponsoring Organizations of the Treadway Commission ( COSO ) criteria, our management, Chief Executive Officer and Chief Financial Officer, have concluded that, as of December 31, 2016, our internal control over financial reporting was effective. However, our independent registered public accounting firm has not yet tested the design or operating effectiveness of our controls over financial reporting or been required to provide an attestation report with respect to our internal control over financial reporting, but will do so at a future date. During the course of our or their subsequent review and testing, material weaknesses or significant deficiencies may be identified that we may be unable to remediate them before we must provide the required reports. If material weaknesses or significant

deficiencies in our internal control over financial reporting are identified in the future, we may not detect or remediate errors on a timely basis and our consolidated financial statements may be materially misstated. We or our independent registered public accounting firm may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall. In addition, as a public company we are required to file accurate and timely quarterly and annual reports with the SEC under the Exchange Act. Any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from The NASDAQ Global Select Market or other adverse consequences that would materially harm our business.

**Table of Contents**

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

We are an emerging growth company as defined in the JOBS Act, and we have elected to take advantage of some of the exemptions from reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. We will remain an emerging growth company until the earliest of (1) December 31, 2020, (2) the last day of the fiscal year in which we have total annual gross revenue of at least \$1.07 billion, (3) the last day of the fiscal year in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds \$700 million as of the prior June 30th or (4) the date on which we have issued more than \$1.07 billion in non-convertible debt during the prior three-year period. We cannot predict if investors will find our common stock less attractive because we may rely on certain reporting exemptions available to emerging growth companies. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

Based on our non-affiliate public float as of June 30, 2017, on December 31, 2017, we will lose our status as an emerging growth company, our auditors will be required to formally attest to the effectiveness of our internal control over financial reporting pursuant to Section 404 and we will no longer be able to take advantage of exemptions from reporting requirements available to emerging growth companies.

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

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

adverse results or delays in our nonclinical studies or clinical trials;

reports of adverse events in other treatments for SCD, IPF or other indications that we may pursue, or clinical trials of such products;

any delay in filing an IND or NDA for any of our product candidates that we may develop and any adverse development or perceived adverse development with respect to the FDA's review of that IND or NDA;

failure to develop successfully and commercialize our lead product candidate GBT440 or any other product candidates that we may develop;

adverse regulatory decisions affecting our product candidates or development programs;



inability to obtain additional funding;

our failure to prosecute, maintain or enforce our intellectual property rights;

changes in laws or regulations applicable to future products;

inability to obtain adequate product supply for our product candidates or the inability to do so at acceptable prices;

introduction of new products, services or technologies by our competitors;

failure to enter into strategic collaborations;

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

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

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

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

additions or departures of key scientific or management personnel;

significant lawsuits, including patent or stockholder litigation;

changes in the market valuations of similar companies;

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

trading volume of our common stock; and

the other risks described in this Risk Factors section.



**Table of Contents**

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

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

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

the timing and cost of, and level of investment in, research and development activities relating to our product candidates, which may change from time to time;

the timing and success or failure of clinical trials for our product candidates or competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners;

our ability to obtain regulatory approval for our product candidates, and the timing and scope of any such approvals we may receive;

the cost of manufacturing our product candidates, which may vary depending on the quantity of production and the terms of our agreements with manufacturers;

our ability to attract, hire and retain qualified personnel;

expenditures that we will or may incur to acquire or develop additional product candidates and technologies;

the level of demand for our product candidates, should they receive approval, which may vary significantly;

future accounting pronouncements or changes in our accounting policies;

the risk/benefit profile, cost and reimbursement policies with respect to our products candidates, if approved, and existing and potential future drugs that compete with our product candidates; and

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

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

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

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

## **Table of Contents**

Pursuant to our 2015 Stock Option and Incentive Plan, or the 2015 Plan, we are authorized to grant stock options and other equity-based awards to our employees, directors and consultants. The number of shares available for future grant under the 2015 Plan will automatically increase each year by up to 4% of all shares of our capital stock outstanding as of December 31 of the prior calendar year, subject to the ability of our board of directors or compensation committee to take action to reduce the size of the increase in any given year. In addition, in January 2017 our board of directors approved our 2017 Inducement Equity Plan, or 2017 Inducement Plan, to enable us and our subsidiaries to grant non-qualified stock options and other equity-based awards to induce highly-qualified prospective officers and employees who are not currently employed by us or our subsidiaries to accept employment with us or our subsidiaries. The number of shares initially reserved for grant under the 2017 Inducement Plan is 300,000 shares, subject to adjustment for reorganization, recapitalization, stock dividend, stock split, or similar changes in our capital stock. In addition, we have reserved shares of common stock for issuance pursuant to our 2015 Employee Stock Purchase Plan, or 2015 ESPP, which number of shares will automatically increase each year on January 1, from January 1, 2016 to January 1, 2025, by the lesser of (i) 3,000,000 shares of common stock, (ii) 1% of all shares of our capital stock outstanding as of December 31 of the prior calendar year, or (iii) such lesser number of shares as determined by the administrator of our 2015 ESPP. Currently, we plan to register the increased number of shares available for issuance under the 2015 Plan and the 2015 ESPP each year. If our board of directors elects to increase the number of shares available for future grant under the 2015 Plan, the 2017 Inducement Plan or the 2015 ESPP, our stockholders may experience additional dilution, and our stock price may fall.

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

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

We have also registered all shares of our common stock subject to options or other equity awards issued or reserved for future issuance under our equity incentive plans. As a result, these shares will be available for sale in the public market subject to vesting arrangements and exercise of options, and restrictions under applicable securities laws. In addition, our directors, executive officers and certain affiliates have established or may in the future establish programmed selling plans under Rule 10b5-1 of the Securities Exchange Act of 1934, as amended, for the purpose of effecting sales of our common stock. If any of these events cause a large number of our shares to be sold in the public market, the sales could reduce the trading price of our common stock and impede our ability to raise future capital.

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

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

Our executive officers, directors, five percent stockholders and their affiliates beneficially owned approximately 37.4% of our outstanding common stock as of July 31, 2017, based on the latest publicly available information.

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

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

We have broad discretion over the use of our capital resources consisting of cash and cash equivalents and short and long-term marketable securities. You may not agree with our decisions, and our use of our capital resources may not yield any returns to our stockholders. We expect to use our existing capital resources to continue the clinical development of GBT440 for the treatment of SCD, including our Phase 3 HOPE study and our ongoing Phase 2a clinical trial in SCD and planned clinical pharmacology studies, our Phase 1 and Phase 2a clinical trials of GBT440 for the treatment of IPF and other hypoxemic pulmonary disorders, our other research and development activities, and for working capital and general corporate purposes. Our failure to apply our capital resources effectively could compromise our ability to pursue our growth strategy and we might not be able to yield a significant return, if any, on our investment of these resources. Our stockholders will not have the opportunity to influence our decisions on how to use our capital resources.

**Table of Contents**

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

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

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

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

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

prohibit stockholder action by written consent;

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

provide that our directors may be removed only for cause;

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

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

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

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

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

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

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

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

We have incurred substantial losses during our history and do not expect to become profitable in the near future and we may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire. Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an ownership change, generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards, or NOLs, and other pre-change tax attributes (such as research tax credits) to offset its post-change income or taxes may be limited. We experienced an ownership change as a result of our IPO, however we do not believe that this ownership change will significantly limit our ability to use these pre-change NOL carryforwards. We may experience subsequent shifts in our stock ownership, including as a result of our follow-on offering, some of which are outside of our control. As a result, if we earn net taxable income, our ability to use our pre-change NOL carryforwards to offset U.S. federal taxable income may become subject to limitations, which could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.



**Table of Contents**

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

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

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

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

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

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

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

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

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

**Table of Contents**

**Item 2. Unregistered Sales of Equity Securities and Use of Proceeds**

a) *Sales of Unregistered Securities*

None.

b) *Use of Proceeds from our Initial Public Offering of Common Stock*

No change.

c) *Repurchases of Shares or of Company Equity Securities*

None.

**Item 3. Defaults Upon Senior Securities**

None.

**Item 4. Mine Safety Disclosures**

Not applicable.

**Item 5. Other Information**

None.

**Item 6. Exhibits**

See the Exhibit Index on the page immediately following the signature page to this Quarterly Report on Form 10-Q for a list of the exhibits filed as part of this Quarterly Report, which Exhibit Index is incorporated herein by reference.

**Table of Contents**

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

**Global Blood Therapeutics, Inc.**

Date: August 7, 2017

By: /s/ Ted W. Love, M.D.  
Ted W. Love, M.D.  
President and Chief Executive Officer  
(Principal Executive Officer)

Date: August 7, 2017

By: /s/ Jeffrey Farrow  
Jeffrey Farrow  
Chief Financial Officer  
(Principal Financial Officer)

**Table of Contents****EXHIBIT INDEX**

<b>Exhibit</b>	<b>Exhibit Description</b>	<b>Incorporated by Reference</b>			<b>Filed</b>
		<b>Form</b>	<b>Date</b>	<b>Number</b>	
3.1	Restated Certificate of Incorporation.	S-1/A	7/31/2015	3.2	
3.2	Amended and Restated Bylaws.	S-1/A	7/31/2015	3.4	
4.1	Specimen Common Stock Certificate	S-1/A	7/31/2015	4.1	
31.1	Certification of Principal Executive Officer required by Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				X
31.2	Certification of Principal Financial Officer required by Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				X
32.1*	Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				X
101.INS	XBRL Instance Document				X
101.SCH	XBRL Taxonomy Extension Schema Document				X
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document				X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document.				X
101.LAB	XBRL Taxonomy Extension Label Linkbase Document.				X
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document.				X

\* The certification attached as Exhibit 32.1 that accompanies this Quarterly Report on Form 10-Q is not deemed filed with the SEC and is not to be incorporated by reference into any filing of Global Blood Therapeutics, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Form 10-Q, irrespective of any general incorporation language contained in such filing.