

**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 September 30, 2020

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)

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

**181 Oyster Point Boulevard**  
**South San Francisco, CA 94080**  
(Address of principal executive offices)

**(650) 741-7700**  
(Registrant's telephone number, including area code)

**Securities registered pursuant to Section 12(b) of the Act:**

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value \$0.001 per share	GBT	The NASDAQ Global Select Market

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 every Interactive Data File required to be submitted 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 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.

Large accelerated filer	<input checked="" type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/>	Smaller reporting company	<input type="checkbox"/>
		Emerging growth company	<input type="checkbox"/>

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.

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

As of October 30, 2020, there were 61,796,443 shares of the registrant's Common Stock, par value \$0.001 per share, outstanding.

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PART I. – FINANCIAL INFORMATION

Item 1. Financial Statements

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

	<u>September 30, 2020</u>	<u>December 31, 2019</u>
	<u>(Unaudited)</u>	
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 418,402	\$ 302,237
Short-term marketable securities	113,523	307,732
Accounts receivable, net	14,130	2,637
Inventories	33,808	1,277
Prepaid expenses and other current assets	14,801	14,114
Total current assets	594,664	627,997
Property and equipment, net	38,697	27,113
Long-term marketable securities	3,275	85,030
Operating lease right-of-use assets	51,337	52,775
Restricted cash	2,417	2,395
Other assets, noncurrent	874	789
Total assets	\$ 691,264	\$ 796,099
<b>Liabilities and Stockholders' Equity</b>		
Current liabilities:		
Accounts payable	\$ 7,882	\$ 10,621
Accrued liabilities	47,466	41,358
Accrued compensation	17,953	17,578
Other liabilities, current	4,645	1,896
Total current liabilities	77,946	71,453
Long-term debt	73,880	73,559
Operating lease liabilities, noncurrent	80,439	72,359
Other liabilities, noncurrent	1,344	34
Total liabilities	233,609	217,405
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, \$0.001 par value, 5,000,000 shares authorized as of September 30, 2020 (unaudited) and December 31, 2019; no shares issued and outstanding	—	—
Common stock, \$0.001 par value, 150,000,000 shares authorized as of September 30, 2020 (unaudited) and December 31, 2019, respectively; 61,756,658 and 60,644,380 shares issued and outstanding as of September 30, 2020 (unaudited) and December 31, 2019, respectively	61	61
Additional paid-in capital	1,381,537	1,316,795
Accumulated other comprehensive income	720	754
Accumulated deficit	(924,663)	(738,916)
Total stockholders' equity	457,655	578,694
Total liabilities and stockholders' equity	\$ 691,264	\$ 796,099

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

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

	<u>Three Months Ended September 30,</u>		<u>Nine Months Ended September 30,</u>	
	<u>2020</u>	<u>2019</u>	<u>2020</u>	<u>2019</u>
Product sales, net	\$ 36,889	\$ —	\$ 82,508	\$ —
Costs and operating expenses:				
Cost of sales	513	—	1,025	—
Research and development	40,196	39,088	114,054	109,564
Selling, general and administrative	54,491	29,654	151,227	72,503
Total costs and operating expenses	<u>95,200</u>	<u>68,742</u>	<u>266,306</u>	<u>182,067</u>
Loss from operations	(58,311)	(68,742)	(183,798)	(182,067)
Other income (expense):				
Interest income	881	4,372	5,251	11,909
Interest expense	(2,291)	(146)	(6,887)	(487)
Other expenses, net	(160)	(31)	(313)	(146)
Total other income (expense), net	<u>(1,570)</u>	<u>4,195</u>	<u>(1,949)</u>	<u>11,276</u>
Net loss	(59,881)	(64,547)	(185,747)	(170,791)
Other comprehensive loss:				
Net unrealized gain (loss) on marketable securities, net of tax	(507)	(213)	(35)	1,026
Comprehensive loss	<u>\$ (60,388)</u>	<u>\$ (64,760)</u>	<u>\$ (185,782)</u>	<u>\$ (169,765)</u>
Basic and diluted net loss per common share	<u>\$ (0.97)</u>	<u>\$ (1.07)</u>	<u>\$ (3.04)</u>	<u>\$ (2.96)</u>
Weighted-average number of shares used in computing basic and diluted net loss per common share	<u>61,573,877</u>	<u>60,098,093</u>	<u>61,160,984</u>	<u>57,637,318</u>

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

**GLOBAL BLOOD THERAPEUTICS, INC.**  
**Condensed Consolidated Statements of Stockholders' Equity**  
**(Unaudited)**  
**(In thousands, except share amounts)**

	Common Stock		Additional Paid- In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2019	60,644,380	\$ 61	\$1,316,795	\$ 754	\$ (738,916)	\$ 578,694
Issuance of common stock upon exercise of stock options	33,937	—	967	—	—	967
Issuance of common stock upon vesting of restricted share units, net of shares withheld for employee taxes	160,594	—	(2,099)	—	—	(2,099)
Issuance of common stock pursuant to ESPP purchases	47,460	—	1,870	—	—	1,870
Stock-based compensation expense	—	—	16,705	—	—	16,705
Net unrealized gain on marketable securities	—	—	—	461	—	461
Net loss	—	—	—	—	(73,026)	(73,026)
Balance at March 31, 2020	60,886,371	\$ 61	\$1,334,238	\$ 1,215	\$ (811,942)	\$ 523,572
Issuance of common stock upon exercise of stock options	334,454	—	8,018	—	—	8,018
Issuance of common stock upon vesting of restricted share units, net of shares withheld for employee taxes	110,162	—	(74)	—	—	(74)
Stock-based compensation expense	—	—	17,128	—	—	17,128
Net unrealized gain on marketable securities	—	—	—	12	—	12
Net loss	—	—	—	—	(52,840)	(52,840)
Balance at June 30, 2020	61,330,987	\$ 61	\$1,359,310	\$ 1,227	\$ (864,782)	\$ 495,816
Issuance of common stock upon exercise of stock options	121,619	—	3,312	—	—	3,312
Issuance of common stock upon vesting of restricted share units, net of shares withheld for employee taxes	253,447	—	(2,990)	—	—	(2,990)
Issuance of common stock pursuant to ESPP purchases	50,605	—	2,266	—	—	2,266
Stock-based compensation expense	—	—	19,639	—	—	19,639
Net unrealized loss on marketable securities	—	—	—	(507)	—	(507)
Net loss	—	—	—	—	(59,881)	(59,881)
Balance at September 30, 2020	<u>61,756,658</u>	<u>\$ 61</u>	<u>\$1,381,537</u>	<u>\$ 720</u>	<u>\$ (924,663)</u>	<u>\$ 457,655</u>

	Common Stock		Additional Paid- In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2018	55,640,299	\$ 56	\$1,044,941	\$ (48)	\$ (472,150)	\$ 572,799
Issuance of common stock upon equity offerings, net of issuance costs	511,363	—	21,246	—	—	21,246
Issuance of common stock upon exercise of stock options	52,288	—	817	—	—	817
Issuance of common stock upon vesting of restricted share units, net of shares withheld for employee taxes	78,155	—	(686)	—	—	(686)
Issuance of common stock pursuant to ESPP purchases	30,745	—	1,128	—	—	1,128
Vesting of restricted stock purchases	24,195	—	80	—	—	80
Stock-based compensation expense	—	—	9,453	—	—	9,453
Net unrealized gain on marketable securities	—	—	—	624	—	624
Net loss	—	—	—	—	(48,923)	(48,923)
Balance at March 31, 2019	56,337,045	\$ 56	\$1,076,979	\$ 576	\$ (521,073)	\$ 556,538
Issuance of common stock upon equity offerings, net of issuance costs	3,375,527	3	192,294	—	—	192,297
Issuance of common stock upon exercise of stock options	123,513	1	2,331	—	—	2,332
Issuance of common stock upon vesting of restricted share units, net of shares withheld for employee taxes	47,258	—	(1,297)	—	—	(1,297)
Vesting of restricted stock purchases	22,856	—	78	—	—	78
Stock-based compensation expense	—	—	10,948	—	—	10,948
Net unrealized gain on marketable securities	—	—	—	615	—	615
Net loss	—	—	—	—	(57,321)	(57,321)
Balance at June 30, 2019	59,906,199	\$ 60	\$1,281,333	\$ 1,191	\$ (578,394)	\$ 704,190
Issuance of common stock upon equity offerings, net of issuance costs	100,000	—	6,126	—	—	6,126
Issuance of common stock upon exercise of stock options	18,439	—	386	—	—	386
Issuance of common stock upon vesting of restricted share units, net of shares withheld for employee taxes	151,120	—	(1,532)	—	—	(1,532)
Issuance of common stock pursuant to ESPP purchases	32,535	—	1,234	—	—	1,234
Stock-based compensation expense	—	—	12,453	—	—	12,453
Net unrealized loss on marketable securities	—	—	—	(213)	—	(213)
Net loss	—	—	—	—	(64,547)	(64,547)
Balance at September 30, 2019	<u>60,208,293</u>	<u>\$ 60</u>	<u>\$1,300,000</u>	<u>\$ 978</u>	<u>\$ (642,941)</u>	<u>\$ 658,097</u>

See accompanying notes to unaudited condensed consolidated financial statements.

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

	<b>Nine Months Ended</b>	
	<b>September 30,</b>	
	<b>2020</b>	<b>2019</b>
<b>CASH FLOWS FROM OPERATING ACTIVITIES:</b>		
Net loss	\$(185,747)	\$(170,791)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	6,925	6,294
Amortization (accretion) of premium (discount) on marketable securities	37	(1,724)
Non-cash interest expense	1,243	—
Amortization of operating lease right-of-use assets	901	332
Stock-based compensation	52,100	32,854
Changes in operating assets and liabilities:		
Accounts receivables	(11,493)	—
Inventories	(30,853)	—
Prepaid expenses and other assets	(1,764)	(5,217)
Accounts payable	(2,821)	1,088
Accrued liabilities	2,299	5,557
Accrued compensation	375	415
Other liabilities, current	(651)	(30)
Operating lease liabilities	1,309	(858)
Other liabilities, noncurrent	1,344	—
Net cash used in operating activities	<u>(166,796)</u>	<u>(132,080)</u>
<b>CASH FLOWS FROM INVESTING ACTIVITIES:</b>		
Purchase of property and equipment	(4,190)	(1,198)
Purchase of marketable securities	(57,936)	(330,130)
Maturities of marketable securities	333,828	233,837
Net cash provided by (used in) investing activities	<u>271,702</u>	<u>(97,491)</u>
<b>CASH FLOWS FROM FINANCING ACTIVITIES:</b>		
Proceeds from issuance of common stock in public offering, net of issuance costs	—	219,443
Proceeds from issuance of common stock in settlement of employee stock purchase plan and exercise of stock options	16,574	5,890
Payments of debt issuance costs	(130)	—
Tax paid related to net share settlement of equity awards	(5,163)	(3,515)
Net cash provided by financing activities	<u>11,281</u>	<u>221,818</u>
Net increase (decrease) in cash, cash equivalents and restricted cash	116,187	(7,753)
Cash, cash equivalents and restricted cash at beginning of period	304,632	277,752
Cash, cash equivalents and restricted cash at end of period	<u>\$ 420,819</u>	<u>\$ 269,999</u>
<b>SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:</b>		
Cash paid for interest	<u>\$ 5,144</u>	<u>\$ —</u>
<b>SUPPLEMENTAL DISCLOSURES OF NON-CASH INVESTING AND FINANCING INFORMATION:</b>		
Leasehold improvements paid for by landlord	<u>\$ 10,709</u>	<u>\$ 4,367</u>
Accrued purchase of property and equipment	<u>\$ 3,943</u>	<u>\$ 76</u>
Accrued issuance costs	<u>\$ (52)</u>	<u>\$ —</u>
Operating lease liabilities arising from obtaining right-of-use assets	<u>\$ 205</u>	<u>\$ 25,930</u>
<b>RECONCILIATION OF CASH, CASH EQUIVALENTS, AND RESTRICTED CASH TO THE CONDENSED CONSOLIDATED BALANCE SHEETS</b>		
Cash and cash equivalents	\$ 418,402	\$ 267,604
Restricted cash	2,417	2,395
Total cash and cash equivalents and restricted cash	<u>\$ 420,819</u>	<u>\$ 269,999</u>

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



**GLOBAL BLOOD THERAPEUTICS, INC.**  
**Notes to Unaudited Condensed Consolidated Financial Statements**

**1. Organization and Basis of Presentation**

Global Blood Therapeutics, Inc., or the Company, we, us, or our, was incorporated in Delaware in February 2011 and commenced operations in May 2012. We are a biopharmaceutical company dedicated to the discovery, development and delivery of life-changing treatments that provide hope to underserved patient communities. In late November 2019, we received U.S. Food and Drug Administration, or FDA, accelerated approval for our first medicine, Oxbryta® (voxelotor) tablets for the treatment of sickle cell disease, or SCD, in adults and children 12 years of age and older. In early December 2019, we began to make Oxbryta available to patients through our specialty pharmacy partner network. Our principal operations are based in South San Francisco, California, and we operate in one segment.

***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 commercial launch of Oxbryta, research and development and business development activities. Since inception through September 30, 2020, we have incurred cumulative net losses of \$924.7 million. We expect to incur additional losses for the foreseeable future to commercialize Oxbryta and conduct product research and development, and expect to potentially raise additional capital to fully implement our business plan. If needed, we intend to raise such capital through borrowings, the issuance of additional equity, and potentially through strategic alliances with partner companies or other transactions. 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 twelve months subsequent to the issuance of these financial statements.

**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, or U.S. GAAP, and applicable rules and regulations of the Securities and Exchange Commission, or 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, 2019 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 nine months ended September 30, 2020 are not necessarily indicative of the results to be expected for the year ending December 31, 2020 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, 2019 included in our Annual Report on Form 10-K, filed with the SEC on February 26, 2020.

***Use of Estimates***

The preparation of the accompanying 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 consolidated financial statements, and the reported amounts of revenues 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.

***Concentration of Risk***

***Credit Risk***

We invest in a variety of financial instruments and, by our Board approved investment policy, limit the amount of credit exposure with any one issuer, industry or geographic area for investments other than instruments backed by the U.S. federal government.

### *Major Customers*

We have entered into distribution agreements with certain limited specialty pharmacies and specialty distributors. For the nine months ended September 30, 2020, our two largest customers represented approximately 94% of our product revenue and approximately 86% of our accounts receivable balance at September 30, 2020.

### *Major Suppliers*

We do not currently have any of our own manufacturing facilities, and therefore depend on an outsourced manufacturing strategy for the production of Oxbritya for commercial use and for the production of our product candidates for clinical trials. We have contracts in place with one third-party manufacturer that is approved for the commercial production of Oxbritya and one third-party supplier that is approved for Oxbritya's active pharmaceutical ingredient. Although there are potential sources of supply other than our existing manufacturers and suppliers, any new supplier would be required to qualify under applicable regulatory requirements.

### *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, 2019.

### *Accounting Pronouncements Adopted*

In August 2018, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, No. 2018-15, *Intangibles—Goodwill and Other—Internal-Use Software (Subtopic 350-40), Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract*, or ASU 2018-15. ASU No. 2018-15 requires a customer that is a party to a cloud computing service contract to follow the internal-use software guidance in Subtopic 350-40 to determine which implementation costs to capitalize and which costs to expense. The amendments in this update are effective for annual reporting periods beginning after December 15, 2019, and interim periods within those fiscal years. The amendments in this update should be applied either retrospectively or prospectively to all implementation costs incurred after the date of adoption. We adopted ASU No. 2018-15 in the first quarter of 2020 and applied the guidance prospectively to the implementation costs incurred in our implementations of various cloud computing arrangements that are service contracts. The adoption of this new standard did not have a material impact on our condensed consolidated financial statements.

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement (Topic 820)*. The new standard modifies the disclosure requirements on fair value measurements in Topic 820, Fair Value Measurement, including removals of, modification to, and additional disclosure requirements from Topic 820. The amendment of ASU No. 2018-13 removes disclosure requirements from Topic 820 in the areas of (1) the amount of and reasons for transfers between Level 1 and Level 2 of the fair value hierarchy, (2) the policy for timing of transfers between levels, and (3) the valuation processes for Level 3 fair value measurements. The amendments in this update are effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019. Except for certain amendments related to Level 3 fair value measurements, all the other amendments should be applied retrospectively to all periods presented upon their effective date. We adopted ASU No. 2018-13 in the first quarter of 2020 and applied the guidance retrospectively. The adoption of this new standard did not have a material impact on our condensed consolidated financial statements.

In June 2016, the FASB issued ASU No. 2016-13, *Measurement of Credit Losses on Financial Instruments (Topic 326)*, which amends the guidance on the impairment of financial instruments. The new standard adds to U.S. GAAP an impairment model that is based on expected losses rather than incurred losses, which is known as the current expected credit loss, or CECL model. The CECL model applies to most debt instruments (other than those measured at fair value), trade and other receivables, financial guarantee contracts, and loan commitments. Available-for-sale debt securities are scoped out of this guidance. Our investment portfolio primarily consists of available-for-sale debt securities carried at fair value. Our accounts receivable are not long term in nature and we do not expect to write off accounts receivable. The amendments in this update are effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019. We adopted ASU No. 2016-13 in the first quarter of 2020 and applied the guidance prospectively. The adoption of this new standard did not have a material impact on our condensed consolidated financial statements.

### 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, accounts receivables, 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.

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):

	September 30, 2020			
	Total	Level 1	Level 2	Level 3
<b>Financial Assets:</b>				
Money market funds	\$417,136	\$417,136	\$ —	\$ —
Corporate debt securities	56,315	—	56,315	—
U.S. government agency securities	20,988	—	20,988	—
Certificates of deposits	1,706	—	1,706	—
U.S. government securities	37,789	—	37,789	—
<b>Total financial assets</b>	<b>\$533,934</b>	<b>\$417,136</b>	<b>\$116,798</b>	<b>\$ —</b>
	December 31, 2019			
	Total	Level 1	Level 2	Level 3
<b>Financial Assets:</b>				
Money market funds	\$250,535	\$250,535	\$ —	\$ —
Corporate debt securities	152,149	—	152,149	—
U.S. government agency securities	95,032	—	95,032	—
Certificates of deposits	6,282	—	6,282	—
U.S. government securities	140,244	—	140,244	—
<b>Total financial assets</b>	<b>\$644,242</b>	<b>\$250,535</b>	<b>\$393,707</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 September 30, 2020 and December 31, 2019, 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 or A/A2, or higher, by Moody's and Standard and Poor's.

#### 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):

	September 30, 2020				December 31, 2019			
	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	\$417,136	\$ —	\$ —	\$ 417,136	\$250,535	\$ —	\$ —	\$ 250,535
Corporate debt securities	55,905	410	—	56,315	151,773	384	(8)	152,149
U.S. government agency securities	20,912	76	—	20,988	94,963	73	(4)	95,032
Certificates of deposits	1,696	10	—	1,706	6,239	43	—	6,282
U.S. government securities	37,565	224	—	37,789	139,978	266	—	140,244
<b>Total</b>	<b>\$533,214</b>	<b>\$ 720</b>	<b>\$ —</b>	<b>\$ 533,934</b>	<b>\$643,488</b>	<b>\$ 766</b>	<b>\$ (12)</b>	<b>\$ 644,242</b>

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

	September 30, 2020	December 31, 2019
Cash and cash equivalents	\$ 417,136	\$ 251,480
Short-term marketable securities	113,523	307,732
Long-term marketable securities	3,275	85,030
<b>Total</b>	<b>\$ 533,934</b>	<b>\$ 644,242</b>

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.

#### 5. Balance Sheet Components

##### *Inventories*

We began capitalizing inventories in November 2019 once the FDA approved Oxbryta. Inventories consist of the following (in thousands):

	September 30, 2020	December 31, 2019
Raw materials	\$ 9,043	\$ 700
Work-in-process	23,355	525
Finished goods	1,410	52
<b>Total inventories</b>	<b>\$ 33,808</b>	<b>\$ 1,277</b>

## Property and Equipment, Net

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

	September 30, 2020	December 31, 2019
Laboratory equipment	\$ 11,559	\$ 8,314
Computer equipment	2,590	2,224
Leasehold improvements	32,281	13,785
Construction-in-progress	761	19,289
Total property and equipment	47,191	43,612
Less: accumulated depreciation and amortization	(8,494)	(16,499)
Property and equipment, net	<u>\$ 38,697</u>	<u>\$ 27,113</u>

## Accrued liabilities

Accrued liabilities consist of the following (in thousands):

	September 30, 2020	December 31, 2019
Accrued research and development costs	\$ 9,694	\$ 26,480
Accrued manufacturing costs	23,779	9,466
Accrued professional and consulting services	3,411	4,564
Accrued sales deductions	6,116	529
Other	4,466	319
Total accrued liabilities	<u>\$ 47,466</u>	<u>\$ 41,358</u>

## Other liabilities, current

Other liabilities consist of the following (in thousands):

	September 30, 2020	December 31, 2019
Operating lease liabilities, current	\$ 4,645	\$ 1,866
Other payable	—	30
Total other liabilities, current	<u>\$ 4,645</u>	<u>\$ 1,896</u>

## 6. Long-term Debt

### Term Loan

On December 17, 2019, we entered into the Loan Agreement, or Term Loan, with funds managed by Pharmakon Advisors LP, which are BioPharma Credit PLC, as collateral agent, Biopharma Credit Investments V (Master) LP, as a lender, and BPCR Limited Partnership, as a lender, and collectively, the Lenders, for a senior secured credit facility consisting of an initial tranche of \$75.0 million and the option to draw an additional \$75.0 million until December 31, 2020. The first tranche, in the amount of \$75.0 million, was funded in connection with the closing date of the Term Loan in December 2019. In June 2020, in accordance with the terms of the Loan Agreement, we provided notification to Lenders of our intention to draw the second tranche of the Term Loan, in the amount of \$75.0 million, prior to December 31, 2020, subject to certain closing conditions. As of September 30, 2020, the second tranche of the Term Loan has not been drawn.

The Term Loan carries a 72-month term. The Term Loan bears interest at a floating per annum interest rate equal to 7.00% plus the greater of (a) the 3-month LIBOR rate and (b) 2%. In the event we default, the interest rate would be 3% above the rate that is otherwise applicable thereto. Interest on amounts outstanding are payable quarterly in arrears. The Term Loan repayment schedule provides for interest only payments for the first 39 months, followed by consecutive equal quarterly payments of principal and interest commencing in March 2023 and continuing through the maturity of December 2025.

We have the option to prepay all or a portion of the borrowed amounts under the Term Loan. If we exercise this option, we must pay a prepayment fee between 1% and 3% of the principal amount being prepaid depending on the timing of the prepayment, or Prepayment Fee. If the prepayment occurs before December 2022, we must also pay an amount equal to the sum of all interest that would have accrued and been payable from date of prepayment through December 2022, or Make Whole Amount. We are obligated to pay an additional fee to the Lenders determined by multiplying the principal amount being paid or prepaid multiplied by 2%, or Paydown Fee, when such payments are made.

In the event of default or change in control, all unpaid principal and all accrued and unpaid interest amounts (if any) become immediately due and payable, at which point, we will be subject to the Prepayment Fee, the Make Whole Amount (if any) and the Paydown Fee. Events of default include, but are not limited to, a payment default, a material adverse change, and insolvency. The obligations under the Term Loan are secured by a first priority security interest in and a lien on substantially all of our assets, subject to certain exceptions.

Debt issuance costs paid directly to the Lenders of \$1.1 million and the other debt issuance costs of \$0.4 million were accounted for as discounts on the Term Loan. These debt discounts along with the Paydown Fee are being amortized or accreted to interest expenses throughout the life of the Term Loan using the effective interest rate method. As of September 30, 2020, there were unamortized issuance costs and debt discounts of \$1.4 million, which were recorded as a direct deduction from the Term Loan on the condensed consolidated balance sheet. In addition, we paid the Lenders \$1.1 million for the option to draw the additional \$75.0 million, which was capitalized as a deferred asset and which is included in other assets, current and amortized on a straight-line basis through December 31, 2020. As of September 30, 2020, the unamortized fee for the option to draw the additional funds was \$0.3 million.

Future payments of principal and interest on the Term Loan as of September 30, 2020 were as follows (in thousands):

<u>Year ending December 31,</u>	<u>Amount</u>
2020 (three months)	\$ 1,688
2021	6,750
2022	6,750
2023	31,406
2024	29,156
2025	26,906
Total minimum payments	102,656
Less amount representing interest	(26,156)
Less amount representing Paydown Fee	(1,500)
Long-term debt, gross	75,000
Discount on notes payable	(1,386)
Accretion of Paydown Fee	266
Long-term debt	<u>\$ 73,880</u>

## 7. Commitments and Contingencies

### Leases

We have operating leases for our headquarters, where we have office and research and development laboratory facilities, and equipment. Our leases have remaining lease terms of 1 to 10 years. Most of these leases require monthly lease payments that may be subject to annual increases throughout the lease term. Certain of these leases include renewal options at our election, with renewal terms that can extend the lease term from 1 to 10 years. These optional periods have not been considered in the determination of the right-of-use, or ROU, assets or lease liabilities associated with these leases as we did not consider it reasonably certain that we would exercise the options.

Lease costs included in operating expenses in the consolidated statement of operations in relation to these operating leases were \$3.1 million and \$1.4 million for the three months ended September 30, 2020 and 2019, respectively; and \$9.3 million and \$4.6 million for the nine months ended September 30, 2020 and 2019, respectively. Included in these lease costs were variable lease costs, which were not included within the measurement of our operating ROU assets and operating lease liabilities in the amount of \$0.7 million and \$0.4 million for the three months ended September 30, 2020 and 2019, respectively; and \$2.0 million and \$1.8 million for the nine months ended September 30, 2020 and 2019, respectively. The variable lease cost is comprised primarily of our proportionate share of operating expenses, property taxes, and insurance in relation with our facility lease. These costs are classified as operating lease expense due to our election to not separate lease and non-lease components.

Supplemental cash flow information related to leases for the period reported is as follows (in thousands, except weighted-average remaining lease term and weighted-average discount rate):

	<b>Nine Months Ended September 30,</b>	
	<b>2020</b>	<b>2019</b>
ROU assets obtained in exchange for new operating lease	\$ 205	\$ 14,177
Cash paid for amounts included in the measurement of lease liabilities	4,811	3,352
Weighted-average remaining lease term of operating leases (in years)	9.5	8.2
Weighted-average discount rate of operating leases	8.7%	13.2%

The majority of our lease costs are driven by our operating lease for our headquarters in South San Francisco, where we have office and research and development laboratory facilities.

In March 2017, we entered into a noncancelable operating lease, or Original Lease, for approximately 67,185 square feet of space in South San Francisco, California, or Prior Premises. The Original Lease term commenced in November 2017 as we gained control over physical access to the Prior Premises. We acquired \$11.1 million of leasehold improvements at the Prior Premises with the tenant inducement allowance provided under the Original Lease. We are required to repay \$1.7 million of the tenant inducement allowance, or Initial Allowance, to the landlord in the form of additional monthly rent with interest applied over the term of the Original Lease.

In August 2018, we entered into an amendment to the Original Lease, or Lease Amendment, to relocate the leased premises from the Prior Premises to a to-be-constructed building consisting of approximately 164,150 rentable square feet of space, or Substitute Premises. The date on which we became responsible for paying rent under the Lease Amendment was March 13, 2020, or the Substitute Premises Payment Commencement Date. The Lease Amendment has a contractual term, or Substitute Premises Term, of 10 years from the Substitute Premises Payment Commencement Date, which was subsequently determined to be in March 2020. The Lease Amendment grants us an option to extend the Lease Amendment for an additional 10-year period. Future minimum rental payments under the Lease Amendment during the 10-year term are \$121.5 million in the aggregate. Under the Lease Amendment, we are obligated to pay to the landlord certain costs, including taxes and operating expenses. On October 1, 2019, we determined that the Lease Amendment for the Substitute Premises had commenced as we had the right to control the Substitute Premises. The Lease Amendment also provides a tenant inducement allowance of up to \$27.9 million, of which \$4.1 million, if utilized, would be repaid to the landlord in the form of additional monthly rent with interest applied. As of September 30, 2020, we have capitalized \$32.3 million of costs in leasehold improvements within property and equipment, net for construction of leasehold improvements at the Substitute Premises, which were mostly acquired with the tenant inducement provided under the Lease Amendment.

We vacated the Prior Premises and surrendered and delivered the Prior Premises to the landlord in May 2020, upon which time we had no further obligations with respect to the Prior Premises other than with respect to the Initial Allowance, which we will repay to the landlord in the form of additional monthly rent with interest applied over the term of the Original Lease. Upon signing of the Lease Amendment, we re-evaluated the remaining useful life of the leasehold improvements at the Prior Premises and started to amortize the leasehold improvements over the remaining period of expected use, resulting in an acceleration of depreciation expenses for approximately \$3.8 million and \$5.2 million for the nine months ended September 30, 2020 and 2019, respectively.

As of September 30, 2020, the maturities of our operating lease liabilities were as follows (in thousands):

<b><u>Year ending December 31,</u></b>	<b><u>Amount</u></b>
2020 (three months)	\$ 2,885
2021	11,841
2022	12,222
2023	12,584
2024	12,948
2025	13,368
Thereafter	60,507
Total lease payments	126,355
Less: Imputed interest	(41,271)
Present value of operating lease liabilities	<u>\$ 85,084</u>

## Contingencies

In the ordinary course of business, we may be subject to legal claims and regulatory actions that could have a material adverse effect on our business or financial position. We assess our potential liability in such situations by analyzing potential outcomes, assuming various litigation, regulatory and settlement strategies. If we determine a loss is probable and its amount can be reasonably estimated, we accrue an amount equal to the estimated loss.

No losses and no provision for a loss contingency have been recorded to date.

## 8. Stock-Based Compensation

We have three stock-based compensation plans – the Amended and Restated 2017 Inducement Equity Plan, or 2017 Inducement Plan, the Amended and Restated 2015 Stock Option and Incentive Plan, or 2015 Plan, and the 2012 Stock Option and Grant Plan, or 2012 Plan. As of September 30, 2020, there were 1,521,896 shares reserved under the 2017 Inducement Plan and 4,626,324 shares reserved under the 2015 Plan for the future issuance of equity awards. Upon adoption of the 2015 Plan in July 2015, no new awards or grants are permitted under the 2012 Plan. See Note 10 to the Consolidated Financial Statements included in our Annual Report on Form 10-K for the year ended December 31, 2019 for additional information related to these stock-based compensation plans.

### Stock Options

The following summarizes option activity under the 2017 Inducement Plan, 2015 Plan and 2012 Plan:

	Number of Options	Weighted- Average Exercise Price
Outstanding — December 31, 2019	3,573,860	\$ 36.24
Options granted	688,061	65.84
Options exercised	(490,010)	25.10
Options canceled	(355,861)	52.59
Outstanding — September 30, 2020	<u>3,416,050</u>	<u>\$ 42.10</u>

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2020	2019	2020	2019
Expected term (in years)	6.1	6.1	5.1-6.1	5.3-6.1
Volatility	70.7%-71.0%	70.4%-71.2%	69.6%-71.8%	70.4%-72.2%
Risk-free interest rate	0.3%-0.4%	1.4%-1.9%	0.3%-1.8%	1.4%-2.6%
Dividend yield	—	—	—	—

### Restricted Stock Units

The following table summarizes activity of restricted stock units, or RSUs, granted to employees with service-based vesting under the 2017 Inducement Plan and 2015 Plan and related information:

	Number of RSUs	Weighted- Average Grant Date Fair Value
Non-vested units — December 31, 2019	1,848,772	\$ 49.19
RSUs granted	1,338,747	66.14
RSUs vested	(602,579)	50.90
RSUs forfeited	(402,143)	55.93
Non-vested units — September 30, 2020	<u>2,182,797</u>	<u>\$ 57.88</u>



### Market-Condition RSUs Granted to Employees

The Compensation Committee of our Board of Directors granted, effective June 1, 2020, awards of up to an aggregate of 414,700 RSUs to certain of our senior management, including our executive officers, under the 2015 Plan, the vesting of which is contingent upon the achievement of three escalating stock price targets. Upon the achievement of the respective stock price targets, fifty percent of the RSUs allotted to that tranche will vest, while the remaining fifty percent will vest on the first anniversary of the date the stock price target was achieved, subject to the employee's continued employment or other service relationship with the Company through such vesting date. Under the terms of the awards, if the stock price targets are not achieved for all or some of the tranches on or before June 30, 2024, the unvested awards will be automatically terminated and forfeited. The compensation cost for the RSUs with a market condition is not reversed when the market condition is not satisfied. The target prices and vesting tranches are set forth in the table below:

Stock Price Targets	Number of Units Allotted
\$109.20	82,940
\$145.60	145,145
\$182.00	186,615

The grant date fair value of the market-condition awards was estimated using a Monte Carlo simulation model, which includes variables such as the expected volatility of the Company's share price and interest rates to generate potential future outcomes. We recognize the related compensation expense on a straight-line basis over the applicable derived service periods, which are the estimated periods of time that would be required to satisfy the market conditions.

The following table summarizes activity of the market-condition awards under the 2015 Plan and related information (in thousands, except share, per share amounts and vesting period):

	Number of Units	Weighted-Average Grant Date Fair Value	Weighted-Average Remaining Vesting Period (years)	Aggregate Intrinsic Value
Non-vested market-condition awards — December 31, 2019	—	\$ —	—	
Granted	421,000	49.95		
Vested	—	—		
Forfeited	(6,300)	49.95		
Non-vested market-condition awards — September 30, 2020	<u>414,700</u>	\$ 49.95	1.46	<u>\$ 22,867</u>

The following table summarizes the assumptions used to estimate the fair value of the market-condition awards as of the grant date:

Valuation date stock price	\$68.67
Volatility	68.1%
Risk-free interest rate	0.26%
Dividend yield	—

At September 30, 2020, total unrecognized compensation expense related to non-vested market-condition awards was \$16.4 million, which is expected to be recognized over their respective remaining derived service periods. The weighted average derived service period is 1.79 years. For the three months and nine months ended September 30, 2020, we recognized \$3.3 million and \$4.4 million, respectively, in stock-based compensation expense related to the market-condition awards.

### *Stock-Based Compensation Expense*

Total stock-based compensation recognized by function included in the condensed consolidated statements of operations and comprehensive loss was as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2020	2019	2020	2019
Research and development	\$ 4,234	\$ 5,109	\$13,014	\$13,847
Selling, general and administrative	14,928	7,344	39,086	19,007
Total stock-based compensation expense	<u>\$19,162</u>	<u>\$12,453</u>	<u>\$52,100</u>	<u>\$32,854</u>

### **9. 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.

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2020	2019	2020	2019
Options to purchase common stock	3,416,050	3,792,500	3,416,050	3,792,500
Restricted stock units	2,597,497	1,685,777	2,597,497	1,685,777
Total	<u>6,013,547</u>	<u>5,478,277</u>	<u>6,013,547</u>	<u>5,478,277</u>

## 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, 2019, included in our Annual Report on Form 10-K filed with the Securities and Exchange Commission on February 26, 2020, 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 biopharmaceutical company dedicated to the discovery, development and delivery of life-changing treatments that provide hope to underserved patient communities. Founded in 2011, we are delivering on our goal to transform the treatment and care of sickle cell disease, or SCD, a lifelong, devastating inherited blood disorder that 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. As a result of the historic lack of treatment options, patients with SCD suffer serious morbidity and premature mortality.

It is estimated the prevalence of SCD is approximately 100,000 individuals in the United States, where newborn screening is mandatory, more than 100,000 people age 12 years and older in the Gulf Cooperation region, and approximately 52,000 individuals in Europe. The global incidence of SCD is estimated to be 250,000 to 300,000 births annually, and SCD is concentrated in populations of African, Middle Eastern and South Asian descent.

In November 2019, we received U.S. Food and Drug Administration, or FDA, accelerated approval for our first medicine, Oxbryta<sup>®</sup> (voxelotor) tablets for the treatment of SCD in adults and children 12 years of age and older. Oxbryta, an oral therapy taken once daily, is the first FDA-approved treatment that directly inhibits sickle hemoglobin polymerization, the root cause of red blood cell sickling in SCD.

The accelerated approval of Oxbryta is based on clinically meaningful and statistically significant improvements in hemoglobin levels, accompanied by reductions in RBC destruction (hemolysis). Data from the Phase 3 HOPE (Hemoglobin Oxygen Affinity Modulation to Inhibit HbS PolymErization) Study of 274 patients 12 years of age and older with SCD showed that, after 24 weeks of treatment, 51.1% of patients receiving Oxbryta achieved a greater than 1 g/dL increase in hemoglobin compared with 6.5% receiving placebo (p<0.001). The HOPE data also demonstrated corresponding improvements in other markers of hemolysis as well as a favorable safety and tolerability profile for Oxbryta.

In December 2019, we began to make Oxbryta available to patients through our specialty pharmacy partner network. As part of the product launch, we are focused on securing reimbursement and expanding patient access, and we established GBT Source Solutions<sup>™</sup>, a comprehensive program for patients who are prescribed Oxbryta that provides a wide range of practical, educational and financial support customized to each patient's needs.

We are conducting and plan to conduct additional studies of Oxbryta, including our Phase 2a HOPE-KIDS 1 Study (an open-label, single- and multiple-dose Phase 2a study that is evaluating the safety, tolerability, pharmacokinetics and exploratory treatment effect of Oxbryta in pediatric patients aged 4 to 17 years with SCD) and, as a condition of accelerated approval, our Phase 3 HOPE-KIDS 2 Study (a post-approval confirmatory study we initiated in December 2019 that is using transcranial Doppler, or TCD, flow velocity to seek to demonstrate a decrease in stroke risk in children 2 to 15 years of age). We also expect to conduct additional clinical studies of Oxbryta, including to seek to expand the potential approved product label into younger pediatric populations, as well as other post-marketing studies.

In June 2020, we announced plans to submit by mid-2021 a New Drug Application, or NDA, for Oxbryta, which will include a new age-appropriate formulation, for the treatment of SCD in children ages 4 to 11 years under the FDA's accelerated approval pathway. The NDA will include clinical data from our Phase 2a HOPE-KIDS 1 study. The FDA's accelerated approval pathway can

allow for earlier approval of drugs that treat serious conditions and that fill an unmet medical need based on a surrogate endpoint. In addition, we are initiating a multi-center Early Access Program, or EAP, in the United States for pediatric patients to provide access to treatment with Oxbryta prior to potential market authorization for children ages 4 to 11 who, in the judgment of their treating physician, have an urgent need for treatment for their SCD, have no comparable or satisfactory treatment options and are unable to participate in our clinical trials.

In June 2020, we announced plans to submit by mid-2021 a Marketing Authorization Application, or MAA, to the European Medicines Agency, or EMA, seeking full marketing authorization of Oxbryta to treat hemolytic anemia (which is low hemoglobin due to red blood cell destruction) in SCD patients ages 12 years and older. The planned MAA will include data from our Phase 3 HOPE Study and our Phase 2 HOPE-KIDS 1 Study, both of which enrolled patients at clinical sites in Europe. In addition, we announced our intention to initiate an EAP in Europe for patients and physicians who may need access to Oxbryta prior to potential marketing authorization.

In September 2020, we announced our entry into an exclusive agreement with Biopharma-Middle East and Africa to distribute Oxbryta in Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, and the United Arab Emirates, collectively known as the Gulf Cooperation Council, or GCC, region. In the GCC region, the U.S. approval of Oxbryta can be referenced to allow for access to the medicine while health authorities conduct their reviews.

Beyond Oxbryta, we are also engaged in other research and development activities, all of which are currently in earlier development stages, including working on new targets to develop the next generation of treatments for SCD. As part of our efforts to build our pipeline, we regularly evaluate opportunities to in-license, acquire or invest in new business, technology or assets or engage in related discussions with other business entities.

In August 2018, we entered into the License Agreement, or Roche Agreement, with F. Hoffmann-La Roche Ltd. and Hoffmann-La Roche Inc. (together, "Roche") pursuant to which Roche granted us an exclusive and sublicensable worldwide license under certain patent rights and know-how to develop and commercialize inclacumab, a p-selectin inhibitor in development to address pain crises associated with the disease, including any modified compounds targeting p-selectin and derived from inclacumab, for all indications and uses, except diagnostic use. Roche retained a non-exclusive, worldwide, perpetual, royalty-free license to inclacumab solely for any diagnostic use. We are developing inclacumab as a treatment for vaso-occlusive crises, or VOCs, in patients with SCD, and we expect to be able to leverage the safety data from Roche's prior clinical studies, which were not in patients with SCD, as we proceed with our development of inclacumab. We expect to initiate a pivotal clinical study by the end of the first half of 2021.

In December 2019, we entered into the License and Collaboration Agreement, or Syros Agreement, with Syros Pharmaceuticals, Inc., or Syros, to discover, develop and commercialize novel therapies for SCD and beta thalassemia. Under the agreement, Syros will use its leading gene control platform to identify therapeutic targets and discover drugs that potentially induce fetal hemoglobin, and we have an option to obtain an exclusive worldwide license to develop, manufacture and commercialize any compounds or products resulting from the collaboration, subject to Syros' option to co-promote the first product in the United States.

The outbreak of the novel coronavirus, SARS-CoV-2, which causes coronavirus disease 2019 (COVID-19), has evolved into a global pandemic that has impacted our business, including our commercialization of Oxbryta and our research and development activities. For example, we have implemented a temporary work from home policy, temporarily suspended our field team from most in-person interactions, including visits to physician offices, clinics and hospitals as well as in-person meetings with payors, and temporarily delayed or paused certain research and development activities, including screening and enrollment in all GBT-sponsored studies, including our Phase 2a HOPE-KIDS 1 Study, our Phase 3 HOPE-KIDS 2 Study and our dose optimization study that is intended to assess doses of Oxbryta of up to 3,000 mg per day. As we continue to monitor and work toward resumption of all trial activities, we are continuing with administrative trial-start up activities (such as contracting and IRB/EC approvals). Notably, the COVID-19 pandemic has not significantly impacted our supply of Oxbryta. We continue to believe we have an adequate supply of Oxbryta to sustain estimated patient need through the remainder of this year and into late 2021, and we are continuing to produce Oxbryta tablets. In addition, we are continuing to engage with healthcare professionals and payors through increased use of digital and internet-based education and outreach. We have seen a significant decrease in weekly new patient prescriptions for Oxbryta from a peak in early March, and we expect the rate of new patient prescriptions to remain lower, possibly through the fourth quarter of 2020, and potentially longer depending on the course of the pandemic. While we intend to resume normal operations as soon as practicable, we do not know for certain the extent or duration of these and other disruptions or the long-term impact on our business.

We own or jointly own and have exclusively licensed rights to Oxbryta and our product candidates in the United States, Europe and other major markets. We are the sole owner of issued U.S. patents covering Oxbryta, including its composition of matter, methods of use, formulations and polymorphs of Oxbryta. These issued U.S. patents covering Oxbryta will expire between 2032 and 2037, 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 Oxbryta.

We are not profitable and have incurred losses and negative cash flows from operations each year since our inception. Our net losses were \$185.7 million and \$170.8 million for the nine months ended September 30, 2020 and 2019, respectively. As of September 30, 2020, we had an accumulated deficit of \$924.7 million. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs and from selling, general and administrative costs associated with our operations. We had \$418.4 million in cash and cash equivalents and \$116.8 million in marketable securities as of September 30, 2020.

### 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.

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.

### Results of Operations

#### Comparison of the Three Months Ended September 30, 2020 and 2019

	Three Months Ended September 30,		\$ Change	% Change
	2020	2019		
	(in thousands, except percentages)			
Product sales, net	\$ 36,889	\$ —	\$36,889	*
Costs and operating expenses:				
Cost of sales	513	—	513	*
Research and development	40,196	39,088	1,108	3%
Selling, general and administrative	54,491	29,654	24,837	84%
Total costs and operating expenses	95,200	68,742	26,458	38%
Loss from operations	(58,311)	(68,742)	10,431	(15)%
Interest income	881	4,372	(3,491)	(80)%
Interest expenses	(2,291)	(146)	(2,145)	*
Other expenses, net	(160)	(31)	(129)	416%
Net loss	\$(59,881)	\$(64,547)	\$ 4,666	(7)%

\* Change is not meaningful

#### Product sales, net

Product sales consist of sales of Oxbryta, which was approved by the FDA in late November 2019. We commenced shipments of Oxbryta and fully launched with a deployed sales force in December 2019.

The following table summarizes activity with respect to our sales allowances and accruals for the three months ended September 30, 2020 (in thousands):

	Rebates, co-payment assistance, Medicare Part D coverage gap, product returns and distributor fees	Prompt payment discounts and chargebacks	Total
<b>Balances at June 30, 2020</b>	\$ 5,302	\$ 284	\$ 5,586
Provision related to current period sales	4,205	1,462	5,667
Credit or payments made during the period	(3,391)	(1,125)	(4,516)
<b>Balance at September 30, 2020</b>	<b>\$ 6,116</b>	<b>\$ 621</b>	<b>\$ 6,737</b>

### *Cost of sales*

Cost of sales of \$0.5 million for the three months ended September 30, 2020 consists of manufacturing costs incurred after FDA approval for the cost of Oxbritya sold. Prior to receiving FDA approval for Oxbritya in November 2019, we recorded all costs incurred in the manufacture of Oxbritya as research and development expense. We expect to sell inventory previously expensed to research and development over approximately the current year and into late 2021, and accordingly, we expect our costs of product sales of Oxbritya to increase as a percentage of net sales in future periods as we produce and sell inventory that reflects the full cost of manufacturing the product.

### *Research and development*

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

- employee-related expenses, which include salaries, benefits and stock-based compensation;
- expenses incurred under agreements with consultants, third-party research firms, manufacturing organizations for products not approved by the FDA and other regulatory authorities, 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;
- payments upon achievement of certain clinical development and regulatory milestones in relation with license agreement; 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.

A significant component of our total operating expenses is our investment in research and development activities, including the clinical development of Oxbritya. We allocate research and development salaries, benefits, stock-based compensation and indirect costs to Oxbritya, inclacumab 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 Oxbritya and product candidates, and as programs advance into later stages of development and we begin to conduct additional or larger clinical trials. The process of conducting the necessary clinical research to obtain, expand the scope of, and maintain regulatory approvals is costly and time-consuming, and research and development 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 additional revenue from the commercialization and sale of any of our product candidates.

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

	Three Months Ended September 30,		\$ Change	% Change
	2020	2019		
<b>Costs incurred by development program:</b>				
Oxbryta for the treatment of SCD	\$21,082	\$29,294	\$(8,212)	(28)%
Other preclinical programs	11,716	7,664	4,052	53%
Inclacumab for the treatment of SCD	7,398	2,130	5,268	247%
<b>Total research and development expenses</b>	<b><u>\$40,196</u></b>	<b><u>\$39,088</u></b>	<b><u>\$ 1,108</u></b>	<b>3%</b>

Research and development, or R&D, expenses increased by \$1.1 million or 3%, to \$40.2 million for the three months ended September 30, 2020 from \$39.1 million for the three months ended September 30, 2019. The increase was due to a \$5.3 million increase in external costs related to our inclacumab program driven by manufacturing scale-up activities and a \$4.1 million increase in internal and external costs associated with our preclinical programs, including increased pre-clinical research activities related to the Syros Agreement, which we entered into in December 2019. Following the approval of Oxbryta in November 2019, we capitalize manufacturing costs to inventory. The increase was offset by a \$8.2 million decrease in external costs for Oxbryta primarily related to the manufacturing costs that were previously expensed to R&D. R&D related stock-based compensation expense was \$4.2 million for the three months ended September 30, 2020 and \$5.1 million for the three months ended September 30, 2019.

#### ***Selling, general and administrative expenses***

Selling, general and administrative expenses consist primarily of costs incurred in our commercial, executive, finance, corporate development, human resource, information technology, legal, compliance and other general and administrative functions, which include:

- employee-related expenses, which include salaries, benefits and stock-based compensation;
- fees to third party vendors providing customer support services;
- expenses incurred under agreements with consultants; 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 selling, general and administrative costs in the periods in which they are incurred. We expect our selling, general and administrative expenses to continue to grow as we progress through the commercial launch of Oxbryta for the treatment of SCD.

Selling, general and administrative, or SG&A, expenses increased by \$24.8 million or 84%, to \$54.5 million for the three months ended September 30, 2020 from \$29.7 million for the three months ended September 30, 2019. The increase was primarily due to an increase of \$9.2 million in salary and benefit costs due to higher headcount primarily in the commercial function, an increase of \$7.6 million in stock-based compensation expense as a result of our hiring additional personnel, stock price appreciation and issuance of market-condition restricted stock units, or RSUs, an increase of \$6.0 million in professional and consulting services due to the growth of our operations and the commercialization of Oxbryta, and an increase of \$2.0 million in other general and administrative expenses due to the growth of our operations, such as higher rent expenses resulting from our move into the new facility. SG&A related stock-based compensation expense was \$14.9 million for the three months ended September 30, 2020 and \$7.3 million for the three months ended September 30, 2019.

Comparison of the Nine Months Ended September 30, 2020 and 2019

	Nine Months Ended September 30,		\$ Change	% Change
	2020	2019		
Product sales, net	\$ 82,508	\$ —	\$ 82,508	*
Costs and operating expenses:				
Cost of sales	1,025	—	1,025	*
Research and development	114,054	109,564	4,490	4%
Selling, general and administrative	151,227	72,503	78,724	109%
Total costs and operating expenses	266,306	182,067	84,239	46%
Loss from operations	(183,798)	(182,067)	(1,731)	1%
Interest income	5,251	11,909	(6,658)	(56)%
Interest expenses	(6,887)	(487)	(6,400)	*
Other expenses, net	(313)	(146)	(167)	114%
Net loss	<u>\$(185,747)</u>	<u>\$(170,791)</u>	<u>\$(14,956)</u>	9%

\* Change is not meaningful

**Product sales, net**

Product sales consist of sales of Oxbryta, which was approved by the FDA in late November 2019. We commenced shipments of Oxbryta and fully launched with a deployed sales force in December 2019.

The following table summarizes activity with respect to our sales allowances and accruals for the nine months ended September 30, 2020 (in thousands):

	Rebates, co-payment assistance, Medicare Part D coverage gap, product returns and distributor fees	Prompt payment discounts and chargebacks	Total
<b>Balances at December 31, 2019</b>	\$ 529	\$ 113	\$ 642
Provision related to current period sales	9,613	2,725	12,338
Credit or payments made during the period	(4,026)	(2,217)	(6,243)
<b>Balance at September 30, 2020</b>	<u>\$ 6,116</u>	<u>\$ 621</u>	<u>\$ 6,737</u>

**Cost of sales**

Cost of sales of \$1.0 million for the nine months ended September 30, 2020 consists of manufacturing costs incurred after FDA approval for the cost of Oxbryta sold. Prior to receiving FDA approval for Oxbryta in November 2019, we recorded all costs incurred in the manufacture of Oxbryta as research and development expense. We expect to sell inventory previously expensed to research and development over approximately the current year and into late 2021, and accordingly we expect our costs of product sales of Oxbryta to increase as a percentage of net sales in future periods as we produce and sell inventory that reflects the full cost of manufacturing the product.



## Research and development

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

	Nine Months Ended September 30,		\$ Change	% Change
	2020	2019		
<b>Costs incurred by development program:</b>				
Oxbryta for the treatment of SCD	\$ 62,164	\$ 86,516	\$(24,352)	(28)%
Other preclinical programs	31,209	18,183	13,206	72%
Inclacumab for the treatment of SCD	20,681	4,865	15,816	325%
Total research and development expenses	<u>\$114,054</u>	<u>\$109,564</u>	<u>\$ 4,490</u>	<u>4%</u>

Research and development, or R&D, expenses increased by \$4.5 million or 4%, to \$114.1 million for the nine months ended September 30, 2020 from \$109.6 million for the nine months ended September 30, 2019. The increase was primarily due to an increase of \$15.8 million in external costs related to our inclacumab program driven by manufacturing scale-up activities. In addition, there was an increase of \$13.2 million in internal and external costs associated with our preclinical programs, including increased pre-clinical research activities related to the Syros Agreement. The increase is partially offset by a \$24.4 million decrease in external costs for Oxbryta primarily due to the manufacturing costs that were previously expensed to R&D. Following the approval of Oxbryta in November 2019, we capitalize manufacturing costs to inventory. R&D related stock-based compensation expense was \$13.0 million for the nine months ended September 30, 2020 and \$13.8 million for the nine months ended September 30, 2019.

## Selling, general and administrative expenses

SG&A expenses increased by \$78.7 million or 109%, to \$151.2 million for the nine months ended September 30, 2020 from \$72.5 million for the nine months ended September 30, 2019. The increase was primarily due to an increase of \$32.9 million in salary and benefit costs due to higher headcount primarily in the commercial function, an increase of \$20.0 million in stock-based compensation expense as a result of our hiring additional personnel and stock price appreciation, an increase of \$19.7 million in professional and consulting services due to the growth of our operations and the commercialization of Oxbryta, and an increase of \$6.0 million in other general and administrative expenses due to the growth of our operations, such as higher rent expenses resulting from our recent move into the new facility. SG&A related stock-based compensation expense was \$39.1 million for the nine months ended September 30, 2020 and \$19.0 million for the nine months ended September 30, 2019.

## 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. We have financed our operations primarily through sale of equity securities. As of September 30, 2020, we had \$418.4 million in cash and cash equivalents and \$116.8 million in marketable securities. On December 17, 2019, we entered into the Loan Agreement, or Term Loan, with funds managed by Pharmakon Advisors LP, which are BioPharma Credit PLC, as collateral agent, Biopharma Credit Investments V (Master) LP, as a lender, and BPCR Limited Partnership, as a lender, and collectively, the Lenders, for a senior secured credit facility consisting of an initial tranche of \$75.0 million and the option to draw an additional \$75.0 million until December 31, 2020. The first tranche, in the amount of \$75.0 million, was funded in connection with the closing date of the Term Loan in December 2019. In June 2020, in accordance with the terms of the Loan Agreement, we provided notification to Lenders of our intention to draw the second tranche of the Term Loan, in the amount of \$75.0 million, prior to December 31, 2020, subject to certain closing conditions. As of September 30, 2020, the second tranche of the Term Loan has not been drawn.

On August 5, 2020, we filed a shelf registration statement on Form S-3, or Shelf Registration Statement, with the SEC relating to the registration of our common stock, preferred stock, debt securities, warrants and units or any combination thereof. Concurrently with the filing of the Shelf Registration Statement, we entered into a Sales Agreement with SVB Leerink LLC, or Sales Agent, to provide for the offering, issuance and sale by us of up to an aggregate of \$200.0 million of our common stock from time to time in “at-the-market” offerings under the Shelf Registration Statement, or Sales Agreement. We have agreed to pay to the Sales Agent cash commissions of up to 3.0% of the gross proceeds from sales of common stock pursuant to the Sales Agreement. We have not issued any shares or received any proceeds pursuant to the Sales Agreement through September 30, 2020.

Our primary use of cash is to fund operations. 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.

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 believe we may continue to require additional financing to commercialize Oxbryta, advance

Oxbryta through clinical development, to develop other potential product candidates and to fund operations for the foreseeable future. We may 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:

- our ability to successfully commercialize Oxbryta, inclacumab and any other product candidates we may identify and develop in any territories;
- the manufacturing, selling, and marketing costs associated with the commercialization of Oxbryta and the potential commercialization of inclacumab and any other product candidates we may identify and develop, including the cost and timing of establishing or maintaining our sales and marketing capabilities in any territory(ies);
- the amount and timing of sales and other revenues from Oxbryta, inclacumab and any other product candidates we may identify and develop, including the sales price and the availability of adequate third-party reimbursement;
- the time and cost necessary to conduct and complete multiple ongoing studies (including our HOPE-KIDS 1 Study, Phase 3 HOPE-KIDS 2 Study, our EAPs in the United States and Europe, and our multi-national open label extension, or OLE, study in Phase 3 HOPE Study countries);
- the time and cost necessary to conduct and complete any additional clinical studies required to pursue additional regulatory approvals for Oxbryta for SCD, including our Phase 3 HOPE-KIDS 2 Study (which is intended as our required confirmatory study to move from our current Subpart H approval to a full approval of Oxbryta) and any studies to support potential label expansions into younger SCD pediatric populations, or any other post-marketing studies for Oxbryta for SCD;
- the progress, data and results of clinical trials of Oxbryta and product candidates;
- 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 ongoing and future clinical trials of Oxbryta, inclacumab or any other product candidate that we may identify and develop;
- the costs of obtaining clinical and commercial supplies of Oxbryta, inclacumab and any other product candidates we may identify and develop;
- our ability to advance our development programs, including for Oxbryta, inclacumab and any other potential product candidate programs we may identify and pursue, the timing and scope of these development activities, and the availability of approval for any of our other product candidates;
- our ability to successfully obtain any additional regulatory approvals from any regulatory authorities, and the scope of any such regulatory approvals, to market and sell Oxbryta, inclacumab and any other product candidates we may identify and develop in any territory(ies);
- 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, and the costs and timing associated with any such acquisitions or in-licenses;
- 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 commercialization, clinical trials and other research and development expenditures. With the exception of our Term Loan, 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 Oxbryta and other product candidates and ongoing developments in connection with the COVID-19 pandemic, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated commercialization, clinical trials and research and development activities.

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

	Nine Months Ended September 30,	
	2020	2019
Cash used in operating activities	\$(166,796)	\$(132,080)
Cash provided by (used in) investing activities	271,702	(97,491)
Cash provided by financing activities	11,281	221,818
Net increase in cash, cash equivalents and restricted cash	<u>\$ 116,187</u>	<u>\$ (7,753)</u>

#### ***Cash flows from operating activities***

Cash used in operating activities for the nine months ended September 30, 2020 was \$166.8 million, consisting of a net loss of \$185.7 million, which was partially offset by non-cash charges of \$52.1 million for stock-based compensation and \$9.1 million for net depreciation and amortization expense. The change in our net operating assets and liabilities was due primarily to an increase of \$30.9 million in inventories as we began capitalizing manufacturing of Oxbryta as inventory upon receipt of FDA approval in November 2019, an increase in accounts receivable of \$11.5 million due to timing of cash receipts associated with Oxbryta commercial sales, a decrease of \$2.8 million in accounts payable due to timing of payments, an increase of \$2.3 million in accrued liabilities due to growth of our operations and timing of receipt of invoices, an increase of \$1.3 million in other liabilities, noncurrent, due to employer payroll tax deferral under the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act, and an increase of \$1.8 million in prepaid expenses and other assets due to advance payments made in connection with pre-clinical research activities and commercialization activities for Oxbryta.

Cash used in operating activities for the nine months ended September 30, 2019 was \$132.1 million, consisting of a net loss of \$170.8 million, which was partially offset by non-cash charges of \$32.9 million for stock-based compensation and \$4.9 million for net depreciation and amortization expense. The change in our net operating assets and liabilities was due primarily to an increase of \$5.6 million in accrued liabilities due to growth of our operations and timing of receipt of invoices, an increase of \$5.2 million in prepaid expenses and other assets due to advance payments made in connection with inlacumab pre-clinical research activities and our preparation for the potential commercial launch of Oxbryta, and an increase of \$1.1 million in accounts payable due to timing of payments and receipt of invoices.

#### ***Cash flows from investing activities***

Cash provided by investing activities for the nine months ended September 30, 2020 was \$271.7 million, consisting of maturities of marketable securities of \$333.8 million, which are partially offset by purchases of marketable securities of \$57.9 million and purchases of property and equipment of \$4.2 million.

Cash used in investing activities for the nine months ended September 30, 2019 was \$97.5 million, consisting of purchases of property and equipment for our office and laboratory facility of \$1.2 million and purchases of marketable securities of \$330.1 million, which are partially offset by maturities of marketable securities of \$233.8 million.

#### ***Cash flows from financing activities***

Cash provided by financing activities for the nine months ended September 30, 2020 was \$11.3 million, primarily from proceeds of \$16.6 million from the issuance of common stock to participants in the employee stock purchase plan and exercise of stock options, which are partially offset by \$5.2 million tax paid related to net share settlement of equity awards.

Cash provided by financing activities for the nine months ended September 30, 2019 was \$221.8 million, primarily from net proceeds of \$219.4 million from the issuance of common stock in connection with the follow-on offering completed in June 2019 and overallotment options exercised by our underwriters in January 2019 and July 2019, and to a lesser extent, proceeds of \$5.9 million from the issuance of common stock to participants in the employee stock purchase plan and exercise of stock options, which are partially offset by \$3.5 million in taxes paid related to net share settlement of equity awards.

#### **Off-Balance Sheet Arrangements**

As of September 30, 2020, we had no off-balance sheet arrangements as defined in Item 303(a)(4) of Regulation S-K as promulgated by the SEC.

## Contractual Obligations and Other Commitments

As of the date of this report, there were no material changes to our contractual obligations and commitments outside the ordinary course of business during the nine months ended September 30, 2020, as compared to those disclosed in our Annual Report on Form 10-K for the year ended December 31, 2019.

## Accounting Pronouncements Adopted

In August 2018, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, No. 2018-15, *Intangibles—Goodwill and Other—Internal-Use Software (Subtopic 350-40), Customer’s Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract*, or ASU 2018-15. ASU No. 2018-15 requires a customer that is a party to a cloud computing service contract to follow the internal-use software guidance in Subtopic 350-40 to determine which implementation costs to capitalize and which costs to expense. The amendments in this update are effective for annual reporting periods beginning after December 15, 2019, and interim periods within those fiscal years. The amendments in this update should be applied either retrospectively or prospectively to all implementation costs incurred after the date of adoption. We adopted ASU No. 2018-15 in the first quarter of 2020 and applied the guidance prospectively to the implementation costs incurred in our implementations of various cloud computing arrangements that are service contracts. The adoption of this new standard did not have a material impact on our condensed consolidated financial statements.

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement (Topic 820)*. The new standard modifies the disclosure requirements on fair value measurements in Topic 820, Fair Value Measurement, including removals of, modification to, and additional disclosure requirements from Topic 820. The amendment of ASU No. 2018-13 removes disclosure requirements from Topic 820 in the areas of (1) the amount of and reasons for transfers between Level 1 and Level 2 of the fair value hierarchy, (2) the policy for timing of transfers between levels, and (3) the valuation processes for Level 3 fair value measurements. The amendments in this update are effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019. Except for certain amendments related to Level 3 fair value measurements, all the other amendments should be applied retrospectively to all periods presented upon their effective date. We adopted ASU No. 2018-13 in the first quarter of 2020 and applied the guidance retrospectively. The adoption of this new standard did not have a material impact on our condensed consolidated financial statements.

In June 2016, the FASB issued ASU No. 2016-13, *Measurement of Credit Losses on Financial Instruments (Topic 326)*, which amends the guidance on the impairment of financial instruments. The new standard adds to U.S. GAAP an impairment model that is based on expected losses rather than incurred losses, which is known as the current expected credit loss, or CECL model. The CECL model applies to most debt instruments (other than those measured at fair value), trade and other receivables, financial guarantee contracts, and loan commitments. Available-for-sale debt securities are scoped out of this guidance. Our investment portfolio primarily consists of available-for-sale debt securities carried at fair value. Our accounts receivable are not long term in nature and we do not expect to write off accounts receivable. The amendments in this update are effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019. We adopted ASU No. 2016-13 in the first quarter of 2020 and applied the guidance prospectively. The adoption of this new standard did not have a material impact on our condensed consolidated financial statements.

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

Our market risks as of September 30, 2020 have not changed materially from those discussed in Item 7A of our Annual Report on Form 10-K for the year ended December 31, 2019, filed with the SEC on February 26, 2020.

## 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 September 30, 2020. Based on the evaluation of our disclosure controls and procedures as of September 30, 2020, our Chief Executive Officer and Chief Financial Officer have concluded that, as of September 30, 2020, our disclosure controls and procedures were effective at the reasonable assurance level.

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

During the first quarter of the current fiscal year, we implemented controls related to the accounting for product sales and related reserves, accounts receivable, and inventory and their related financial statement reporting. There were no changes in our internal controls over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the three months ended September 30, 2020 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 September 30, 2020 and consolidated financial statements as of December 31, 2019 and the notes accompanying those consolidated financial statements.*

#### Risks Related to Commercialization

***Our business is substantially dependent on our ability to successfully commercialize Oxbryta, and the commercial success of Oxbryta or any future drug we may develop or obtain will depend upon the degree of market acceptance by physicians, patients, third-party payors and others in the medical community and marketplace.***

Our business depends heavily on our ability to successfully commercialize our first approved product, Oxbryta, for the treatment of sickle cell disease, or SCD. Oxbryta or any future drug of ours approved for commercial sale may fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community and marketplace. If Oxbryta or any other approved drug 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 the drug, in addition to treating the target indication, also provides incremental health benefits to patients. For example, there have been numerous instances of government and private payors placing restrictions on coverage for products approved by the U.S. Food and Drug Administration, or FDA, under the FDA's Subpart H regulations, or Subpart H, so even though the FDA granted Oxbryta accelerated approval, healthcare payors may place restrictions on coverage for Oxbryta because of its accelerated approval status, labeling limitations or other factors. Our efforts to educate the medical community and third-party payors about the benefits of Oxbryta or any future drug approved for commercial sale will require significant resources and may never be successful. The degree of market acceptance of Oxbryta and any other approved drugs that we may pursue will depend on a wide range of factors, including:

- the demonstrated efficacy and potential advantages of our drugs compared to alternative treatments;
- our ability to offer our drugs for sale at competitive prices;
- the availability of third-party coverage and adequate reimbursement;
- the convenience and ease of administration of our drugs compared to alternative current and future treatments;
- the willingness of the SCD or other target patient populations to try new therapies and of physicians to prescribe these therapies;
- the availability of our drugs and our ability to meet market demand, including a reliable supply for long-term chronic treatment;
- the strength of labeling, marketing and distribution support;
- the clinical indications and approved labeling for which the drug is approved, including labeling restrictions for drugs approved under Subpart H, such as Oxbryta;
- 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.

For example, shortly after we launched Oxbryta, the outbreak of the novel coronavirus, SARS-CoV-2, which causes coronavirus disease 2019 (COVID-19), evolved into a global pandemic that has significantly impacted people and entities throughout the world. In light of the COVID-19 pandemic, we have temporarily suspended our field team from most in-person interactions, including visits to physician offices, clinics and hospitals as well as in-person meetings with payors. The COVID-19 pandemic has also reduced our ability to engage with the medical and investor communities. These and other measures may significantly impact our ability to commercialize Oxbryta and our business in general, and we may continue to experience disruptions to our commercial efforts as well as other disruptions that could materially impact our business.

***If our sales and marketing capabilities for Oxbryta in the United States are not effective, or we are unable to establish or secure effective sales and marketing capabilities for any future drug approved for commercial sale in the United States or another geographic market, we may be unsuccessful in our commercial efforts.***

In 2019, we established the infrastructure we believe is adequate for the commercial launch of Oxbryta in the United States, which occurred in December 2019. This included establishing a sales and marketing organization with technical expertise and supporting distribution capabilities to commercialize Oxbryta in the United States. Our commercialization of Oxbryta in the United States will continue to be expensive, difficult, risky and time consuming, and we may not deploy or have adequate resources over time to support the successful commercialization of Oxbryta. Any failures or delays in our commercial efforts, including with respect to any changes in related resources or activities following launch, could adversely impact the commercialization of Oxbryta or any other products, if any are approved.

Although many of our employees have experience with commercializing products while employed at other companies, our 2019 launch of Oxbryta is our first experience marketing and selling a drug together as a management team. To successfully commercialize Oxbryta or any other drugs we may develop or obtain, we will need to continue to develop and strengthen our commercial capabilities, either on our own or with others. 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 Oxbryta or any other product candidates, if any. For example, we may have hired substantially more sales representatives than required and may incur excess costs as a result.

In light of the COVID-19 pandemic, we have temporarily suspended our field team from most in-person interactions, including visits to physician offices, clinics and hospitals as well as in-person meetings with payors. While we are continuing to engage with healthcare professionals and payors through digital and internet-based education and outreach, the impact of temporarily suspending our field force from in-person interactions is unknown. We have seen a significant decrease in weekly new patient prescriptions for Oxbryta from a peak in early March, and we expect the rate of new patient prescriptions to remain lower, possibly through the fourth quarter of 2020, and potentially longer depending on the course of the pandemic.

Another potential challenge for our commercial efforts is frequency of doctor visits by SCD patients. We believe that nearly half of Medicaid and Medicare patients living with SCD do not see a hematologist at least once per year. This infrequency of doctor visits may impede prescriptions for Oxbryta.

With respect to certain geographical markets, we may seek to 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 Oxbryta or future drugs, 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 also be competing with companies that currently have extensive and well-funded marketing and sales operations. For example, in November 2019, the FDA approved Novartis' biologic, crizanlizumab for the reduction of the frequency of vaso-occlusive crises, or VOCs, in patients with SCD, and, in October 2020, Novartis announced that the European Commission has approved crizanlizumab for the prevention of recurrent VOCs in patients with SCD. Without an effective internal team or the support of a third party to perform marketing and sales functions, we would be unable to compete successfully against more established companies, and our commercial efforts and ability to generate revenues would be impaired.

***Our profitability will depend significantly on our ability to sell sufficient amounts of product at competitive prices and on the availability of adequate coverage and reimbursement through governmental or private third-party payors. The insurance coverage and reimbursement status of newly approved products is uncertain in the United States and elsewhere, and failure to obtain or maintain adequate coverage and reimbursement for Oxbryta or any other products we may develop due to price controls, resource constraints or reimbursement limitations could limit our ability to market those products and impair our ability to generate revenue.***

Our target patient populations are small, and, accordingly, the pricing, coverage and reimbursement of Oxbryta or any of our product candidates, if approved, must be adequate to support our commercial infrastructure. To achieve profitability, our per-patient prices must be sufficient to recover our development and manufacturing costs, and we must be able to sell sufficient amounts of product at these prices. Additionally, the availability of government funded or private insurance coverage for Oxbryta and any other product candidates for any approved indications, if any, and the extent of reimbursement by governmental and private payors, will be essential for most patients to be able to afford Oxbryta or any of our other specialty products, if approved. In particular, the list price for Oxbryta in the United States is \$125,000 per year, and a significant percentage of patients with SCD in the United States rely on government programs, such as Medicare and Medicaid, for their coverage of drugs and other medical care, so the availability of federal and state coverage of Oxbryta is critical to the success of our commercialization efforts for Oxbryta in the United States. Sales of Oxbryta or any future drug we may develop or obtain will depend substantially, both domestically and abroad, on the extent to which the costs of such drugs 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 programs. If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize Oxbryta or any future drug we may develop or obtain. 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, and even more uncertainty related to the insurance coverage for products, such as Oxbryta, that receive accelerated approval by the FDA under Subpart H (including in the period before required post-marketing confirmatory studies to verify clinical benefit). 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 formula, which might not include all of the FDA-approved products for a particular indication. Moreover, a third-party payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. For example, the payor's reimbursement payment rate may not be adequate or may require co-payments that patients find unacceptably high. Additionally, coverage and reimbursement for products can differ significantly from payor to payor.

In the United States, significant decisions about reimbursement for new medicines are made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, as CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare, and federal and state programs enter into contracts with drug manufacturers for discounted drug prices for Medicare, VA/Federal Supply Schedule, 340B and Medicaid under the Medicaid Drug Rebate Program, among others. The practices and requirements relating to these arrangements are highly complex and subject to differing regulatory requirements and time frames, which will impact the commercialization of Oxbryta. For example, 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. Limitations could also come from entities such as local Medicare carriers, fiscal intermediaries, or Medicare Administrative Contractors. Further, Medicare Part D, which provides a pharmacy benefit to certain Medicare patients, does not require participating prescription drug plans to cover all drugs within a class of products. Our business could be materially adversely affected if private or governmental payors, including Medicare Part D prescription drug plans, were to limit access to, or deny or limit reimbursement of, Oxbryta or any of our product candidates, if approved.

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 potential pricing and usage of Oxbryta and any future drugs we may develop or obtain. 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 addition, the prices of medicines under such systems are, in general, 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 outside of the United States. 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.

In many non-U.S. jurisdictions, including some countries in the European Union, or EU, the proposed pricing for a drug must be approved before it may be lawfully marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted and reimbursement may in some cases be unavailable. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, which may negatively impact the revenues we are able to generate from the sale of the product in that country. The requirements governing drug pricing vary widely from country to country and products may be subject to continuing governmental control following approval. For example, reimbursement in the EU must be negotiated on a country-by-country basis and, in many countries, the product cannot be commercially launched until reimbursement is approved. Furthermore, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use, including by approving a specific price for the medicinal product or adopting a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. In addition, 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. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products or product candidates.

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 Oxbryta or our product candidates. We expect to experience pricing pressures in connection with the sale of Oxbryta and any future drugs we may develop or obtain, 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. For example, third-party payors are increasingly requiring higher levels of evidence of the benefits and clinical outcomes of new technologies, benchmarking against other therapies, seeking performance-based discounts, and challenging the prices charged. We cannot be sure that coverage will be available for Oxbryta or any other product we commercialize and, if available, that the reimbursement rates will be adequate, as 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 are or may be sold, and drug pricing and other healthcare costs continue to be subject to intense political and social pressures that we anticipate will continue and escalate on a global basis.

Our future profitability will depend, in part, on our ability to commercialize and obtain reimbursement for Oxbryta and our product candidates in markets within and outside of the United States and Europe. If reimbursement for Oxbryta, or our product candidates, if approved, is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, in the United States or, based on the large population of patients with SCD who reside in foreign countries, abroad, our business and operations 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.

***Our future growth may depend, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.***

If we commercialize Oxbryta and any future drugs we may develop or obtain in foreign markets, we would be subject to additional risks and uncertainties, including:

- the burden of complying with complex and changing foreign regulatory, tax, accounting, compliance and legal requirements;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- import or export licensing requirements;
- longer accounts receivable collection times;
- longer lead times for shipping;
- language barriers for technical training;
- reduced protection of intellectual property rights in some foreign countries, and related prevalence of bioequivalent or generic alternatives to therapeutics;
- foreign currency exchange rate fluctuations;
- potential resource constraints, including with respect to patients' ability to obtain reimbursement for our products in foreign markets; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

Any of these factors could impair our ability to commercialize Oxbryta and any future drugs we may develop or obtain outside the United States, which could have a material adverse effect on our business and results of operations.

***With the FDA approval of Oxbryta, and with respect to any other product candidate that receives regulatory approval in any jurisdiction, we will be subject to ongoing regulatory obligations and scrutiny, which may include significant restrictions relating to product labeling, distribution or other post-marketing requirements.***

Even if a product candidate 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. For example, because the FDA approved Oxbryta under the accelerated approval pathway under Subpart H, we must conduct at least one post-marketing confirmatory study to verify clinical risk/benefit, which we intend to satisfy through our HOPE-KIDS 2 Study, and we may not be able to successfully and timely complete this study or any other post-marketing confirmatory study as required to maintain approval or achieve full approval. Also, the FDA has restricted the indicated use of Oxbryta under the approved label to patients 12 years and older. While we plan to conduct additional studies to potentially lower the indicated age range down to 9 months of age, failure to reach agreement with the FDA on these studies, failure to obtain adequate results from them, or disagreements with regulatory authorities over the interpretation of the results may prevent expansion of the age range within our approved label.

Furthermore, any new legislation addressing drug safety or other drug related issues could result in delays or increased costs to assure compliance. With respect to Oxbryta and any other product candidate that is 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 labeling claims that are necessary or desirable for the successful commercialization of Oxbryta, inlacumab or any other product candidates. For example, the development of Oxbryta 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 Oxbryta 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 cGMPs. For Oxbryta, inlacumab 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 are also 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 Oxbryta and any future products. In addition, we are subject to very rapid reporting obligations relating to any adverse events or serious adverse events relating to Oxbryta and our product candidates. Our failure to report adverse events we become aware of within the prescribed timeframes could have serious negative consequences for our commercialization, 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 Oxbryta or any other approved product, if any, could have serious negative consequences for our commercialization activities, 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 a sponsor's activities relating to the promotion, marketing, or labeling of a product, these regulatory agencies may impose restrictions or sanctions on that product or us, including requiring withdrawal of the product from the market. In addition, in the United States, a wide range of commercialization and pre-launch activities relating to a drug candidate are subject to potential for significant civil and/or criminal liability and sanctions under federal anti-kickback and fraud and abuse statutes and regulations. If we fail to comply with any of these complex applicable regulatory requirements, a regulatory agency or enforcement authority may:

- issue untitled or warning letters;
- impose civil or criminal penalties;
- impose injunctions;
- impose fines;
- impose additional specialized restrictions on the company's activities and practices;
- suspend regulatory approval;
- suspend ongoing clinical trials;
- seek voluntary product recalls and impose publicity requirements;
- refuse to approve pending applications or supplements to approved applications submitted by us;
- impose restrictions on our operations, including closing our contract manufacturers' facilities; or
- seize or detain products.

As a company, we have limited 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 continue to take significant effort and management attention to address compliance with these requirements with respect to Oxbryta in the United States and in any jurisdiction for which we seek to commercialize Oxbryta or any other product candidate, if approved. 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 commercialize and generate revenues from Oxbryta or to obtain approval for, launch, commercialize and generate revenues from inlacumab 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.

***Our business operations and current and future relationships with investigators, health care professionals, consultants, third-party payors and customers are or 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.***

Our current and future operations are or will 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 sales, marketing, distribution, commercialization, medical and educational programs and our clinical research activities, and they may constrain our business and financial arrangements and relationships with healthcare providers, physicians and other parties through which we market, sell and distribute Oxbryta and any future drugs we may develop or obtain. 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 federal Anti-Kickback Statute, the federal False Claims laws, the U.S. Federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, the Physician Payment Sunshine Act, and analogous state laws and regulations such as state anti-kickback and false claims laws and analogous non-U.S. fraud and abuse laws and regulations, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors.

Ensuring that our business activities (including our operations and arrangements with third parties) comply with applicable healthcare laws and regulations is complex, time-consuming, costly and could materially impact our operations. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse, price reporting or other healthcare laws and regulations.

Although an effective compliance program can mitigate the risk of investigation and prosecution for violations of these requirements, these risks cannot be entirely eliminated. Moreover, achieving and sustaining compliance with applicable federal, state and foreign privacy, security, and fraud requirements is costly. Any action against us for violation of these requirements, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from our business and operations, and could negatively impact the price of our common stock.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform and other factors. Federal and state enforcement bodies in the United States regularly pursue a large number of investigations, prosecutions, convictions and settlements in the healthcare industry, and in the EU, GDPR enforcement is increasing. 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 may 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 of products or individuals 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 requirements, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment. If any of the above occur, it could adversely affect our ability to operate our business and our results of operations.

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

In the United States, there have been and continue to be a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could restrict or regulate post-approval activities, affect our ability to profitably sell Oxbryta and any other drug candidates for which we obtain marketing approval, and prevent or delay marketing approval of our drug candidates. 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 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.

Since its enactment, there have been many judicial, President, and Congressional challenges to numerous aspects of the ACA.

The full impact on our business of the ACA, the potential impacts of any challenges, including any laws repealing and/or replacing elements of it, as well as the political uncertainty surrounding any repeal or replacement legislation, remain unclear.

Additionally, at the federal level, statutes and regulations routinely impact a variety of parameters relating to federal programs and Medicaid. For example, CMS's final rule regarding the Medicaid drug rebate program, issued in 2016, revised the manner in which the "average manufacturer price" is to be calculated by manufacturers participating in the program. At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. The full impact of these federal and state laws and regulations, as well as other new laws and reform measures that may be proposed and adopted in the future, remains uncertain, but may result in additional reductions in Medicaid and other health care funding, or higher production costs which could have a material adverse effect on our customers and, accordingly, our financial operations.

There have been multiple recent U.S. congressional inquiries and proposed and adopted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs and biologics. In addition, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. While any proposed measures will require authorization through additional legislation to become effective, Congress and the current U.S. presidential administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs.

At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for Oxbritya and our drug candidates, once approved, or put pressure on our product pricing over time.

Moreover, there have been a number of other legislative and regulatory changes in recent years aimed at the biopharmaceutical industry. For instance, the Drug Quality and Security Act imposes obligations on manufacturers of biopharmaceutical products related to product tracking and tracing. Among the requirements of this legislation, manufacturers are required to provide certain information regarding the product to individuals and entities to which product ownership is transferred, will be required to label products with a product identifier, and are required keep certain records regarding the product. The transfer of information to subsequent product owners by manufacturers will eventually be required to be done electronically. Manufacturers are also required to verify that purchasers of the manufacturers' products are appropriately licensed. Further, manufacturers have product investigation, quarantine, disposition, and FDA and trading partner notification responsibilities related to counterfeit, diverted, stolen, and intentionally adulterated products that would result in serious adverse health consequences or death to humans, as well as products that are the subject of fraudulent transactions or which are otherwise unfit for distribution such that they would be reasonably likely to result in serious health consequences or death.

We expect federal and state healthcare reform measures that may be adopted in the future in the United States may result in more rigorous coverage criteria, increased regulatory burdens and operating costs, decreased net revenue from our pharmaceutical products and additional downward pressure on the price that we receive for Oxbritya and any of our drug candidates approved for use. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. These legislative and executive efforts have significantly increased uncertainty regarding the availability of healthcare programs, insurance coverage and reimbursement as a general matter as well as for Oxbritya and our product candidates, and we cannot predict how these events will impact our business or operations. Accordingly, at this time it is difficult to determine the full impact of these efforts on our business. In the United States many patients with SCD participate in the Medicaid program, and the impact of uncertainty or changes relating to the ACA or healthcare programs, insurance coverage or reimbursement generally have a particularly significant impact on our business or results of operations.

***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 Oxbritya and 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 are or may compete with Oxbritya and inlacumab for the potential treatment of SCD. For example, the FDA approved Novartis' crizanlizumab in November 2019. Both crizanlizumab and inlacumab are human monoclonal antibodies against p-selectin for the treatment of VOCs in patients with SCD. The FDA's approval of crizanlizumab resulted in another new and innovative SCD product entering the United States SCD market approximately one week earlier than Oxbritya, and substantially earlier than any potential approval of our

inlacumab product candidate (which could be a direct competitor to crizanlizumab). As a result, the commercialization of crizanlizumab may also impact our commercialization of Oxbryta in the United States, as well as inlacumab if we are successful in developing and obtaining approval for it for SCD patients. In addition, Novartis announced in October 2020 that the European Commission has approved crizanlizumab for the prevention of recurrent VOCs in patients with SCD.

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 Oxbryta or our product candidates uneconomical or obsolete, and we may not be successful in marketing any drugs or product candidates against competitors.

***If the market opportunities for Oxbryta or 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 development and commercialization efforts are focused on the potential of Oxbryta to treat SCD. Our projections of both the number of people who have SCD, as well as the subset of people with SCD who have the potential to benefit from treatment with Oxbryta, 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 SCD. 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 Oxbryta and our product candidates may be limited or may not be amenable to treatment with Oxbryta or 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. Restrictions on labeling of any approved product, including any restrictions that may be imposed in connection with any approval under Subpart H, may also limit the size of the potential market for Oxbryta and our product candidates. Further, even if we obtain significant market share for Oxbryta or any other drug we may develop or obtain, because the potential target populations are small, we may never achieve profitability despite obtaining such significant market share.

#### **Risks Related to Our Financial Position and Need for Additional Capital**

***We are a biopharmaceutical company with only one drug approved for marketing in the United States and 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 generated limited 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 biopharmaceutical company with only one drug, Oxbryta, approved for marketing, and such approval is only for the United States. We also have 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 Oxbryta, and our current clinical development activities are focused on Oxbryta and inlacumab. In August 2018, we entered into an exclusive worldwide license agreement with F. Hoffman-LaRoche and Hoffman-La Roche Inc., collectively, Roche, for the development and commercialization of inlacumab.

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 nine months ended September 30, 2020 and 2019 were \$185.7 million and \$170.8 million, respectively. As of September 30, 2020, we had an accumulated deficit of \$924.7 million. We have only recently begun to generate revenues with the December 2019 commercial launch of Oxbryta, 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:

- commercialize Oxbryta and continue related clinical development, including conducting (i) our Phase 2a HOPE-KIDS 1 Study of Oxbryta, (ii) our Phase 3 HOPE-KIDS 2 Study, which we intend to serve as our post-confirmatory study of Oxbryta in SCD (and any other post-marketing studies that may be required by regulatory authorities, if any), and (iii) any additional clinical trials of Oxbryta we may conduct now or in the future in SCD patients or for any other indications for Oxbryta, inlacumab or any other product candidates, if any;

- establish and maintain manufacturing and supply relationships with third parties that can provide adequate supplies (in amount and quality) of Oxbryta, inclacumab or any other product candidates to support commercialization and further clinical development;
- seek and obtain additional regulatory and marketing approvals for Oxbryta for SCD, including for younger pediatric patient populations, or any potential approvals we may pursue;
- maintain a sales and marketing organization and enter into selected collaborations to commercialize Oxbryta for SCD or any other approved indication, as well as for any other product candidates;
- maintain a medical affairs organization to advance our engagement with healthcare providers and stakeholders;
- advance our other programs, including inclacumab and any other product candidates, through nonclinical and clinical development and commence development activities for any additional product candidates we may identify and pursue; and
- expand our organization to support our commercialization, research, development and medical activities and our operations as a public company.

Prior to the December 2019 commercial launch of Oxbryta, we had never generated any revenues from product sales, and we may never be able to achieve significant revenues or 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 commercialize Oxbryta, advance our development programs or achieve approval to commercialize any other 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, market Oxbryta, diversify our research and development pipeline, market 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 may require substantial additional funds to achieve our business goals. If we are unable to obtain such funds when needed and on acceptable terms, we could be forced to delay, limit or terminate our commercialization activities for Oxbryta, 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 Oxbryta, our product candidates or technologies.***

We are currently commercializing Oxbryta and investigating Oxbryta in clinical development to support its potential full approval by the FDA and opportunities for potential label expansion. Among other activities, we are evaluating the safety and pharmacokinetics of single and multiple doses of Oxbryta in our HOPE-KIDS 1 Study, a Phase 2a clinical trial in adolescent and pediatric patients with SCD, which we expanded to include a new single-dose cohort in children aged 6-11. Our clinical program for Oxbryta also includes multi-national open label extension, or OLE, clinical studies for adult and pediatric patients in HOPE Study countries who have completed participation in the ongoing Phase 3 HOPE Study and elect to continue to receive Oxbryta. We are also conducting our HOPE-KIDS 2 Study, which is our TCD post-confirmatory study of Oxbryta in SCD (to potentially satisfy the FDA's requirement for a post-confirmatory study under Subpart H). In light of the COVID-19 pandemic, we temporarily delayed or paused our research and development activities, including temporarily pausing screening and enrollment on all GBT-sponsored clinical studies (including our HOPE-KIDS 2 Study). Activities on our clinical trials have now resumed, with appropriate measures in place. Assessment of the long-term impact of COVID-19 on our clinical trials is ongoing. Oxbryta is currently our only compound in clinical development, although we are conducting nonclinical research activities in other programs.

Discovering, developing and commercializing biopharmaceutical products is expensive and time-consuming, and we expect our selling, general and administrative and research and development expenses to increase substantially in connection with our ongoing activities, particularly as we continue to commercialize Oxbryta and engage in research and development efforts for Oxbryta, inclacumab and other product candidates that we may identify and pursue in clinical trials. As of September 30, 2020 and December 31, 2019, we had working capital of \$516.7 million and \$556.5 million, respectively, and capital resources consisting of cash and cash equivalents and short and long-term marketable securities totaling \$535.2 million and \$695.0 million, respectively. 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. Because the outcome of commercialization, reimbursement and any clinical development and regulatory approval process is highly uncertain, we cannot reasonably estimate the actual capital amounts necessary to successfully commercialize Oxbryta and complete our ongoing and planned additional development of activities for Oxbryta or any other future product candidates.

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 Oxbryta, inclacumab 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:

- our ability to successfully commercialize Oxbryta, inclacumab and any other product candidates we may identify and develop in any territories;
- the manufacturing, selling, and marketing costs associated with the commercialization of Oxbryta and the potential commercialization of inclacumab and any other product candidates we may identify and develop, including the cost and timing of establishing or maintaining our sales and marketing capabilities in any territory(ies);
- the amount and timing of sales and other revenues from Oxbryta, inclacumab and any other product candidates we may identify and develop, including the sales price and the availability of adequate third-party reimbursement;
- the time and cost necessary to conduct and complete multiple ongoing studies (including our HOPE-KIDS 1 Study, Phase 3 HOPE-KIDS 2 Study and our OLE study in Phase 3 HOPE Study countries);
- the time and cost necessary to conduct and complete any additional clinical studies required to pursue additional regulatory approvals for Oxbryta for SCD, including our Phase 3 HOPE-KIDS 2 Study (which is necessary to move from our current Subpart H approval to a full approval) and any studies to support potential label expansions into younger SCD pediatric populations, or any other post-marketing studies for Oxbryta for SCD;
- the progress, data and results of clinical trials of Oxbryta;
- 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 ongoing and future clinical trials of Oxbryta, inclacumab or any other product candidate that we may identify and develop;
- the costs of obtaining clinical and commercial supplies of Oxbryta, inclacumab and any other product candidates we may identify and develop;
- our ability to advance our development programs, including for Oxbryta, inclacumab and any other potential product candidate programs we may identify and pursue, the timing and scope of these development activities, and the availability of approval for any of our other product candidates;
- our ability to successfully obtain any additional regulatory approvals from any regulatory authorities, and the scope of any such regulatory approvals, to market and sell Oxbryta, inclacumab and any other product candidates we may identify and develop in any territory(ies);
- 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, and the costs and timing associated with any such acquisitions or in-licenses;
- 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 development or commercialization activities for Oxbryta, inclacumab or for any other product candidates we may identify and pursue, 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.

***We are party to a loan and security agreement that contains operating and financial covenants that may restrict our business and financing activities.***

In December 2019, we entered into a loan agreement, or Term Loan, with funds managed by Pharmakon Advisors LP, which are BioPharma Credit PLC, as collateral agent, Biopharma Credit Investments V (Master) LP, as a lender, and BPCR Limited Partnership, as a lender, for a senior secured credit facility consisting of an initial term loan of \$75.0 million, with an option to draw an additional \$75.0 million until December 31, 2020. Borrowings under the Term Loan are secured by a first priority security interest in and a lien on substantially all of our assets, subject to certain exceptions.

The Term Loan restricts our ability, among other things, to:

- sell, transfer or otherwise dispose of any of our business or property, subject to limited exceptions;
- make certain changes to our organizational structure;
- consolidate or merge with other entities or acquire other entities;
- incur additional indebtedness or create encumbrances on our assets;
- pay dividends, other than dividends paid solely in shares of our common stock, or make distributions on and, in certain cases, repurchase our stock;
- repay subordinated indebtedness; or
- make certain investments.

In addition, we are required under the Term Loan to comply with various operating covenants and default clauses that may restrict our ability to finance our operations, engage in business activities or expand or fully pursue our business strategies. A breach of any of these covenants or clauses could result in a default under the Term Loan, which could cause all of the outstanding indebtedness under the facility to become immediately due and payable.

If we are unable to generate sufficient cash to repay our debt obligations when they become due and payable, we may not be able to obtain additional debt or equity financing on favorable terms, if at all, which may negatively affect our business operations and financial condition.

### **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 additional jurisdictions for Oxbryta or one or more jurisdictions for inclacumab 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 such as the European Medicines Agency, or EMA, 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 only obtained regulatory approval for Oxbryta in the United States. In June 2020, we announced plans to submit by mid-2021 a New Drug Application, or NDA, for Oxbryta which will include a new age-appropriate formulation for the treatment of SCD in children ages 4 to 11 years old for potential approval under the FDA's accelerated approval pathway. We also announced plans to submit by mid-2021 a Marketing Authorization Application, or MAA, to the EMA for potential full marketing authorization of Oxbryta to treat hemolytic anemia (which is low hemoglobin due to red blood cell destruction) in SCD patients ages 12 years and older. It is possible that we will never obtain these or any other regulatory approvals for Oxbryta, for inclacumab or any other product candidates we may seek to develop in the future.

Applications for product candidates 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 regulatory authorities (including the EMA) that Oxbryta, inclacumab 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 or expectations regarding the pathways and endpoints for approval, including the availability of accelerated 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 Oxbryta, inclacumab and any other product candidates that we may identify and pursue may not be sufficient to support the submission for regulatory approval;
- 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 Oxbryta, inclacumab 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 studies and clinical trials, and our reliance on third-party manufacturers for any product candidates, may result in our failure to obtain regulatory approval to market Oxbryta outside of the United States or to market inclacumab or 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.

***Expedited development and regulatory approval programs for Oxbryta, such as the accelerated approval under Subpart H, may not lead to a faster development or regulatory review or approval process, may not lead to any approval, and may lead to an approval that is later withdrawn.***

The FDA approved Oxbryta through the accelerated approval process under Subpart H, and we plan to seek approval under the accelerated approval process under Subpart H for an NDA for Oxbryta with a new age-appropriate formulation for the treatment of SCD in children ages 4 to 11 years. While the FDA approved Oxbryta under Subpart H, we cannot be assured that our planned pediatric NDA will benefit from or receive accelerated approval under Subpart H, or that any other product candidates that we may develop will qualify for or benefit from any such expedited programs in the United States, including under Subpart H, or in any foreign regulatory jurisdictions.

In June 2017, the EMA granted PRIME designation for Oxbryta for the treatment of SCD. The PRIME program is a 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. We cannot be assured that Oxbryta or any other product candidates that we may develop will benefit from a PRIME program designation.

The FDA grants accelerated approval under Subpart H for new drugs that address serious or life-threatening illnesses and that provide meaningful therapeutic benefit to patients over existing treatments. Under Subpart H, the FDA may grant marketing approval for a new drug product on the basis of adequate and well-controlled clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity.

Drugs approved under Subpart H are required to be further evaluated in at least one post-marketing study to verify clinical benefit. To satisfy such requirement, we are conducting our TCD post-confirmatory study, the HOPE-KIDS 2 Study. We previously announced that the FDA agreed that TCD flow velocity would be an acceptable primary endpoint in a post-approval confirmatory study of Oxbryta to demonstrate stroke risk reduction for purposes of full approval by the FDA and that we had reached final agreement with the FDA on the design of the TCD post-confirmatory study.

We temporarily paused screening and enrollment on our HOPE-KIDS 2 Study due to the impact of the COVID-19 pandemic. Activities on our clinical trials have now resumed, with appropriate measures in place. Assessment of the long-term impact of COVID-19 on our clinical trials is ongoing and we may not be able to complete this study or any other successful post-marketing confirmatory study as required to maintain approval and achieve full approval, or data and results from our required post-marketing confirmatory program may not verify Oxbryta's clinical benefit to maintain approval and achieve full approval, in which case the product may be required to be withdrawn from market approval.

Access to any expedited program, including through the FDA (such as accelerated approval under Subpart H), may be withdrawn by the FDA or a foreign regulatory authority if it believes that the program is no longer supported by data from our clinical development, and accelerated approval under Subpart H may be withdrawn if, among other reasons, required post-marketing confirmatory studies are not completed or if the FDA determines the results of post-marketing confirmatory studies do not verify clinical benefit.



***All of our programs other than Oxbryta are still in earlier development stages, so we remain very reliant on the potential success of Oxbryta in the clinic and in the marketplace. If we are unable to successfully commercialize Oxbryta for SCD or complete clinical development of Oxbryta, 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 Oxbryta, including conducting nonclinical studies and clinical trials, submitting and obtaining approval for an NDA, and providing general and administrative support for these operations. We do not have any other clinical product candidates at this time, and our only clinical development program for Oxbryta is in SCD. Our future success is highly dependent on our ability to successfully continue to develop, obtain and maintain regulatory approval for, and commercialize Oxbryta inside and outside the United States for SCD.

We are evaluating Oxbryta in SCD patients in our ongoing HOPE-KIDS 1 Study, our HOPE-KIDS 2 Study (which is our post-approval confirmatory study), and other ongoing and planned clinical trials. We are also generating additional clinical data regarding Oxbryta in SCD patients in our OLE studies for HOPE Study sites in multiple countries. In light of the COVID-19 pandemic, we temporarily delayed certain of our research and development activities, including temporarily pausing screening and enrollment on all GBT-sponsored clinical studies. Activities on our clinical trials have now resumed, with appropriate measures in place. Assessment of the long-term impact of COVID-19 on our clinical trials is ongoing.

All of our other programs are in earlier stages of research and development, and we have no other product candidates in clinical trials other than Oxbryta. As a result, even after in-licensing the inclacumab program, we are very dependent on Oxbryta 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 clinical program for Oxbryta, including the HOPE-KIDS 2 Study. The primary endpoint of the HOPE-KIDS 2 Study relates to TCD measurement, and we have not previously conducted any Phase 3 clinical study of Oxbryta in SCD patients using this primary endpoint, nor do we believe this measure has been used as a primary endpoint for any registrational studies for any other SCD therapies.

As we continue our clinical development of Oxbryta, the additional data we generate could be different from, including less favorable in terms of efficacy and/or safety, than the data generated and discussed with the FDA to date. If this were to occur, it could significantly impact our continued development and commercialization of Oxbryta. In addition, depending on the results we obtain from our HOPE-KIDS 2 Study, which we intend to satisfy our post-approval confirmatory requirement under Subpart H, accelerated approval of Oxbryta under Subpart H may be withdrawn (which would also mean full approval would not be achieved, and could also mean that Oxbryta could be required to be removed from the market) if the required post-marketing confirmatory program is not completed or if the FDA determines the results do not verify clinical risk/benefit. If our planned pediatric NDA for Oxbryta with a new age-appropriate formulation for the treatment of SCD in children ages 4 to 11 years is approved and our HOPE-KIDS 2 Study also serves as the post-approval confirmatory study under Subpart H for any such pediatric approval, any accelerated approval of Oxbryta in this pediatric population, if any, may be withdrawn as well depending on the results we obtain from the HOPE-KIDS 2 Study. We do not have a special protocol assessment agreement in place with the FDA for our HOPE-KIDS 2 Study.

We cannot be certain that Oxbryta, inclacumab or any other product candidates that we seek to develop will be successful in nonclinical studies or clinical trials or receive and maintain any regulatory approvals. If we do not receive regulatory approval for, regulatory approval is withdrawn from, or we otherwise fail to successfully commercialize Oxbryta, inclacumab 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 Oxbryta as a potential disease-modifying anti-sickling agent in SCD patients represents a novel therapeutic approach, and there is a risk that the outcomes of our clinical trials will not be favorable or otherwise support any further decision to seek or grant or maintain 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, and our future success depends on the success 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 are only four approved therapies for SCD, Oxbryta, crizanlizumab, hydroxyurea, and L-glutamine, and Oxbryta is the first approved therapy 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 product candidate such as Oxbryta 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 Oxbryta 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 determined to measure change in hemoglobin levels as the primary endpoint in the Phase 3 HOPE Study. This primary endpoint has not been used previously in a registration study for any SCD treatment. As a result, regulators outside of the United States have not determined that such data would signify a clinically meaningful result in SCD patients or would support seeking or obtaining regulatory approval.

We did not achieve statistically significant results with respect to either potential key secondary endpoint in Part A of the HOPE Study (relating to episodes of VOCs and to the Patient Reported Outcome, or PRO, instrument developed by us), and we may not achieve key endpoints in other clinical trials, such as any post-marketing confirmatory studies. In addition, we may not achieve the same results with respect to the primary endpoint in Part A of the HOPE Study in other ongoing or future clinical trials, including our ongoing TCD post-confirmatory study, the HOPE-KIDS 2 Study. Any inability to design clinical trials with protocols and endpoints acceptable to applicable regulatory authorities, and to obtain and maintain regulatory approvals for Oxbryta, inclacumab and any other product candidates that we may pursue, would have an adverse impact on our business, prospects, financial condition and results of operations.

***Results of earlier studies may not be predictive of future clinical trial results, and initial studies may not establish or maintain an adequate safety or efficacy profile for Oxbryta, inclacumab or 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 Oxbryta, inclacumab and of any 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 Oxbryta 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 in clinical trials or in the general patient population. In addition, the results obtained in our development program for SCD patients aged 12 years and older, such as in our Phase 3 HOPE Study, may not be replicated in our ongoing studies in pediatric populations, including our HOPE-KIDS 1 Study and HOPE-KIDS 2 Study.

Products evaluated in post-marketing studies and product candidates in later stages of clinical trials may fail to demonstrate the desired safety and efficacy despite having progressed through nonclinical studies and earlier 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. Since Oxbryta was approved under Subpart H requiring successful completion of a confirmatory clinical trial to obtain full FDA approval, if the results of our confirmatory study fail to demonstrate efficacy and safety adequate to obtain full regulatory approval for Oxbryta and maintain its marketing approval in the United States, this would have a substantial impact on our business, prospects, financial condition and results of operations.

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. In addition, data and results from later studies or programs may conflict with earlier findings.

Our failure to demonstrate the required characteristics to support continued marketing of Oxbryta in the United States, full FDA approval, marketing approval for Oxbryta outside of the United States, or marketing approval for inclacumab 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 obtain any marketing approval for Oxbryta outside of the United States, foreign regulatory authorities may impose additional requirements, the scope of which are not fully known at this time.***

Before we can obtain any marketing approval for a drug candidate for any potential indication, we must successfully complete 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, and a confirmatory study would have been difficult to conduct on ethical grounds.

The FDA approved Oxbryta for the treatment of SCD under the accelerated approval pathway under Subpart H, and approval under this accelerated pathway means that we are required to conduct at least one post-marketing confirmatory study sufficient to verify Oxbryta's clinical benefit, which we intend to satisfy through our HOPE-KIDS 2 Study. With respect to Europe, we announced

plans to submit a MAA to the EMA for potential full marketing authorization of Oxbryta to treat hemolytic anemia in SCD patients ages 12 years and older, with such MAA expected to include data from our Phase 3 HOPE Study and our Phase 2 HOPE-KIDS 1 Study, both of which enrolled patients at clinical sites in Europe.

Foreign authorities may not consider the results of our ongoing, planned or potential future clinical trials of Oxbryta to be sufficient to maintain any approval outside of the United States. Any post-marketing confirmatory studies, if required, would result in increased costs and potential delays in the clinical development and marketing approval process outside the United States, 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 or other application for marketing authorization, as applicable, which may cause us to alter our development, regulatory and/or commercialization strategies.

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

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. In addition, because the FDA approved Oxbryta under the accelerated approval pathway under Subpart H, we must conduct at least one post-marketing confirmatory study to verify clinical risk/benefit, which we intend to satisfy through our HOPE-KIDS 2 Study. Clinical testing is expensive, time-consuming and uncertain as to outcome, and we cannot guarantee that any of our current or future clinical trials for Oxbryta or any other product candidates we may pursue will be conducted as planned or completed on schedule, if at all. For example, in light of the COVID-19 pandemic, we have temporarily paused all site activation, screening and enrollment activities for our HOPE-KIDS 2 Study (other than, where feasible, contracting and other administrative study start-up activities). Activities on our clinical trials have now resumed, with measures in place that we believe are appropriate. Assessment of the long-term impact of COVID-19 on our clinical trials is ongoing, and it is unknown whether we will be required to pause or delay such activities again in the future. 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 Oxbryta or our product candidates or study related devices to the clinical sites and patients;
- delays in having patients enroll or complete participation in a study in accordance with applicable protocols or protocol amendments 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 Oxbryta or our product candidates;
- the occurrence of serious adverse events or other safety concerns associated with Oxbryta or 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 Oxbryta or 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 Oxbryta or a drug candidate. In addition, if we make manufacturing or formulation changes to Oxbryta or our product candidates, we may need to conduct additional studies to bridge the development program from the data and results for the previous version to the modified version.

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

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

Identifying and qualifying patients to participate in our ongoing and planned clinical trials of Oxbryta, inclacumab, 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 estimates by the Centers for Disease Control and Prevention, the prevalence of SCD, for which Oxbryta is indicated, is approximately 100,000 individuals in the United States. Accordingly, there are limited patient pools from which to draw for clinical trials in our target indications. We may not be able to identify, recruit, and enroll a sufficient number of subjects to complete our clinical trials of Oxbryta because of the perceived risks and benefits of Oxbryta, 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 or other requirements in our clinical trials, we may not be able to generate clinical data acceptable to the FDA or comparable regulatory authorities in our trials. For example, successful conduct of our HOPE-KIDS 2 Study (our post-approval confirmatory study) will require consistency in TCD measurements, which is why we are providing specific training and equipment to participating clinical trial sites in such clinical trial. Failure to achieve consistent high-quality readings could result in data that are difficult to interpret or that delay or confound the results. If clinical sites or 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 Oxbryta, or any other product candidates we may pursue, our costs are likely to increase, and our ability to obtain and maintain regulatory approval (or achieve full regulatory approval of Oxbryta) and generate product revenue from Oxbryta and 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 Oxbryta or 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. For example, our Phase 3 HOPE Study in SCD patients represents only a very small fraction of all patients with SCD. Side effects of Oxbryta, inclacumab or any other product candidates that we may develop may be uncovered only in later stages of clinical trials, or only in trials involving different patient populations (such as pediatric patients), or only during post-approval studies, such as our HOPE-KIDS 2 Study (our TCD confirmatory study), or the safety reporting required for approved products. Many approved drugs and 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 Oxbryta in non-humans and clinical trials involving other hemoglobin modifiers (other than

Oxbryta) 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 Oxbryta have not shown evidence of tissue hypoxia. However, if Oxbryta 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. In addition, with respect to Oxbryta, such a result may also significantly impact or require us to terminate our commercialization of Oxbryta.

***Although the FDA and the European Commission have each granted orphan drug designation for Oxbryta for the potential treatment of SCD, we may not receive orphan drug designation for inclacumab or 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 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 Oxbryta 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 Oxbryta for the treatment of SCD, we may apply for orphan drug designation for Oxbryta in other jurisdictions or for other indications, or for inclacumab or 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 from the FDA and the EMA, or may receive from any other regulatory authorities (if any), may not effectively protect Oxbryta or any other product candidate we pursue 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. In addition, legislators or regulators may elect to modify orphan drug exclusivity laws or regulations in ways that could materially impact existing or future orphan drug designations. 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. In addition, even if any orphan drug designations we receive are maintained, we may be unable to realize significant commercial benefits from these regulatory exclusivities for Oxbryta or any other product candidate we pursue.

### **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 Oxbryta, 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 current 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 suspend regulatory approval or 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 product for our trials and commercialization, 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 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, obtain or maintain regulatory approval for or successfully commercialize Oxbritya or 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.

In addition, in connection with any NDA for our product candidates, pre-approval inspections by the FDA of our facilities and/or those of third parties involved in the drug development program may occur, including at clinical trial sites, CMOs or other third parties on which we are very reliant. Significant negative results from pre-approval inspections, if any, could materially delay potential approval of the drug candidate. Accordingly, our dependence on third-party CROs, other key vendors and other third parties 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 Oxbritya, inclacumab and for any other product candidates we may pursue for nonclinical studies and clinical trials, and we expect to continue to do so for the commercialization of Oxbritya in the United States and for any other product commercialization we may conduct. 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 commercialization of Oxbritya and for any clinical trials we are conducting or may conduct for Oxbritya, inclacumab or any other future product candidates, and we do not presently expect that we will establish or acquire the resources necessary 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, as well as for commercial manufacture or any required post-marketing studies of Oxbritya, and we expect to do the same with respect to any other product candidates, if any, that 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 Oxbritya as well as for inclacumab or any other product candidates, if approved.

We may be unable to establish or maintain any agreements with third-party manufacturers for Oxbritya, inclacumab 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 Oxbritya, inclacumab 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, including, without limitation, potential impact on supply chain due to the impact of public health risks, such as the COVID-19 pandemic;
- 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.

Our reliance on third-party manufacturers in connection with inlacumab entails additional potential risks, in connection with the transfer of technology from Roche to our third-party manufacturer for inlacumab, and the requirement for approval by the FDA of any Investigational New Drug application, or IND, from the new site, which may not be successful. In addition, because of our lack of experience manufacturing a biologic product, we will have greater reliance on the expertise and experience of our third-party manufacturer for inlacumab.

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 third-party 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 Oxbryta or 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 commercialize Oxbryta or develop, obtain additional regulatory approval for or further market, as applicable, Oxbryta or our product candidates, if approved.

Oxbryta, inlacumab and any future product candidates that we may identify and pursue 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 or impair clinical development, marketing approval or commercialization. Although we believe we have adequate supplies to commercialize Oxbryta and 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 continued commercialization and clinical development activities. Our current and anticipated future dependence upon others for the manufacturing of Oxbryta, our product candidates and any other marketed drugs may adversely affect our future profit margins and our ability to commercialize Oxbryta or any other 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 Oxbryta, 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 Oxbryta or 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 Oxbryta, inlacumab 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. 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 for Oxbryta. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of Oxbryta, inlacumab 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, additional regulatory approval of Oxbryta or regulatory approval of inlacumab or any of our other future product candidates may never be granted or may be substantially delayed.

In addition, at any time following approval of a product for sale, the regulatory authorities also may audit the manufacturing facilities of our third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that could be costly 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 Oxbryta or 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 Oxbryta and to conduct other aspects of our clinical development activities, as well as for inlacumab and any other product candidates we may pursue, 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 Oxbryta or 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 Oxbryta, inlacumab and other product candidates that we may pursue may be impaired. Changes in patent policy and rules could impair our ability to protect our products and increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.***

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

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 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 Oxbryta, inclacumab or any future product candidates that we may develop.***

We cannot assure that Oxbryta, inclacumab 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 Oxbryta 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 Oxbryta, inclacumab 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 Oxbryta, inclacumab or any other of 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 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 Oxbryta and 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 Oxbryta and 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 intellectual property litigation, if we were to initiate legal proceedings against a third party to enforce a patent covering Oxbryta or one of our product candidates, the defendant could counterclaim that the patent covering Oxbryta or our product candidate is invalid and/or unenforceable. In addition, there is an abbreviated regulatory pathway, under the Biologics Price Competition and Innovation Act of 2009, for the regulatory approval of biosimilar or interchangeable biologic products, which could create a litigation pathway for a third party to challenge patents covering inclacumab. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are multiple potential grounds for a validity challenge or an unenforceability assertion. The outcome following legal assertions of invalidity and unenforceability is often highly unpredictable.

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

In addition, our defense of litigation, interference or derivation proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our business and operations including our ability to commercialize Oxbryta, 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 Oxbryta and our product candidates to domestic and foreign markets.

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 commercialize Oxbryta, 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, we have exclusively licensed from the Regents of the University of California, or Regents, worldwide patent rights covering Oxbryta and certain Oxbryta analogs, some of which patent rights we jointly own with the Regents. Additionally, in the United States, each co-owner may be required to be joined as a party to any claim or action we may wish to bring to enforce these patent rights, which may limit our ability to pursue third party infringement claims.

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

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

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

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

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

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

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

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

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

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

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

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological complexity and legal complexity. Therefore, obtaining and enforcing biopharmaceutical patents is costly, time-consuming and inherently uncertain. In addition, the 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 has developed 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, the courts have yet to address many of these provisions and it is not clear what, if any, impact the AIA will have on the operation of our business. 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 Our Business and Industry**

***Pandemics such as the one caused by the novel strain of coronavirus, SARS-CoV-2, which causes COVID-19, as well as similar outbreaks and other public health crises, could adversely impact our business, including our commercialization activities, clinical trials and preclinical studies.***

Pandemics, similar outbreaks and other public health crises could adversely impact our business. For example, the outbreak of the novel coronavirus, SARS-CoV-2, which causes coronavirus disease 2019 (COVID-19), has evolved into a global pandemic that has significantly impacted people and entities throughout the world. As a result of the COVID-19 pandemic, we have experienced and may continue to experience disruptions that could materially impact our business. The extent to which this pandemic or other health crises, or changes in laws and regulations such as shelter-in-place orders, impact our business and operating results will depend on future developments that are highly uncertain and cannot be accurately predicted, including new information that may emerge concerning COVID-19 and the actions taken to contain COVID-19 or treat its impact, among others.

As a result of the COVID-19 pandemic, various aspects of our business operations have been, and could continue to be, disrupted. In response to the pandemic, we implemented a work from home policy, with our administrative and certain other employees continuing their work outside of our offices, and restricted on-site staff to only a limited number of employees who have critical needs to be in the facility. The increase in working remotely could increase our cyber security risk, create data accessibility concerns, and make us more susceptible to communication disruptions, any of which could adversely impact our business operations or delay necessary interactions with local and federal regulators, ethics committees, manufacturing sites and clinical trial sites. In addition, as a result of shelter-in-place orders or other mandated travel restrictions, staff conducting on-site research and development may have limited access to our laboratory space, and these core activities may be significantly limited or curtailed, possibly for an extended period of time.

The COVID-19 pandemic has also reduced the ability to engage with the medical and investor communities, including due to the cancellation of conferences scheduled throughout the year. For example, in light of the COVID-19 pandemic, we have temporarily suspended our field team from most in-person interactions, including visits to physician offices, clinics and hospitals as well as in-person meetings with payors. These and other measures may significantly impact our ability to commercialize Oxbryta, such as by impacting new patient enrollments.

In addition, our ongoing and planned clinical trials have been and will likely continue to be affected by the COVID-19 pandemic. For example, in light of the COVID-19 pandemic, we temporarily paused screening and enrollment in all GBT-sponsored clinical studies (other than, where feasible, certain contracting and other administrative study start-up activities). Activities on our clinical trials have now resumed, with measures in place that we believe are appropriate. Assessment of the long-term impact of COVID-19 on our clinical trials is ongoing, and it is unknown whether we will be required to pause or delay such activities again in the

future. Any prolongation or de-prioritization of our clinical trials or delay in regulatory review resulting from such disruptions could materially affect the development and study of Oxbryta or our product candidates. Study procedures (particularly any procedures that may be deemed non-essential), site initiation, participant recruitment and enrollment, participant dosing, shipment of our study compound, distribution of clinical trial materials, study monitoring, site inspections and data analysis may be delayed or paused due to changes in hospital or research institution policies, federal, state or local regulations, prioritization of hospital and other medical resources toward pandemic efforts, or other reasons related to the pandemic. If COVID-19 continues to spread, some participants and clinical investigators may not be able to comply with clinical trial protocols and we may experience increased patient study withdrawals or protocol deviations. For example, this may occur if quarantines or other travel limitations (whether voluntary or required) may impede participant movement, affect access to study sites, or interrupt healthcare services for a prolonged period of time. As a result, we may be unable to conduct our clinical trials. Furthermore, the COVID-19 pandemic could result in interruption or delays in the operations of the FDA and other domestic or foreign regulatory agencies, which could impact the conduct of our clinical trials, the ability to seek agency input on our regulatory strategies and potential filings or interactions with regulatory agencies that oversee our research, development and promotional activities. The extent and impact of such disruptions are currently unpredictable.

Our and our vendors' and collaborators' research, preclinical development, and manufacturing operations also may be adversely impacted by the COVID-19 pandemic. We currently utilize third parties to, among other things, supply and manufacture raw materials, components, and Oxbryta and our product candidates, to ship Oxbryta and our product candidates and manufacturing materials, and to perform certain testing relating to Oxbryta and our product candidates. If we, or any third parties in our supply chain for materials which are used in either the manufacture of Oxbryta or our product candidates or the conduct of our research and development, are adversely impacted by restrictions resulting from the coronavirus outbreak, our supply chain may be disrupted and our ability to manufacture and ship Oxbryta and our product candidates for commercial and research and development activities may be limited.

In addition, the trading prices for our common stock and other biopharmaceutical companies have been highly volatile as a result of the COVID-19 pandemic. As a result, we may face difficulties raising capital through equity or debt financings, or such financing transactions may be on unfavorable terms. While the potential economic impact brought by and the duration of the pandemic may be difficult to assess or predict, it has already caused, and is likely to result in further, significant disruption of global financial markets, which may reduce our ability to access capital either at all or on favorable terms. Furthermore, a recession, depression or other sustained adverse market event resulting from the spread of COVID-19 could materially and adversely affect our business and the value of our common stock.

The ultimate impact of the COVID-19 pandemic, or any other health epidemic, is highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts on our business, our commercialization activities, our clinical and preclinical programs, our clinical, preclinical, research, manufacturing, and regulatory activities, healthcare systems or the global economy as a whole. However, these effects could have a material adverse impact on our operations, and we will continue to monitor the situation closely.

***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, commercial, research and development, clinical, financial and business development expertise of our executive officers, as well as the other members of our team. 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, clinical, technical operations personnel and 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. The COVID-19 pandemic, as well as similar outbreaks or other significant business disruptions, may make such efforts more challenging. Furthermore, to the extent we hire personnel from competitors, we may be subject to allegations that they have been improperly solicited or that they have divulged proprietary or other confidential information, or that their former employers own their research output. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

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

With our recent establishment of infrastructure required for commercialization of Oxbryta and our current and planned product development activities, we have experienced significant and rapid growth in the number of our employees and the scope of our operations, particularly in the areas of sales, marketing and distribution, regulatory affairs, research and drug development. To manage this and 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, train and retain a sufficient number of 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 our recent or future 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 could be impaired.***

Although a substantial amount of our effort will focus on the continued commercialization, clinical testing and seeking of additional regulatory approval of Oxbryta, 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, such as inclacumab. With the exception of Oxbryta, all of our other potential product candidates remain in the earlier development stages. 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 inclacumab or any 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 Oxbryta.

***If successful product liability claims are brought against us, we may incur substantial liability and costs. If the use of Oxbryta or our product candidates harms patients, or is perceived to harm patients even when such harm is unrelated to Oxbryta or 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 commercialization of Oxbryta, the use of Oxbryta and our product candidates, including inclacumab, in clinical trials and the sale of any other 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 Oxbryta or our product candidates may induce adverse events. The risk of product liability claims may be increased now that Oxbryta is approved and being sold in the United States. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- impairment of our business reputation;

- withdrawal of clinical trial participants;
- costs due to related litigation;
- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- increased warnings on product labels or additional restrictions imposed by regulatory authorities;
- the recall of Oxbryta or our product candidates;
- the inability to commercialize Oxbryta or our product candidates; and
- decreased demand for Oxbryta or 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 commercial activities and clinical programs, but we may not be able to obtain and maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. 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 products or 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 products or 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 inlacumab, may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic collaboration, licensing or other partnering arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate, or we may allocate internal resources to a product candidate in a therapeutic area in which it would have been more advantageous to enter into a partnering arrangement.



***Any collaboration, distribution or other 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, distribution or other arrangements with pharmaceutical or biotechnology companies for the development or commercialization of Oxbryta, inclacumab and potential future product candidates. For example, in December 2019, we announced our entry into the License and Collaboration Agreement with Syros Pharmaceuticals, Inc., to discover, develop and commercialize novel therapies for SCD and beta thalassemia, and, in September 2020, we announced our entry into an exclusive agreement with Biopharma-Middle East and Africa, or Biopharma-MEA, to distribute Oxbryta in Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, and the United Arab Emirates, collectively known as the Gulf Cooperation Council, or GCC, region. We may enter into additional collaboration, distribution or other arrangements on a selective basis depending on the merits of retaining commercialization rights for ourselves as compared to entering into selective arrangements with leading pharmaceutical or biotechnology companies for our products or product candidates, both in the United States and internationally. To the extent that we decide to enter into such arrangements, we will face significant competition in seeking appropriate partners. Whether we reach a definitive agreement for any collaboration, distribution or other arrangement will depend, among other things, upon our assessment of the partner's resources and expertise, the terms and conditions of the proposed arrangement and the proposed partner'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 or a product candidate, the costs and complexities of manufacturing and delivering a product or 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, these arrangements are complex and time consuming to negotiate, document and implement, and we may not be successful in our efforts to establish and implement additional 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 collaboration, distribution or other arrangement that we enter into may not be successful and may increase our potential liabilities. The success of our arrangements will depend heavily on the efforts and activities of us and our partners, who generally have significant discretion in determining the efforts and resources that they will apply to these collaborations. Disagreements between parties to an arrangement regarding research, development and commercialization matters can lead to delays in the development process or commercializing the applicable product or product candidate and, in some cases, costly and time-consuming disputes or termination of the 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. In addition, we are reliant on our partners' compliance with applicable laws and regulations in the region in which they operate, such as in the GCC region with respect to our arrangement with Biopharma-MEA. A partner's failure to comply with applicable law could result in liability for us, and negatively impact our operations and business reputation. Many of such arrangements 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 evaluate data from our Phase 3 HOPE Study, plan to conduct additional studies inside and outside the United States, and plan to seek to obtain regulatory approval to commercialize Oxbryta in additional patient populations inside the United States as well as in patient populations outside the United States. Doing business internationally involves a number of risks, including but not limited to:

- restrictions and obligations imposed by privacy regulations, such as provisions under the General Data Protection Regulation 2016/679, known as GDPR, applicable to the collection and use of personal health data in the European Union;
- multiple, conflicting, and changing laws and regulations such as 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 our current and potential 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 FCPA, its books and records provisions, or its anti-bribery provisions.

Any such factors may impose additional responsibilities, obligations or liability in relation to our current and planned activities outside the United States, and we may be required to put in place additional mechanisms and make additional expenditures to ensure compliance with existing and new requirements, which 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, these 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 activities outside the United States to increase over time. We engage third parties for clinical trials and/or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals, have entered into an exclusive agreement with Biopharma-MEA to distribute Oxbryta in the GCC region, and expect to contract with additional third parties with respect to the distribution and commercialization of Oxbryta and our other product candidates in territories outside the United States, if approved for marketing in any such territories. 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 (particularly as a result of the COVID-19 pandemic), 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. Additionally, the availability of healthcare services and resources is currently constrained due to the COVID-19 pandemic. If fewer patients are seeking medical care because they do not have insurance coverage or are unable to obtain medical care for their conditions due to resource constraints on the healthcare system, we may experience difficulties in the commercialization of Oxbryta and 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 U.K., held a referendum in which voters supported the exit of the U.K. from the EU (known 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. On January 31, 2020, the U.K. officially left 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, changes in, and legal uncertainty with regard to, national and international laws and regulations may present difficulties for our clinical and regulatory strategy.

A severe or prolonged economic downturn, including as a result of the COVID-19 pandemic, 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 COVID-19 pandemic, current economic climate and financial market conditions could adversely impact our business.

***Misconduct or other improper activities of our employees, agents, contractors or collaborators could adversely affect our reputation and our business, prospects, operating results and financial conditions.***

We cannot ensure that our compliance controls, policies, and procedures will in every instance protect us from acts committed by our employees, agents, contractors or collaborators that would violate the law or regulations of the jurisdictions in which we operate, including FDA, healthcare, employment, foreign corrupt practices, environmental, competition, and patient privacy regulations. Misconduct by our employees, agents, contractors, or collaborators could include intentional or unintentional failures to:

- comply with EMA or FDA regulations or similar regulations of comparable foreign regulatory authorities;
- provide accurate information to the FDA or EMA or comparable foreign regulatory authorities;
- comply with cGMP regulations and manufacturing standards that we have established and comply with applicable healthcare fraud and abuse regulations in the jurisdictions in which we operate;
- report financial information or data accurately; or
- disclose unauthorized activities to us.

In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Misconduct could also involve the improper use of, including trading on, information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation.

Additionally, our business activities may be subject to the FCPA and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate. The FCPA generally prohibits offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to a non-U.S. government official in order to influence official action, or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. Our business is heavily regulated and, therefore, involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, the health care providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these prescribers and purchasers are subject to regulation under the FCPA.

There is no certainty that all of our employees, agents, contractors, or collaborators, or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these requirements. We have adopted a code of conduct, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may be ineffective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these requirements. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business.

***We or the third parties upon whom we depend may be adversely affected by earthquakes, outbreaks of disease (such as the COVID-19 pandemic) or other natural disasters, and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.***

Earthquakes, outbreaks of disease (such as the COVID-19 pandemic) 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. As a result of the COVID-19 pandemic, we have been prevented from using all or a significant portion of our headquarters, and future events (including pandemics, earthquakes, power outages or natural disasters) may prevent us in the future from using all or a significant portion of our facilities. In addition, damage to or restrictions on the use of critical infrastructure, such as the manufacturing facilities of our third-party contract manufacturers or other facilities critical to our research and development activities, may render it difficult

or, in certain cases, impossible for us to continue certain aspects of our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

***Our internal computer systems, or those of our third-party vendors, may fail or suffer security breaches, which could result in a material disruption of our business and operations.***

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, and the prevalent use of mobile devices that access confidential information increases the risk of data security breaches. With respect to our data and information technology infrastructure, we continue to invest in the protection of such infrastructure, but there can be no assurance that our efforts will prevent service interruptions or identify breaches in our systems.

If any such event were to occur and cause interruptions in our operations, it could adversely affect our business and operations or result in the loss of critical or sensitive information, which could result in financial, legal, business or reputational harm to us. For example, the loss of data from completed or ongoing clinical trials or nonclinical studies for Oxbryta or any of our product candidates could harm our commercialization activities, 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. In addition, our liability insurance may not be sufficient in type or amount to cover us against claims related to security breaches, cyber-attacks and other related breaches. As a result, any such cyber-attacks or breaches could have a material adverse effect on our business.

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

***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:

- failure to successfully develop and commercialize Oxbryta, inclacumab or any other product candidates, including results relating to our launch and commercialization of Oxbryta in the United States;
- adverse results or delays in, or the halting of, our nonclinical studies or clinical trials, especially in our ongoing or future clinical program for Oxbryta for the treatment of SCD;
- reports of adverse events from our commercialization or clinical trials of Oxbryta, or from clinical trials of any other product candidates that we may develop;
- any delay in the review of, or potential action with respect to, our planned filing of any IND, NDA or MAA for Oxbryta, inclacumab or for any other product candidates that we may develop and any adverse development or perceived adverse development with respect to the FDA's or any other regulatory agency's review of such filing;
- adverse regulatory decisions affecting Oxbryta, inclacumab or any other product candidates we may develop, including any delay in or denial of potential approval in accordance with our plans and expectations;
- inability to obtain additional funding;
- failure to prosecute, maintain or enforce our intellectual property rights;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- changes in laws or regulations applicable to Oxbryta or future products;
- inability to obtain adequate product supply for Oxbryta or 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 or perform under 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;
- additions or departures of key scientific or management personnel;
- significant lawsuits, including patent or stockholder litigation;
- changes in the market valuations of similar companies;
- sales of our common stock by us or our stockholders in the future;
- trading volume of our common stock; and
- the other risks described in this “Risk Factors” section.

In addition, companies trading in the stock market in general, and the NASDAQ Stock Market, or NASDAQ, 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, including the effects of the COVID-19 pandemic on the global economy, 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:

- our ability to successfully commercialize Oxbryta or any of our product candidates, if approved, and the timing and costs of our commercialization activities;
- the timing and cost of, and level of investment in, research and development activities relating to Oxbryta and our product candidates, which may change from time to time;
- the timing and success or failure of clinical trials for Oxbryta and 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 and maintain full regulatory approval for Oxbryta in the United States (including potential pediatric approval) and to obtain regulatory approval of Oxbryta outside of the United States (including potential European approval) as well as regulatory approval for our product candidates, and the timing and scope of any such approvals we may receive;
- the cost of manufacturing Oxbryta and 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, train 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 Oxbryta and our product candidates, if approved, which may vary significantly;
- future accounting pronouncements or changes in our accounting policies;
- the risk/benefit profile, cost and reimbursement policies with respect to Oxbryta and our products candidates, if approved, and existing and potential future drugs that compete with Oxbryta and our product candidates;
- whether Oxbryta or any of our product candidates are subject to any compliance-related challenges or sanctions, or any intellectual-property related challenges; and
- the changing and volatile U.S., European and global economic environments, including economic volatility as a result of the COVID-19 pandemic.

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.

***We incur significant costs, and expend significant time and effort, to comply with the rules applicable to us as a public company, including Section 404 of the Sarbanes-Oxley Act of 2002. If we fail to comply with these rules, including maintaining proper and effective systems of disclosure controls and internal controls over financial reporting, 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, or Exchange Act, Section 404, or Section 404, of the Sarbanes-Oxley Act of 2002, or Sarbanes-Oxley, and the rules and regulations of NASDAQ. The Exchange Act requires us to file accurate and timely quarterly, annual and current reports with the SEC. Section 404 generally requires our management and independent registered public accounting firm to report on the effectiveness of our internal control over financial reporting and requires us to include an opinion from our independent registered public accounting firm on the effectiveness of our internal control over financial reporting. We are also subject to significant corporate governance and executive compensation-related provisions of the Dodd-Frank Wall Street Reform and Consumer Protection Act, or Dodd-Frank, including the “say on pay” rules adopted by the SEC under Dodd-Frank. We incur significant legal, accounting and other expenses, and expend significant time and effort by management and other personnel, to comply with the rules applicable to us as a public company.

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, or COSO, criteria, our management, Chief Executive Officer and Chief Financial Officer, have concluded that, as of December 31, 2019, our internal control over financial reporting was effective. As required under Section 404 of Sarbanes-Oxley, our independent registered public accounting firm has tested the design and operating effectiveness of our controls over financial reporting and been required to provide an attestation report with respect to our internal control over financial reporting. During the course of our or their subsequent review and testing, however, material weaknesses or significant deficiencies may be identified and 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, any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from NASDAQ or other adverse consequences that would materially harm our business.

Moreover, stockholder activism, the current political environment, and increased levels of government scrutiny and regulatory reform may lead to substantial new regulations and disclosure obligations for public companies, 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 any new compliance initiatives. In addition, any new 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 Sarbanes-Oxley and rules adopted by the SEC and by NASDAQ, would likely result in increased costs to us as we respond to their requirements.

***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. In August 2020, we filed a registration statement on Form S-3 pursuant to which we may issue up to \$200.0 million in shares of common stock in sales deemed to be “at-the-market offerings” as defined by the Securities Act of 1933, as amended, and an unlimited amount of shares of our common stock, preferred stock, debt securities, warrants and/or units. Any sale or issuance of securities pursuant to this registration statement or otherwise may result in dilution to our stockholders and may cause the market price of our stock to decline. Furthermore, new investors purchasing securities that we may issue and sell in the future could obtain rights superior to the rights of our existing stockholders.

We are also authorized to grant stock options and other equity-based awards to our employees, directors and consultants pursuant to our Amended and Restated 2015 Stock Option and Incentive Plan, or 2015 Plan. 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, and thereafter amended and restated the plan as the Amended and Restated 2017 Inducement Plan, or the 2017 Inducement Plan. The 2017 Inducement Plan enables us and our subsidiaries to grant non-qualified stock options and other equity-based awards to induce employees who are not currently employed by us or our subsidiaries to accept employment with us or our subsidiaries. As of September 30, 2020, there were 1,521,896 shares reserved under the 2017 Inducement Plan (subject to adjustment for reorganization, recapitalization, stock dividend, stock split, or similar changes in our capital stock) for issuance to new employees entering into employment with us. In addition, we have reserved shares of common stock for issuance pursuant to our Amended and Restated 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 significant stockholders. Sales by our stockholders of a substantial number of shares, or the expectation that such sales may occur, could significantly reduce the market price of our common stock.

We have also registered or intend to register 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 Exchange Act 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.

***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 57.0% of our outstanding common stock as of September 30, 2020, 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 commercialization and clinical development of Oxbryta for the treatment of SCD, including in our Phase 2a HOPE-KIDS 1 Study, our Phase 3 HOPE-KIDS 2 Study, our other research and development activities including other clinical and nonclinical studies, including for inclacumab, 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.

***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 and an ownership change as a result of our follow-on offerings, however we do not believe that these ownership changes will significantly limit our ability to use these pre-change NOL carryforwards. We may experience subsequent shifts in our stock ownership, including as a result of our future follow-on offering, some of which are outside of our control. As a result, if we earn net taxable income, our ability to use our pre-change NOL carryforwards to offset U.S. federal taxable income may become subject to limitations, which could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. On June 29, 2020, California enacted legislation AB 85 limiting our ability to use our state NOLs and imposing a cap on the amount of business incentives tax credits (R&D credit) for taxable years 2020, 2021, and 2022. In addition, pursuant to the Tax Cuts and Jobs Act of 2017 (as modified by the Coronavirus Aid, Relief, and Economic Security Act of 2020), we may not use net operating loss carry-forwards arising in taxable years beginning after December 31, 2017 to reduce our taxable income in any year beginning after December 21, 2020 by more than 80% and we may not carry back any net operating losses arising in taxable years ending after December 31, 2020 to prior years. These new rules apply regardless of the occurrence of an “ownership change.”



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

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

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

**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*

Not applicable.

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.

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**Item 6. Exhibits**

See the Exhibit Index on the page prior to 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.

**EXHIBIT INDEX**

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
3.1	<a href="#">Restated Certificate of Incorporation</a>	S-1/A	7/31/2015	3.2	
3.2	<a href="#">Amended and Restated Bylaws</a>	S-1/A	7/31/2015	3.4	
4.1	<a href="#">Specimen Common Stock Certificate</a>	S-1/A	7/31/2015	4.1	
10.1	<a href="#">Sales Agreement dated as of August 5, 2020, by and between the Registrant and SVB Leerink LLC</a>	S-3	8/5/2020	1.2	
31.1	<a href="#">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</a>	—	—	—	X
31.2	<a href="#">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</a>	—	—	—	X
32.1*	<a href="#">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</a>	—	—	—	X
101.SCH	Inline XBRL Taxonomy Extension Schema Document	—	—	—	X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document	—	—	—	X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document	—	—	—	X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document	—	—	—	X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document	—	—	—	X
104	Cover Page Interactive Data File (formatted as inline XBRL with applicable taxonomy extension information contained in Exhibits 101.)	—	—	—	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.

**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: November 5, 2020

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

Date: November 5, 2020

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

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER  
PURSUANT TO RULES 13a-14(a) AND 15d-14(a) OF THE SECURITIES EXCHANGE ACT, AS ADOPTED  
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Ted W. Love, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Global Blood Therapeutics, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f) for the registrant and have:
  - a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 5, 2020

/s/ Ted W. Love, M.D.

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Ted W. Love, M.D.

*President and Chief Executive Officer*  
*(Principal Executive Officer)*

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER  
PURSUANT TO RULES 13a-14(a) AND 15d-14(a) OF THE SECURITIES EXCHANGE ACT, AS ADOPTED PURSUANT TO  
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Jeffrey Farrow, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Global Blood Therapeutics, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f) for the registrant and have:
  - a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 5, 2020

/s/ Jeffrey Farrow

Jeffrey Farrow

*Chief Financial Officer*

*(Principal Financial Officer)*

GLOBAL BLOOD THERAPEUTICS, INC.  
CERTIFICATION PURSUANT TO  
18 U.S.C. SECTION 1350,  
AS ADOPTED PURSUANT TO  
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Quarterly Report of Global Blood Therapeutics, Inc. (the "Company") on Form 10-Q for the quarter ended September 30, 2020, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Ted W. Love, President and Chief Executive Officer of the Company, and Jeffrey Farrow, Chief Financial Officer, do each hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to my knowledge:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and
2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ Ted W. Love, M.D.

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Ted W. Love, M.D.

*President and Chief Executive Officer*

*(Principal Executive Officer)*

November 5, 2020

/s/ Jeffrey Farrow

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Jeffrey Farrow

*Chief Financial Officer*

*(Principal Financial Officer)*

November 5, 2020

This certification accompanies the Form 10-Q to which it relates, is not deemed filed with the Securities and Exchange Commission 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 the Form 10-Q), irrespective of any general incorporation language contained in such filing.