bluebird bio, Inc.
Form 10-Q
November 02, 2016

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, DC 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, 2016

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: 001-35966

bluebird bio, Inc.

(Exact Name of Registrant as Specified in Its Charter)

Delaware	13-3680878
(State or Other Jurisdiction of Incorporation or Organization)	(IRS Employer Identification No.)
150 Second Street	02141

Cambridge, Massachusetts
(Address of Principal Executive Offices) (Zip Code)

(339) 499-9300

(Registrant's Telephone Number, Including Area Code)

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

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

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

Large accelerated filer Accelerated filer

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

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 28, 2016, there were 37,303,678 shares of the registrant's Common Stock, par value $0.01 per share, outstanding.

This Quarterly Report on Form 10-Q contains forward-looking statements that involve risks and uncertainties, as well as assumptions that, if they never materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such forward-looking statements. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. All statements other than statements of historical facts contained in this Quarterly Report on Form 10-Q are forward-looking statements. In some cases, you can identify forward-looking statements by words such as "anticipate," "believe," "contemplate," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "target," "would," or the negative of these words or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- the initiation, timing, progress and results of our preclinical and clinical studies, and our research and development programs;
- our ability to advance product candidates into, and successfully complete, clinical studies;
- our ability to advance our viral vector and drug product manufacturing capabilities;
- the timing or likelihood of regulatory filings and approvals for our product candidates;
- the timing or success of commercialization of our product candidates, if approved;
- the pricing and reimbursement of our product candidates, if approved;
- the implementation of our business model, strategic plans for our business, product candidates and technology;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology;
- estimates of our expenses, future revenues, capital requirements and our needs for additional financing;
- the potential benefits of strategic collaboration agreements and our ability to enter into strategic arrangements;
- our ability to maintain and establish collaborations and licenses;
- developments relating to our competitors and our industry; and
- other risks and uncertainties, including those listed under Part II, Item 1A. Risk Factors.

Any forward-looking statements in this Quarterly Report on Form 10-Q reflect our current views with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under Part II, Item 1A. Risk Factors and elsewhere in this Quarterly Report on Form 10-Q. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This Quarterly Report on Form 10-Q also contains estimates, projections and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources.

bluebird bio, Inc.

Form 10-Q

For the three and nine months ended September 30, 2016

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PART I. FINANCIAL INFORMATION

Item 1. Financial Statements

bluebird bio, Inc.

Condensed Consolidated Balance Sheets

(unaudited)

(in thousands, except par value amounts)

	September 30, 2016	December 31, 2015
Assets		
Current assets:		
Cash and cash equivalents	$ 245,154	$ 164,269
Marketable securities	355,806	353,680
Prepaid expenses and other current assets	7,875	6,016
Total current assets	608,835	523,965
Marketable securities	126,681	347,814
Property and equipment, net	131,737	82,614
Intangible assets, net	21,634	24,456
Goodwill	13,128	13,128
Restricted cash and other non-current assets	16,247	10,360
Total assets	$ 918,262	$ 1,002,337
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 6,710	$ 6,334
Accrued expenses and other current liabilities	54,672	28,145
Deferred revenue, current portion	6,209	5,889
Total current liabilities	67,591	40,368
Deferred rent, net of current portion	10,995	8,294
Deferred revenue, net of current portion	41,756	35,959
Contingent consideration, net of current portion	3,267	5,082
Construction financing lease obligation	99,991	61,901
Other non-current liabilities	149	237
Total liabilities	223,749	151,841
Commitments and contingencies (Note 7)		
Stockholders' equity:		
Preferred stock, $0.01 par value, 5,000 shares authorized; 0 shares issued and outstanding at September 30, 2016 and December 31, 2015	—	—
Common stock, $0.01 par value, 125,000 shares authorized; 37,296 and 36,894 shares	373	369

issued and outstanding at September 30, 2016 and December 31, 2015, respectively		
Additional paid-in capital	1,201,286	1,166,585
Accumulated other comprehensive loss	(836)	(2,291)
Accumulated deficit	(506,310)	(314,167)
Total stockholders' equity	694,513	850,496
Total liabilities and stockholders' equity	$ 918,262	$ 1,002,337

See accompanying notes to unaudited condensed consolidated financial statements.

bluebird bio, Inc.

Condensed Consolidated Statements of Operations and Comprehensive Loss

(unaudited)

(in thousands, except per share data)

	Three months ended September 30,		Nine months ended September 30,	
	2016	2015	2016	2015
Revenue:				
Collaboration revenue	$1,552	$1,324	$4,603	$12,607
Total revenue	1,552	1,324	4,603	12,607
Operating expenses:				
Research and development	63,971	30,395	147,642	98,380
General and administrative	14,623	13,704	48,941	31,765
Change in fair value of contingent consideration	1,098	352	3,515	2,540
Total operating expenses	79,692	44,451	200,098	132,685
Loss from operations	(78,140)	(43,127)	(195,495)	(120,078)
Other income, net	937	263	2,803	630
Loss before income taxes	(77,203)	(42,864)	(192,692)	(119,448)
Income tax benefit (expense)	178	(60)	549	(60)
Net loss	$(77,025)	$(42,924)	$(192,143)	$(119,508)
Net loss per share - basic and diluted:	$(2.07)	$(1.18)	$(5.19)	$(3.52)
Weighted-average number of common shares used in computing net loss per share - basic and diluted:	37,201	36,384	37,026	33,979
Other comprehensive (loss) income:				
Unrealized (loss) gain on available-for-sale securities, net of tax (benefit) expense of ($0.1) and $0.8 million for the three and nine months ended September 30, 2016, respectively	(194)	103	1,455	121
Comprehensive loss	$(77,219)	$(42,821)	$(190,688)	$(119,387)

See accompanying notes to unaudited condensed consolidated financial statements.

bluebird bio, Inc.

Condensed Consolidated Statements of Cash Flows

(unaudited)

(in thousands)

	Nine months ended September 30,	
	2016	2015
Operating activities		
Net loss	$(192,143)	$(119,508)
Adjustments to reconcile net loss to net cash used in operating activities:		
Change in fair value of contingent consideration	2,099	2,015
Depreciation and amortization	7,132	5,381
Stock-based compensation expense	30,831	31,011
Other non-cash items	2,166	528
Changes in operating assets and liabilities:		
Prepaid expenses and other assets	(3,857)	(2,717)
Accounts payable	1,210	623
Accrued expenses and other liabilities	24,099	5,320
Deferred revenue	6,117	12,643
Deferred rent	1,805	(640)
Net cash (used in) operating activities	(120,541)	(65,344)
Investing activities		
Restricted cash	(4,379)	(8,816)
Purchase of property and equipment	(15,005)	(3,618)
Purchases of marketable securities	(145,135)	(470,499)
Proceeds from maturities of marketable securities	356,684	132,239
Proceeds from sales of marketable securities	7,500	—
Net cash provided by (used in) investing activities	199,665	(350,694)
Financing activities		
Cash paid for contingent purchase price consideration	(2,025)	(453)
Proceeds from public offering of common stock, net of issuance costs	—	477,247
Proceeds from issuance of common stock	3,786	8,909
Net cash provided by financing activities	1,761	485,703
Increase in cash and cash equivalents	80,885	69,665
Cash and cash equivalents at beginning of period	164,269	347,845
Cash and cash equivalents at end of period	$245,154	$417,510
Non-cash investing and financing activities:		
Construction financing lease obligation	$38,090	$43,777
Purchases of property and equipment included in accounts payable and accrued expenses	$2,479	$1,475
Stock option exercise proceeds receivable	$374	$24

See accompanying notes to unaudited condensed consolidated financial statements.

bluebird bio, Inc.

Notes to Condensed Consolidated Financial Statements

(unaudited)

1. Description of the business

bluebird bio, Inc. (the “Company” or “bluebird”) was incorporated in Delaware on April 16, 1992, and is headquartered in Cambridge, Massachusetts. The Company researches, develops, manufactures and plans to commercialize gene therapies for the treatment of severe genetic and rare diseases and in the field of T cell-based immunotherapy. Since its inception, the Company has devoted substantially all of its resources to its research and development efforts relating to its product candidates, including activities to manufacture product candidates, conduct clinical studies of its product candidates, perform preclinical research to identify new product candidates and provide general and administrative support for these operations.

2. Summary of significant accounting policies and basis of presentation

Basis of presentation and principles of consolidation

The accompanying condensed consolidated financial statements are unaudited and have been prepared by the Company in accordance with accounting principles generally accepted in the United States (“GAAP”) as found in the Accounting Standards Codification (“ASC”) and Accounting Standards Update (“ASU”) of the Financial Accounting Standards Board (“FASB”). Certain information and footnote disclosures normally included in the Company’s annual financial statements have been condensed or omitted. These interim condensed consolidated financial statements, in the opinion of management, reflect all normal recurring adjustments necessary for a fair presentation of the Company’s financial position and results of operations for the interim periods ended September 30, 2016 and 2015.

The results of operations for the interim periods are not necessarily indicative of the results of operations to be expected for the full year. These interim financial statements should be read in conjunction with the audited financial statements as of and for the year ended December 31, 2015, and the notes thereto, which are included in the Company’s Annual Report on Form 10-K filed with the Securities and Exchange Commission (the “SEC”) on February 25, 2016.

The accompanying condensed consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries: Precision Genome Engineering, Inc. (“Pregenen”), bluebird bio France – SARL, bluebird bio Australia Pty Ltd., bluebird bio (UK) Ltd., bluebird bio (Bermuda) Ltd. and bluebird bio Securities Corporation. All intercompany balances and transactions have been eliminated in consolidation. Any reference in these notes to applicable guidance is meant to refer to GAAP. The Company views its operations and manages its business in one operating segment. All material long-lived assets of the Company reside in the United States.

Summary of accounting policies

The significant accounting policies and estimates used in the preparation of the condensed consolidated financial statements are described in the Company's audited financial statements as of and for the year ended December 31, 2015, and the notes thereto, which are included in the Company's Annual Report on Form 10-K. There have been no material changes in the Company's significant accounting policies during the nine months ended September 30, 2016.

Net income (loss) per share

Basic net income (loss) per share is calculated by dividing net income (loss) attributable to common stockholders by the weighted average number of common shares outstanding during the period. Diluted net income per share is calculated by dividing the net income attributable to common stockholders by the weighted-average number of common stock equivalent shares outstanding for the period, including any dilutive effect from outstanding stock options, unvested restricted stock, restricted stock units, employee stock purchase plan, and warrants using the treasury stock method.

Use of estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts in the financial statements and accompanying notes. Estimates are used in the following areas, among others: fair value estimates used to assess potential impairment of long-lived assets, construction financing lease obligations, contingent consideration, stock-based compensation expense, accrued expenses, revenue and income taxes. Actual results could materially differ from those estimates.

bluebird bio, Inc.

Notes to Condensed Consolidated Financial Statements

(unaudited)

Recently issued accounting pronouncements

In May 2014, the FASB issued ASU No. 2014-09, Revenue from Contracts with Customers (“Topic 606”), which supersedes all existing revenue recognition requirements, including most industry-specific guidance. The new standard requires a company to recognize revenue when it transfers goods or services to customers in an amount that reflects the consideration that the company expects to receive for those goods or services. The new standard will be effective on January 1, 2018 and earlier application is permitted only for annual reporting periods beginning after December 15, 2016, including interim reporting periods within that reporting period. The Company is currently evaluating the potential impact that Topic 606 may have on its financial position and results of operations.

In February 2016, the FASB issued ASU 2016-02, Leases, (“ASU 2016-02”), which requires a lessee to recognize assets and liabilities on the balance sheet for operating leases and changes many key definitions, including the definition of a lease. The new standard includes a short-term lease exception for leases with a term of 12 months or less, as part of which a lessee can make an accounting policy election not to recognize lease assets and lease liabilities. Lessees will continue to differentiate between finance leases (previously referred to as capital leases) and operating leases using classification criteria that are substantially similar to the previous guidance. The new standard will be effective beginning January 1, 2019, and early adoption is permitted for public entities. The Company is currently evaluating the potential impact ASU 2016-02 may have on its financial position and results of operations.

In March 2016, the FASB issued ASU 2016-09, Improvements to Employee Share-Based Payment Accounting (“ASU No. 2016-09”), which simplifies share-based payment accounting through a variety of amendments. The standard will be effective for annual reporting periods and interim periods within those annual periods, beginning after December 15, 2016, and early adoption is permitted. The Company is currently evaluating the potential impact ASU 2016-09 may have on its financial position and results of operations.

In August 2016, the FASB issued ASU 2016-15, Statement of Cash Flows: Classification of Certain Cash Receipts and Cash Payments (“Topic 230”). The new standard clarifies certain aspects of the statement of cash flows, including the classification of contingent consideration payments made after a business combination and several other clarifications not currently applicable to the Company. The new standard also clarifies that an entity should determine each separately identifiable source or use within the cash receipts and cash payments on the basis of the nature of the underlying cash flows. In situations in which cash receipts and payments have aspects of more than one class of cash flows and cannot be separated by source or use, the appropriate classification should depend on the activity that is likely to be the predominant source or use of cash flows for the item. The new standard will be effective for the Company on January 1, 2018. The adoption of this standard is not expected to have a material impact on our statements of cash flows upon adoption.

3. Marketable securities

The following table summarizes the available-for-sale securities held at September 30, 2016 and December 31, 2015 (in thousands):

Description	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
September 30, 2016				
U.S. government agency securities and treasuries	$475,344	$ 91	$ (164)	$475,271
Certificates of deposit	7,200	16	—	7,216
Total	$482,544	$ 107	$ (164)	$482,487
December 31, 2015				
U.S. government agency securities and treasuries	$689,425	$ 22	$ (2,300)	$687,147
Certificates of deposit	14,360	—	(13)	14,347
Total	$703,785	$ 22	$ (2,313)	$701,494

No available-for-sale securities held as of September 30, 2016 or December 31, 2015 had remaining maturities greater than three years.

bluebird bio, Inc.

Notes to Condensed Consolidated Financial Statements

(unaudited)

4. Fair value measurements

The following table sets forth the Company's assets and liabilities that are measured at fair value on a recurring basis as of September 30, 2016 and December 31, 2015 (in thousands):

Description	Total	Quoted prices in active markets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)
September 30, 2016				
Assets:				
Cash and cash equivalents	$245,154	$245,154	$—	$ —
Marketable securities:				
U.S. government agency securities and treasuries	475,271	—	475,271	—
Certificates of deposit	7,216	—	7,216	—
Total assets	$727,641	$245,154	$482,487	$ —
Liabilities:				
Contingent consideration	$7,180	$—	$—	$ 7,180
Total liabilities	$7,180	$—	$—	$ 7,180
December 31, 2015				
Assets:				
Cash and cash equivalents	$164,269	$158,269	$6,000	$ —
Marketable securities:				
U.S. government agency securities and treasuries	687,147	—	687,147	—
Certificates of deposit	14,347	—	14,347	—
Total assets	$865,763	$158,269	$707,494	$ —
Liabilities:				
Contingent consideration	$8,665	$—	$—	$ 8,665
Total liabilities	$8,665	$—	$—	$ 8,665

Cash and cash equivalents

The Company considers all highly liquid securities with original final maturities of three months or less from the date of purchase to be cash equivalents. As of September 30, 2016, cash and cash equivalents comprise funds in cash, money market accounts, and federally insured deposits. As of December 31, 2015, cash and cash equivalents comprise

funds in cash, money market accounts, U.S. Treasury securities and federally insured deposits.

Marketable securities

The amortized cost of available-for-sale securities is adjusted for amortization of premiums and accretion of discounts to maturity. At September 30, 2016 and December 31, 2015, the balance in the Company's accumulated other comprehensive loss was composed solely of activity related to the Company's available-for-sale marketable securities. There were no material realized gains on the sale or maturity of available-for-sale securities during the nine months ended September 30, 2016, and as a result, the Company did not reclassify any material amounts out of accumulated other comprehensive loss for the same period.

The aggregate fair value of securities held by the Company in an unrealized loss position for less than twelve months as of September 30, 2016 and December 31, 2015 was $255.8 million and $638.1 million, respectively. There were no securities held by the Company in an unrealized loss position for more than twelve months as of September 30, 2016. The Company has the intent and ability to hold such securities until recovery. The Company determined that there was no material change in the credit risk of the above investments. As a result, the Company determined it did not hold any investments with any other-than-temporary impairment as of September 30, 2016 and December 31, 2015.

bluebird bio, Inc.

Notes to Condensed Consolidated Financial Statements

(unaudited)

Contingent consideration

On June 30, 2014, the Company acquired Pregenen. In connection with the acquisition, the Company recorded contingent consideration pertaining to the amounts potentially payable to Pregenen's former equityholders pursuant to the Stock Purchase Agreement (the "Stock Purchase Agreement") by and among the Company, Pregenen and Pregenen's former equityholders. Contingent consideration is measured at fair value and is based on significant inputs not observable in the market, which represents a Level 3 measurement within the fair value hierarchy. The valuation of contingent consideration uses assumptions the Company believes would be made by a market participant. The Company assesses these estimates on an on-going basis as additional data impacting the assumptions is obtained. Future changes in the fair value of contingent consideration related to updated assumptions and estimates are recognized within the condensed consolidated statements of operations and comprehensive loss.

Contingent consideration may change significantly as development progresses and additional data are obtained, impacting the Company's assumptions regarding probabilities of successful achievement of related milestones used to estimate the fair value of the liability and the timing in which they are expected to be achieved. In evaluating the fair value information, considerable judgment is required to interpret the market and internal data used to develop the estimates. The estimates of fair value may not be indicative of the amounts that could be realized in a current market exchange. Accordingly, the use of different market and internal assumptions and/or different valuation techniques could result in materially different fair value estimates.

The significant unobservable inputs used in the measurement of fair value of the Company's contingent consideration are probabilities of successful achievement of preclinical, clinical and commercial milestones, the period in which these milestones are expected to be achieved ranging from 2017 to 2026 and discount rates ranging from 9.9% to 12.7%. Significant increases or decreases in any of the probabilities of success would result in a significantly higher or lower fair value measurement, respectively. Significant increases or decreases in these other inputs would result in a significantly lower or higher fair value measurement, respectively.

The table below provides a roll-forward of fair value of the Company's contingent consideration obligations, which include Level 3 inputs (in thousands):

	Nine Months Ended September 30, 2016
Beginning balance	$ 8,665
Additions	—
Changes in fair value	3,515
Payments	(5,000)
Ending balance	$ 7,180

The Company may be required to make up to $129.0 million in remaining future contingent cash payments to the former equityholders of Pregenen upon the achievement of certain milestones related to the Pregenen technology, of which $9.0 million relates to preclinical milestones, $20.1 million relates to clinical milestones, and $99.9 million relates to commercial milestones. As of September 30, 2016, $3.9 million of the fair value of the Company's total contingent consideration obligations was reflected as a component of accrued expenses and other current liabilities within the condensed consolidated balance sheets, with the remaining balance of $3.3 million reflected as a non-current liability.

bluebird bio, Inc.

Notes to Condensed Consolidated Financial Statements

(unaudited)

5. Property and equipment, net

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

	September 30, 2016	December 31, 2015
Computer equipment and software	$ 1,350	$ 1,259
Office equipment	1,427	1,104
Laboratory equipment	15,273	10,520
Leasehold improvements	13,839	11,010
Construction-in-progress	110,922	65,542
Total property and equipment, gross	142,811	89,435
Less accumulated depreciation and amortization	(11,074)	(6,821)
Total property and equipment, net	$ 131,737	$ 82,614

Construction-in-progress as of September 30, 2016 includes $109.7 million related to construction costs at 60 Binney Street in Cambridge, Massachusetts, of which $100.0 million was incurred by the landlord. Please refer to Note 7, "Commitments and contingencies," for further information.

6. Accrued expenses and other current liabilities

Accrued expenses and other current liabilities consist of the following (in thousands):

	September 30, 2016	December 31, 2015
Employee compensation	$ 8,920	$ 5,935
Accrued goods and services	23,855	15,876
Accrued license and milestone fees	15,208	277
Accrued professional fees	2,103	1,014
Deferred rent, current portion	68	964
Contingent consideration, current portion	3,913	3,584
Other	605	495
Total accrued expenses and other current liabilities	$ 54,672	$ 28,145

Accrued license and milestone fees as of September 30, 2016 includes a $15.0 million upfront fee related to a research collaboration and license agreement entered into during the third quarter of 2016. This upfront fee was paid in the fourth quarter of 2016.

7. Commitments and contingencies

The Company is party to various agreements, principally relating to licensed technology, that require future payments relating to milestones not met at September 30, 2016 and December 31, 2015 or royalties on future sales of specified products.

The Company enters into standard indemnification agreements in the ordinary course of business. Pursuant to these agreements, the Company indemnifies, holds harmless, and agrees to reimburse the indemnified party for losses suffered or incurred by the indemnified party, generally the Company's business partners or customers, in connection with claims by any third party with respect to the Company's products or business activities. The term of these indemnification agreements is generally perpetual any time after execution of the agreement. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is unlimited. The Company has never incurred costs to defend lawsuits or settle claims related to these indemnification agreements.

bluebird bio, Inc.

Notes to Condensed Consolidated Financial Statements

(unaudited)

The Company's wholly-owned subsidiary bluebird bio France – SARL participates in the French Crédit d'Impôt Recherche ("CIR") program, which allows companies to monetize up to 30% of eligible research expenses. As of September 30, 2016, the Company received aggregate reimbursement of €2.3 million related to years 2013 through 2015. The Company has not yet applied for the €0.6 million related to the nine months ended September 30, 2016. The years 2013 through 2016 are open and subject to examination.

Operating Lease Commitments

On June 3, 2013, the Company entered into a nine-year building lease for approximately 43,600 square feet of space located at 150 Second Street, Cambridge, Massachusetts, which commenced in December 2013. This lease was amended in June 2014 to add approximately 9,900 square feet. The lease originally had monthly lease payments of $0.2 million for the first 12 months, which increased to $0.3 million per month beginning in December 2014 due to the lease amendment, with annual rent escalations thereafter. Rent expense is recognized on a straight-line basis over the term of the lease. The Company has the option to extend this lease by an additional five years. The lease provided a contribution from the landlord towards the initial build-out of the space of up to $7.8 million. The Company capitalizes the leasehold improvements as property and equipment and records the landlord incentive payments received as deferred rent and amortizes these amounts as reductions to rent expense over the lease term. In addition, in accordance with the lease, the Company entered into a cash-collateralized irrevocable standby letter of credit in the amount of $1.3 million, naming the landlord as beneficiary, which has a balance of $0.6 million as of September 30, 2016.

On September 30, 2016, the Company entered into an Assignment and Assumption of Lease ("Assignment") relating to its lease at 150 Second Street. Under the Assignment, the Company will assign all of its rights, interests, obligations and responsibilities under the lease, to be effective as of the later of May 1, 2017 or the first day following the Company's surrender of the leased premises in accordance with the lease. The Company expects to vacate the premises by mid-2017 and as a result, no longer expects to pay $20.6 million in lease payments between 2017 and 2022, including $2.2 million in 2017, $3.5 million in 2018, $3.6 million in 2019, $3.7 million in 2020 and $7.6 million in 2021 and thereafter.

On June 29, 2015, the Company entered into a lease agreement for additional office space located at 215 First Street, Cambridge, Massachusetts. Under the terms of the lease, the Company leased approximately 15,120 square feet starting on July 13, 2015 for $0.5 million per year in base rent, which is subject to a 3% annual rent increase plus certain operating expenses and taxes. The lease will continue until the end of the 60th full calendar month following the date the landlord delivers the premises to the Company, and includes early termination provisions that could allow the Company to terminate the lease without penalty at the end of the 20th full calendar month following the delivery of the premises if the Company meets certain conditions specified within the lease. Under the terms of the lease, the Company has also leased an additional 8,075 square feet of office space in the same premises starting on January 1, 2016 for an additional $0.3 million per year in base rent, which is subject to a 3% annual rent increase plus certain operating expenses and taxes. The Company expects to terminate the lease by mid-2017.

On June 3, 2016, the Company entered into a strategic manufacturing agreement for the future commercial production of the Company's Lenti-D and LentiGlobin product candidates with a contract manufacturing organization. Under this 12 year agreement, the contract manufacturing organization will complete the design, construction, validation and process validation of the leased suites prior to anticipated commercial launch of the product candidates. During construction, the Company is required to pay $12.5 million upon the achievement of certain construction milestones, and may pay up to $8.0 million in additional construction milestones if the Company elects its option to lease additional suites. The Company paid $2.0 million for the achievement of the first milestone during the third quarter of 2016, which is reflected as a component of other non-current assets within the condensed consolidated balance sheets. Following construction completion, the Company will pay $5.1 million per year in fixed suite fees as well as certain fixed labor, raw materials, testing and shipping costs for manufacturing services, and may pay additional suite fees if it elects its option to reserve or lease additional suites. The Company may terminate this agreement any time after July 1, 2016 upon payment of a one-time termination fee and up to 24 months of fixed suite and labor fees. The Company concluded that this agreement contains an embedded lease as the suites are designated for the Company's exclusive use during the term of the agreement. The Company concluded that it is not the deemed owner during construction nor is it a capital lease. As a result, the Company will account for the agreement as an operating lease and expense the rental payments on a straight-line basis over the term of the embedded lease.

bluebird bio, Inc.

Notes to Condensed Consolidated Financial Statements

(unaudited)

60 Binney Street Lease Commitments

On September 21, 2015, the Company entered into a lease agreement, which was amended for certain administrative matters on June 21, 2016, for additional office and laboratory space located in a building (the "Building") under construction at 60 Binney Street, Cambridge, Massachusetts (the "60 Binney Lease"). Under the terms of the 60 Binney Lease, starting on October 1, 2016, the Company will lease approximately 253,108 square feet of office and laboratory space at $72.50 per square foot per year, or $18.4 million per year in base rent, which is subject to scheduled annual rent increases of 1.75% plus certain operating expenses and taxes. The Company also executed a $9.2 million letter of credit upon signing the 60 Binney Lease, which was required to be collateralized with a bank account at a financial institution in accordance with the 60 Binney Lease agreement. This letter of credit was increased to $13.8 million during the third quarter of 2016 as required under the terms of the lease. Subject to the terms of the lease and certain reduction requirements specified therein, including market capitalization requirements, this amount may decrease back to $9.2 million over time. The 60 Binney Lease will continue until the end of the 120th full calendar month following April 2017 or the earlier the date the Company occupies the Building or other conditions specified in the 60 Binney Lease occur. Pursuant to a work letter entered into in connection with the 60 Binney Lease, the landlord will contribute an aggregate of $42.4 million toward the cost of construction and tenant improvements for the Building. The purpose of the 60 Binney Lease is to supplement and eventually replace the Company's current leased premises at 150 Second Street and 215 First Street in Cambridge, Massachusetts and the Company intends to move its corporate headquarters to 60 Binney Street in mid-2017. The Company has the option to extend the 60 Binney Lease for two successive five-year terms.

Because the Company is involved in the construction project, including having responsibility to pay for a portion of the costs of finish work and mechanical, electrical, and plumbing elements of the Building, the Company is deemed for accounting purposes to be the owner of the Building during the construction period. Accordingly, the Company has recorded project construction costs incurred by the landlord as an asset in "Property and equipment, net" and a related financing obligation in "Construction financing lease obligation" on the Company's condensed consolidated balance sheet.

The Company bifurcates its future lease payments pursuant to the 60 Binney Lease into (i) a portion that is allocated to the Building and (ii) a portion that is allocated to the land on which the Building is being constructed, which is recorded as rental expense. Although the Company estimates that the Company will not begin making lease payments pursuant to the 60 Binney Lease until April 2017, the portion of the lease obligation allocated to the land is treated for accounting purposes as an operating lease that commenced upon execution of the 60 Binney Lease in September 2015. During the three and nine months ended September 30, 2016, the Company recognized $0.5 and $1.4 million of non-cash rental expense attributable to the land.

As of September 30, 2016, Property and equipment, net, includes $109.7 million related to construction costs for the Building. The construction financing lease obligation related to the Building is $100.0 million. No cash has been paid to the landlord to date.

Once the landlord completes the construction of the Building, the Company will evaluate the 60 Binney Lease in order to determine whether or not the 60 Binney Lease meets the criteria for "sale-leaseback" treatment. If the 60 Binney Lease meets the "sale-leaseback" criteria, the Company will remove the asset and the related liability from its

consolidated balance sheet and treat the 60 Binney Lease as either an operating or a capital lease based on the Company's assessment of the accounting guidance. The Company expects that upon completion of construction of the Building the 60 Binney Lease will not meet the "sale-leaseback" criteria. If the 60 Binney Lease does not meet "sale-leaseback" criteria, the Company will treat the 60 Binney Lease as a financing obligation and will depreciate the asset in accordance with the Company's accounting policy.

8. Significant agreements

Celgene Corporation

Original Collaboration Agreement

On March 19, 2013, the Company entered into a Master Collaboration Agreement (the "Collaboration Agreement") with Celgene Corporation ("Celgene") to discover, develop and commercialize potentially disease-altering gene therapies in oncology. The collaboration is focused on applying gene therapy technology to genetically modify a patient's own T cells, known as chimeric antigen receptor, or CAR T cells, to target and destroy cancer cells. Additionally, on March 19, 2013, the Company entered into a Platform Technology Sublicense Agreement (the "Sublicense Agreement") with Celgene pursuant to which the Company obtained a sublicense to certain intellectual property from Celgene, originating under Celgene's license from Baylor College of Medicine, for use in the collaboration.

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Under the terms of the Collaboration Agreement, the Company received a $75.0 million up-front, non-refundable cash payment. The Company was responsible for conducting discovery, research and development activities through completion of Phase I clinical studies, if any, during the initial term of the Collaboration Agreement, or three years. The collaboration is governed by a joint steering committee ("JSC") formed by an equal number of representatives from the Company and Celgene. The JSC, among other activities, reviews the collaboration program, reviews and evaluates product candidates and approves regulatory plans. In addition to the JSC, the Collaboration Agreement provides that the Company and Celgene each appoint representatives to a patent committee, which is responsible for managing the intellectual property developed and used during the collaboration.

Amended Collaboration Agreement

On June 3, 2015, the Company and Celgene amended and restated the Collaboration Agreement (the "Amended Collaboration Agreement"). Under the Amended Collaboration Agreement, the parties will now focus the collaboration exclusively on anti- B-cell maturation antigen ("BCMA") product candidates for a new three-year term. In connection with the Amended Collaboration Agreement, the Company received an upfront, one-time, non-refundable, non-creditable payment of $25.0 million to fund research and development under the collaboration. The collaboration will continue to be governed by the JSC.

Under the terms of the Amended Collaboration Agreement, for up to two product candidates selected for development under the collaboration, the Company is responsible for conducting and funding all research and development activities performed up through completion of the initial Phase I clinical study of such product candidate.

On a product candidate-by-product candidate basis, up through a specified period following enrollment of the first patient in an initial Phase I clinical study for such product candidate (the "Option Period"), the Company has granted Celgene an option to obtain an exclusive worldwide license to develop and commercialize such product candidate pursuant to a written agreement, the form of which the Company has already agreed upon. In the event that Celgene exercises its option with respect to any product candidate, the Company may elect to co-develop and co-promote the product candidate in the United States, provided that, if the Company does not exercise its option co-develop and co-promote the first product candidate in-licensed by Celgene under the Amended Collaboration Agreement, then the Company will not be permitted to exercise its option to co-develop and co-promote any future product candidates under the Amended Collaboration Agreement. If Celgene elects to exercise its option to exclusively in-license a product candidate, it must pay the Company an option fee in the amount of $10.0 million for the first product candidate and $15.0 million for any additional product candidates.

On February 10, 2016, Celgene exercised its option to obtain an exclusive worldwide license to develop and commercialize bb2121, the first product candidate under the Amended Collaboration Agreement, pursuant to an executed license agreement entered into by the parties on February 16, 2016 and paid the associated $10.0 million option fee. The Company may now elect to co-develop and co-promote the product candidate in the United States and will receive an additional fee in the amount of $10.0 million in the event the Company does not exercise its option to co-develop and co-promote bb2121 with Celgene. On February 17, 2016, the parties further amended the Amended Collaboration Agreement to update the timing of certain deliverables in connection with Celgene's option exercise for the license of the bb2121 product candidate.

Accounting Analysis

The Company's Amended Collaboration Agreement with Celgene contains the following deliverables: (i) research and development services, (ii) participation on the JSC, (iii) participation on the patent committee, (iv) a license to the first product candidate, (v) manufacture of vectors and associated payload for incorporation into the first optioned product candidate under the license, and (vi) participation on the JGC under the co-development and co-promotion agreement for the first optioned product candidate under the license.

The license to the first product candidate was considered a deliverable at the inception of the arrangement and therefore the associated option fee was included in allocable arrangement consideration as the Company believed there was minimal risk with regard to whether Celgene will exercise the option based on the successful completion of preclinical activities and proximity of enrollment of the first patient in an initial Phase I clinical study for this product candidate. The Company determined that the obligation within the license to manufacture or have manufactured supplies of vectors and associated payloads for incorporation into the first optioned product candidate is a deliverable, consistent with the option to license the first product candidate.

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However, the Company determined that the options to license any additional product candidates are substantive options and therefore were not considered deliverables at execution of the Amended Collaboration Agreement. Celgene is not contractually obligated to exercise the options. Additionally, as a result of the uncertain outcome of the discovery, research and development activities, the Company is at risk with regard to whether Celgene will exercise the options to license additional product candidates. Moreover, the Company determined that the options are not priced at a significant and incremental discount. Accordingly, the options to other product candidates are not considered deliverables and the associated option fees are not included in allocable arrangement consideration.

Upon execution of the Amended Collaboration Agreement in June 2015, the Company concluded that each of the three delivered elements at the inception of the agreement (research and development services, participation on the JSC and participation on the patent committee) had standalone value from the other undelivered elements. Additionally, the Amended Collaboration Agreement does not include return rights related to the collaboration term. Accordingly, each deliverable qualified as a separate unit of accounting.

The Company determined that each of the delivered elements had the same period of performance (the three year term through projected initial Phase I clinical study substantial completion) and the same pattern of revenue recognition, ratably over the period of performance as there was no other discernible pattern of recognition. The Company identified the allocable arrangement consideration as the $25.0 million up-front research and development funding payment, $10.0 million option fee for the first product candidate, $20.0 million related to remaining deferred revenue from the original Collaboration Agreement, and $54.1 million of contingent revenue related to the estimated amounts that will be received from Celgene for manufacturing services. The $109.0 million total allocable arrangement consideration was allocated based on the relative estimated selling price of the separate units of accounting at the inception of the amended agreement, resulting in $17.3 million allocated to the three delivered elements at the inception of the agreement, which will be recognized over an initial three year term.

The Company is required to reassess its conclusions on standalone value of deliverables upon delivery, and therefore, upon Celgene’s exercise of its option to obtain an exclusive worldwide license to develop and commercialize bb2121 in February 2016, the Company updated its assessment. The Company determined that there were no changes in standalone value of the research and development services as the option was previously determined to be non-substantive, the Company continues to have an obligation to provide research and development services for bb2121 and other product candidates, and this obligation is separate and unrelated to the execution of the license agreement. Participation on the JSC and participation on the patent committee also continue to have standalone value from the other undelivered elements as there has been no change in facts that would change this conclusion. Accordingly, each of these three deliverables continues to qualify as a separate unit of accounting.

The Company determined that each of the identified deliverables that qualify as a separate unit of accounting continue to have the same period of performance (the three year term through projected initial Phase I clinical study substantial completion) and the same pattern of revenue recognition, ratably over the period of performance as there is no other discernible pattern of recognition, and therefore there is no change in the recognition of $17.3 million allocated to these three elements. As of September 30, 2016, this will continue to be recognized over a three year term that began in June 2015.

However, the Company concluded that the license to bb2121 does not have standalone value from one of the undelivered elements, the post-initial Phase I the manufacture of vectors and associated payload for bb2121 under the license, because the manufacturing is essential to the license agreement. Accordingly, these two deliverables qualify as a single combined unit of accounting.

The single combined unit of accounting comprised of the license to bb2121 and the manufacture of vectors and associated payload for bb2121 were allocated consideration of $91.7 million, which will begin to be recognized upon the commencement of manufacturing services for bb2121 for Celgene post-initial Phase I, not in excess of the fixed consideration and assuming other revenue recognition criteria have been met. The Company currently expects this to commence in the second half of 2017 or first half of 2018. Revenue for the combined unit of account will be recognized on a proportional performance method or ratably over the period of performance if there is no other discernible pattern of recognition. This period of performance and recognition pattern will be revisited as the development plan changes or if other events impacting the deliverables occur.

The Company evaluated all of the milestones that may be received in connection with Celgene’s option to license a product candidate resulting from the collaboration. In evaluating if a milestone is substantive, the Company assesses whether: (i) the consideration is commensurate with either the Company’s performance to achieve the milestone or the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the Company’s performance to achieve the milestone, (ii) the

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consideration relates solely to past performance and (iii) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. All clinical and regulatory milestones that may be received under the option to the license agreement are considered substantive on the basis of the contingent nature of the milestone, specifically reviewing factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the milestone as well as the level of effort and investment required. Accordingly, such amounts will be recognized as revenue in full in the period in which the associated milestone is achieved, assuming all other revenue recognition criteria are met. All commercial milestones will be accounted for in the same manner as royalties and recorded as revenue upon achievement of the milestone, assuming all other revenue recognition criteria are met.

During the three months ended September 30, 2016 and 2015, the Company recognized $1.6 million and $1.3 million, respectively, of revenue associated with its collaboration with Celgene related to the recognition of discovery, research and development services. During the nine months ended September 30, 2016 and 2015 the Company recognized $4.6 million and $12.6 million, respectively, of revenue associated with its same collaboration. As of September 30, 2016 and December 31, 2015, there was $48.0 million and $41.8 million, respectively, of total deferred revenue related to the Company's collaboration with Celgene, which is classified as current or non-current in the condensed consolidated balance sheets, $10.3 million of which is currently expected to be recognized through the first half of 2018 with the remaining amount deferred until a later date, as described above.

9. Stock-based compensation

In January 2016, the number of shares of common stock available for issuance under the 2013 Stock Option and Incentive Plan ("2013 Plan") was increased by approximately 1.5 million shares as a result of the automatic increase provision of the 2013 Plan. As of September 30, 2016, the total number of shares of common stock available for issuance under the 2013 Plan was approximately 1.2 million.

Stock-based compensation expense

Stock-based compensation expense by award type included within the condensed consolidated statements of operations and comprehensive loss was as follows (in thousands):

	Three months ended		Nine months ended	
	September 30,		September 30,	
	2016	2015	2016	2015
Stock options	$8,294	$8,407	$26,278	$28,472

Restricted stock units	1,495	1,056	4,248	2,341
Employee stock purchase plan	116	66	305	198
	$9,905	$9,529	$30,831	$31,011

As of September 30, 2016, the Company had $89.4 million of unrecognized stock-based compensation expense, net of estimated forfeitures, related to unvested stock options, restricted stock units and the employee stock purchase plan, which is expected to be recognized over a weighted-average period of 2.6 years.

Stock-based compensation expense by classification included within the condensed consolidated statements of operations and comprehensive loss was as follows (in thousands):

	Three months ended		Nine months ended	
	September 30,		September 30,	
	2016	2015	2016	2015
Research and development	$5,399	$4,426	$15,410	$19,726
General and administrative	4,506	5,103	15,421	11,285
	$9,905	$9,529	$30,831	$31,011

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In the first quarter of 2015, the Company modified outstanding options held by its former Chief Scientific Officer in connection with the termination of his employment. The incremental value of the modification was $3.0 million. As a result of the modification, the Company recognized $0.2 million and $3.0 million of stock-based compensation expense during the three and nine months ended September 30, 2015, respectively.

In the second quarter of 2015, the Company modified the vesting conditions of a stock option award held by a non-employee founder, which resulted in $6.7 million of stock-based compensation expense recognized to research and development expense during the second quarter of 2015.

Stock options

The following table summarizes the stock option activity under the Company's equity award plans (shares in thousands):

	Shares	Weighted-average exercise price per share
Outstanding at December 31, 2015	3,532	$ 48.74
Granted	944	$ 50.55
Exercised	(273)	$ 11.71
Canceled or forfeited	(336)	$ 48.88
Outstanding at September 30, 2016	3,867	$ 51.74
Exercisable at September 30, 2016	1,850	$ 38.04
Vested and expected to vest at September 30, 2016	3,776	$ 51.53

Options exercisable for 0.3 million shares of common stock were exercised during the nine months ended September 30, 2016, resulting in total proceeds to the Company of $3.2 million. In accordance with the Company's equity award plans, the shares were issued from a pool of shares reserved for issuance under the equity award plans.

Restricted stock units

The following table summarizes the restricted stock unit activity under the Company's equity award plans (shares in thousands):

	Shares	Weighted-average grant date fair value
Unvested balance at December 31, 2015	148	$ 65.79
Granted	236	$ 50.55
Vested	(110)	$ 45.57
Forfeited	(20)	$ 41.63
Unvested balance at September 30, 2016	254	$ 62.23

Employee stock purchase plan

On June 3, 2013, the Company's board of directors adopted its 2013 Employee Stock Purchase Plan ("2013 ESPP"), which was subsequently approved by its stockholders and became effective upon the closing of the Company's IPO on June 24, 2013. The 2013 ESPP authorizes the initial issuance of up to a total of 238,000 shares of the Company's common stock to participating employees. The first offering period under the 2013 ESPP opened on August 1, 2014. During the nine months ended September 30, 2016 and 2015, 18,338 shares and 10,545 shares of common stock were issued under the 2013 ESPP, respectively.

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10. Income taxes

Deferred tax assets and deferred tax liabilities are recognized based on temporary differences between the financial reporting and tax basis of assets and liabilities using statutory rates. A valuation allowance is recorded against deferred tax assets if it is more likely than not that some or all of the deferred tax assets will not be realized. Due to the uncertainty surrounding the realization of the favorable tax attributes in future tax returns, the Company has recorded a full valuation allowance against the Company's otherwise recognizable net deferred tax assets.

For the three and nine months ended September 30, 2016, the Company recognized an income tax benefit of $0.2 and $0.5 million and an income tax (benefit) expense in other comprehensive loss of $(0.1) and $0.8 million related to the unrealized gain (loss) on available-for-sale securities. As of September 30, 2016, the Company recorded an accrued income tax provision of $0.2 million related to this tax benefit included within accrued expenses and other current liabilities in the condensed consolidated balance sheet, which is expected to be generated from continuing operations.

11. Net loss per share

The following common stock equivalents were excluded from the calculation of diluted net loss per share for the periods indicated because including them would have had an anti-dilutive effect (in thousands):

	For the three and nine months ended September 30,	
	2016	2015
Outstanding stock options	3,867	3,661
Restricted stock units	254	149
ESPP shares	12	3
Acquisition holdback	—	94
	4,133	3,907

Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations

The following information should be read in conjunction with the unaudited financial information and the notes thereto included in this Quarterly Report on Form 10-Q and the audited financial information and the notes thereto included in our Annual Report on Form 10-K, which was filed with the Securities and Exchange Commission, or the SEC, on February 25, 2016.

Except for the historical information contained herein, the matters discussed in this Quarterly Report on Form 10-Q may be deemed to be forward-looking statements that involve risks and uncertainties. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. In this Quarterly Report on Form 10-Q, words such as "may," "expect," "anticipate," "estimate," "intend," "plan," and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements.

Our actual results and the timing of certain events may differ materially from the results discussed, projected, anticipated, or indicated in any forward-looking statements. We caution you that forward-looking statements are not guarantees of future performance and that our actual results of operations, financial condition and liquidity, and the development of the industry in which we operate may differ materially from the forward-looking statements contained in this Quarterly Report. In addition, even if our results of operations, financial condition and liquidity, and the development of the industry in which we operate are consistent with the forward-looking statements contained in this Quarterly Report, they may not be predictive of results or developments in future periods.

The following information and any forward-looking statements should be considered in light of factors discussed elsewhere in this Quarterly Report on Form 10-Q, including those risks identified under Part II, Item 1A. 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. We disclaim any obligation, except as specifically required by law and the rules of the SEC, to publicly update or revise any such statements to reflect any change in our expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.

Overview

We are a clinical-stage biotechnology company committed to developing potentially transformative gene therapies for severe genetic and rare diseases and in the field of T cell-based immunotherapy. With our lentiviral-based gene therapy and gene editing capabilities, we have built an integrated product platform with broad potential application in these areas. We believe that gene therapy for severe genetic diseases has the potential to change the way these patients are treated by correcting the underlying genetic defect that is the cause of their disease, rather than offering treatments that only address their symptoms. We and our scientific collaborators have generated what we believe is human proof-of-concept data for our gene therapy platform in three underserved diseases.

We are conducting four clinical studies of our LentiGlobin product candidate: a Phase I/II study in the United States, Australia, and Thailand, called the Northstar Study, for the treatment of transfusion-dependent -thalassemia, or TDT; a global, multi-center Phase III study called the Northstar-2 Study, for the treatment of patients with TDT who do not have a $^{0}/^{0}$ genotype; a single-center Phase I/II study in France (HGB-205) for the treatment of TDT and severe sickle cell disease, or severe SCD; and a Phase I study in the United States (HGB-206) for the treatment of severe SCD. We have achieved our enrollment target of 18 patients in the Northstar Study. Both TDT and severe SCD are rare, hereditary blood disorders that often lead to severe anemia and shortened lifespans. Our LentiGlobin product candidate has been granted Orphan Drug status by the U.S. Food and Drug Administration, or FDA, and the European

Medicines Agency, or EMA, for both -thalassemia and SCD. Our LentiGlobin product candidate was granted Fast-Track designation by the FDA for the treatment of -thalassemia major in January 2013 and for the treatment of certain patients with severe SCD in May 2014. In January 2015, the FDA granted Breakthrough Therapy designation to our LentiGlobin product candidate for the treatment of transfusion-dependent patients with -thalassemia major. In September 2016, the EMA has granted access to its Priority Medicines (PRIME) scheme for our LentiGlobin product candidate for the treatment of TDT. Also in September 2016, we initiated our NorthStar-2 Study, which we expect will enroll approximately 15 adult and adolescent patients with TDT who do not have a $^{0}/^{0}$ genotype, with an additional pediatric cohort of up to eight patients for a total enrollment of approximately 23 patients. We expect to evaluate the patients for 24 months following treatment, and anticipate that the primary endpoint of this study will be 12 months of transfusion independence following treatment. We have discussed with the FDA and EMA the design of our planned Phase III study (HGB-212) of our LentiGlobin product candidate for patients with TDT who have a $^{0}/^{0}$ genotype, and we anticipate that the primary endpoint of this study will be transfusion reduction.

We are also conducting a Phase II/III clinical study, called the Starbeam Study, of our Lenti-D product candidate, to evaluate its safety and efficacy in subjects with cerebral adrenoleukodystrophy, or CALD, a rare, hereditary neurological disorder that is often fatal. In October 2013, we announced that the first subject had been treated in this study and in May 2015 we announced the achievement of enrollment of 18 subjects in this study. We are also conducting an observational study of subjects with CALD treated by allogeneic hematopoietic stem-cell transplant referred to as the ALD-103 study. Our Lenti-D product candidate has been granted Orphan Drug status by the FDA and the EMA for the treatment of adrenoleukodystrophy.

In March 2013, we entered into a global strategic collaboration with Celgene Corporation, or Celgene, to discover, develop and commercialize chimeric antigen receptor-modified T cells, or CAR T cells, as potentially disease-altering therapies in oncology. This collaboration had an initial term of three years, and Celgene made a $75.0 million up-front, non-refundable cash payment to us as consideration for entering into the collaboration. In June 2015, we amended and restated the collaboration agreement, or the Amended Collaboration Agreement, to focus exclusively on anti-BCMA product candidates for a new three-year term. B-cell maturation antigen, or BCMA, is a cell surface protein that is expressed on normal plasma cells and on most multiple myeloma cells, but is absent from other normal tissues. As consideration for the Amended Collaboration Agreement, we received an upfront, non-refundable cash payment of $25.0 million to fund research and development under the collaboration. In February 2016, we treated the first subject in our Phase I clinical study of bb2121, the first anti-BCMA product candidate from this collaboration. This study will enroll up to 40 patients who have received three prior regimens for treatment of multiple myeloma. In February 2016, Celgene exercised its option to obtain an exclusive worldwide license to develop and commercialize bb2121 and as a result, has paid to us an option fee in the amount of $10.0 million in the first quarter of 2016. We may elect to co-develop and co-promote bb2121, and any other product candidates in the United States under this collaboration arrangement. In May 2016, the FDA granted Orphan Drug status to our bb2121 product candidate for the treatment of multiple myeloma.

In June 2014, we acquired Precision Genome Engineering, Inc., or Pregenen, a privately-held biotechnology company headquartered in Seattle, Washington. Through the acquisition, we obtained rights to Pregenen's gene editing and cell signaling technology. The agreement provided for up to $135.0 million in future contingent cash payments by us upon the achievement of certain preclinical, clinical and commercial milestones related to the Pregenen technology, of which $15.0 million relates to preclinical milestones, $20.1 million relates to clinical milestones and $99.9 million relates to commercial milestones. We estimate future contingent cash payments have a fair value of $7.2 million as of September 30, 2016, $3.9 million of which is classified as a current liability.

As of September 30, 2016, we had cash, cash equivalents and marketable securities of approximately $727.6 million. We expect that our existing cash, cash equivalents and marketable securities will be sufficient to fund our current operations through 2018.

Since our inception in 1992, we have devoted substantially all of our resources to our development efforts relating to our product candidates, including activities to manufacture product candidates in compliance with good manufacturing practices, or GMP, to conduct clinical studies of our product candidates, to provide general and administrative support for these operations and to protect our intellectual property. We do not have any products approved for sale and have not generated any revenue from product sales. We have funded our operations primarily through the sale of common stock in our public offerings, private placements of preferred stock and warrants and through collaborations.

We have never been profitable and have incurred net losses in each year since inception. Our net loss was $192.1 million for the nine months ended September 30, 2016 and our accumulated deficit was $506.3 million as of September 30, 2016. Substantially all of our net losses resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We expect to

continue to incur significant expenses and increasing operating losses for at least the next several years. We expect our expenses will increase substantially in connection with our ongoing and planned activities, as we:

- conduct clinical studies for our LentiGlobin, Lenti-D, and bb2121 product candidates;
- increase research and development-related activities for the discovery and development of oncology product candidates;
- continue our research and development efforts;
- manufacture clinical study materials and develop large-scale manufacturing capabilities;
- seek regulatory approval for our product candidates; and
- add personnel to support our product development and commercialization efforts.

We do not expect to generate revenue from product sales unless and until we successfully complete development and obtain regulatory approval for one or more of our product candidates, which we expect will take a number of years and is subject to significant uncertainty. We have no commercial-scale manufacturing facilities, and all of our manufacturing activities are contracted out to third parties. Additionally, we currently utilize third-party contract research organizations, or CROs, to carry out our clinical development activities; and we do not yet have a sales and marketing organization. If we seek to obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses as we prepare for product sales, marketing, manufacturing, and distribution. Accordingly, we will seek to fund our operations through public or private equity or debt financings, strategic collaborations, or other sources. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. Our failure to raise capital or enter into such other arrangements as and when needed would have a negative impact on our financial condition and our ability to develop our products.

Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate revenues from the sale of our products, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce our operations.

Financial operations overview

Revenue

To date, we have not generated any revenues from the sale of products. Our revenues have been derived from collaboration arrangements, research fees, license fees and grant revenues.

Collaboration revenue is generated exclusively from our collaboration arrangement with Celgene, which was amended in 2015. The terms of this amended arrangement contain multiple deliverables, which include: (i) research and development services, (ii) participation on the joint steering committee, (iii) participation on the patent committee, (iv) a license to the first product candidate, (v) manufacture of vectors and associated payload for incorporation into the first optioned product candidate under the license, and (vi) participation on the joint governance committee under the co-development and co-promotion agreement for the first optioned product candidate under the license. We recognize arrangement consideration allocated to each unit of accounting when all of the revenue recognition criteria in Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 605, Revenue Recognition, or ASC 605, are satisfied for that particular unit of accounting. We expect that $17.3 million of revenue from the Celgene arrangement associated with discovery, research and development services, joint steering committee services and patent committee services will be recognized ratably over the associated period of performance, which was initially estimated to be three years from the date of the agreement in June 2015. We expect that $91.7 million of revenue, not in excess of the fixed consideration and assuming other revenue recognition criteria have been met, from the Celgene arrangement associated with the license to the first product candidate, bb2121, and the manufacture of vector and associated payload for bb2121 following the initial Phase I study will be recognized on a proportional performance method or ratably over the period of performance if there is no other discernible pattern of recognition. This period of performance and recognition pattern will be revisited as the development plan changes or if other events impacting the deliverables occur.

Research and development expenses

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

- employee-related expenses, including salaries, benefits, travel and stock-based compensation expense;
- expenses incurred under agreements with CROs and clinical sites that conduct our clinical studies;
- costs of acquiring, developing, and manufacturing clinical study materials;
- facilities, depreciation, and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance, information technology, and other supplies;
- costs associated with our research platform and preclinical activities;
- costs associated with in-licensing other product candidates or technologies for use in preclinical and clinical activities;
- costs associated with our regulatory, quality assurance and quality control operations; and
- amortization of intangible assets.

Research and development costs are expensed as 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 our clinical sites. We cannot determine with certainty the duration and completion costs of the current or future clinical studies of our product candidates or if, when, or to what extent we will generate revenues from the commercialization and sale of any of our product candidates that obtain regulatory approval. We may never succeed in achieving regulatory approval for any of our product candidates. The duration, costs, and timing of clinical studies and development of our product candidates will depend on a variety of factors, including:

- the scope, rate of progress, and expense of our ongoing as well as any additional clinical studies and other research and development activities we undertake;
- future clinical study results;
- uncertainties in clinical study enrollment rates;
- changing standards for regulatory approval; and
- the timing and receipt of any regulatory approvals.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the FDA, or another regulatory authority were to require us to conduct clinical studies beyond those that we currently anticipate will be required for the completion of clinical development of a product candidate or if we experience significant delays in enrollment in any of our clinical studies, we could be required to expend significant additional financial resources and time on the completion of clinical development for our product candidates.

We plan to increase our research and development expenses for the foreseeable future as we continue to advance the clinical development of our Lenti-D and LentiGlobin product candidates, conduct research and development activities in the field of oncology and continue the research and development of product candidates using our gene editing technology platform. Our research and development activities include the following:

- We are conducting a Phase II/III clinical study to examine the safety and efficacy of our Lenti-D product candidate in the treatment of CALD. In October 2013, we announced that the first subject had been treated in this study and in May 2015 we announced the achievement of enrollment of 18 subjects in this study. We are also conducting an observational study of subjects with CALD treated by allogeneic hematopoietic stem-cell transplant.
- We are conducting a Phase I/II clinical study in the United States, Australia and Thailand to study the safety and efficacy of our LentiGlobin product candidate in the treatment of subjects with TDT. In March 2014, we announced that the first subject had been treated in this study.
- We are conducting a Phase I/II clinical study in France to study the safety and efficacy of our LentiGlobin product candidate in the treatment of subjects with TDT and severe SCD. In December 2013, we announced that the first subject with TDT had been treated in this study and in October 2014, we announced that the first subject with severe SCD had been treated in this study.
- We are conducting a Phase I clinical study in the United States to study the safety and efficacy of our LentiGlobin product candidate in the treatment of subjects with severe SCD. In June 2015, we announced that the first patient with severe SCD had been treated in this study.
- We are conducting a global, multi-center Phase III clinical study to study the safety and efficacy of our LentiGlobin product candidate in the treatment of patients with a diagnosis of TDT who have non-$^{0}/^{0}$ genotypes.
- We are planning to initiate in 2017, a global, multi-center Phase III clinical study to study the safety and efficacy of our LentiGlobin product candidate in the treatment of patients with a diagnosis of TDT who have $^{0}/^{0}$ genotypes.
- We are conducting a Phase I clinical study in the United States to study the safety and efficacy of our bb2121 product candidate in the treatment of subjects with relapsed/refractory multiple myeloma. In February 2016, we announced that the first subject with relapsed/refractory multiple myeloma had been treated in this study.
- We will continue to manufacture clinical study materials in support of our clinical studies.

Our direct research and development expenses consist principally of external costs, such as fees paid to investigators, consultants, central laboratories and CROs in connection with our clinical studies, costs to in-license product candidates and new technologies, and costs related to acquiring and manufacturing clinical study materials. We allocate salary and benefit costs directly related to specific programs. We do not allocate personnel-related discretionary bonus or stock-based compensation costs, costs associated with our general discovery platform improvements, depreciation or other indirect costs that are deployed across multiple projects under development and, as such, the costs are separately classified as personnel and other expenses in the table below:

	Three months ended September 30,		Nine months ended September 30,	
	2016	2015	2016	2015
	(in thousands)		(in thousands)	
LentiGlobin	$16,154	$10,937	$45,898	$25,070
Lenti-D	5,663	2,837	10,956	10,729
bb2121	3,613	—	8,900	—
Pre-clinical programs	20,856	3,680	29,378	11,596
Total direct research and development expense	46,286	17,454	95,132	47,395
Employee-and contractor-related expenses	4,015	3,568	12,401	9,029
Stock-based compensation expense	5,399	4,426	15,410	19,726
Platform-related expenses	2,767	2,985	9,178	17,047
Facility expenses	5,209	1,724	14,606	4,710
Other expenses	295	238	915	473
Unallocated personnel and other expenses	17,685	12,941	52,510	50,985
Total research and development expense	$63,971	$30,395	$147,642	$98,380

The costs associated with our bb2121 program were included within pre-clinical programs in the table shown above for the three and nine months ended September 30, 2015, and are separately shown for the three and nine months ended September 30, 2016.

General and administrative expenses

General and administrative expenses consist primarily of salaries and related costs for personnel, including stock-based compensation and travel expenses for our employees in executive, operational, finance, legal, business development, commercial and human resource functions. Other general and administrative expenses include allocated facility-related information technology costs, professional fees for accounting, consulting and legal services, directors' fees and expenses associated with obtaining and maintaining patents.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support our continued research and development and potential commercialization of our product candidates.

Other income, net

Other income, net consists primarily of interest income earned on investments.

Critical accounting policies and estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in accordance with generally accepted accounting principles. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, and expenses and the disclosure of contingent assets and liabilities in our financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to accrued research and development expenses, revenue, construction financing lease obligations, stock-based compensation, income taxes, contingent consideration and fair value estimates used to assess potential impairment of long-lived assets. We base our estimates on historical experience, known trends and events and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. In making estimates and judgments, management employs critical accounting policies. During the nine months ended September 30, 2016, there were no material changes to our critical accounting policies as reported in our Annual Report on Form 10-K for the year ended December 31, 2015, which was filed with the SEC on February 25, 2016.

Results of Operations

Comparison of the three months ended September 30, 2016 and 2015:

	Three months ended September 30,		
	2016	2015	Change
	(in thousands)		
Revenue:			
Collaboration revenue	$1,552	$1,324	$228
Total revenue	1,552	1,324	228
Operating expenses:			
Research and development	63,971	30,395	33,576
General and administrative	14,623	13,704	919
Change in fair value of contingent consideration	1,098	352	746
Total operating expenses	79,692	44,451	35,241
Loss from operations	(78,140)	(43,127)	35,013
Other income, net	937	263	(674)
Loss before income taxes	(77,203)	(42,864)	34,339
Income tax benefit (expense)	178	(60)	(238)
Net loss	$(77,025)	$(42,924)	$34,101

Revenue. Total revenue was $1.6 for the three months ended September 30, 2016, compared to $1.3 for the three months ended September 30, 2015. The increase was primarily attributable to the timing of recognition of revenue associated with our Celgene agreement.

Research and development expenses. Research and development expenses were $64.0 million for the three months ended September 30, 2016, compared to $30.4 million for the three months ended September 30, 2015. The increase of $33.6 million was primarily attributable to the following:

- $4.0 million of increased employee compensation and benefit expense, primarily due to an increase in headcount.
- $14.4 million of increased license and milestones fees, primarily due to a $15.0 million one-time upfront payment owed in the third quarter of 2016, offset by license and milestone fees incurred during the first quarter of 2015.
- $8.4 million of increased manufacturing expenses, $2.1 million of increased lab expenses, and $0.9 million of increased clinical trial related costs to support the advancement of our clinical and pre-clinical programs.
- $3.5 million of increased facilities and information technology expenses.

General and administrative expenses. General and administrative expenses were $14.6 million for the three months ended September 30, 2016, compared to $13.7 million for the three months ended September 30, 2015. The increase of $0.9 million was primarily attributable to increased compensation and benefit expenses to support overall growth offset by a decrease in stock-based compensation expense.

Other income, net. The change in other income, net was primarily related to increased interest income of $0.6 million due to increased marketable securities balances.

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Comparison of the nine months ended September 30, 2016 and 2015:

	Nine months ended September 30,		
	2016	2015	Change
	(in thousands)		
Revenue:			
Collaboration revenue	$4,603	$12,607	$(8,004)
Total revenue	4,603	12,607	(8,004)
Operating expenses:			
Research and development	147,642	98,380	49,262
General and administrative	48,941	31,765	17,176
Change in fair value of contingent consideration	3,515	2,540	975
Total operating expenses	200,098	132,685	67,413
Loss from operations	(195,495)	(120,078)	75,417
Other income, net	2,803	630	(2,173)
Loss before income taxes	(192,692)	(119,448)	73,244
Income tax benefit (expense)	549	(60)	(609)
Net loss	$(192,143)	$(119,508)	$72,635

Revenue. Total revenue was $4.6 million for the nine months ended September 30, 2016 compared to $12.6 million for the nine months ended September 30, 2015. The decrease of $8.0 million was primarily attributable to a reduction in collaboration revenue as a result of the amendment to our collaboration agreement with Celgene in June 2015.

Research and development expenses. Research and development expenses were $147.6 million for the nine months ended September 30, 2016, compared to $98.4 million for the nine months ended September 30, 2015. The increase of $49.2 million was primarily attributable to the following:

- $6.4 million of increased employee compensation and benefit expense, primarily due to $10.7 million of increased payroll and bonus expense offset by $4.3 million of decreased stock-based compensation expense. The decrease in stock-based compensation expense is due to one-time charges of $9.5 million incurred during the first half of 2015 related to the modification of stock option awards of a non-employee founder and a former officer, offset by an increase in expense related to increased headcount.
- $6.0 million of increased license and milestones fees, primarily due to a $15.0 million one-time upfront payment owed in the third quarter of 2016, offset by license and milestone fees incurred during the first three quarters of 2015.
- $15.9 million of increased manufacturing costs, $4.9 million of increased lab expenses, and $3.7 million of increased clinical trial related costs necessary to support the advancement of our clinical and pre-clinical programs.
- $9.9 million of increased facilities and information technology expenses.

General and administrative expenses. General and administrative expenses were $48.9 million for the nine months ended September 30, 2016, compared to $31.8 million for the nine months ended September 30, 2015. The increase of $17.1 million was primarily attributable to $16.8 million of increased employee, contractor and consultant expenses to support increased headcount and overall growth, of which $5.2 million was increased salary and benefit expense, $4.1 million was stock-based compensation expense and $6.7 million related to increased consulting costs.

Other income, net. The change in other income, net was primarily related to increased interest income of $2.1 million due to increased marketable securities balances resulting from our underwritten public offering in June 2015.

Liquidity and Capital Resources

As of September 30, 2016, we had cash, cash equivalents and marketable securities of approximately $727.6 million. We expect cash, cash equivalents and marketable securities to fund our planned operations through 2018. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to liquidity and capital preservation. As of September 30, 2016, our funds are held in U.S. Treasury securities, U.S. government agency securities, federally insured deposits, certificates of deposit and money market funds.

We have incurred losses and cumulative negative cash flows from operations since our inception in April 1992, and as of September 30, 2016 we had an accumulated deficit of $506.3 million. We anticipate that we will continue to incur losses for at least the next several years. We expect that our research and development and general and administrative expenses will continue to increase and, as a result, we will need additional capital to fund our operations, which we may raise through public or private equity or debt financings, strategic collaborations, or other sources. In connection with our 60 Binney Street lease, we increased our letter of credit from $9.2 million to $13.8 million during the third quarter of 2016, which is presented in "Restricted cash and other non-current assets" in our condensed consolidated balance sheet. Please refer to Note 7, "Commitments and contingencies," for further information.

We have funded our operations principally from the sale of common stock, preferred stock and through the Celgene collaboration. On June 24, 2013, we completed our initial public offering, or IPO, whereby we sold 6,832,352 shares of common stock at a price of $17.00 per share for aggregate net proceeds received by us of $104.9 million. On July 14, 2014, we sold 3,450,000 shares of common stock (inclusive of 450,000 shares of common stock sold by us pursuant to the full exercise of an overallotment option granted to the underwriters in connection with the offering) through an underwritten public offering at a price of $34.00 per share for aggregate net proceeds to us of $109.8 million. On December 19, 2014, we sold 3,047,500 shares of common stock (inclusive of 397,500 shares of common stock sold by us pursuant to the full exercise of an overallotment option granted to the underwriters in connection with the offering) through an underwritten public offering at a price of $85.00 per share for aggregate net proceeds to us of $243.3 million. On June 29, 2015, we sold 2,941,176 shares of common stock through an underwritten public offering at a price of $170.00 per share for aggregate net proceeds to us of $477.2 million.

Sources of Liquidity

Cash Flows

The following table sets forth the primary sources and uses of cash for each of the periods below:

	Nine months ended September 30,	
	2016	2015
	(in thousands)	
Net cash provided by (used in):		
Operating activities	$(120,541)	$(65,344)
Investing activities	199,665	(350,694)
Financing activities	1,761	485,703
Increase in cash and cash equivalents	$80,885	$69,665

Cash Flows from Operating Activities. The $55.2 million increase in cash used in operating activities for the nine months ended September 30, 2016, compared to the nine months ended September 30, 2015, was primarily due to the increase in net loss during this period which was primarily attributable to increased payroll-related expense, in-license milestones and fees, and spending on our clinical and pre-clinical stage programs. Net loss was $192.1 million for the nine months ended September 30, 2016 compared to $119.5 million for the nine months ended September 30, 2015, an increase of $72.6 million.

Cash Flows from Investing Activities. The net cash provided by investing activities was $199.7 million for the nine months ended September 30, 2016 and was primarily due to $356.7 million in maturities of marketable securities offset in part by $145.1 million in purchases of marketable securities.

Cash Flows from Financing Activities. The $483.9 million decrease in net cash provided by financing activities was primarily due to the absence of $477.2 million in net proceeds from an offering of our common stock that occurred during the nine months ended September 30, 2015 and a decrease in the proceeds from stock option exercises.

Contractual Obligations and Commitments

There have been no material changes to our contractual obligations and commitments as included in our Annual Report on Form 10-K, which was filed with the SEC on February 25, 2016, except as noted below:

- On June 3, 2016, we entered into a strategic manufacturing agreement for the future commercial production of our Lenti-D and LentiGlobin product candidates. Under this 12 year agreement, we are required to pay $12.5 million upon the achievement of certain construction milestones. The first milestone was achieved during the third quarter of 2016 and we paid $2.0 million accordingly. We expect to pay another $6.0 million during the fourth quarter of 2016 and to pay the remainder of the contract in early 2017. Following construction completion, we expect to pay $5.1 million per year in fixed suite fees as well as certain fixed labor, raw materials, testing and shipping costs for manufacturing services. We may terminate this agreement any time after July 1, 2016 upon our payment of a one-time termination fee and up to 24 months of fixed suite and labor fees.
- On September 29, 2016, we entered into a research collaboration and license agreement with a clinical stage immunotherapy company to research, develop and commercialize T cell receptor immunotherapies against four undisclosed targets. Under this agreement, we are required to pay $15.0 million upon execution of the agreement. We made the upfront payment of $15.0 million during the fourth quarter of 2016.
- On September 30, 2016, we entered into an Assignment and Assumption of Lease relating to our leased office and laboratory premises at 150 Second Street, Cambridge, Massachusetts. Under the Assignment and Assumption of Lease, we will assign all of our rights, interests, obligations and responsibilities under the lease to a third party, to be effective as of the later of May 1, 2017, or the first day following our surrender of the leased premises in accordance with the terms of the lease. As a result of the lease assignment, we expect to be absolved of $20.6 million in lease commitments between 2017 and 2022, of which $2.2 million relates to 2017, $3.5 million relates to 2018, $3.6 million relates to 2019, $3.7 million relates to 2020 and $7.6 million relates to 2021 and thereafter.

We have obligations to make future payments to third parties that become due and payable on the achievement of certain development, regulatory and commercial milestones. In addition to the commitments described in our Annual Report on Form 10-K, the following commitments are not on our balance sheet because the achievement and timing of these milestones are not fixed and determinable:

- Under a license agreement with Biogen Inc., pursuant to which we license certain patents and patent applications related to our bb2121 product candidate, we will be required to make certain payments related to certain development milestone obligations and must report on our progress in achieving these milestones on a periodic basis. We may be obligated to pay up to $24.0 million in the aggregate for a licensed product upon the achievement of these milestones. Upon commercialization of our products covered by the in-licensed intellectual property, we will be obligated to pay a percentage of net sales as a royalty in the low single digits.
- Under a license agreement with the National Institutes of Health, pursuant to which we license certain patents and patent applications related to our bb2121 product candidate, we have agreed to certain development and regulatory milestone obligations and must report on our progress in achieving these milestones on a periodic basis. We may be obligated to pay up to $9.7 million in the aggregate for a licensed product upon the achievement of these milestones. Upon commercialization of our products covered by the in-licensed intellectual property, we will be obligated to pay NIH a percentage of net sales as a royalty in the low single digits. The royalties payable under this license agreement are subject to reduction for any third party payments required to be made, with a minimum floor in the low single digits.

Off-Balance Sheet Arrangements

As of September 30, 2016, we did not have any off-balance sheet arrangements as defined in the rules and regulations of the SEC.

Item 3. Quantitative and Qualitative Disclosures about Market Risks

We are exposed to market risk related to changes in interest rates. As of September 30, 2016 and December 31, 2015, we had cash, cash equivalents and marketable securities of $727.6 million and $865.8 million, respectively, primarily invested in U.S. government agency securities, federally insured certificates of deposit and money market mutual funds invested in U.S. Treasuries or U.S. government agency securities. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are in short-term securities. Our available for sale securities are subject to interest rate risk and will fall in value if market interest rates increase. If market interest rates were to increase immediately and uniformly by 100 basis points, or one percentage point, from levels at September 30, 2016, the net fair value of our interest-sensitive marketable securities would have resulted in a hypothetical decline of approximately $3.7 million.

Item 4. Controls and Procedures

Management's Evaluation of our Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Securities and Exchange Act of 1934 is (1) recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms and (2) accumulated and communicated to our management, including our principal executive officer and principal financial officer, to allow timely decisions regarding required disclosure.

As of September 30, 2016, our management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities and Exchange Act of 1934). Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our principal executive officer and principal financial officer have concluded based upon the evaluation described above that, as of September 30, 2016, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Control over Financial Reporting

With the exception of the migration of certain of our financial processing systems to an enterprise-wide systems solution, there have been no changes in our internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15(d)-15(f) promulgated under the Securities Exchange Act of 1934 during the third quarter of 2016 that have materially affected, or is reasonably likely to materially affect, our internal control over financial reporting. In connection with this implementation and the resulting business process changes, we continue to enhance the design and documentation of our internal control over financial reporting processes to maintain effective controls over our financial reporting.

PART II. OTHER INFORMATION

Item 1. Legal Proceedings

In the ordinary course of business, we are from time to time involved in lawsuits, claims, investigations, proceedings, and threats of litigation relating to intellectual property, commercial arrangements, employment and other matters. While the outcome of these proceedings and claims cannot be predicted with certainty, as of September 30, 2016, we were not party to any legal or arbitration proceedings that may have, or have had in the recent past, significant effects on our financial position. No governmental proceedings are pending or, to our knowledge, contemplated against us. We are not a party to any material proceedings in which any director, member of executive management or affiliate of ours is either a party adverse to us or our subsidiaries or has a material interest adverse to us or our subsidiaries.

Item 1A. Risk Factors

An investment in shares of our common stock involves a high degree of risk. You should carefully consider the following information about these risks, together with the other information appearing elsewhere in this Quarterly Report on Form 10-Q, including our financial statements and related notes hereto, before deciding to invest in our common stock. The occurrence of any of the following risks could have a material adverse effect on our business, financial condition, results of operations and future growth prospects. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment.

Those risk factors below denoted with a "*" are newly added or have been materially updated from our Annual Report on 10-K filed with the Securities and Exchange Commission, or the SEC, on February 25, 2016.

Risks related to the discovery and development of our product candidates

* Our gene therapy product candidates are based on a novel technology, which makes it difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval. At the moment, no gene therapy products have been approved in the United States and only a few products have been approved in the European Union, or EU.

We have concentrated our therapeutic product research and development efforts on our gene therapy platform, and our future success depends on the successful development of this therapeutic approach. There can be no assurance that any development problems we experience in the future related to our gene therapy platform will not cause significant delays or unanticipated costs, or that such development problems can be solved. We may also experience delays in developing a sustainable, reproducible and commercial-scale manufacturing process or transferring that process to commercial partners, which may prevent us from completing our clinical studies or commercializing our products on a timely or profitable basis, if at all.

In addition, the clinical study requirements of the U.S. Food and Drug Administration, or FDA, the European Medicines Agency, or EMA and other regulatory agencies and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other, better known or more extensively studied pharmaceutical or other product candidates. At the moment, only a few gene therapy products have been approved in the Western world, including UniQure's Glybera, which received marketing authorization in the EU in 2012, and GlaxoSmithKline's Strimvelis, which received marketing authorization in the EU in 2016. Given the few precedents of approved gene therapy products, it is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in the United States, the EU or other jurisdictions. Approvals by the EMA and the European Commission may not be indicative of what the FDA may require for approval.

Regulatory requirements governing gene and cell therapy products have evolved and may continue to change in the future. For example, the FDA has established the Office of Cellular, Tissue and Gene Therapies within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. Gene therapy clinical studies conducted at institutions that receive funding for recombinant DNA research from the U.S. National Institutes of Health, or NIH, are also subject to review by the NIH Office of Biotechnology Activities' Recombinant DNA Advisory Committee, or RAC. Although the FDA decides whether individual gene therapy protocols may proceed, the RAC review process can impede the initiation of a clinical study, even if the FDA has reviewed the study and approved its initiation. Clinical trial sites in the United States that receive NIH funding for research involving recombinant or synthetic nucleic acid molecules are required to follow RAC recommendations, or risk losing NIH funding for such research or needing NIH pre-approval before conducting such research. In addition, the FDA can put an investigational new drug application, or IND, on clinical hold if the information in an IND is not sufficient to assess the risks in pediatric patients. Before a clinical study can begin at any institution, that institution's institutional review board, or IRB, and its Institutional Biosafety Committee will have to review the proposed clinical study to assess the safety of the study. Moreover, serious adverse events or developments in clinical trials of gene therapy product candidates conducted by others may cause the FDA or other regulatory bodies to initiate a clinical hold on our clinical trials or otherwise change the requirements for approval of any of our product candidates.

These regulatory review agencies, committees and advisory groups and the new requirements and guidelines they promulgate may lengthen the regulatory review process, require us to perform additional or larger studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates or lead to significant post-approval studies, limitations or restrictions.

As we advance our product candidates, we will be required to consult with these regulatory and advisory groups and comply with applicable requirements and guidelines. If we fail to do so, we may be required to delay or discontinue development of our product candidates. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenue to maintain our business.

We may find it difficult to enroll patients in our clinical studies, which could delay or prevent clinical studies of our product candidates.

Identifying and qualifying patients to participate in clinical studies of our product candidates is critical to our success. The timing of our clinical studies depends on the speed at which we can recruit eligible patients to participate in testing our product candidates. We have experienced delays in some of our clinical studies, and we may experience similar delays in the future. If patients are unwilling to participate in our gene therapy studies because of negative publicity from adverse events in the biotechnology or gene therapy industries or for other reasons, including competitive clinical studies for similar patient populations, the timeline for recruiting patients, conducting studies and obtaining regulatory approval of potential products may be delayed. These delays could result in increased costs, delays in advancing our product development, delays in testing the effectiveness of our technology or termination of the clinical studies altogether.

We may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics to achieve diversity in a study, to complete our clinical studies in a timely manner. Patient enrollment is affected by factors including:

- severity of the disease under investigation;
- design of the study protocol;
- size of the patient population;
- eligibility criteria for the study in question;
- perceived risks and benefits of the product candidate under study, including as a result of adverse effects observed in similar or competing therapies;
- proximity and availability of clinical study sites for prospective patients;
- availability of competing therapies and clinical studies;
- efforts to facilitate timely enrollment in clinical studies;
- patient referral practices of physicians; and
- ability to monitor patients adequately during and after treatment.

In particular, each of the conditions for which we plan to evaluate our current hematopoietic stem cell, or HSC, product candidates are rare genetic disorders with limited patient pools from which to draw for clinical studies. It has been estimated that about 1.5% (80 to 90 million people) of the global population are carriers of ß-thalassemia, with about 60,000 symptomatic individuals born annually, the great majority in the developing world. According to Thalassemia International Federation, about 288,000 patients with transfusion-dependent -thalassemia, or TDT, are alive and registered as receiving regular treatment around the world, of which we estimate that about 10,000-15,000 live in the United States and Europe. The global incidence of SCD is estimated to be 250,000-300,000 births annually with a global prevalence estimated to be about 20-25 million. The worldwide incidence rate for adrenoleukodystrophy, the superset of cerebral adrenoleukodystrophy, or CALD, is approximately one in 21,000 male births. CALD in young boys accounts for about 30-40% of patients diagnosed with adrenoleukodystrophy. Further, because newborn screening for CALD is not widely adopted, and it can be difficult to diagnose CALD in the absence of a genetic screen, we may have difficulty finding patients who are eligible to participate in our study. The eligibility criteria of our clinical studies will further limit the pool of available study participants. Additionally, the process of finding and diagnosing patients may prove costly. Finally, our treatment process requires that the procurement of autologous cells from subjects be conducted where the cells can be shipped to a transduction facility within the required timelines, as the HSCs and T cells, in the case of our oncology product candidate, have limited viability following harvest.

Our current product candidates are being developed to treat rare conditions and certain cancers. We plan to seek initial marketing approval in the United States and the European Union. We may not be able to initiate or continue clinical studies if we cannot enroll a sufficient number of eligible patients to participate in the clinical studies required by the FDA or the EMA or other regulatory agencies. Our ability to successfully initiate, enroll and complete a clinical study in any foreign country is subject to numerous risks unique to conducting business in foreign countries, including:

- difficulty in establishing or managing relationships with contract research organizations, or CROs, and physicians;
- different standards for the conduct of clinical studies;
- our inability to locate qualified local consultants, physicians and partners; and
- the potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment.

If we have difficulty enrolling a sufficient number of patients to conduct our clinical studies as planned, we may need to delay, limit or terminate ongoing or planned clinical studies, any of which would have an adverse effect on our business.

We may encounter substantial delays in our clinical studies or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities.

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

- delays in reaching a consensus with regulatory agencies on study design;
- delays in obtaining required IRB or Institutional Ethics Committee approval at each clinical study site;
- delays in recruiting suitable patients to participate in our clinical studies;
- imposition of a clinical hold by regulatory agencies, after an inspection of our clinical study operations or study sites or due to unforeseen safety issues;
- failure by our CROs, other third parties or us to adhere to clinical study requirements;
- failure to perform in accordance with the FDA's good clinical practices, or GCP, or applicable regulatory requirements in other countries;
- delays in the testing, validation, manufacturing and delivery of our product candidates to the clinical sites;
- failure to obtain sufficient cells from patients to manufacture enough drug product or achieve target cell doses;
- delays in having patients complete participation in a study or return for post-treatment follow-up;
- clinical study sites or patients dropping out of a study;
- occurrence of serious adverse events associated with the product candidate that are viewed to outweigh its potential benefits; or
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols.

Any inability to successfully complete preclinical and clinical development could result in additional costs to us or impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties. In addition, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional studies to demonstrate comparability of our modified product candidates to earlier versions. Clinical study delays could also shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

If the results of our clinical studies are inconclusive or if there are safety concerns or adverse events associated with our product candidates, we may:

- be delayed in obtaining regulatory approval for our product candidates, if at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be required to perform additional clinical studies or clinical studies of longer duration to support approval or be subject to additional post-marketing testing requirements;
- have regulatory authorities withdraw their approval of the product or impose restrictions on its use;
- be subject to the addition of labeling statements, such as warnings or contraindications;
- be sued; or
- experience damage to our reputation.

Treatment with our gene therapy product candidates involves chemotherapy and myeloablative treatments, which can cause side effects or adverse events that are unrelated to our product candidates, but may still impact the success of our clinical studies. Additionally, our product candidates could potentially cause other adverse events that have not yet been predicted. The inclusion of critically ill patients in our clinical studies may result in deaths or other adverse medical events due to other therapies or medications that such patients may be using, or the progression of their disease. As described above, any of these events could prevent us from achieving or maintaining market acceptance of our product candidates and impair our ability to commercialize our products.

We have not completed any clinical studies of our current viral vectors or product candidates derived from these viral vectors. Initial success in our ongoing clinical studies may not be indicative of results obtained when these studies are completed. Furthermore, success in early clinical studies may not be indicative of results obtained in later studies.

Our current viral vectors and our product candidates first initiated evaluation in human clinical studies in 2013, and we may experience unexpected results in the future. Earlier gene therapy clinical studies, which we believe serve as proof-of-concept for our product candidates, utilized lentiviral vectors similar to ours. However, these studies should not be relied upon as evidence that our ongoing or future clinical studies will succeed. Study designs and results from previous studies are not necessarily predictive of our future clinical study designs or results, and initial results may not be confirmed upon full analysis of the complete study data. There is limited data concerning long-term safety and efficacy following treatment with our gene therapy product candidates. These data, or other positive data, may not continue or occur for these subjects or for any future subjects in our ongoing or future clinical studies, and may not be repeated or observed in ongoing or future studies involving our product candidates. For instance, while patients with TDT or severe SCD who have been treated with our LentiGlobin product candidate may experience a reduction or temporary elimination of transfusion support, there can be no assurance that they will not require transfusion support in the future. Furthermore, our product candidates may also fail to show the desired safety and efficacy in later stages of clinical development despite having successfully advanced through initial clinical studies. There can be no assurance that any of these studies will ultimately be successful or support further clinical advancement or regulatory approval of our product candidates.

There is a high failure rate for drugs and biologics proceeding through clinical studies. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later stage clinical studies even after achieving promising results in earlier stage clinical studies. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, regulatory delays or rejections may be encountered as a result of many factors, including changes in regulatory policy during the period of product development.

Patients with different genotypes may respond differently to treatment with our product candidates, which may result in the delay of our clinical development and commercialization plans.

Initial results from our ongoing clinical studies suggest that patients with TDT who do not have a $^{0}/^{0}$ genotype respond better to treatment with our LentiGlobin product candidate than patients who do have a $^{0}/^{0}$ genotype. Consequently, we expect to seek FDA approval of our LentiGlobin product candidate initially for the treatment of TDT in patients who do not have a $^{0}/^{0}$ genotype. These differences in responsiveness require us to engage regulatory authorities in additional discussions. In order to support an application for FDA approval of our LentiGlobin product candidate in patients who have a $^{0}/^{0}$ genotype, we intend to conduct a Phase III clinical study (HGB-212), but we do not yet have plans for when our LentiGlobin product candidate may be commercially available to all genotypes.

The results from our Starbeam Study may not be sufficiently robust to support the submission of marketing approval for our Lenti-D product candidate. Before we submit our Lenti-D product candidate for marketing approval, the FDA and the EMA may require us to enroll additional subjects, conduct additional clinical studies, or evaluate subjects for

an additional follow-up period.

The FDA has advised us that our Starbeam Study, which is a single-arm, open-label study to evaluate the safety and efficacy of our Lenti-D product candidate to halt the progression of CALD, may not be deemed to be a pivotal study or may not provide sufficient support for a Biologics License Application, or BLA, submission. The FDA normally requires two pivotal clinical studies to approve a drug or biologic product, and thus the FDA may require that we conduct larger or additional clinical studies of our Lenti-D product candidate prior to a BLA submission. The FDA typically does not consider a single clinical study to be adequate to serve as a pivotal study unless it is, among other things, well-controlled and demonstrates a clinically meaningful effect on mortality, irreversible morbidity, or prevention of a disease with potentially serious outcome, and a confirmatory study would be practically or ethically impossible. Due to the nature of CALD and the limited number of patients with this condition, we believe a placebo-controlled and blinded study is not practicable for ethical and other reasons. However, it is still possible that, even if we achieve favorable results in the Starbeam Study, the FDA may require us to enroll additional subjects or conduct additional clinical studies, possibly involving a larger sample size or a different clinical study design, particularly if the FDA does not find the results from the Starbeam Study to be sufficiently persuasive to support a BLA submission. The FDA may also require that we conduct a longer follow-up period of subjects treated with our Lenti-D product candidate prior to accepting our BLA submission.

In addition, the Starbeam Study was not designed to achieve a statistically significant efficacy determination. Rather, we anticipate that the safety and efficacy of our Lenti-D product candidate will be evaluated in light of the data collected in our retrospective ALD-101 Study and our observational ALD-103 study. However, due to the retrospective nature of the ALD-101 study, and the limited number of patients with this condition, the FDA has advised us that the ALD-101 Study is not sufficiently robust to serve as a conventional historical control group and as a basis of comparison against the results of the Starbeam Study. Thus, we expect that the FDA will assess the totality of the safety and efficacy data from our CALD clinical studies in reviewing any future BLA submission for our Lenti-D product candidate. Based on this assessment, the FDA may require that we conduct additional preclinical or clinical studies prior to submitting or approving a BLA for this indication.

It is possible that the FDA or the EMA may not consider the results of this study to be sufficient for approval of our Lenti-D product candidate for this indication. If the FDA or the EMA requires additional studies, we would incur increased costs and delays in the marketing approval process, which may require us to expend more resources than we have available. In addition, it is possible that the FDA and the EMA may have divergent opinions on the elements necessary for a successful BLA and Marketing Authorization Application, or MAA, respectively, which may cause us to alter our development, regulatory and/or commercialization strategies.

* We cannot be certain that our Northstar-2 clinical study in patients with TDT who do not have a 0/ 0 genotype, or our planned Phase III clinical study in patients with TDT who have a 0/ 0 genotype, together with data from our Northstar and HGB-205 clinical studies, will be sufficient to form the basis for a BLA submission for our LentiGlobin product candidate.

In general, the FDA requires the successful completion of two pivotal trials to support approval of a BLA, but in certain circumstances, will approve a BLA based on only one pivotal trial. If successful, we believe the results from our Northstar-2 clinical study, together with data from our Northstar and HGB-205 clinical studies, could be sufficient to form the basis for a BLA submission for our LentiGlobin product candidate to treat patients with TDT who do not have a $^{0}/_{0}$ genotype. In addition, if successful, we believe the results from our planned Phase III clinical study HGB-212, together with data from our Northstar, Northstar-2 and HGB-205 clinical studies, could be sufficient to form the basis for a BLA supplement submission for our LentiGlobin product candidate to treat patients with TDT who do have a $^{0}/_{0}$ genotype. However, it should be noted that our ability to submit and obtain approval of a BLA is ultimately an FDA review decision, which will be dependent upon the data available at such time, and the available data may not be sufficiently robust from a safety and/or efficacy perspective to support the submission or approval of a BLA. Depending on the outcome of these planned and ongoing clinical studies, the FDA may require that we conduct additional or larger pivotal trials before we can submit or obtain approval for a BLA for our LentiGlobin product candidate for the treatment of TDT.

Before beginning our planned Phase III clinical studies of our LentiGlobin product candidate, the FDA must review the final protocols for the studies, along with additional information supporting the respective proposed study designs. Concurrent with starting the studies, the FDA will review certain updated chemistry, manufacturing and controls, or CMC, information that we are required to submit. If the FDA does not approve the protocols for the planned studies in the forms in which we submit them, or if the FDA is not satisfied with the additional CMC information we plan to provide, the start or continuation of these clinical studies may be delayed or the design of the studies may change.

There can be no assurance that we will ultimately receive conditional marketing approval of our LentiGlobin product candidate in the European Union, or the nature of the conditions that would be imposed on us if conditionally approved.

The EMA Adaptive Pathways program in which we are participating is intended to facilitate either an initial approval in a well-defined patient subgroup with a high medical need and subsequent widening of the indication to a larger

patient population, or an early regulatory approval (e.g. conditional approval), which is prospectively planned, and where uncertainty is reduced through the collection of post-approval data on a drug's use in patients. Based on our discussions with the EMA, we believe our LentiGlobin product candidate may be eligible for conditional approval under this program for the treatment of patients with TDT on the basis of the totality of clinical data, in particular reduction in transfusion need, from the ongoing Northstar and Northstar-2 studies, the supportive HGB-205 study, and our planned HGB-212 clinical study.

However, it should be noted that the EMA Adaptive Pathways program is a pilot program, and as such there is limited information and precedent regarding the potential outcomes for sponsors that participate in this program. Whether our LentiGlobin product candidate is eligible for conditional approval will ultimately be determined at the discretion of the EMA and will be dependent upon the data available at such time, and the available data may not be sufficiently robust from a safety and/or efficacy perspective to support conditional approval. Depending on the outcome of our planned and ongoing clinical trials, the EMA may require that we conduct additional or larger clinical trials before our LentiGlobin product candidate is eligible for conditional approval. Even if conditional approval is obtained, the conditions to be imposed on us under this program are unknown and will be imposed at the time of any such conditional approval.

Changes in our manufacturing processes may cause delays in our clinical development and commercialization plans.

The manufacturing processes for our lentiviral vectors and our product candidates are complex. As we develop a commercial-scale manufacturing process for our LentiGlobin and Lenti-D product candidates, we are exploring improvements to the manufacturing process for both producing our lentiviral vectors and for our product candidates on a continual basis. In some circumstances, changes in the manufacturing process may require us to perform additional comparability studies or to collect additional data from patients prior to undertaking additional clinical studies. The FDA may also require us to file a new IND with respect to such changes in our manufacturing process. These requirements may lead to delays in our clinical development and commercialization plans.

In previous clinical studies involving viral vectors for gene therapy, some subjects experienced serious adverse events, including the development of leukemia due to vector-related insertional oncogenesis. If our vectors demonstrate a similar effect, we may be required to halt or delay further clinical development of our product candidates.

A significant risk in any gene therapy product based on viral vectors is that the vector will insert in or near cancer-causing oncogenes leading to uncontrolled clonal proliferation of mature cancer cells in the patient. For example, in 2003, 20 subjects treated for X-linked severe combined immunodeficiency in two gene therapy studies using a murine, or mouse-derived, gamma-retroviral vector showed correction of the disease, but the studies were terminated after five subjects developed leukemia (four of whom were subsequently cured). The cause of these adverse events was shown to be insertional oncogenesis, which is the process whereby the corrected gene inserts in or near a gene that is important in a critical cellular process like growth or division, and this insertion results in the development of a cancer (often leukemia). Using molecular diagnostic techniques, it was determined that clones from these subjects showed retrovirus insertion in proximity to the promoter of the LMO2 proto-oncogene. Earlier generation retroviruses like the one used in these two studies have been shown to preferentially integrate in regulatory regions of genes that control cell growth.

These well-publicized adverse events led to the development of new viral vectors, such as lentiviral vectors, with improved safety profiles and also the requirement of enhanced safety monitoring in gene therapy clinical trials, including periodic analyses of the therapy's genetic insertion sites. In published studies, lentiviral vectors have demonstrated an improved safety profile over gamma-retroviral vectors, with no disclosed events of gene therapy-related adverse events, which we believe is due to a number of factors including the tendency of these vectors to integrate within genes rather than in areas that control gene expression, as well as their lack of strong viral enhancers. However, it should be noted that in our Phase I/II study (the LG001 Study) of autologous HSCs transduced ex vivo using an earlier generation of our LentiGlobin vector, called HPV569, we initially observed in one subject that a disproportionate number of the cells expressing our functional gene had the same insertion site. Tests showed that this partial clonal dominance contained an insertion of the functional gene in the HMGA2 gene that persisted for a period of two to three years. Although there was some initial concern that the observed clonal dominance might represent a pre-leukemic event, there have been no adverse clinical consequences of this event, or any signs of cancer, in over seven years since the observation was made. The presence of the HMGA2 clone has steadily declined in this subject over time to the point that it is no longer the most common clone observed in this subject.

Notwithstanding the historical data regarding the potential safety improvements of lentiviral vectors, the risk of insertional oncogenesis remains a significant concern for gene therapy and we cannot assure that it will not occur in any of our ongoing or planned clinical studies. There is also the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biological activity of the genetic material or other components of products used to carry the genetic material. The FDA has stated that lentiviral vectors possess characteristics that may pose high risks of delayed adverse events. If any such adverse events occur, further advancement of our clinical studies could be halted or delayed, which would have a material adverse effect on our business and operations.

* In previous clinical studies involving T cell-based immunotherapies, some subjects experienced serious adverse events. Our T cell-based immunotherapy product candidates may demonstrate a similar effect or have other properties that could halt their clinical development, prevent their regulatory approval, limit their commercial potential, or result in significant negative consequences.

Our bb2121 product candidate is a chimeric antigen receptor, or CAR, T cell-based immunotherapy. In previous clinical studies involving CAR T cell products by other companies or academic researchers, many subjects experienced side effects such as neurotoxicity and cytokine release syndrome. There have been life threatening events related to severe neurotoxicity and cytokine release syndrome, requiring intense medical intervention such as intubation or pressor support, and in several cases, resulted in death. Severe neurotoxicity is a condition that is currently defined clinically by cerebral edema, confusion, drowsiness, speech impairment, tremors, seizures, or other central nervous system side effects, when such side effects are serious enough to lead to intensive care. In some cases, severe neurotoxicity was thought to be associated with the use of certain lymphodepletion regimens used prior to the administration of the CAR T cell products. Cytokine release syndrome is a condition that is currently defined clinically by certain

symptoms related to the release of cytokines, which can include fever, chills, low blood pressure, when such side effects are serious enough to lead to intensive care with mechanical ventilation or significant vasopressor support. The exact cause or causes of cytokine release syndrome and severe neurotoxicity in connection with treatment of CAR T cell products is not fully understood at this time. In addition, subjects have experienced other adverse events in these studies, such as a reduction in the number of blood cells (in the form of neutropenia, thrombocytopenia, anemia or other cytopenias), febrile neutropenia, chemical laboratory abnormalities (including elevated liver enzymes), and renal failure.

Undesirable side effects caused by our bb2121 product candidate, or our other T cell-based immunotherapy product candidates, could cause us or regulatory authorities to interrupt, delay or halt clinical studies and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign regulatory authorities. Results of our studies could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Treatment-related side effects could also affect patient recruitment or the ability of enrolled subjects to complete the studies or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff, as toxicities resulting from T cell-based immunotherapies are not normally encountered in the general patient population and by medical personnel. We expect to have to train medical personnel regarding our T cell-based immunotherapy product candidates to understand their side effects for both our planned clinical trials and upon any commercialization of any T cell-based immunotherapy product candidates. Inadequate training in recognizing or managing the potential side effects of T cell-based immunotherapy product candidates could result in patient deaths. Any of these occurrences may harm our business, financial condition and prospects significantly.

Even if we complete the necessary preclinical and clinical studies, we cannot predict when or if we will obtain regulatory approval to commercialize a product candidate or the approval may be for a more narrow indication than we expect.

We cannot commercialize a product until the appropriate regulatory authorities have reviewed and approved the product candidate. Even if our product candidates demonstrate safety and efficacy in clinical studies, the regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee or other regulatory advisory group or authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical studies and the review process. Regulatory agencies also may approve a treatment candidate for fewer or more limited indications than requested or may grant approval subject to the performance of post-marketing studies. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our treatment candidates. For example, the development of our product candidates for pediatric use is an important part of our current business strategy, and if we are unable to obtain regulatory approval for the desired age ranges, our business may suffer.

Even if we obtain regulatory approval for a product candidate, our products will remain subject to regulatory scrutiny.

Even if we obtain regulatory approval in a jurisdiction, the regulatory authority may still impose significant restrictions on the indicated uses or marketing of our product candidates, or impose ongoing requirements for potentially costly post-approval studies, post-market surveillance or patient or drug restrictions. For example, the FDA typically advises that patients treated with gene therapy undergo follow-up observations for potential adverse events for a 15-year period. Additionally, the holder of an approved BLA is obligated to monitor and report adverse events and any failure of a product to meet the specifications in the BLA. The holder of an approved BLA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Advertising and promotional materials must comply with FDA rules and are

subject to FDA review, in addition to other potentially applicable federal and state laws.

In addition, product manufacturers and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with good manufacturing practices, or GMP, and adherence to commitments made in the BLA. If we or a regulatory agency discovers previously unknown problems with a product such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions relative to that product or the manufacturing facility, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

If we fail to comply with applicable regulatory requirements following approval of any of our product candidates, a regulatory agency may:

- issue a warning letter asserting that we are in violation of the law;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;

- suspend any ongoing clinical studies;
- refuse to approve a pending marketing application, such as a BLA or supplements to a BLA submitted by us;
- seize product; or
- refuse to allow us to enter into supply contracts, including government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenues.

Risks related to our reliance on third parties

We expect to rely on third parties to conduct some or all aspects of our vector production, drug product manufacturing, research and preclinical and clinical testing, and these third parties may not perform satisfactorily.

We do not expect to independently conduct all aspects of our vector production, product manufacturing, research and preclinical and clinical testing. We currently rely, and expect to continue to rely, on third parties with respect to these items. In some cases these third parties are academic, research or similar institutions that may not apply the same quality control protocols utilized in certain commercial settings.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibility to ensure compliance with all required regulations and study protocols. For example, for product candidates that we develop and commercialize on our own, we will remain responsible for ensuring that each of our IND-enabling studies and clinical studies are conducted in accordance with the study plan and protocols.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our studies in accordance with regulatory requirements or our stated study plans and protocols, we will not be able to complete, or may be delayed in completing, the preclinical and clinical studies required to support future IND and BLA submissions and approval of our product candidates.

Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it could delay our product development activities.

Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured the product candidates ourselves, including:

- the inability to negotiate manufacturing agreements with third parties under commercially reasonable terms;
- reduced control as a result of using third-party manufacturers for all aspects of manufacturing activities;
- the risk that these activities are not conducted in accordance with our study plans and protocols;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us; and
- disruptions to the operations of our third-party manufacturers or suppliers caused by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier.

Any of these events could lead to clinical study delays or failure to obtain regulatory approval, or impact our ability to successfully commercialize future products. Some of these events could be the basis for FDA action, including injunction, recall, seizure or total or partial suspension of production.

We and our contract manufacturers are subject to significant regulation with respect to manufacturing our products. The manufacturing facilities on which we rely may not continue to meet regulatory requirements and have limited capacity.

We currently have relationships with a limited number of suppliers for the manufacturing of our viral vectors and product candidates. Each supplier may require licenses to manufacture such components if such processes are not owned by the supplier or in the public domain and we may be unable to transfer or sublicense the intellectual property rights we may have with respect to such activities.

All entities involved in the preparation of therapeutics for clinical studies or commercial sale, including our existing contract manufacturers for our product candidates, are subject to extensive regulation. Some components of a finished therapeutic product approved for commercial sale or used in late-stage clinical studies must be manufactured in accordance with GMP. These regulations govern manufacturing processes and procedures (including record keeping) 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 adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We or our contract manufacturers must supply all necessary documentation in support of a BLA or MAA on a timely basis and where required, must adhere to the FDA's or other regulator's good laboratory practices, or GLP, and GMP regulations enforced by the FDA or other regulator through facilities inspection programs. Some of our contract manufacturers have not produced a commercially-approved product and therefore have not obtained the requisite FDA or other regulatory approvals to do so. Our facilities and quality systems and the facilities and quality systems of some or all of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our product candidates or any of our other potential products. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidates or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted. If these facilities do not pass a pre-approval plant inspection, FDA or other regulatory approval of the products will not be granted.

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

If we or any of our third-party manufacturers fail to maintain regulatory compliance, the FDA or other regulators can impose regulatory sanctions including, among other things, refusal to approve a pending application for a biologic product, or revocation of a pre-existing approval. As a result, our business, financial condition and results of operations may be materially harmed.

Additionally, if supply from one approved manufacturer is interrupted, there could be a significant disruption in commercial supply. The number of manufacturers with the necessary manufacturing capabilities is limited. In addition, an alternative manufacturer would need to be qualified through a BLA supplement or similar regulatory submission which could result in further delay. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

These factors could cause the delay of clinical studies, regulatory submissions, required approvals or commercialization of our product candidates, cause us to incur higher costs and prevent us from commercializing our products successfully. 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 studies may be delayed or we could lose potential revenue.

We expect to rely on third parties to conduct, supervise and monitor our clinical studies, and if these third parties perform in an unsatisfactory manner, it may harm our business.

We expect to rely on CROs and clinical study sites to ensure our clinical studies are conducted properly and on time. While we will have agreements governing their activities, we will have limited influence over their actual performance. We will control only certain aspects of our CROs' activities. Nevertheless, we will be responsible for ensuring that each of our clinical studies is 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 are required to comply with the FDA's GCPs for conducting, recording and reporting the results of clinical studies to assure that the data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical study participants are protected. The FDA enforces these GCPs through periodic inspections of study sponsors, principal investigators and clinical study sites. If we or our CROs fail to comply with applicable GCPs, the clinical data generated in our future clinical studies may be deemed unreliable and the FDA may require us to perform additional clinical studies before approving any marketing applications. Upon inspection, the FDA may determine that our clinical studies did not comply with GCPs. In addition, our future clinical studies will require a sufficient number of test subjects to evaluate the safety and efficacy of our product candidates. Accordingly, if our CROs fail to comply with these regulations or fail to recruit a sufficient number of patients, we may be required to repeat such clinical studies, which would delay the regulatory approval process.

Employees of our CROs are not our employees, and we are therefore unable to directly monitor whether or not they devote sufficient time and resources to our clinical and nonclinical programs, which must be conducted in accordance with GCPs and GLPs, respectively. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical studies or other drug development activities that could harm our competitive position. If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements, or for any other reasons, our clinical studies may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase, and our ability to generate revenues could be delayed.

We also expect to rely on other third parties to store and distribute our vectors and products for any clinical studies that we may conduct. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, if approved, producing additional losses and depriving us of potential product revenue.

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

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

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

Risks related to our financial condition and capital requirements

We have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future.

We are a clinical-stage biotechnology company, and we have not yet generated significant revenues. We have incurred net losses in each year since our inception in 1992, including net losses of $77.0 million and $42.9 million for the three months ended September 30, 2016 and 2015, respectively. As of September 30, 2016 and December 31, 2015, we had an accumulated deficit of $506.3 million and $314.2 million, respectively.

We have devoted most of our financial resources to research and development, including our clinical and preclinical development activities. To date, we have financed our operations primarily through the sale of equity securities and, to a lesser extent, through collaboration agreements and grants from governmental agencies and charitable foundations. The amount of our future net losses will depend, in part, on the rate of our future expenditures and our ability to obtain funding through equity or debt financings, strategic collaborations or additional grants. We have not completed pivotal clinical studies for any product candidate and it will be several years, if ever, before we have a product candidate ready for commercialization. Even if we obtain regulatory approval to market a product candidate, our future revenues will depend upon the size of any markets in which our product candidates have received approval, and our ability to achieve sufficient market acceptance, reimbursement from third-party payors and adequate market share for our product candidates in those markets.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if and as we:

- continue our research and preclinical and clinical development of our product candidates;
- expand the scope of our current clinical studies for our product candidates;
- initiate additional preclinical, clinical or other studies for our oncology product candidates;
- further develop the manufacturing process for our vectors or our product candidates;
    - change or add additional manufacturers or suppliers;
- seek regulatory and marketing approvals for our product candidates that successfully complete clinical studies;
- seek to identify and validate additional product candidates;
- acquire or in-license other product candidates and technologies;
- make milestone or other payments under any license agreements or our stock purchase agreement with the former equityholders of Pregenen;
- maintain, protect and expand our intellectual property portfolio;
- establish a sales, marketing and distribution infrastructure in the United States and Europe to commercialize any products for which we may obtain marketing approval;
- attract and retain skilled personnel;
- build additional infrastructure to support our operations as a public company and our product development and planned future commercialization efforts; and
- experience any delays or encounter issues with any of the above.

The net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. In any particular quarter or quarters, our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline.

We have never generated any revenue from product sales and may never be profitable.

Our ability to generate revenue and achieve profitability depends on our ability, alone or with strategic collaboration partners, to successfully complete the development of, and obtain the regulatory, pricing and reimbursement approvals necessary to commercialize our product candidates. We do not anticipate generating revenues from product sales for the foreseeable future, if ever. Our ability to generate future revenues from product sales depends heavily on our success in:

- completing research and preclinical and clinical development of our product candidates;
- seeking and obtaining regulatory and marketing approvals for product candidates for which we complete clinical studies;
- developing a sustainable, commercial-scale, reproducible, and transferable manufacturing process for our vectors and product candidates;
- establishing and maintaining supply and manufacturing relationships with third parties that can provide adequate (in amount and quality) products and services to support clinical development and the market demand for our product candidates, if approved;
- launching and commercializing product candidates for which we obtain regulatory and marketing approval, either by collaborating with a partner or, if launched independently, by establishing a sales force, marketing and distribution infrastructure;
- obtaining sufficient pricing and reimbursement for our product candidates from third-party and governmental payors;
- obtaining market acceptance of our product candidates and gene therapy as a viable treatment option;
- addressing any competing technological and market developments;
- identifying and validating new gene therapy product candidates;

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- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter; and
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how.

Even if one or more of the product candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Our expenses could increase beyond expectations if we are required by the FDA, the EMA, or other regulatory agencies, domestic or foreign, to perform clinical and other studies in addition to those that we currently anticipate. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations.

From time to time, we will need to raise additional funding, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations.

We are currently advancing our LentiGlobin, Lenti-D and bb2121 product candidates through clinical development and other product candidates through preclinical development. Developing gene therapy products is expensive, and we expect our research and development expenses to increase substantially in connection with our ongoing activities, particularly as we advance our product candidates in clinical studies.

As of September 30, 2016, our cash, cash equivalents and marketable securities were $727.6 million. We expect that our existing cash, cash equivalents, and marketable securities will be sufficient to fund our current operations through 2018. However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or a combination of these approaches. In any event, we will require additional capital to obtain regulatory approval for, and to commercialize, our product candidates. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic objectives.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborative partners or otherwise at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any product candidates or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations.

Risks related to commercialization of our product candidates

* We intend to rely on third-party manufacturers to produce our vector, product candidates and