bluebird bio, Inc.
Form 10-Q
August 07, 2015
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

FORM 10-Q

(Mark One)

x QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the quarterly period ended June 30, 2015

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 x 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 x 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	x	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 x

As of July 31, 2015, there were 36,263,621 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,” “will,” “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 manufacturing and transduction capabilities;
the timing or likelihood of regulatory filings and approvals;
the 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 or obtain additional grant funding;
our financial performance;
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 six months ended June 30, 2015

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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)

	June 30, 2015	December 31, 2014
Assets		
Current assets:		
Cash and cash equivalents	$593,299	$ 347,845
Marketable securities	217,208	125,710
Deferred tax assets	399	1,913
Prepaid expenses and other current assets	4,546	4,521
Total current assets	815,452	479,989
Marketable securities	125,938	18,448
Property and equipment, net	16,803	15,740
Intangible assets, net	26,337	28,219
Goodwill	13,128	13,128
Restricted cash and other non-current assets	1,511	1,215
Total assets	$999,169	$ 556,739
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$2,339	$ 2,954
Accrued expenses and other current liabilities	20,024	14,649
Deferred revenue, current portion	5,670	25,375
Total current liabilities	28,033	42,978
Deferred rent, net of current portion	8,223	8,674
Deferred revenue, net of current portion	38,724	5,302
Contingent consideration, net of current portion	4,590	6,321
Deferred tax liabilities	399	1,913
Other non-current liabilities	234	294
Total liabilities	80,203	65,482
Commitments and contingencies (Note 6)		
Stockholders' equity:		
Preferred stock, $0.01 par value, 5,000 shares authorized; 0 shares issued and outstanding at June 30, 2015	—	—

and December 31, 2014		
Common stock, $0.01 par value, 125,000 shares authorized;		
35,958 and 32,340 shares issued and outstanding at June 30, 2015		
and December 31, 2014, respectively	360	323
Additional paid-in capital	1,142,625	638,389
Accumulated other comprehensive loss	(53)	(71)
Accumulated deficit	(223,966)	(147,384)
Total stockholders' equity	918,966	491,257
Total liabilities and stockholders' equity	$999,169	$ 556,739

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 June 30,		Six months ended June 30,	
	2015	2014	2015	2014
Revenue:				
Collaboration revenue	$4,940	$6,250	$11,284	$12,500
Research and license fees	—	85	—	170
Total revenue	4,940	6,335	11,284	12,670
Operating expenses:				
Research and development	44,266	13,931	67,985	25,394
General and administrative	10,724	5,738	18,060	11,277
Change in fair value of contingent consideration	1,973	—	2,188	—
Total operating expenses	56,963	19,669	88,233	36,671
Loss from operations	(52,023)	(13,334)	(76,949)	(24,001)
Other income, net	228	11	367	69
Loss before income taxes	(51,795)	(13,323)	(76,582)	(23,932)
Benefit from income taxes	—	11,797	—	11,797
Net loss	$(51,795)	$(1,526)	$(76,582)	$(12,135)
Other comprehensive loss:				
Unrealized gain on available-for-sale securities, net of tax	70	—	18	—
Comprehensive loss	$(51,725)	$(1,526)	$(76,564)	$(12,135)
Net loss per share - basic and diluted:	$(1.57)	$(0.06)	$(2.34)	$(0.50)
Weighted-average number of common shares used in computing net loss per share - basic and diluted:	32,955	24,474	32,757	24,312

See accompanying notes to unaudited condensed consolidated financial statements.

bluebird bio, Inc.

Condensed Consolidated Statements of Cash Flows

(unaudited)

(in thousands)

	Six months ended June 30,	
	2015	2014
Operating activities		
Net loss	$(76,582)	$(12,135)
Adjustments to reconcile net loss to net cash used in operating activities:		
Non-cash benefit on release of tax valuation allowance	—	(11,797)
Depreciation and amortization	3,509	1,017
Stock-based compensation expense	21,482	4,843
Change in fair value of contingent consideration	2,188	—
Other non-cash items	269	168
Changes in operating assets and liabilities:		
Prepaid expenses and other assets	(1,059)	854
Accounts payable	(418)	(2,702)
Accrued expenses and other liabilities	1,098	7,674
Deferred revenue	13,716	(12,670)
Deferred rent	(480)	1,490
Net cash used in operating activities	(36,277)	(23,258)
Investing activities		
Restricted cash	359	—
Purchase of property and equipment	(2,568)	(4,534)
Acquisition of business, net of cash acquired	—	(4,673)
Purchases of marketable securities	(261,440)	—
Proceeds from maturities of marketable securities	62,680	—
Net cash used in investing activities	(200,969)	(9,207)
Financing activities		
Proceeds from public offering of common stock, net of issuance costs	477,179	—
Proceeds from issuance of common stock	5,521	1,896
Net cash provided by financing activities	482,700	1,896
Increase (decrease) in cash and cash equivalents	245,454	(30,569)
Cash and cash equivalents at beginning of period	347,845	206,279
Cash and cash equivalents at end of period	$593,299	$175,710
Non-cash investing and financing activities:		
Assets acquired in acquisition	$—	$43,759
Liabilities assumed in acquisition	$—	$12,768
Equity issued in acquisition	$—	$19,348
Purchases of property and equipment included in	$524	$344

accounts payable and accrued expenses		
Offering expenses included in accounts payable and accrued expenses	$115	$45
Stock option exercise proceeds receivable	$181	$75

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 was formed to develop, manufacture and market therapies to safely and effectively deliver genes useful in 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.

In June 2015, the Company sold 2,941,176 shares of common stock through an underwritten public offering at a price of $170.00 per share. The aggregate net proceeds received by the Company from the offering were $477.2 million, net of underwriting discounts and commissions and estimated offering expenses payable by the Company of approximately $22.8 million.

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 June 30, 2015 and 2014.

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, 2014, 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, 2015.

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. 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 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, 2014, 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 six months ended June 30, 2015.

Contingent consideration

Each reporting period, the Company revalues the contingent consideration obligations associated with business combinations to their fair value and records within operating expenses increases in their fair value as contingent consideration expense and decreases in the fair value as contingent consideration income. Changes in contingent consideration result from changes in the assumptions regarding probabilities of successful achievement of related milestones, the estimated timing in which the milestones are achieved and the discount rate used to estimate the fair value of the liability. Contingent consideration may change significantly as development of the Company's programs in certain indications progress and additional data are obtained, impacting the Company's assumptions. The assumptions used in estimating fair value require significant judgment. The use of different assumptions and judgments could result in a materially different estimate of fair value. See Note 4, "Fair value measurements," for additional information.

bluebird bio, Inc.

Notes to Condensed Consolidated Financial Statements

(unaudited)

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 equivalent shares outstanding for the period, including any dilutive effect from outstanding stock options, unvested restricted stock, restricted stock units, employee stock purchase plan, warrants, and acquisition holdback shares 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, contingent consideration, stock-based compensation expense, accrued expenses, revenue and income taxes. Actual results could materially differ from those estimates.

3. Marketable securities

The following table summarizes the available-for-sale securities held at June 30, 2015 and December 31, 2014 (in thousands):

Description	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
June 30, 2015				
U.S. government agency securities	$ 329,359	$ 29	$ (89)	$ 329,299
Certificates of deposit	13,840	8	(1)	13,847
Total	$ 343,199	$ 37	$ (90)	$ 343,146
December 31, 2014				
U.S. government agency securities	$ 131,589	$ 6	$ (59)	$ 131,536
Certificates of deposit	12,640	—	(18)	12,622
Total	$ 144,229	$ 6	$ (77)	$ 144,158

No available-for-sale securities held as of June 30, 2015 or December 31, 2014 had remaining maturities greater than two years.

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bluebird bio, Inc.

Notes to Condensed Consolidated Financial Statements

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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 June 30, 2015 and December 31, 2014 (in thousands):

Description	Total	Quoted prices in active markets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)
June 30, 2015				
Assets:				
Cash and cash equivalents	$593,299	$593,299	$—	$ —
Marketable securities:				
U.S. government agency securities	329,299	—	329,299	—
Certificates of deposit	13,847	—	13,847	—
Total assets	$936,445	$593,299	$343,146	$ —
Liabilities:				
Contingent consideration	$7,984	$—	$—	$ 7,984
Total liabilities	$7,984	$—	$—	$ 7,984
December 31, 2014				
Assets:				
Cash and cash equivalents	$347,845	$347,845	$—	$ —
Marketable securities:				
U.S. government agency securities	131,536	—	131,536	—
Certificates of deposit	12,622	—	12,622	—
Total assets	$492,003	$347,845	$144,158	$ —
Liabilities:				
Contingent consideration	$6,796	$—	$—	$ 6,796
Total liabilities	$6,796	$—	$—	$ 6,796

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 June 30, 2015 and December 31, 2014, cash and cash equivalents comprise funds in cash and money market accounts.

Marketable securities

The amortized cost of available-for-sale securities is adjusted for amortization of premiums and accretion of discounts to maturity. At June 30, 2015 and December 31, 2014, 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 realized gains or losses recognized on the sale or maturity of available-for-sale securities during the six months ended June 30, 2015, and as a result, the Company did not reclassify any amounts out of accumulated other comprehensive income 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 June 30, 2015 and December 31, 2014 was $181.3 million and $134.4 million, respectively. 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 an other-than-temporary impairment as of June 30, 2015 and December 31, 2014.

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Contingent consideration

In connection with the acquisition of Pregenen, 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 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 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 2016 to 2026 and discount rates ranging from 10.5% to 14.7%. 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):

	Six Months Ended June 30, 2015
Beginning balance	$6,796
Additions	—
Changes in fair value	2,188
Reclassification to accrued expenses	(1,000)
Payments	—
Ending balance	$7,984

As of June 30, 2015, $3.4 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 $4.5 million reflected as a non-current liability. During the second quarter of 2015, a $1.0 million milestone under the Stock Purchase Agreement was achieved and was recorded in accrued expenses and other current liabilities as of June 30, 2015. $1.0 million was paid to the former equityholders of Pregenen during the third quarter of 2015.

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5. Accrued expenses and other current liabilities

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

	June 30, 2015	December 31, 2014
Employee compensation	$3,937	$ 4,943
Accrued good and services	10,303	7,358
Accrued professional fees	1,090	428
Deferred rent, current portion	885	914
Contingent consideration, current portion	3,394	475
Other	415	531
Total accrued expenses and other current liabilities	$20,024	$ 14,649

The change in fair value of contingent consideration was primarily related to an increase in the probability of successful achievement of milestones expected to be achieved within the next twelve months.

6. 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 June 30, 2015 and December 31, 2014 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.

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. The Company received aggregate reimbursement of €1.1 million related to years 2011 through 2013. The Company applied for €0.7 million related to 2014, which was classified in current assets within the condensed consolidated balance sheets as of June 30, 2015 and was received during the third quarter of 2015. The Company has not yet applied for €0.3 million related to the six months ended June 30, 2015, which is classified as non-current assets within the condensed

consolidated balance sheets as of June 30, 2015. The years 2011 through 2015 are open and subject to examination.

On June 30, 2014, the Company acquired Pregenen. During the second quarter of 2015, a $1.0 million milestone under the Stock Purchase Agreement was achieved, which resulted in a $1.0 million payment to the former equityholders of Pregenen during the third quarter of 2015. The Company may be required to make up to an additional $134.0 million in future contingent cash payments to the former equityholders of Pregenen upon the achievement of certain preclinical, clinical and commercial milestones related to the Pregenen technology, of which $14.0 million relates to preclinical milestones, $20.1 million relates to clinical milestones and $99.9 million relates to commercial milestones. In accordance with accounting for business combinations guidance, contingent consideration liabilities are required to be recognized on the condensed consolidated balance sheets at fair value. Estimating the fair value of contingent consideration requires the use of significant assumptions primarily relating to probabilities of successful achievement of certain preclinical, clinical and commercial milestones, the expected timing in which these milestones will be achieved and discount rates. The use of different assumptions could result in materially different estimates of fair value. See Note 4, “Fair value measurements,” for additional information.

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 $483,840 per year in base rent, which is subject to a 3% annual increase plus certain operating expenses and taxes. The lease will continue until the end of the sixtieth full calendar month following the date the landlord delivers the premises to the Company. Under

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the terms of the lease, the Company will also lease an additional 8,075 square feet of office space in the same premises starting on January 1, 2016 for an additional $258,400 per year in base rent, which is subject to a 3% annual increase plus certain operating expenses and taxes.

7. 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.

Under the terms of the Collaboration Agreement, the Company received a $75.0 million up-front, non-refundable cash payment. The Company is responsible for conducting discovery, research and development activities through completion of Phase I clinical studies, if any, during the initial term of the 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, review the collaboration program, review and evaluate product candidates and approve 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.

Summary of the 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 an additional 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, if any, 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, provided that, if Celgene does not exercise its option with respect to the first product candidate under the Amended Collaboration Agreement prior to the expiration of the applicable Option Period then it will not be permitted to exercise its option with respect to any future product candidates under the Amended Collaboration Agreement. 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, plus 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 that product candidate in the United States. In addition to the applicable option fee, for each product candidate that is in-licensed by Celgene, and for which the Company does not exercise its option to co-develop and co-promote in the United States, the Company will be eligible to receive up to $10.0 million in clinical milestone payments, up to $117.0 million in regulatory milestone payments and up to $78.0 million in commercial milestone payments. The Company will also be eligible to receive a percentage of net sales as a royalty in a

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Notes to Condensed Consolidated Financial Statements

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range from the mid-single digits to low-teens. The royalties payable to the Company are subject to certain reductions, including for any royalty payments required to be made by Celgene to acquire patent rights, with an aggregate minimum floor. Celgene will assume certain development obligations and must report on its progress in achieving these milestones on a quarterly basis.

If the Company elects to co-develop and co-promote a product candidate licensed by Celgene, then the Company and Celgene would share equally in all costs incurred relating to the development, commercialization and manufacturing of the product candidate within the United States and share equally in the profits generated by such product candidate in the United States. Additionally, if the Company elects to co-develop and co-promote a product candidate, then the milestones and royalties would decrease compared to those described above. Under this scenario, the Company would receive, per product, up to $10.0 million in clinical milestone payments and, outside of the United States, up to $54.0 million in regulatory milestone payments and up to $36.0 million in commercial milestone payments. In addition, to the extent any of the product candidates licensed by Celgene and co-developed and co-promoted by the Company are commercialized, the Company would be entitled to receive tiered royalty payments ranging from the mid-single digits to low-teens based on a percentage of net sales from sales generated outside of the United States. The royalties payable to the Company are subject to certain reductions, including for any royalty payments required to be made by Celgene to acquire patent rights, with an aggregate minimum floor. The co-development and co-promotion agreement would be governed by a joint governance committee, or JGC, formed by representatives from the Company and Celgene. The JGC will, among other activities, supervise the overall performance of the development and commercialization of elected product candidates and licensed products for United States administration.

Celgene is solely responsible for the manufacture and supply of drug product for any optioned product candidate. Under the Amended Collaboration Agreement, subject to customary “back-up” supply rights granted to Celgene, the Company has the sole right to manufacture or have manufactured supplies of vectors and associated payloads manufactured for incorporation into the optioned product candidate. Celgene would reimburse the Company for its costs to manufacture and supply such vectors and associated payloads, plus a mid-single digit mark-up.

If Celgene does not exercise its option with respect to any product candidate prior to expiration of the applicable option period, then the Company has the right to develop that product candidate outside the scope of the Amended Collaboration Agreement.

Either party may terminate the Amended Collaboration Agreement upon written notice to the other party in the event of the other party’s uncured material breach. Celgene may terminate the Amended Collaboration Agreement for any reason upon prior written notice to the Company. If the agreement is terminated, rights to product candidates in development at the time of such termination will be allocated to the parties through a mechanism included in the agreement. In addition, if Celgene terminates the agreement for the Company’s breach, any then-existing co-development and co-promotion agreement will be automatically terminated and replaced with a license agreement for such product candidate and any amounts payable by Celgene under any then-existing product license agreements will be reduced.

Under the Amended Collaboration Agreement, the so-called “call option” under the prior collaboration agreement, pursuant to which Celgene had the option to terminate the collaboration agreement and obtain fully paid-up licenses to product candidates in the event of a change of control transaction involving the Company, has been eliminated.

Under the Sublicense Agreement, the Company will continue to have access to certain intellectual property rights in-licensed to Celgene pursuant to its collaboration agreement with the Baylor College of Medicine, which was first established in connection with the initiation of the original Collaboration Agreement between the Company and Celgene.

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 is considered a deliverable at the inception of the arrangement and therefore the associated option fee is included in allocable arrangement consideration. The Company believes there is minimal risk with regard to whether Celgene will exercise the option based on the successful completion of preclinical activities and proximity of enrollment of

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the first patient in an initial Phase I clinical study for this product candidate. Further, Celgene loses the right to option any other product candidates if it does not agree to license the first product candidate. The Company has 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.

However, the Company has determined that the options to license any additional product candidates are substantive options and therefore are 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 has determined that the options are not priced at a significant and incremental discount. Accordingly, the options to other product candidates are not considered deliverables at the inception of the arrangement and the associated option fees are not included in allocable arrangement consideration.

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) has 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 qualifies as a separate unit of accounting.

The Company determined that each of the identified deliverables have the same period of performance (the three year term through projected initial Phase I study completion) and have the same pattern of revenue recognition, ratably over the period of performance as there is 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. This initial term will be revisited as the development plan timing changes or other events that impact the period over which the Company’s obligations relate.

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 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 each of the six months ended June 30, 2015 and 2014, the Company recognized $11.3 million and $12.5 million, respectively, of revenue associated with its collaboration with Celgene related to the recognition of discovery, research and development services. As of June 30, 2015 and December 31, 2014, there was $44.4 million and $30.7 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, $16.9 million of which will be recognized over three years with the remaining amount deferred until a later date.

8. Stock-based compensation and warrants

In January 2015, the number of shares of common stock available for issuance under the 2013 Stock Option and Incentive Plan ("2013 Plan") was increased by approximately 1.3 million shares as a result of the automatic increase provision of the 2013 Plan. As

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of June 30, 2015, the total number of shares of common stock available for issuance under the 2013 Plan was approximately 0.9 million.

Stock-based compensation expense

Stock-based compensation expense by award type was as follows (in thousands):

	Three months ended June 30,		Six months ended June 30,	
	2015	2014	2015	2014
Stock options	$15,310	$2,335	$20,065	$4,812
Restricted stock awards	—	16	—	31
Restricted stock units	668	—	1,285	—
Employee stock purchase plan	72	—	132	—
	$16,050	$2,351	$21,482	$4,843

As of June 30, 2015, the Company had $80.5 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 that is expected to be recognized over a weighted-average period of 2.9 years.

On January 29, 2015, the Company entered into a Transitional Services and Separation Agreement with its Chief Scientific Officer, ending his employment with the Company effective July 6, 2015. Subsequent to this separation date, he is serving as a member of the Company's Scientific Advisory Board. Under the terms of the agreement, outstanding options held by the Chief Scientific Officer were modified. The incremental value of the modification was estimated to be $3.0 million using a Black-Scholes option valuation model, which is being recognized within research and development expense on a straight-line basis through the date of separation. As a result of the modification, the Company recognized $1.8 million and $2.8 million of stock-based compensation expense during the three and six months ended June 30, 2015, respectively.

On April 10, 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.

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, 2014	179	$ 30.47
Granted	25	$ 179.30
Vested	—	—
Forfeited	(1)	$ 30.47
Unvested balance at June 30, 2015	203	$ 48.77

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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, 2014	3,652	$ 12.30
Granted	915	$ 106.87
Exercised	(671)	$ 7.97
Canceled or forfeited	(43)	$ 44.68
Outstanding at June 30, 2015	3,853	$ 35.15
Exercisable at June 30, 2015	1,325	$ 7.89
Vested and expected to vest at June 30, 2015	3,776	$ 35.61

Options exercisable for approximately 0.7 million shares of common stock were exercised during the six months ended June 30, 2015, resulting in total proceeds to the Company of $5.3 million. In accordance with the Company's stock option plans, the shares were issued from a pool of shares reserved for issuance under the stock option plans.

Employee stock purchase plan

The Company's 2013 Employee Stock Purchase Plan ("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 closed on January 31, 2015, resulting in the purchase of 6,780 common shares.

Warrants

As of June 30, 2015 and December 31, 2014, the Company had 0.2 million warrants outstanding to purchase common stock. During the six months ended June 30, 2015, there were no warrants exercised and no cancellations or expirations.

9. 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. The Company has allocated its valuation allowance in accordance with the provisions of ASC 740, Income Taxes, which resulted in a current deferred tax asset of $0.4 million and a non-current deferred tax liability of $0.4 million as of June 30, 2015.

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10. 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):

	Three and six months ended June 30,	
	2015	2014
Warrants	177	338
Outstanding stock options	3,853	4,112
Unvested restricted stock	—	27
Restricted stock units	203	—
ESPP shares	4	—
Acquisition holdback	94	94
	4,331	4,571

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, 2015.

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," "will," "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, each of which has been granted orphan drug status by U.S. and European regulatory authorities.

We are conducting a Phase II/III clinical study, called the Starbeam Study, of our most advanced product candidate, Lenti-D, to evaluate its safety and efficacy in subjects with childhood cerebral adrenoleukodystrophy, or CCALD, a rare, hereditary neurological disorder affecting young boys 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 CCALD treated by allogeneic

hematopoietic stem-cell transplant referred to as the ALD-103 study.

We are also conducting two Phase I/II clinical studies in the United States, Australia, and Thailand and in France, called the Northstar (HGB-204) and HGB-205 studies, respectively, of our product candidate, LentiGlobin, to evaluate its safety and efficacy in subjects with beta-thalassemia major and sickle cell disease, or SCD, which are rare, hereditary blood disorders that often lead to severe anemia and shortened lifespans. We have initiated a Phase I clinical study in the United States, called the HGB-206 Study, to evaluate the safety and efficacy of LentiGlobin in subjects with severe SCD. In June 2015, we announced that the first patient with severe SCD had been infused in the HGB-206 Study.

We recently announced clinical data from our ongoing clinical studies of LentiGlobin in subjects with beta-thalassemia major and SCD. These data are summarized below.

· In December 2014, at the annual meeting of the American Society of Hematology (ASH), we announced data from the first eight subjects treated with LentiGlobin in these studies. As of December 2014, in the first four subjects, each of whom had at

least three months of follow-up, treatment with LentiGlobin resulted in sufficient hemoglobin production to reduce or eliminate the need for transfusion support among patients with beta-thalassemia major who would otherwise require chronic blood transfusions. These data included the first five subjects treated in the Northstar study and the first three subjects (two with beta-thalassemia major and one with severe SCD) from the HGB-205 study.

- In June 2015, at the 20th Congress of the European Hematology Association, we announced long-term follow up of two subjects with beta-thalassemia major and early safety and efficacy data in the first subject with severe SCD treated with LentiGlobin in the HGB-205 study. As of May 2015, the two patients with beta-thalassemia major remained transfusion-independent for 16 and 14 months, respectively, and neither experienced a LentiGlobin-related adverse event. As of May 2015, the proportion of anti-sickling hemoglobin being produced by the first-ever subject with severe SCD treated with gene therapy has risen steadily and accounted for 45% of all hemoglobin production at the patient's six-month visit post-drug product infusion; this is above the 30% threshold expected to potentially achieve a disease-modifying clinical effect. Further, as of May 2015, the patient with severe SCD had been free of transfusions for more than three months without complications or hospitalizations for SCD-related events post-transplant, and has demonstrated improvement in hemolysis markers.

We also plan to initiate two new clinical trials of LentiGlobin, called HGB-207, for adult and adolescent patients with beta-thalassemia major, and HGB-208, for pediatric patients with beta-thalassemia major. Each of these trials, once initiated, are expected to enroll approximately 15 patients to be evaluated for 24 months following treatment, and we expect that the primary endpoint of these trials will be 12 months of transfusion independence following treatment.

In May 2015, we announced that we believe we have reached general agreement with regulatory authorities in Europe and the United States regarding our development plans for LentiGlobin, which could potentially result in accelerated approvals in these jurisdictions. These discussions are summarized below.

- In Europe, we are participating in the Adaptive Pathways (formerly referred to as Adaptive Licensing) pilot program of the European Medicines Agency, or EMA. Based on our discussions with EMA, we believe it is possible to seek conditional approval of LentiGlobin for the treatment of adults and adolescents with beta-thalassemia major on the basis of the totality of clinical data, in particular reduction in transfusion need, from the ongoing Northstar study and supportive HGB-205 study. We believe that conversion to full approval will be subject to the successful completion of the HGB-207 and HGB-208 clinical trials, and collection of supportive long-term follow-up data and "real-life" post-approval data.
- In the United States, we believe we have reached general agreement with the U.S. Food and Drug Administration, or FDA, on the major elements of our planned HGB-207 and HGB-208 clinical trials. Based on our discussions with the FDA, we believe that the data from these trials, together with data from our ongoing beta-thalassemia major clinical studies (Northstar and HGB-205), could form the basis for a Biologics License Application, or BLA, submission for LentiGlobin for the treatment of beta-thalassemia major.

In June 2015, the National Institutes of Health (NIH) Recombinant DNA Advisory Committee's (RAC) recommended that we delay the initiation of the HGB-208 clinical trial for pediatric patients with beta-thalassemia major for an additional one to two years in order to obtain more safety and efficacy data in adults and adolescents to demonstrate a higher benefit with LentiGlobin as compared to alternative treatments. We believe this recommendation has no impact on our planned HGB-207 clinical trial for adult and adolescent patients with beta-thalassemia major. We still expect to initiate the HGB-208 clinical trial for pediatric patients in the United States and Europe after consultation with the appropriate regulatory agencies, institutional review boards and clinical trial sites.

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 an additional three-year term. B-cell maturation antigen, or BCMA, is a cell

surface protein that is expressed in normal plasma cells and in 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. During the three and six months ended June 30, 2015, we recognized $4.9 million and $11.3 million, respectively, of revenue associated with our collaboration with Celgene related to the research and development services performed. As of June 30, 2015, we have classified $44.4 million of deferred revenue related to our collaboration with Celgene in the accompanying balance sheets. We expect the first product candidate from this collaboration, bb2121, to enter clinical trials in early 2016.

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. During the second quarter of 2015, a $1.0 million milestone was achieved, which resulted in a $1.0 million payment to the former equityholders of Pregenen during the third quarter of 2015. We estimate future contingent cash payments have a fair value of $7.9 million as of June 30, 2015, $3.4 million of which is current.

As of June 30, 2015, we had cash, cash equivalents and marketable securities of approximately $936.4 million. We expect our cash, cash equivalents and marketable securities to fund 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 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 losses were $76.6 million for the six months ended June 30, 2015 and our accumulated deficit was $224.0 million as of June 30, 2015. Substantially all 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 Lenti-D and LentiGlobin 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 obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to 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. The terms of this 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. $17.3 million of revenue from the Celgene arrangement associated with research and development services, joint steering committee services and patent committee services will be recognized ratably over the associated period of performance, which is initially estimated to be three years.

Research and license fee revenue is primarily generated through license and research and development agreements with strategic partners and nonprofit organizations for the development and commercialization of our product candidates. There are no performance, cancellation, termination, or refund provisions in any of our arrangements that contain material financial consequences to us.

Nonrefundable license fees are recognized as revenue upon delivery provided there are no undelivered elements in the arrangement. Research fees are recognized as revenue over the period we perform the associated services or on a straight-line basis if the pattern of performance cannot be estimated.

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, 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 CCALD. 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 CCALD 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 beta-thalassemia major. In March 2014, we announced that the first subject had been treated in this study. We recently amended the protocol for this study to expand enrollment to include up to three adolescent patients.
- 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 beta-thalassemia major and severe SCD. In December 2013, we announced that the first subject beta-thalassemia major had been treated in this study and in October 2014, we announced that the first subject with SCD had been treated in this study.
- We have initiated 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 infused in the HGB-206 Study.
- We are conducting research and development activities in the field of oncology and expect the first product candidate from our collaboration with Celgene, bb2121 to treat multiple myeloma, to enter clinical trials in early 2016.
- We are planning to initiate two new clinical trials of LentiGlobin, called HGB-207, for adult and adolescent patients with beta-thalassemia major, and HGB-208, for pediatric patients with beta-thalassemia major.
- 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 June 30,		Six months ended June 30,	
	2015	2014	2015	2014
	(in thousands)		(in thousands)	
Lenti-D	$3,440	$2,232	$7,892	$5,042
LentiGlobin	7,042	6,273	14,133	10,138
Pre-clinical programs	5,266	1,160	7,916	2,257
Total direct research and development expense	15,748	9,665	29,941	17,437
Employee- and contractor-related expenses	2,993	1,295	5,461	2,233
Stock-based compensation expense	12,066	1,061	15,300	2,124
Platform-related expenses	11,885	250	14,062	516
Facility expenses	1,483	1,005	2,986	2,060
Other expenses	91	655	235	1,024
Unallocated personnel and other expenses	28,518	4,266	38,044	7,957

Total research and development expense	$44,266	$13,931	$67,985	$25,394

Refer to the “Results of Operations” section below for additional discussion on one-time, non-recurring charges included within unallocated personnel and other expenses.

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, and human

resource functions. Other general and administrative expenses include facility-related costs, professional fees for accounting 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. Additionally, if and when we believe a regulatory approval of the first product candidate appears likely, we anticipate an increase in payroll and related expenses as a result of our preparation for commercial operations, especially as it relates to the sales and marketing of our product candidates.

Other income, net

Other income, net consists primarily of interest income earned on investments, foreign currency gain or loss and tax incentives from the Massachusetts Life Sciences Center.

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, stock-based compensation, income taxes and contingent consideration. 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 six months ended June 30, 2015, 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, 2014, which was filed with the SEC on February 25, 2015.

Results of Operations

Comparison of the three months ended June 30, 2015 and 2014:

	Three months ended June 30,		
	2015	2014	Change
	(in thousands)		
Revenue:			
Collaboration revenue	$4,940	$6,250	$(1,310)
Research and license fees	—	85	(85)
Total revenue	4,940	6,335	(1,395)
Operating expenses:			
Research and development	44,266	13,931	30,335
General and administrative	10,724	5,738	4,986

Change in fair value of contingent consideration	1,973	—	1,973
Total operating expenses	56,963	19,669	37,294
Loss from operations	(52,023)	(13,334)	38,689
Other income, net	228	11	(217)
Loss before income taxes	(51,795)	(13,323)	38,472
Benefit from income taxes	—	11,797	11,797
Net loss	$(51,795)	$(1,526)	$50,269

Revenue. Total revenue was $4.9 million for the three months ended June 30, 2015 compared to $6.3 million for the three months ended June 30, 2014. The decrease of $1.4 million was primarily attributable to a reduction in collaboration revenue as a result of the amendment to our collaboration agreement with Celgene executed in the second quarter of 2015.

Research and development expenses. Research and development expenses were $44.3 million for the three months ended June 30, 2015, compared to $13.9 million for the three months ended June 30, 2014. The increase of $30.3 million was primarily attributable to the following:

- $11.0 million of increased stock-based compensation expense, $6.7 million of which related to the modification of a stock option award held by a non-employee founder and $1.8 million of which related to the modification of a stock option award held by our former Chief Scientific Officer, which are one-time charges.
- $10.7 million of non-recurring in-license milestones and fees, of which $5.4 million related to an upfront payment for amending and restating an existing patent sublicense agreement; $3.3 million (€3.0 million) related to an upfront payment for amending an existing license agreement with Institut Pasteur; and $1.5 million related to an upfront payment for a new license and collaboration agreement with Five Prime Therapeutics, Inc.
- $3.0 million of increased other employee compensation and benefit expense and $1.7 million of increased lab expenses necessary to support the advancement of our clinical and pre-clinical programs.
- $0.9 million of amortization expense related to intangible assets acquired in June 2014.

General and administrative expenses. General and administrative expenses were $10.7 million for the three months ended June 30, 2015, compared to $5.7 million for the three months ended June 30, 2014. The increase of $5.0 million was primarily attributable to $3.5 million of increased employee compensation and benefit expense to support our overall growth, of which $2.7 million was stock-based compensation expense.

Change in fair value of contingent consideration. The change in fair value of contingent consideration of $2.0 million was primarily related to an increase in the probability of successful achievement of milestones expected to be achieved within the next twelve months.

Comparison of the six months ended June 30, 2015 and 2014

	Six months ended June 30,		
	2015	2014	Change
	(in thousands)		
Revenue:			
Collaboration revenue	$11,284	$12,500	$(1,216)
Research and license fees	—	170	(170)
Total revenue	11,284	12,670	(1,386)
Operating expenses:			
Research and development	67,985	25,394	42,591
General and administrative	18,060	11,277	6,783
Change in fair value of contingent consideration	2,188	—	2,188
Total operating expenses	88,233	36,671	51,562
Loss from operations	(76,949)	(24,001)	52,948
Other income (expense), net	367	69	(298)
Loss before income taxes	(76,582)	(23,932)	52,650
Benefit from income taxes	—	11,797	11,797
Net loss	$(76,582)	$(12,135)	$64,447

Revenue. Total revenue was $11.3 million for the six months ended June 30, 2015 compared to $12.7 million for the six months ended June 30, 2014. The decrease of $1.4 million was primarily attributable to a reduction in

collaboration revenue as a result of the amendment to our collaboration agreement with Celgene executed in the second quarter of 2015. We expect collaboration revenue to be lower in the second half of 2015 as compared to the first half of 2015 as a result of this amendment.

Research and development expenses. Research and development expenses were $68.0 million for the six months ended June 30, 2015 compared to $25.4 million for the six months ended June 30, 2014. The increase of $42.6 million was primarily attributable to the following:

- $13.2 million of increased stock-based compensation expense, $6.7 million of which related to the modification of a stock option award held by a non-employee founder and $2.8 million of which related to the modification of a stock option award held by our former Chief Scientific Officer, which are one-time charges.
- $10.8 million of non-recurring in-license milestones and fees, of which $5.4 million related to an upfront payment for amending and restating an existing patent sublicense agreement; $3.3 million (€3.0 million) related to an upfront payment for

amending an existing license agreement with Institut Pasteur; and $1.5 million related to an upfront payment for a new license and collaboration agreement with Five Prime Therapeutics, Inc.

- $5.3 million of increased other employee compensation and benefit expense, $3.0 million of increased manufacturing related costs, $2.9 million of increased clinical trial related costs, and $2.2 million of increased lab expenses necessary to support the advancement of our clinical and pre-clinical programs.
- $1.9 million of amortization expense related to intangible assets acquired in June 2014.

General and administrative expenses. General and administrative expenses were $18.1 million for the six months ended June 30, 2015 compared to $11.3 million for the six months ended June 30, 2014. The increase of $6.8 million was primarily attributable to $4.6 million of increased employee and contractor related costs to support our overall growth, of which $3.4 million was stock-based compensation expense, $0.5 million of increased professional services costs and $0.5 million of consulting costs.

Change in fair value of contingent consideration. The change in fair value of contingent consideration of $2.2 million was primarily related to an increase in the probability of successful achievement of milestones expected to be achieved within the next twelve months.

Liquidity and Capital Resources

As of June 30, 2015, we had cash, cash equivalents and marketable securities of approximately $936.4 million. We expect cash, cash equivalents and marketable securities to fund 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 June 30, 2015, our funds are held 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.

We have incurred losses and cumulative negative cash flows from operations since our inception in April 1992, and as of June 30, 2015 we had an accumulated deficit of $224.0 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.

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:

	Six months ended June 30,	
	2015	2014
	(in thousands)	
Net cash provided by (used in):		
Operating activities	$(36,277)	$(23,258)
Investing activities	(200,969)	(9,207)
Financing activities	482,700	1,896
Net decrease in cash and cash equivalents	$245,454	$(30,569)

Cash Flows from Operating Activities. The $13.0 million increase in cash used in operating activities for the six months ended June 30, 2015, compared to the six months ended June 30, 2014, was primarily due to the increase in net loss during this period which

was primarily attributable to increased stock-based compensation expense, in-license milestones and fees, and spending on our clinical and pre-clinical stage programs, partially offset by cash received in connection with the Amended Collaboration Agreement with Celgene Corporation. Net loss was $76.6 million for the six months ended June 30, 2015 compared to $12.1 million for the six months ended June 30, 2014, an increase of $64.5 million.

Cash Flows from Investing Activities. The net cash used in investing activities was $201.0 million for the six months ended June 30, 2015 and was primarily due to our purchase of $261.4 million of marketable securities partially offset by proceeds by maturities of marketable securities of $62.7 million.

Cash Flows from Financing Activities: The net cash provided by financing activities was $482.7 million for the six months ended June 30, 2015 and was due to $477.2 million net proceeds from an offering of our common stock and $5.5 million of proceeds from the exercise of stock options and ESPP contributions.

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, 2015, except as noted below:

- On April 1, 2015, we amended an existing license agreement with Institut Pasteur, which resulted in a payment of $3.3 million (€3.0 million) that was paid during the second quarter of 2015.
- On April 6, 2015, we amended and restated an existing patent sublicense agreement, which resulted in a license fee payment of $5.4 million that was paid during the second quarter of 2015. As a result of this amendment, aggregate payments of $1.3 million that were previously included in our contractual obligations and commitments table in our Annual Report on Form 10-K filed with the SEC on February 25, 2015 are no longer due.
- On June 29, 2015, we entered into a lease agreement for additional office space located at 215 First Street, Cambridge, Massachusetts. Under the terms of the lease, we leased approximately 15,120 square feet starting on July 13, 2015 for $483,840 per year in base rent, which is subject to a 3% annual increase plus certain operating expenses and taxes. The lease will continue until the end of the sixtieth full calendar month following the date the landlord delivers the premises to us. Under the terms of the lease, we will also lease an additional 8,075 square feet of office space in the same premises starting on January 1, 2016 for an additional $258,400 per year in base rent, which is subject to a 3% annual increase plus certain operating expenses and taxes.

Off-Balance Sheet Arrangements

As of June 30, 2015, 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 June 30, 2015 and December 31, 2014, we had cash, cash equivalents and marketable securities of $936.4 million and $492.0 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 June 30, 2015, the net fair value of our interest-sensitive marketable securities would have resulted in a hypothetical decline of approximately $3.0 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 June 30, 2015, 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 June 30, 2015, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Control over Financial Reporting

During the quarter ended June 30, 2015, 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, that have materially affected, or are reasonably likely to materially affect, our internal control over 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 June 30, 2015, 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, 2015.

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 one product has 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 extensively studied pharmaceutical or other product candidates. At the moment, only one gene therapy product, UniQure's Glybera, which received marketing

authorization in the EU in 2012, has been approved in the Western world, which makes it 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 the NIH, are also subject to review by the NIH Office of Biotechnology Activities' Recombinant DNA Advisory Committee, or the 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. For example, although in May 2015 we believe we reached general agreement with the FDA on the design of our planned HGB-208 pediatric study protocol for our LentiGlobin product candidate, in June 2015, the RAC completed its public review and recommended a delay of initiation of the HGB-208 study in the United States for an additional one to two years. We cannot predict if this recommendation may delay enrollment of the HGB-208 study. 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 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 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 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;
- 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 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 beta-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 beta-thalassemia major 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, or ALD, the superset of CCALD, is approximately one in 20,000 newborn males. CCALD accounts for about 30-40% of patients diagnosed with ALD. Further, because newborn screening for CCALD is not widely adopted, and it can be difficult to diagnose CCALD 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 hematopoietic stem cells, or HSCs, 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 Institutional Review Board, or 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 candidate, 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. 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. 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 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. 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 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.

*Initial success in our ongoing clinical studies may not be indicative of results obtained when these studies are completed.

In December 2014, at the Annual Meeting of the American Society of Hematology (ASH), we announced data from the first eight subjects treated with our LentiGlobin BB305 product candidate. In June 2015, at the 20th Congress of the European Hematology Association, we announced long-term follow up of two patients with beta-thalassemia major and early safety and efficacy data in the first patient with severe SCD treated with our LentiGlobin BB305

product candidate in the HGB 205 Study. Although the initial clinical data on these subjects are encouraging, the data are preliminary in nature, based on limited periods of time since patient infusion, and the Northstar and HGB-205 Studies are not complete. There is limited data concerning long-term safety and efficacy following treatment with LentiGlobin drug product. These data, or other positive data, may not continue or occur for these subjects or for any future subjects in this study, and may not be repeated or observed in ongoing or future studies involving our LentiGlobin product candidate, including the HGB-205 Study, the Northstar Study or the HGB-206 Study in severe SCD. There can be no assurance that subjects for whom periodic transfusion support has been reduced or temporarily eliminated will not receive transfusion support in the future. Furthermore, there can be no assurance that any of these studies will ultimately be successful or support further clinical advancement of this product candidate. 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 clinical development

even after achieving promising results in earlier studies, and any such setbacks in our clinical development could have a material adverse effect on our business and operating results.

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 Lenti-D 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 CCALD, 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 additional clinical studies of Lenti-D 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 CCALD and the limited number of patients with this condition, 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 Lenti-D safety and efficacy will be evaluated in light of the data collected in our retrospective ALD-101 Study and potentially 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 CCALD 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 Lenti-D 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 planned HGB-207 and HGB-208 clinical trials of LentiGlobin BB305, together with data from our ongoing beta-thalassemia major clinical studies (Northstar and HGB-205), will be sufficient to form the basis for a Biologics License Application, or BLA, submission for LentiGlobin BB305.

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 planned clinical trials, called HGB-207, for adult and adolescent patients with beta-thalassemia major, and HGB-208, for pediatric patients with beta-thalassemia major, together with data from our ongoing beta-thalassemia

major clinical studies (Northstar and HGB-205), could be sufficient to form the basis for a BLA submission for LentiGlobin BB305 to treat patients with beta-thalassemia major. 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 trials, the FDA may require that we conduct additional or larger pivotal trials before we can submit or obtain approval for a BLA for LentiGlobin BB305.

In June 2015, the RAC recommended that we delay the initiation of the HGB-208 trial for pediatric patients with beta-thalassemia major for one to two years. Any delay in the initiation or completion of the HGB-208 clinical trial could similarly delay our ability to submit a BLA for LentiGlobin BB305 or obtain full approval in Europe.

In addition, while we believe we and the FDA are in general agreement on the design and key elements of our planned HGB-207 and HGB-208 clinical trials of LentiGlobin BB305, before beginning these trials, the FDA must review the final protocols for the trials, along with additional information supporting the respective proposed trial designs. Concurrent with starting the trial, 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 trials 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 trials may be delayed or the design of the trials may change.

*There can be no assurance that we will ultimately receive conditional marketing approval of LentiGlobin 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 BB305 product candidate may be eligible for conditional approval under this program for the treatment of patients with beta-thalassemia major on the basis of the totality of clinical data, in particular reduction in transfusion need, from the ongoing Northstar study and supportive HGB-205 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 BB305 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 LentiGlobin BB305 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.

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.

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 or post-market surveillance. 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 $48.7 million and $25.3 million for the years ended December 31, 2014 and 2013, respectively. As of June 30, 2015, we had an accumulated deficit of $224.0 million.

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 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;
- 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 U.S. Food and Drug Administration, or the FDA, the European Medicines Agency, or 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.

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*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 Lenti-D and LentiGlobin 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 June 30, 2015, our cash, cash equivalents and marketable securities were $936.4 million. We expect that our existing cash and cash equivalents 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 other key materials, but we have not entered into binding agreements with any such manufacturers to support commercialization. Additionally, these manufacturers do not have experience producing our vectors and product candidates at commercial levels and may not achieve the necessary regulatory approvals or produce our vectors and products at the quality, quantities, locations and timing needed to support commercialization.

We have not yet secured manufacturing capabilities for commercial quantities of our viral vectors or established transduction facilities in the desired commercialization regions to support commercialization of our products. Although we intend to rely on third-party manufacturers for commercialization, we have only entered into agreements

with such manufacturers to support our clinical studies. We may be unable to negotiate binding agreements with the manufacturers to support our commercialization activities at commercially reasonable terms.

No manufacturer currently has the experience or ability to produce our vectors and product candidates at commercial levels. We are currently developing a commercial-scale manufacturing process for LentiGlobin and Lenti-D, which we are beginning to transfer to one or more contract manufacturers. We may run into technical or scientific issues related to manufacturing or development that we may be unable to resolve in a timely manner or with available funds. Although we have been able to produce our Lenti-D vector at commercial scale, we have not completed the characterization and validation activities necessary for commercial and regulatory approvals. If our manufacturing partners do not obtain such regulatory approvals, our commercialization efforts will be harmed.

Additionally, since the HSCs have a limited window of stability following procurement from the subject, we must set up transduction facilities in the regions where we wish to commercialize our product. Currently, we rely on third-party contract manufacturers in the United States and Europe to produce our product candidates for our clinical studies. Since a portion of our target patient populations will be outside the United States and Europe, we will need to set up additional transduction facilities that can

replicate our transduction process. Establishment of such facilities may be financially impractical or impeded by technical, quality, or regulatory issues related to these new sites and we may also run into technical or scientific issues related to transfer of our transduction process or other developmental issues that we may be unable to resolve in a timely manner or with available funds.

Even if we timely develop a manufacturing process and successfully transfer it to the third-party vector and product manufacturers, if such third-party manufacturers are unable to produce the necessary quantities of viral vectors and our product candidates, or in compliance with GMP or other pertinent regulatory requirements, and within our planned time frame and cost parameters, the development and sales of our products, if approved, may be materially harmed.

In addition, any significant disruption in our supplier relationships could harm our business. We source key materials from third parties, either directly through agreements with suppliers or indirectly through our manufacturers who have agreements with suppliers. There are a small number of suppliers for certain key materials that are used to manufacture our product candidates. Such suppliers may not sell these key materials to our manufacturers at the times we need them or on commercially reasonable terms. We do not have any control over the process or timing of the acquisition of these key materials by our manufacturers. Moreover, we currently do not have any agreements for the commercial production of these key materials.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate any revenues.

We have no experience selling and marketing our product candidates. To successfully commercialize any products that may result from our development programs, we will need to develop these capabilities, either on our own or with others. We may enter into collaborations with other entities to utilize their mature marketing and distribution capabilities, but we may be unable to enter into marketing agreements on favorable terms, if at all. If our future collaborative partners do not commit sufficient resources to commercialize our future products, if any, and we are unable to develop the necessary marketing capabilities on our own, we will be unable to generate sufficient product revenue to sustain our business. We will be competing with many companies that currently have extensive and well-funded marketing and sales operations. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

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

We are engaged in gene therapy and in the field of CAR T cells in oncology, both of which are competitive and rapidly changing fields. We have competitors both in the United States and internationally, including major multinational pharmaceutical companies, biotechnology companies and universities and other research institutions. Some of the pharmaceutical and biotechnology companies we expect to compete with include GlaxoSmithKline plc through their collaboration with TIGET/MolMed, Sangamo BioSciences Inc. through their collaboration with Biogen Idec, Merck & Co., Inc., Novartis AG through their collaboration with the University of Pennsylvania, GlycoMimetics Inc., Acceleron Pharma, Inc., Kite Pharma, Inc., Pfizer Inc. through their collaboration with Cellectis SA, Adaptimmune Inc. and Juno Therapeutics, Inc. through their collaboration with Celgene Corporation. In addition, many universities and private and public research institutes are active in our target disease areas.

Many of our competitors have substantially greater financial, technical and other resources, such as larger research and development staff and experienced marketing and manufacturing organizations. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for

investment in these industries. Our competitors may succeed in developing, acquiring or licensing on an exclusive basis, products that are more effective or less costly than any product candidate that we may develop, or achieve earlier patent protection, regulatory approval, product commercialization and market penetration than us. Additionally, technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing our product candidates against competitors.

Even if we are successful in achieving regulatory approval to commercialize a product candidate faster than our competitors, we may face competition from biosimilars due to the changing regulatory environment. In the United States, the Biologics Price Competition and Innovation Act of 2009 created an abbreviated approval pathway for biological products that are demonstrated to be "highly similar," or biosimilar, to or "interchangeable" with an FDA-approved biological product. This new pathway could allow competitors to reference data from biological products already approved after 12 years from the time of approval. In his proposed budget for fiscal year 2014, President Obama proposed to cut this 12-year period of exclusivity down to seven years. He also proposed to prohibit additional periods of exclusivity due to minor changes in product formulations, a practice often referred to as "evergreening." In Europe, the European Commission has granted marketing authorizations for several biosimilars pursuant to a set of general and product class-specific guidelines for biosimilar approvals issued over the past few years. In Europe, a competitor may reference data from biological products already approved, but will not be able to get on the market until 10 years after the time of

approval. This 10-year period will be extended to 11 years if, during the first eight of those 10 years, the marketing authorization holder obtains an approval for one or more new therapeutic indications that bring significant clinical benefits compared with existing therapies. In addition, companies may be developing biosimilars in other countries that could compete with our products. If competitors are able to obtain marketing approval for biosimilars referencing our products, our products may become subject to competition from such biosimilars, with the attendant competitive pressure and consequences. Expiration or successful challenge of our applicable patent rights could also trigger competition from other products, assuming any relevant exclusivity period has expired.

In addition, although our product candidates have been granted orphan drug status by the FDA and EMA, there are limitations to the exclusivity. In the United States, the exclusivity period for orphan drugs is seven years, while pediatric exclusivity adds six months to any existing patents or exclusivity periods. In Europe, orphan drugs may be able to obtain 10 years of marketing exclusivity and up to an additional two years on the basis of qualifying pediatric studies. However, orphan exclusivity may be reduced to six years if the drug no longer satisfies the original designation criteria. Additionally, a marketing authorization holder may lose its orphan exclusivity if it consents to a second orphan drug application or cannot supply enough drug. Orphan drug exclusivity also can be lost when a second applicant demonstrates its drug is “clinically superior” to the original orphan drug.

Finally, as a result of the expiration or successful challenge of our patent rights, we could face more litigation with respect to the validity and/or scope of patents relating to our competitors’ products. The availability of our competitors’ products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize.

The commercial success of any current or future product candidate will depend upon the degree of market acceptance by physicians, patients, third-party payors and others in the medical community.

Ethical, social and legal concerns about gene therapy and genetic research could result in additional regulations restricting or prohibiting the products and processes we may use. Even with the requisite approvals, the commercial success of our product candidates will depend in part on the medical community, patients, and third-party or governmental payors accepting gene therapy products in general, and our product candidates in particular, as medically useful, cost-effective, and safe. Any product that we bring to the market may not gain market acceptance by physicians, patients, third-party payors and others in the medical community. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenue and may not become profitable. The degree of market acceptance of these product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the potential efficacy and potential advantages over alternative treatments;
- the prevalence and severity of any side effects, including any limitations or warnings contained in a product’s approved labeling;
- the prevalence and severity of any side effects resulting from the chemotherapy and myeloablative treatments associated with the procedure by which our product candidates are administered;
- relative convenience and ease of administration;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support and timing of market introduction of competitive products;
- the pricing of our products;
- publicity concerning our products or competing products and treatments; and
- sufficient third-party insurance coverage or reimbursement.

Even if a potential product displays a favorable efficacy and safety profile in preclinical and clinical studies, market acceptance of the product will not be known until after it is launched. Our efforts to educate the medical community and third-party payors on the benefits of the product candidates may require significant resources and may never be

successful. Such efforts to educate the marketplace may require more resources than are required by the conventional technologies marketed by our competitors.

If we obtain approval to commercialize our product candidates outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

If any of our product candidates are approved for commercialization, we may enter into agreements with third parties to market them on a worldwide basis or in more limited geographical regions. We expect that we will be subject to additional risks related to entering into international business relationships, including:

- different regulatory requirements for approval of drugs and biologics in foreign countries;
- reduced protection for intellectual property rights;
- economic weakness, including inflation, or political instability in particular foreign economies and markets; and
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country.

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

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

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products, including gene therapies. In the United States, the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, as CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare. Private payors tend to follow CMS to a substantial degree. It is difficult to predict what CMS will decide with respect to reimbursement for fundamentally novel products such as ours, as there is no body of established practices and precedents for these new products. Reimbursement agencies in Europe may be more conservative than CMS. For example, a number of cancer drugs have been approved for reimbursement in the United States and have not been approved for reimbursement in certain European countries. In addition, costs or difficulties associated with the reimbursement of Glybera could create an adverse environment for reimbursement of other gene therapies.

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

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

Due to the novel nature of our technology and the potential for our product candidates to offer therapeutic benefit in a single administration, we face uncertainty related to pricing and reimbursement for these product candidates.

Our target patient populations are relatively small, as a result, the pricing and reimbursement of our product candidates, if approved, must be adequate to support commercial infrastructure. If we are unable to obtain adequate levels of reimbursement, our

ability to successfully market and sell our product candidates will be adversely affected. The manner and level at which reimbursement is provided for services related to our product candidates (e.g., for administration of our product to patients) is also important. Inadequate reimbursement for such services may lead to physician resistance and adversely affect our ability to market or sell our products.

If the market opportunities for our product candidates are smaller than we believe they are, our revenues may be adversely affected and our business may suffer. Because the target patient populations of our product candidates are small, we must be able to successfully identify patients and achieve a significant market share to maintain profitability and growth.

We focus our research and product development on treatments for severe genetic and rare diseases. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on estimates. These estimates may prove to be incorrect and new studies may change the estimated incidence or prevalence of these diseases. The number of patients in the United States, Europe and elsewhere may turn out to be lower than expected, may not be otherwise amenable to treatment with our products, or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our results of operations and our business.

Risks related to our business operations

If we undertake business combinations, collaborations or similar strategic transactions, they may disrupt our business, divert management’s attention, dilute stockholder value or be difficult to integrate.

On a regular basis, we consider various business combination transactions, collaborations, license agreements and strategic transactions with third parties, including transactions which may result in us acquiring, or being acquired by, a third party. The consummation or performance of any future business combination, collaboration or strategic transaction may involve risks, such as:

- diversion of managerial resources from day-to-day operations;
- challenges associated with integrating acquired technologies and operations of acquired companies;
- exposure to unforeseen liabilities;
- difficulties in the assimilation of different cultures and practices, as well as in the assimilation and retention of broad and geographically dispersed personnel and operations;
- misjudgment with respect to value, return on investment or strategic fit;
- higher than expected transaction costs; and
- additional dilution to our existing stockholders if we issue equity securities as consideration for any acquisitions.

As a result of these risks, we may not be able to achieve the expected benefits of any such transaction. If we are unsuccessful in completing or integrating any acquisition, we may be required to reevaluate that component of our strategy only after we have incurred substantial expenses and devoted significant management time and resources in seeking to complete and integrate the acquisition.

Future business combinations could involve the acquisition of significant intangible assets. We may need to record write-downs from future impairments of identified intangible assets and goodwill. These accounting charges would increase a reported loss or reduce any future reported earnings. In addition, we could use substantial portions of our available cash to pay the purchase price for company or product candidate acquisitions. Subject to the limitations under our existing indebtedness, it is possible that we could incur additional debt or issue additional equity securities as consideration for these acquisitions, which could cause our stockholders to suffer significant dilution.

The failure to successfully integrate Precision Genome Engineering, Inc.'s business and operations or fully realize the benefits of this acquisition may adversely affect our future results.

On June 30, 2014, we acquired all of the outstanding capital stock of Precision Genome Engineering, Inc., or Pregenen. Based in Seattle, Washington, Pregenen is focused on the development of gene editing and cell signaling technologies. The success of our acquisition of Pregenen will depend, in part, on our ability to successfully integrate Pregenen's business and operations and fully realize the anticipated benefits and synergies from combining our business with Pregenen's business, in particular our ability to advance Pregenen's gene editing and cell signaling technologies to the stage where they can be incorporated into our existing or new product candidates. However, to realize these anticipated benefits, we must successfully combine these businesses and continue the research and development activities previously undertaken by Pregenen as a stand-alone company. If we are unable to achieve these

objectives, the anticipated benefits of our acquisition of Pregenen may not be realized fully or at all or may take longer to realize than expected. Any failure to timely realize these anticipated benefits could have a material adverse effect on our development programs, expenses and operating results.

Negative public opinion and increased regulatory scrutiny of gene therapy and genetic research may damage public perception of our product candidates or adversely affect our ability to conduct our business or obtain regulatory approvals for our product candidates.

Public perception may be influenced by claims that gene therapy is unsafe, and gene therapy may not gain the acceptance of the public or the medical community. In particular, our success will depend upon physicians specializing in the treatment of those diseases that our product candidates target prescribing treatments that involve the use of our product candidates in lieu of, or in addition to, existing treatments they are already familiar with and for which greater clinical data may be available. More restrictive government regulations or negative public opinion would have a negative effect on our business or financial condition and may delay or impair the development and commercialization of our product candidates or demand for any products we may develop. For example, in 2003, 20 subjects treated for X-linked severe combined immunodeficiency in two gene therapy studies using a murine gamma-retroviral vector showed correction of the disease, but the studies were terminated after five subjects developed leukemia (four of whom were subsequently cured). Although none of our current product candidates utilize these gamma-retroviruses, our product candidates use a viral delivery system. Adverse events in our clinical studies, even if not ultimately attributable to our product candidates (such as the many adverse events that typically arise from the transplant process) and the resulting publicity could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our potential product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates.

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

We are highly dependent on principal members of our executive team and key employees, the loss of whose services may adversely impact the achievement of our objectives. While we have entered into employment agreements with each of our executive officers, any of them could leave our employment at any time, as all of our employees are “at will” employees. Recruiting and retaining other qualified employees, consultants and advisors for our business, including scientific and technical personnel, will also be critical to our success. There is currently a shortage of skilled executives in our industry, which is likely to continue. As a result, competition for skilled personnel is intense and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for individuals with similar skill sets. In addition, failure to succeed in preclinical or clinical studies may make it more challenging to recruit and retain qualified personnel. The inability to recruit or loss of the services of any executive, key employee, consultant or advisor may impede the progress of our research, development and commercialization objectives.

*We will need to expand our organization and we may experience difficulties in managing this growth, which could disrupt our operations.

As of June 30, 2015, we had 184 full-time employees. As our business, research and development activities expand, we expect to expand our full-time employee base and to hire more consultants and contractors. Our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require

significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenues could be reduced, and we may not be able to implement our business strategy.

Our employees, principal investigators, consultants and commercial partners may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, principal investigators, consultants and commercial partners. Misconduct by these parties could include intentional failures to comply with the regulations of the FDA and non-U.S. regulators, provide accurate information to the FDA and non-U.S. regulators, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a

wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct could also involve the improper use of information obtained in the course of clinical studies, which could result in regulatory sanctions and cause serious harm to our reputation or could cause regulatory agencies not to approve our product candidates. We have adopted a code of conduct applicable to all of our employees, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

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

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

- impairment of our business reputation;
- withdrawal of clinical study participants;
- costs due to related litigation;
- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- the inability to commercialize our product candidates; and
- decreased demand for our product candidates, if approved for commercial sale.

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

Patients with the diseases targeted by our product candidates are often already in severe and advanced stages of disease and have both known and unknown significant pre-existing and potentially life-threatening health risks. During the course of treatment, patients may suffer adverse events, including death, for reasons that may be related to our product candidates. Such events could subject us to costly litigation, require us to pay substantial amounts of money to injured patients, delay, negatively impact or end our opportunity to receive or maintain regulatory approval to market our products, or require us to suspend or abandon our commercialization efforts. Even in a circumstance in which we do not believe that an adverse event is related to our products, the investigation into the circumstance may be time-consuming or inconclusive. These investigations may interrupt our sales efforts, delay our regulatory approval process in other countries, or impact and limit the type of regulatory approvals our product candidates receive or

maintain. As a result of these factors, a product liability claim, even if successfully defended, could have a material adverse effect on our business, financial condition or results of operations.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste

products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

We may not be successful in our efforts to identify or discover additional product candidates.

The success of our business depends primarily upon our ability to identify, develop and commercialize products based on our gene therapy and gene editing platforms. Although our Lenti-D and LentiGlobin product candidates are currently in clinical development, our research programs, including our oncology research programs, may fail to identify other potential product candidates for clinical development for a number of reasons. Our research methodology may be unsuccessful in identifying potential product candidates or our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval.

If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations. Research programs to identify new product candidates require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful.

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

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

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

As a public company, we have incurred and will continue to incur significant legal, accounting and other expenses. In addition, the Sarbanes-Oxley Act, as well as rules subsequently implemented by the SEC, and The NASDAQ Global Select Market have imposed various requirements on public companies. In July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act, was enacted, resulting in significant corporate governance and executive compensation-related regulations. Stockholder activism, the current political environment

and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain our current levels of such coverage.

Risks related to our intellectual property

If we are unable to obtain or protect intellectual property rights related to our product candidates, we may not be able to compete effectively in our markets.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our product candidates. The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our product candidates in the United States or in other foreign countries. There is no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found, which can invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents do successfully issue and even if such patents cover our product candidates, third parties may challenge their validity, enforceability or scope, which may result in such patents being narrowed or invalidated. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property, provide exclusivity for our product candidates or prevent others from designing around our claims. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

If the patent applications we hold or have in-licensed with respect to our programs or product candidates fail to issue, if their breadth or strength of protection is threatened, or if they fail to provide meaningful exclusivity for our product candidates, it could dissuade companies from collaborating with us to develop product candidates, and threaten our ability to commercialize, future products. Several patent applications covering our product candidates have been filed recently. We cannot offer any assurances about which, if any, patents will issue, the breadth of any such patent or whether any issued patents will be found invalid and unenforceable or will be threatened by third parties. Any successful opposition to these patents or any other patents owned by or licensed to us could deprive us of rights necessary for the successful commercialization of any product candidates that we may develop. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced. Since patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we were the first to file any patent application related to a product candidate. Furthermore, if third parties have filed such patent applications, an interference proceeding in the United States can be initiated by a third party to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. In addition, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available however the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired for a product, we may be open to competition from generic medications.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our product candidate discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors.

Although we expect all of our employees and consultants to assign their inventions to us, and all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed or that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Misappropriation or unauthorized disclosure of our trade secrets could impair our competitive position and may have a material adverse effect on our business. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret. In addition, others may independently discover our trade secrets and proprietary information. For example, the FDA, as part of its Transparency Initiative, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA's disclosure policies may change in the future, if at all.

Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent material disclosure of the non-patented intellectual property related to our technologies to third parties, and there is no guarantee that we will have any such enforceable trade secret protection, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition.

Third-party claims of intellectual property infringement may prevent or delay our development and commercialization efforts.