bluebird bio, Inc.
Form 10-Q
August 02, 2018
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

FORM 10-Q

(Mark One)

QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the quarterly period ended June 30, 2018

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.)
60 Binney Street	02142

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

(339) 499-9300

(Registrant's Telephone Number, Including Area Code)

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

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

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

Large accelerated filer		Accelerated filer
Non-accelerated filer	(Do not check if a smaller reporting company)	Smaller reporting company
		Emerging growth company

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

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

As of July 27, 2018, there were 54,157,916 shares of the registrant's Common Stock, par value $0.01 per share, outstanding.

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

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

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

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

bluebird bio, Inc.

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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)

	As of June 30, 2018	As of December 31, 2017
Assets		
Current Assets:		
Cash and cash equivalents	$333,949	$758,505
Marketable securities	743,010	531,604
Tenant improvement receivable	19	3,112
Prepaid expenses	24,053	21,171
Receivables and other current assets	4,713	8,377
Total current assets	1,105,744	1,322,769
Marketable securities	380,284	324,193
Property, plant and equipment, net	219,226	199,606
Intangible assets, net	15,050	16,931
Goodwill	13,128	13,128
Restricted cash and other non-current assets	28,079	23,940
Total assets	$1,761,511	$1,900,567
Liabilities and Stockholders' Equity		
Current Liabilities:		
Accounts payable	$17,936	$12,873
Accrued expenses and other current liabilities	71,003	57,065
Deferred revenue, current portion	27,323	25,674
Total current liabilities	116,262	95,612
Deferred revenue, net of current portion	27,900	21,763
Contingent consideration	3,027	2,231
Financing lease obligation, net of current portion	154,103	154,749
Other non-current liabilities	2,685	2,780
Total liabilities	303,977	277,135
Commitments and contingencies (Note 7)		
Stockholders' Equity:		
Preferred stock, $0.01 par value, 5,000 shares authorized; 0 shares issued and outstanding at June 30, 2018 and December 31, 2017	—	—

Common stock, $0.01 par value, 125,000 shares authorized; 50,225 and 49,406 shares issued and outstanding at June 30, 2018 and December 31, 2017, respectively	502	494
Additional paid-in capital	2,666,729	2,540,951
Accumulated other comprehensive loss	(5,394)	(4,205)
Accumulated deficit	(1,204,303)	(913,808)
Total stockholders' equity	1,457,534	1,623,432
Total liabilities and stockholders' equity	$1,761,511	$1,900,567

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)

	For the three months ended		For the six months ended	
	June 30, 2018	2017	June 30, 2018	2017
Revenue:				
Collaboration revenue	$7,437	$6,146	$23,045	$12,978
License and royalty revenue	414	10,570	763	10,570
Total revenues	7,851	16,716	23,808	23,548
Operating expenses:				
Research and development	115,014	63,891	212,123	118,919
General and administrative	41,168	21,197	76,094	41,481
Cost of license and royalty revenue	21	420	36	420
Change in fair value of contingent consideration	262	(970)	796	463
Total operating expenses	156,465	84,538	289,049	161,283
Loss from operations	(148,614)	(67,822)	(265,241)	(137,735)
Interest income (expense), net	2,436	(2,242)	3,824	(687)
Other income (expense), net	182	(834)	297	(1,189)
Loss before income taxes	(145,996)	(70,898)	(261,120)	(139,611)
Net loss	$(145,996)	$(70,898)	$(261,120)	$(139,611)
Net loss per share - basic and diluted:	$(2.91)	$(1.73)	$(5.22)	$(3.41)
Weighted-average number of common shares used in computing net loss per share - basic and diluted:	50,153	41,035	50,038	40,936
Other comprehensive loss:				
Other comprehensive loss, net of tax expense of $0.0 and $0.0 million for the three and six months ended June 30, 2018 and 2017, respectively	(345)	(165)	(1,189)	(266)
Total other comprehensive loss	(345)	(165)	(1,189)	(266)
Comprehensive loss	$(146,341)	$(71,063)	$(262,309)	$(139,877)

See accompanying notes to unaudited condensed consolidated financial statements.

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bluebird bio, Inc.

Condensed Consolidated Statements of Cash Flows

(unaudited)

(in thousands)

	For the six months ended June 30,	
	2018	2017
Cash flows from operating activities:		
Net loss	$(261,120)	$(139,611)
Adjustments to reconcile net loss to net cash used in operating activities:		
Change in fair value of contingent consideration	796	463
Depreciation and amortization	8,199	6,281
Stock-based compensation expense	51,051	24,971
Other non-cash items	2,834	2,334
Changes in operating assets and liabilities:		
Prepaid expenses and other assets	(3,279)	(9,594)
Accounts payable	4,097	2,003
Accrued expenses and other liabilities	9,862	(8,509)
Deferred revenue	(21,589)	(7,682)
Deferred rent	(73)	507
Net cash used in operating activities	(209,222)	(128,837)
Cash flows from investing activities:		
Purchase of property, plant and equipment, including assets under financing lease obligation	(20,689)	(39,509)
Purchases of marketable securities	(689,163)	(116,740)
Proceeds from maturities of marketable securities	417,640	210,810
Net cash (used in) provided by investing activities	(292,212)	54,561
Cash flows from financing activities:		
Proceeds from public offering of common stock, net of issuance costs	48,702	436,805
Reimbursement of assets under financing lease obligation	3,098	36,399
Payments on financing lease obligation	(446)	(120)
Proceeds from issuance of common stock	25,624	8,639
Net cash provided by financing activities	76,978	481,723
(Decrease) increase in cash, cash equivalents and restricted cash	(424,456)	407,447
Cash, cash equivalents and restricted cash at beginning of period	772,268	293,277
Cash, cash equivalents and restricted cash at end of period	$347,812	$700,724
Supplemental cash flow disclosures from investing and financing activities:		
Purchases of property, plant and equipment included in accounts payable and accrued expenses	$7,815	$1,194

Assets acquired under financing lease obligation	$—	$2,297
Tenant improvements under financing lease included in tenant improvements receivable	$14	$3,635

See accompanying notes to unaudited condensed consolidated financial statements.

bluebird bio, Inc.

Notes to Condensed Consolidated Financial Statements

(unaudited)

1. Description of the business

bluebird bio, Inc. (the “Company” or “bluebird”) was incorporated in Delaware on April 16, 1992, and is headquartered in Cambridge, Massachusetts. The Company researches, develops, manufactures and plans to commercialize gene therapies for the treatment of severe genetic diseases and cancer. 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.

The Company’s clinical programs in severe genetic diseases include its LentiGlobin® product candidate to treat transfusion-dependent -thalassemia, or TDT, and to treat severe sickle cell disease, or severe SCD, and its Lenti-D™ product candidate to treat cerebral adrenoleukodystrophy, or CALD, a rare hereditary neurological disorder. The Company’s programs in oncology are built upon its leadership in lentiviral gene delivery and T cell engineering, with a focus on developing novel T cell-based immunotherapies, including chimeric antigen receptor (CAR) and T cell receptor (TCR) T cell therapies. bb2121 and bb21217, which are product candidates in oncology under the Company’s collaboration arrangement with Celgene Corporation (“Celgene”), are CAR T cell product candidates for the treatment of multiple myeloma. Refer to Note 8, “Collaboration revenue” for further discussion of the Company’s collaboration with Celgene.

As of June 30, 2018, the Company had cash, cash equivalents and marketable securities of $1.46 billion. Although the Company has incurred recurring losses and expects to continue to incur losses for the foreseeable future, the Company expects that its cash, cash equivalents and marketable securities will be sufficient to fund current operations for at least the next twelve months.

2. Basis of presentation, principles of consolidation and significant accounting policies

Basis of presentation

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, 2018 and 2017.

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, 2017, 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 21, 2018.

Certain items in the prior year's condensed consolidated financial statements have been reclassified to conform to the current presentation. As a result, no subtotals in the prior year condensed consolidated financial statements were impacted.

Amounts reported are computed based on thousands. As a result, certain totals may not sum due to rounding.

Principles of consolidation

The accompanying condensed consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries. As of June 30, 2018, there have been no changes to the Company's subsidiary listing, which is included as an exhibit to its Annual Report on Form 10-K for the year ended December 31, 2017. 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.

Significant accounting policies

The significant accounting policies used in preparation of these condensed consolidated financial statements for the three and six months ended June 30, 2018 are consistent with those discussed in Note 2 to the consolidated financial statements in the Company's 2017 Annual Report on Form 10-K, except as noted below with respect to the Company's revenue recognition, collaboration revenue and license and royalty revenue accounting policies and as noted within the "Recent accounting pronouncements – Recently adopted" section below.

Revenue recognition

Effective January 1, 2018, the Company adopted Accounting Standards Codification ("ASC"), Topic 606, Revenue from Contracts with Customers ("Topic 606"), using the modified retrospective transition method. Under this method, the Company has recognized the cumulative effect of the adoption as an adjustment to the opening balance of accumulated deficit in the current period condensed consolidated balance sheet. The Company has not revised its consolidated financial statements for prior periods. This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as collaboration arrangements and leases.

Under Topic 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of Topic 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price, including variable consideration, if any; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. The Company only applies the five-step model to contracts when it is probable that the entity will collect the consideration to which it is entitled in exchange for the goods or services it transfers to the customer.

Once a contract is determined to be within the scope of Topic 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations. Arrangements that include rights to additional goods or services that are exercisable at a customer's discretion are generally considered options. The Company assesses if these options provide a material right to the customer and if so, they are considered performance obligations. The exercise of a material right is accounted for as a contract modification for accounting purposes.

The Company assesses whether each promised good or service is distinct for the purpose of identifying the performance obligations in the contract. This assessment involves subjective determinations and requires management to make judgments about the individual promised goods or services and whether such are separable from the other aspects of the contractual relationship. Promised goods and services are considered distinct provided that: (i) the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer (that is, the good or service is capable of being distinct) and (ii) the entity's promise to transfer the good or service to the customer is separately identifiable from other promises in the contract (that is, the promise to transfer the good or service is distinct within the context of the contract). In assessing whether a promised good or service is distinct, the Company considers factors such as the research, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. The Company also considers the intended benefit of the contract in assessing whether a promised good or service is separately identifiable from other promises in the contract. If a promised good or service is not distinct, an entity is required to combine that good or service with other promised goods or services until it identifies a bundle of goods or

services that is distinct.

The transaction price is then determined and allocated to the identified performance obligations in proportion to their standalone selling prices ("SSP") on a relative SSP basis. SSP is determined at contract inception and is not updated to reflect changes between contract inception and when the performance obligations are satisfied. Determining the SSP for performance obligations requires significant judgment. In developing the SSP for a performance obligation, the Company considers applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. The Company validates the SSP for performance obligations by evaluating whether changes in the key assumptions used to determine the SSP will have a significant effect on the allocation of arrangement consideration between multiple performance obligations.

If the consideration promised in a contract includes a variable amount, the Company estimates the amount of consideration to which it will be entitled in exchange for transferring the promised goods or services to a customer. The Company determines the amount of variable consideration by using the expected value method or the most likely amount method. The Company includes the unconstrained amount of estimated variable consideration in the transaction price. The amount included in the transaction price is constrained to the amount for which it is probable that a significant reversal of cumulative revenue recognized will not occur. At the end of each subsequent reporting period, the Company re-evaluates the estimated variable consideration included in the transaction price and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis in the period of adjustment.

If an arrangement includes development and regulatory milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the Company's control or the licensee's control, such as regulatory approvals, are generally not considered probable of being achieved until those approvals are received.

In determining the transaction price, the Company adjusts consideration for the effects of the time value of money if the timing of payments provides the Company with a significant benefit of financing. The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the licensees and the transfer of the promised goods or services to the licensees will be one year or less. The Company assessed each of its revenue generating arrangements in order to determine whether a significant financing component exists and concluded that a significant financing component does not exist in any of its arrangements.

The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) each performance obligation is satisfied, either at a point in time or over time, and if over time recognition is based on the use of an output or input method.

Collaboration revenue

To date, the Company's collaboration revenue has been exclusively generated from its collaboration arrangement with Celgene, which was originally entered into in March 2013 and was subsequently amended in June 2015, as further described in Note 8, "Collaboration revenue".

The Company analyzes its collaboration arrangements to assess whether they are within the scope of ASC 808, Collaborative Arrangements ("ASC 808") to determine whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities. This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For collaboration arrangements within the scope of ASC 808 that contain multiple elements, the Company first determines which elements of the collaboration are deemed to be within the scope of ASC 808 and those that are more reflective of a vendor-customer relationship and therefore within the scope of Topic 606. For elements of collaboration arrangements that are accounted for pursuant to ASC 808, an appropriate recognition method is determined and applied consistently, generally by analogy to Topic 606. Amounts that are owed to collaboration partners are recognized as an offset to collaboration revenues as such amounts are incurred by the collaboration partner. Where amounts owed to a collaboration partner exceed the Company's collaboration revenues in each quarterly period, such amounts are classified as research and development expense. For those elements of the arrangement that are accounted for pursuant to Topic 606, the Company applies the five-step model described above.

License and royalty revenue

The Company enters into out-licensing agreements that are within the scope of Topic 606. The Company does not have any material license arrangements that contain more than one performance obligation. The terms of such out-license agreements include the license of functional intellectual property, given the functionality of the intellectual property is not expected to change substantially as a result of the licensor's ongoing activities, and typically include payment of one or more of the following: non-refundable up-front license fees; development and regulatory milestone payments and milestone payments based on the level of sales; and royalties on net sales of licensed products. Nonrefundable up-front license fees are recognized as revenue at a point in time when the licensed intellectual property is made available for the customer's use and benefit, which is generally at the inception of the arrangement. Milestone fees, which are a type of variable consideration, are recognized as revenue to the extent that it is probable that a significant reversal will not occur. For arrangements with licenses of intellectual property that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes royalty revenue and sales-based milestones at the later of (i) when the related sales occur, or (ii) when the performance obligation to which the royalty has been allocated has been satisfied.

For a complete discussion of accounting for collaboration and other revenue-generating arrangements, see Note 8, “Collaboration revenue” and Note 9, “License and royalty revenue”. Additionally, see “Recent accounting pronouncements - Recently adopted” below for discussion of the impact of adopting Topic 606, which was effective on January 1, 2018.

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. Actual results could materially differ from those estimates. Management considers many factors in selecting appropriate financial accounting policies and controls, and in developing the estimates and assumptions that are used in the preparation of these financial statements. Management must apply significant judgment in this process. In addition, other factors may affect estimates, including: expected business and operational changes, sensitivity and volatility associated with the assumptions used in developing estimates, and whether historical trends are expected to be representative of future trends. The estimation process often may yield a range of potentially reasonable estimates of the ultimate future outcomes and management must select an amount that falls within that range of reasonable estimates. This process may result in actual results differing materially from those estimated amounts used in the preparation of the financial statements. Estimates are used in the following areas, among others: subsequent fair value estimates used to assess potential impairment of long-lived assets, including goodwill and intangible assets, financing lease obligation, contingent consideration, stock-based compensation expense, accrued expenses, revenue and income taxes.

Recent accounting pronouncements

Recently adopted

ASU No. 2014-09, Revenue from Contracts with Customers

In May 2014, the FASB issued ASU No. 2014-09, Revenue from Contracts with Customers, which superseded the revenue recognition requirements in ASC 605, Revenue Recognition and created a new Topic 606, Revenue from Contracts with Customers. In 2015 and 2016, the FASB issued additional ASUs related to Topic 606 that delayed the effective date of the guidance and clarified various aspects of the new revenue guidance. The new standard became effective on January 1, 2018. Topic 606 allows for either a full retrospective adoption, in which the standard is applied to all periods presented in an entity’s financial statements, or a modified retrospective approach, in which the standard is applied to the most current period presented in an entity’s financial statements with the cumulative effect of adoption recognized as an adjustment to the opening balance of accumulated deficit in the period of adoption. The Company adopted this new standard on January 1, 2018 using the modified retrospective approach, which has been applied consistently to all contracts, and has elected to use the following practical expedient that is permitted under the rules of adoption:

- For contracts that were modified prior to Topic 606 adoption, the Company has not retrospectively accounted for each contract modification in accordance with the contract modification guidance. Instead, the Company reflected the aggregate effect of all modifications occurring prior to Topic 606 adoption when identifying the satisfied and unsatisfied performance obligations, determining the transaction price and allocating the transaction price.

As a result of adopting Topic 606, the Company recorded a $29.4 million adjustment to the opening balance of accumulated deficit in the first quarter of 2018 primarily as a result of the accounting for the up-front consideration received in March 2013 in connection with the collaboration arrangement with Celgene under ASC 605-25 versus

Topic 606. Refer below for a summary of the amount by which each financial statement line item was affected by the impact of the cumulative adjustment:

	Impact of Topic 606 Adoption on Condensed Consolidated Balance Sheet as of January 1, 2018		
(in thousands)	As reported under Topic 606	Adjustments	Balances without adoption of Topic 606
Deferred revenue, current portion	$45,344	$ 19,670	$ 25,674
Deferred revenue, net of current portion	$31,468	$ 9,705	$ 21,763
Accumulated deficit	$(943,183)	$ (29,375)	$ (913,808)

The amount by which each financial statement line item is affected in the current reporting period by Topic 606 as compared with the guidance that was in effect prior to adoption is disclosed below.

	Impact of Topic 606 Adoption on Condensed Consolidated Balance Sheet as of June 30, 2018		
(in thousands)	As reported under Topic 606	Adjustments	Balances without adoption of Topic 606
Deferred revenue, current portion	$27,323	$ 12,010	$ 15,313
Deferred revenue, net of current portion	$27,900	$ 8,545	$ 19,355
Accumulated deficit	$(1,204,303)	$ (20,555)	$ (1,183,748)

	Impact of Topic 606 Adoption on Condensed Consolidated Statement of Operations and Comprehensive Loss for the Three Months Ended June 30, 2018		
(in thousands, except per share data)	As reported under Topic 606	Adjustments	Balances without adoption of Topic 606
Collaboration revenue	$7,437	$ 887	$ 6,550
Research and development expense	$115,014	$ (1,800)	$ 116,814
Net loss	$(145,996)	$ 2,687	$ (148,683)
Net loss per share - basic and diluted:	$(2.91)	$ 0.05	$ (2.96)

	Impact of Topic 606 Adoption on Condensed Consolidated Statement of Operations and Comprehensive Loss for the Six Months Ended June 30, 2018		
(in thousands, except per share data)	As reported under Topic 606	Adjustments	Balances without adoption of Topic 606

Collaboration revenue	$23,045	$ 7,020	$ 16,025
Research and development expense	$212,123	$ (1,800)	$ 213,923
Net loss	$(261,120)	$ 8,820	$ (269,940)
Net loss per share - basic and diluted:	$(5.22)	$ 0.17	$ (5.39)

	Impact of Topic 606 Adoption on Condensed Consolidated Statement of Cash Flows for the Six Months Ended June 30, 2018		
(in thousands)	As reported under Topic 606	Adjustments	Balances without adoption of Topic 606
Net loss	$(261,120)	$ 8,820	$ (269,940)
Changes in deferred revenue	$(21,589)	$ (8,820)	$ (12,769)

The most significant change above relates to the Company's collaboration revenue, which to date has been exclusively generated from its collaboration arrangement with Celgene. Under ASC 605, the Company accounted for contract modifications to the Celgene collaboration as they occurred and the accounting for those changes was prospective in nature. Through the application of the practical expedient discussed above in connection with the adoption of Topic 606, the Company reflected the aggregate effect of all modifications to the Celgene collaboration when identifying the satisfied and unsatisfied performance obligations, determining the transaction price, and allocating the transaction price. As a result, although the performance obligations identified under Topic 606 were generally consistent with the units of account identified under ASC 605, the timing of the allocation of the transaction price to the identified performance obligations under Topic 606 differed from the allocations of consideration under ASC 605. Accordingly, the transaction price ultimately allocated to each performance obligation under Topic 606 differed from the amounts allocated under ASC 605.

As a result of adopting Topic 606, the Company established a deferred revenue deferred tax asset, and an offsetting valuation allowance, of $7.9 million through its accumulated deficit given it is not more likely than not that the deferred tax asset will be realized due to historical and expected future losses, such that there was no tax impact on the Company's condensed consolidated financial statements as a result of adopting Topic 606.

ASU 2016-15, Statement of Cash Flows: Classification of Certain Cash Receipts and Cash Payments

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

ASU 2016-18, Statement of Cash Flows: Restricted Cash

In November 2016, the FASB issued ASU 2016-18, Statement of Cash Flows: Restricted Cash ("ASU 2016-18"). The amendments in this update require that amounts generally described as restricted cash and restricted cash equivalents be included within cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the statement of cash flows. ASU 2016-18 was effective January 1, 2018. As a result of adopting ASU 2016-18, the Company includes its restricted cash balance in the cash and cash equivalents reconciliation of operating, investing and financing activities. The following table provides a reconciliation of cash, cash equivalents, and restricted cash within the statement of financial position that sum to the total of the same such amounts shown in the statement of cash flows:

(in thousands)	As of June 30, 2018	As of June 30, 2017
Cash and cash equivalents	$333,949	$686,334
Restricted cash included in receivables and other current assets	100	627
Restricted cash included in restricted cash and other non-current assets	13,763	13,763
Total cash, cash equivalents, and restricted cash shown in the statement of cash flows	$347,812	$700,724

ASU 2017-09, Compensation – Stock Compensation (Topic 718): Scope Modification Accounting

In May 2017, the FASB issued ASU 2017-09, Compensation – Stock Compensation (Topic 718): Scope Modification Accounting. The new standard is intended to reduce the diversity in practice and cost and complexity when applying the guidance in Topic 718 to a change to the terms or conditions of a share-based payment award. The new standard was effective beginning January 1, 2018. The adoption of this standard did not have a material impact on the Company's financial position or results of operations upon adoption.

Not yet adopted

ASU 2016-02, Leases

In February 2016, the FASB issued ASU 2016-02, Leases, ("ASU 2016-02"), which requires a lessee to recognize assets and liabilities on the balance sheet for operating leases and changes many key definitions, including the definition of a lease. The new standard includes a short-term lease exception for leases with a term of 12 months or less, as part of which a lessee can make an accounting policy election not to recognize lease assets and lease liabilities. Lessees will continue to differentiate between finance leases (previously referred to as capital leases) and operating leases using classification criteria that are substantially similar to the previous guidance. The new standard will be effective beginning January 1, 2019. The Company is currently evaluating the potential impact ASU 2016-02 may have on its financial position and results of operations. The Company's assessment will include, but is not limited to, evaluating the impact that this standard has on the lease of its corporate headquarters at 60 Binney in Cambridge, Massachusetts, its laboratory space in Seattle, Washington, its office space in Zug, Switzerland, and any of its embedded leases.

ASU 2017-04, Intangibles – Goodwill and Other (Topic 350): Simplifying the Test for Goodwill Impairment

In January 2017, the FASB issued ASU 2017-04, Intangibles – Goodwill and Other (Topic 350): Simplifying the Test for Goodwill Impairment. To address concerns over the cost and complexity of the two-step goodwill impairment test, the amendments in this ASU remove the second step of the test. An entity will instead apply a one-step quantitative test and record the amount of goodwill impairment as the excess of a reporting unit's carrying amount over its fair value, not to exceed the total amount of goodwill allocated to the reporting unit. The new guidance does not amend the optional qualitative assessment of goodwill impairment. The new standard will be effective beginning January 1, 2020 and early adoption is permitted with measurement dates on or after January 1, 2017. The adoption of this standard is not expected to have a material impact on the Company's financial position or results of operations upon adoption.

ASU 2017-08, Receivables – Nonrefundable Fees and Other Costs

In April 2017, the FASB issued ASU 2017-08, Receivables – Nonrefundable Fees and Other Costs ("Subtopic 310-20"). The new standard amends the amortization period for certain purchased callable debt securities held at a premium by shortening the amortization period for the premium to the earliest call date. Subtopic 310-20 calls for a modified retrospective application under which a cumulative-effect adjustment will be made to retained earnings as of the beginning of the first reporting period in which the guidance is adopted. The new standard will be effective beginning January 1, 2019 and early adoption is permitted for public entities. The adoption of this standard is not expected to have a material impact on the Company's financial position or results of operations upon adoption.

ASU 2018-02, Reclassification of Certain Tax Effects from Accumulated Other Comprehensive Income

In February 2018, the FASB issued ASU 2018-02, Reclassification of Certain Tax Effects from Accumulated Other Comprehensive Income ("ASU 2018-02"). The new standard allows for a reclassification from accumulated other comprehensive income to retained earnings for stranded tax effects resulting from the Tax Cuts and Jobs Act. The new standard will be effective beginning January 1, 2019 and early adoption is permitted. The adoption of this standard is not expected to have a material impact on the Company's financial position and results of operations upon adoption.

ASU 2018-07, Improvements to Nonemployee Share-Based Payment Accounting

In June 2018, the FASB issued ASU 2018-07, Improvements to Nonemployee Share-Based Payment Accounting ("ASU 2018-07"). The new standard simplifies the accounting for share-based payments to nonemployees by aligning it with the accounting for share-based payments to employees, with certain exceptions. The new standard will be effective beginning January 1, 2019 and early adoption is permitted. The Company is currently evaluating the potential impact ASU 2018-07 may have on its results of operations upon adoption.

3. Marketable securities

The following table summarizes the available-for-sale securities held at June 30, 2018 and December 31, 2017 (in thousands):

Description	Amortized cost	Unrealized gains	Unrealized losses	Fair value
June 30, 2018				
U.S. government agency securities and treasuries	$1,116,012	$ 36	$ (4,714)	$1,111,334
Certificates of deposit	11,960	—	—	11,960
Total	$1,127,972	$ 36	$ (4,714)	$1,123,294
December 31, 2017				
U.S. government agency securities and treasuries	$841,895	$ —	$ (3,579)	$838,316
Certificates of deposit	17,480	1	—	17,481
Total	$859,375	$ 1	$ (3,579)	$855,797

The amortized cost of available-for-sale securities is adjusted for amortization of premiums and accretion of discounts to maturity. At June 30, 2018 and December 31, 2017, the balance in the Company's accumulated other comprehensive loss was composed primarily of activity related to the Company's available-for-sale marketable securities. There were no material realized gains or losses recognized on the sale or maturity of available-for-sale securities during the six months ended June 30, 2018 or 2017, and as a result, the Company did not reclassify any amounts out of accumulated other comprehensive loss for the same periods.

The aggregate fair value of securities held by the Company in an unrealized loss position for less than twelve months as of June 30, 2018 and December 31, 2017 was $807.2 million and $704.1 million, respectively. As of June 30, 2018 and December 31, 2017, there were $101.2 million and $134.4 million in securities held by the Company in an unrealized loss position for more than twelve months, respectively. The aggregate unrealized loss on securities held by the Company for less than twelve months as of June 30, 2018 and December 31, 2017 was $4.3 million and $3.3 million, respectively. The aggregate unrealized loss on securities held by the Company for more than twelve months as of June 30, 2018 and December 31, 2017 was $0.4 million and $0.3 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 any other-than-temporary impairment as of June 30, 2018 and December 31, 2017.

No available-for-sale securities held as of June 30, 2018 or December 31, 2017 had remaining maturities greater than three years.

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, 2018 and December 31, 2017 (in thousands):

Description	Total	Quoted prices in active markets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)
June 30, 2018				
Assets:				
Cash and cash equivalents	$333,949	$333,949	$—	$ —
Marketable securities:				
U.S. government agency securities and treasuries	1,111,334	—	1,111,334	—
Certificates of deposit	11,960	—	11,960	—
Total assets	$1,457,243	$333,949	$1,123,294	$ —
Liabilities:				
Contingent consideration	$3,027	$—	$—	$ 3,027
Total liabilities	$3,027	$—	$—	$ 3,027
December 31, 2017				
Assets:				
Cash and cash equivalents	$758,505	$758,505	$—	$ —
Marketable securities:				
U.S. government agency securities and treasuries	838,316	—	838,316	—
Certificates of deposit	17,481	—	17,481	—
Total assets	$1,614,302	$758,505	$855,797	$ —
Liabilities:				
Contingent consideration	$2,231	$—	$—	$ 2,231
Total liabilities	$2,231	$—	$—	$ 2,231

Cash, cash equivalents and marketable securities

The Company considers all highly liquid securities with original final maturities of 90 days or less from the date of purchase to be cash equivalents. As of June 30, 2018 and December 31, 2017, cash and cash equivalents comprises funds in cash and money market accounts.

Marketable securities classified as Level 2 within the valuation hierarchy generally consist of U.S. treasury securities and government agency securities. The Company estimates the fair values of these marketable securities by taking into consideration valuations obtained from third-party pricing sources. These pricing sources utilize industry standard valuation models, including both income and market-based approaches, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. These inputs include market pricing based on real-time trade data

for the same or similar securities, issuer credit spreads, benchmark yields, and other observable inputs. The Company validates the prices provided by its third-party pricing sources by understanding the models used, obtaining market values from other pricing sources and analyzing pricing data in certain instances.

Contingent consideration

In connection with its prior acquisition of Pregenen, the Company may be required to pay future consideration that is contingent upon the achievement of specified development, regulatory approvals or sales-based milestone events. 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. In the absence of new information, changes in fair value will reflect changing discount rates and the passage of time.

The significant unobservable inputs used in the measurement of fair value of the Company's contingent consideration are probabilities of successful achievement of clinical and commercial milestones, the period in which these milestones are expected to be achieved ranging from 2021 to 2028 and discount rates ranging from 15.6% to 16.5%. 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 the 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):

	For the six months ended June 30, 2018
Beginning balance	$ 2,231
Additions	—
Changes in fair value	796
Payments	—
Ending balance	$ 3,027

Please refer to Note 7, "Commitments and contingencies" for further information.

5. Property, plant and equipment, net

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

	As of June 30, 2018	As of December 31, 2017
Land	$1,210	$ 1,210
Building	167,155	164,414
Computer equipment and software	5,551	5,134
Office equipment	5,036	4,478
Laboratory equipment	30,293	24,914
Leasehold improvements	272	116
Construction-in-progress	31,876	15,189
Total property, plant and equipment	241,393	215,455
Less accumulated depreciation and amortization	(22,167)	(15,849)
Property, plant and equipment, net	$219,226	$ 199,606

North Carolina manufacturing facility

In November 2017, the Company acquired a manufacturing facility, which is in the process of construction, in Durham, North Carolina for the future manufacture of lentiviral vector for the Company's gene and cell therapies. Construction-in-progress as of June 30, 2018 and December 31, 2017 includes $28.1 million and $12.9 million, respectively, related to the North Carolina manufacturing facility.

60 Binney Street lease

As of June 30, 2018, total property, plant and equipment, gross, includes $167.2 million related to the Company's headquarters at 60 Binney Street in Cambridge, Massachusetts, of which $156.0 million was incurred by the landlord. As of December 31, 2017, total property, plant and equipment, gross, includes $164.4 million related to the Company's headquarters at 60 Binney Street in Cambridge, Massachusetts, of which $156.0 million was incurred by the landlord. Please refer to Note 7, "Commitments and contingencies" for further information.

6. Accrued expenses and other current liabilities

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

	As of June 30, 2018	As of December 31, 2017
Accrued goods and services	$52,683	$ 29,533
Employee compensation	13,383	19,657
Accrued professional fees	1,748	1,402
Financing lease obligation, current portion	1,214	1,051
Accrued license and milestone fees	914	4,584
Other	1,061	838
Total accrued expenses and other current liabilities	$71,003	$ 57,065

7. Commitments and contingencies

Operating lease commitments

On June 3, 2016, the Company entered into a strategic manufacturing agreement for the future commercial production of the Company's Lenti-D and LentiGlobin product candidates with a contract manufacturing organization. Under this 12 year agreement, the contract manufacturing organization will complete the design, construction, validation and process validation of the leased suites prior to anticipated commercial launch of the product candidates. During construction, the Company was required to pay $12.5 million upon the achievement of certain contractual milestones, and may pay up to $8.0 million in additional contractual milestones if the Company elects its option to lease additional suites. The Company paid $5.0 million for the achievement of the first and second contractual milestones during 2016 and paid $5.5 million for the third and fourth contractual milestones achieved during 2017. In March 2018, $1.5 million of the possible $2.0 million related to the fifth contractual milestone was achieved and was paid in the second quarter of 2018. Given that construction was completed in March 2018, beginning in April 2018 the Company will pay $5.1 million per year in fixed suite fees as well as certain fixed labor, raw materials, testing and shipping costs for manufacturing services, and may pay additional suite fees if it elects its option to reserve or lease additional suites. The Company may terminate this agreement at any time upon payment of a one-time termination fee and up to 24 months of fixed suite and labor fees. The Company concluded that this agreement contains an embedded lease as the suites are designated for the Company's exclusive use during the term of the agreement. The Company concluded that it is not the deemed owner during construction nor is it a capital lease under ASC 840-10, Leases – Overall. As a result, the Company accounts for the agreement as an operating lease and expenses the rental payments on a straight-line basis over the non-cancellable term of the embedded lease.

On November 18, 2016, the Company entered into an agreement for future clinical and commercial production of the Company's LentiGlobin and Lenti-D gene therapy drug products with a contract manufacturing organization at an

existing facility. The term of the agreement is five years with a three year renewal at the mutual option of each party. Under the agreement, the Company is required to pay an up-front fee of €3.0 million, €2.0 million of which was paid in the fourth quarter of 2016 and €1.0 million of which is expected to be paid in the third quarter of 2018, and annual maintenance and production fees of up to €9.8 million, depending on its production needs. The Company may terminate this agreement with twelve months' notice and a one-time termination fee. The Company concluded that this agreement contains an embedded lease as the clean rooms are designated for the Company's exclusive use during the term of the agreement, and determined that it is not a capital lease under ASC 840-10, Leases – Overall. As a result, the Company accounts for the agreement as an operating lease and expenses the rental payments on a straight-line basis over the non-cancellable term of the embedded lease.

60 Binney Street Lease commitments

On September 21, 2015, the Company entered into a lease agreement for office and laboratory space located in a building (the "Building") at 60 Binney Street, Cambridge, Massachusetts (the "60 Binney Street Lease") to become its new corporate headquarters with a term through March 31, 2027. Although the Company does not legally own the premises, it is deemed to be the owner of the building for accounting purposes because the Company was involved in the construction project, including having responsibility to pay for a portion of the costs of finish work and mechanical, electrical, and plumbing elements of the Building during the construction period. Accordingly, construction costs that were incurred by the landlord directly or indirectly through reimbursement to the Company as part of its tenant improvement allowance have been recorded as an asset in "Property, plant and equipment, net" with a related financing obligation in "Accrued expenses and other current liabilities" and "Financing lease obligation, net of current portion" on the Company's condensed consolidated balance sheets.

The Company evaluated the 60 Binney Street Lease upon occupancy on March 27, 2017 and determined that the 60 Binney Street Lease did not meet the criteria for "sale-leaseback" treatment. This determination was based on, among other things, the Company's continuing involvement with the property in the form of non-recourse financing to the lessor. Accordingly, upon occupancy, the Company commenced depreciating the building over a useful life of 40 years and incurred interest expense related to the financing obligation of $3.9 million and $7.8 million for the three and six months ended June 30, 2018, respectively. The Company incurred interest expense related to the financing obligation of $3.7 million for the three and six months ended June 30, 2017. The Company currently maintains a $13.8 million letter of credit as required under the terms of the lease. Subject to the terms of the lease and certain reduction requirements specified therein, including market capitalization requirements, this amount may decrease to $9.2 million over time.

Contingent consideration related to business combinations

On June 30, 2014, the Company acquired Pregenen. The Company may be required to make up to $120.0 million in remaining future contingent cash payments to the former equityholders of Pregenen upon the achievement of certain clinical and commercial milestones related to the Pregenen technology, of which $20.1 million relates to clinical milestones and $99.9 million relates to commercial milestones. In accordance with accounting guidance for business combinations, contingent consideration liabilities are required to be recognized on the 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 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. Please refer to Note 4, "Fair value measurements" for additional information.

Other funding commitments

The Company is party to various agreements, principally relating to licensed technology, that require future payments relating to milestones not met at June 30, 2018 and December 31, 2017 or royalties on future sales of specified products. Additionally, the Company is party to various contracts with contract research organizations and contract manufacturers that generally provide for termination on notice, with the exact amounts due in the event of termination to be based on the timing of the termination and the terms of the agreement. In each of 2018 and 2019, the Company expects to make payments of approximately $12.0 million under an agreement with a contract manufacturer.

8. Collaboration revenue

To date, the Company's collaboration revenue has been exclusively generated from its collaboration arrangement with Celgene, which was originally entered into in March 2013 and was subsequently amended in June 2015, as further described below.

Original Collaboration Agreement

On March 19, 2013, the Company entered into a Master Collaboration Agreement (the "Collaboration Agreement") with 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 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 during the initial term of the Collaboration Agreement, or three years. The collaboration is governed by a joint steering committee ("JSC") formed by an equal number of representatives from the Company and Celgene. The JSC, among other activities, reviews the collaboration program, reviews and evaluates product candidates and approves regulatory plans. In addition to the JSC, the Collaboration Agreement provides that the Company and Celgene each appoint representatives to a patent committee, which is responsible for managing the intellectual property developed and used during the collaboration.

Amended Collaboration Agreement

On June 3, 2015, the Company and Celgene amended and restated the Collaboration Agreement (the "Amended Collaboration Agreement"). Under the Amended Collaboration Agreement, the parties narrowed the focus of the collaboration exclusively to anti- B-cell maturation antigen ("BCMA") product candidates for a new three-year term that ended in June 2018. In connection with the Amended Collaboration Agreement, the Company received an upfront, one-time, non-refundable, non-creditable payment of $25.0 million. The collaboration will continue to be governed by the JSC. Under the terms of the Amended Collaboration Agreement, for up to two product candidates selected for development under the collaboration, the Company is responsible for conducting and funding all research and development activities performed up through completion of the initial Phase I clinical study of such product candidate.

On a product candidate-by-product candidate basis, up through a specified period following enrollment of the first patient in an initial Phase I clinical study for such product candidate (the "Option Period"), the Company granted Celgene an option to obtain an exclusive worldwide license to develop and commercialize such product. Following Celgene's license of each product candidate, the Company is entitled to elect to co-develop and co-promote each product candidate in the U.S.

bb2121 License Agreement

On February 10, 2016, Celgene exercised its option to obtain an exclusive worldwide license to develop and commercialize bb2121, the first product candidate under the Amended Collaboration Agreement, pursuant to an executed license agreement ("bb2121 License Agreement") entered into by the parties on February 16, 2016 and paid the Company an option fee of $10.0 million. Pursuant to the bb2121 License Agreement, Celgene is responsible for development and related funding of bb2121 after the substantial completion of the on-going Phase I clinical trial. The Company is responsible for the manufacture of vector and associated payload throughout development and, upon Celgene's request, commercialization, which is fully reimbursed by Celgene, and Celgene is responsible for the manufacture of drug product throughout development and commercialization.

bb2121 Co-Development, Co-Promote and Profit Share Agreement

On March 28, 2018, the Company elected to co-develop and co-promote bb2121 within the U.S. pursuant to the execution of the Amended and Restated Co-Development, Co-Promote and Profit Share Agreement ("bb2121 CCPS"). The responsibilities of the parties remain unchanged from those under the bb2121 License Agreement, however, the Company will share equally in all profits and losses relating to developing, commercializing and manufacturing bb2121 within the U.S. and has the right to participate in the development and promotion of bb2121 in the U.S. Under the bb2121 CCPS, the Company may receive up to $70.0 million in development milestone payments for the first indication to be addressed by the bb2121 product candidate, with the ability to obtain additional milestone payments for a second indication and modified licensed products. In addition, to the extent bb2121 is 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 generated outside of the U.S., subject to certain reductions.

bb21217 License Agreement

On September 22, 2017, Celgene exercised its option to obtain an exclusive worldwide license to develop and commercialize bb21217, the second product candidate under the Amended Collaboration Agreement, pursuant to an executed license agreement ("bb21217 License Agreement") entered into by the parties on September 28, 2017 and paid the Company an option fee of $15.0 million. Pursuant to the bb21217 License Agreement, Celgene is responsible for development and related funding of bb21217 after the substantial completion of the on-going Phase I clinical trial. The Company is responsible for the manufacture of vector and associated payload throughout development and,

upon Celgene's request, commercialization, which is fully reimbursed by Celgene, and Celgene is responsible for the manufacture of drug product throughout development and commercialization.

The Company currently expects it will exercise its option to co-develop and co-promote bb21217 within the U.S. The Company's election to co-develop and co-promote bb21217 must be made by the substantial completion of the ongoing Phase I trial of bb21217. If elected, the Company expects the responsibilities of the parties to remain largely unchanged, however, the Company expects it will share equally in all profits and losses relating to developing, commercializing and manufacturing bb21217 within the U.S. and to have the right to participate in the development and promotion of bb21217 in the U.S. Under this scenario, the Company expects to receive, per product, up to $70.0 million in development milestone payments for the first indication to be addressed by the bb21217 product candidate, with the ability to obtain additional milestone payments for a second indication and modified licensed products. In addition, to the extent bb21217 is 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 generated outside of the U.S., subject to certain reductions.

In the event the Company does not exercise its option to co-develop and co-promote bb21217, the Company will receive an additional fee in the amount of $10.0 million. Under this scenario, the Company may 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. In addition, to the extent bb21217 is 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, subject to certain reductions.

Accounting analysis – bb2121

The Company has elected to use a practical expedient within Topic 606 that allow entities to reflect the aggregate effect of all contract modifications when identifying the satisfied and unsatisfied performance obligations for contracts that were modified prior to Topic 606 adoption. Celgene's option to in-license the first product candidate, bb2121, under the arrangement was considered a material right at the time the Amended Collaboration Agreement was executed in June 2015 given the product candidate had been formally nominated by the JSC and that substantially all investigational new drug application, or IND, enabling activities had been completed by that time. Therefore, Celgene's February 2016 exercise of its option that was considered a material right to obtain an exclusive worldwide license to develop and commercialize the first product candidate, bb2121, under the collaboration represented a contract modification. As a result, the Collaboration Agreement, Amended Collaboration Agreement, and bb2121 License Agreement are combined for accounting purposes and treated as a single arrangement. As of February 2016, Celgene's option to license an additional product candidate under the collaboration did not represent a material right. Therefore, the license to the Company's second product candidate, bb21217, which was executed in September 2017, is accounted for as a separate contract. Refer below for discussion of the bb21217 accounting analysis.

As of the February 2016 contract modification date, the Company concluded the arrangement contained the following promised goods and services: (i) research and development services, (ii) a license to the first product candidate, bb2121, and (iii) manufacture of vectors and associated payload for incorporation into bb2121 through development. The Company determined that the manufacture of commercial vector represents an option to acquire additional goods and services that is not representative of a material right. In addition, at this time Celgene has not exercised its option to purchase any commercial vector. Accordingly, the manufacture of commercial vector is not considered to be a performance obligation at this time.

The Company concluded that the research and development services are distinct from the other promised goods and services under the arrangement and thus such services are considered to be a separate performance obligation. The Company concluded that the license to bb2121 is not distinct from the vector manufacturing services because the manufacturing is essential to the use of the license. Accordingly, these two promised goods and services are considered a single combined performance obligation.

As of June 30, 2018, the total transaction price of $182.5 million comprises the up-front non-refundable fees of $100.0 million, the option fee of $10.0 million, and the estimated variable consideration of $72.5 million related to the estimated reimbursement from Celgene for the manufacture of vectors and associated payload through development. The total transaction price has been allocated to the performance obligations identified based on a relative SSP basis. The Company estimated the SSP of the license after considering potential future cash flows under the license. The Company then discounted these probability-weighted cash flows to their present value. The Company estimated the SSP of each of the research and development services and manufacturing services to be provided based on the Company's estimated cost of providing the services plus an applicable profit margin commensurate with observable market data for similar services.

None of the clinical or regulatory milestones have been included in the transaction price, as all milestone amounts are fully constrained. As part of its evaluation of the constraint, the Company considered numerous factors, including the fact that achievement of the milestones is outside the control of the Company and contingent upon the future success of its clinical trials, the licensee's efforts, and the receipt of regulatory approval. Any consideration related to sales-based milestones (including royalties) will be recognized when the related sales occur as these amounts have been determined to relate predominantly to the license granted to Celgene and therefore are recognized at the later of when the performance obligation is satisfied, or the related sales occur. The Company will re-evaluate the transaction price, including its estimated variable consideration included in the transaction price and all constrained amounts, in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

bb2121 research and development services

The Company allocated $36.0 million of the transaction price to the research and development services. The Company satisfied this performance obligation as the research and development services were performed. The Company determined that the period of performance of the research and development services was three years through projected initial Phase I clinical study substantial completion, or through May 2018. The Company recognized revenue related to research and development services performed using an input method by calculating costs incurred at each period end relative to total costs expected to be incurred. Although the Company has fully satisfied this performance obligation during the second quarter of 2018, any future changes to the total transaction price allocated to the performance obligations under the arrangement may impact the revenue recognized for this performance obligation in the period of change.

The Company recognized revenue related to bb2121 research and development services of $1.0 million and $3.1 million for the three and six months ended June 30, 2018, respectively. The Company recognized revenue related to bb2121 research and development services of $1.6 million and $3.1 million for the three and six months ended June 30, 2017, respectively.

bb2121 license and manufacturing services

The Company allocated $146.4 million of the transaction price to the combined unit of accounting which consists of the license and manufacture of vectors and associated payload for incorporation into bb2121.

The Company accounts for its vector manufacturing services for development in the U.S. and Celgene's U.S. development efforts within the scope of ASC 808 given that both parties are active participants in the activities and both parties are exposed to significant risks and rewards dependent on the commercial success of the activities. The Company recognizes revenue for its U.S. manufacturing services by analogy to Topic 606. The portion of Celgene's U.S. development costs that bluebird is responsible for are recognized as a reduction to its collaboration revenues, or, if in excess of such revenues in a given quarter, the excess is recorded as research and development expense.

Revenue recognition for the combined unit of accounting commenced during the first quarter of 2017. The Company recognizes revenue associated with the combined unit of accounting using the proportional performance method, as the Company will satisfy this performance obligation as the manufacturing services are performed through development. In using this method the Company estimated its development plan for bb2121, including expected demand from Celgene, and the costs associated with the manufacture of vectors and associated payload for incorporation into bb2121. On a quarterly basis, the Company determines the proportion of effort incurred as a percentage of total effort it expects to expend. This ratio is applied to the transaction price, which includes variable consideration, allocated to the combined performance obligation consisting of the bb2121 license and manufacturing services. Management has applied significant judgment in the process of developing its budget estimates and any changes to these estimates will be recognized in the period in which they change as a cumulative catch up.

In developing the SSP for the combined performance obligation, management assumed that the Company would exercise its option to co-develop and co-promote bb2121, and therefore will recognize revenue related to 67.5% of worldwide development costs incurred, which represents the percentage the Company is contractually entitled to bill Celgene under the cost share provisions of the co-development and co-promotion agreement, upon its execution. The Company exercised its option to co-develop and co-promote bb2121 in March 2018. The period of performance and pattern of revenue recognition remained unchanged upon its execution and will be revisited as the development plan changes or if other events occur.

For the three months ended June 30, 2018, the portion of Celgene's U.S. development costs that bluebird is responsible for are in excess of the Company's corresponding U.S. development costs, and, as such, the Company recorded research and development expense of $3.3 million (which is representative of gross revenue of $8.5 million offset by approximately $11.8 million of cost reimbursement to Celgene) related to the combined unit of accounting. For the three months ended March 31, 2018, the Company recognized revenue of $3.9 million (representative of gross revenue of $11.8 million offset by approximately $7.9 million of cost reimbursement to Celgene) related to the combined unit of accounting for its license and vector manufacturing of bb2121 in the U.S.

Revenue related to the combined unit of accounting for its rest of world license and vector manufacturing services is accounted for in accordance with Topic 606 and is recognized as collaboration revenue. The Company recognized $5.8 million and $14.7 million of revenue related to the combined unit of accounting for its rest of world license and

vector manufacturing services for the three and six months ended June 30, 2018, respectively. The Company recognized $6.0 million and $10.9 million of revenue related to the combined unit of accounting of accounting for its license and vector manufacturing services for the three and six months ended June 30, 2017, respectively, in accordance with ASC 605.

As of June 30, 2018, the aggregate amount of the transaction price allocated to the combined performance obligation, which consists of the bb2121 license and manufacturing services, that is unsatisfied, or partially unsatisfied, is $80.8 million, which the Company expects to recognize as revenue as manufacturing services are provided through the remaining development period which is estimated to be through 2020. The Company had $41.8 million remaining deferred revenue as of June 30, 2018 associated with the combined performance obligation consisting of the bb2121 license and manufacturing services.

Accounting analysis – bb21217

On September 22, 2017, Celgene exercised its option to obtain an exclusive worldwide license to develop and commercialize bb21217, the second optioned product candidate, pursuant to the bb21217 License Agreement entered into by the parties on September 28, 2017. The bb21217 License Agreement is considered a separate contract for accounting purposes as the option to obtain an exclusive worldwide license to develop and commercialize bb21217, or any other product candidate, was not considered a material right to Celgene at the time the practical expedient was applied. The Company made this evaluation after considering the significant uncertainty at that time regarding whether any additional product candidates would be identified under the Amended Collaboration Agreement. In particular, the Company considered that bb21217 had not been formally nominated as a product candidate under the collaboration at that time, primarily due to a lack of pre-clinical data as well as uncertainty surrounding the ability to successfully complete various IND-enabling activities.

At contract inception, the Company concluded that the arrangement contained the following promised goods and services: (i) research and development services, (ii) a license to the second product candidate, bb21217, and (iii) manufacture of vectors and associated payload for incorporation into bb21217 through development. The Company determined that the manufacture of commercial vector represents an option to acquire additional goods and services that is not representative of a material right. In addition, at this time Celgene has not exercised its option to purchase any commercial vector. Accordingly, the manufacture of commercial vector is not considered to be a performance obligation at this time.

The Company concluded that the research and development services are distinct from the other promised goods and services under the arrangement and thus is considered to be a performance obligation. Similar to bb2121, the Company concluded that the license to bb21217 is not distinct from the vector manufacturing services because the manufacturing is essential to the use of the license. Accordingly, these two promised goods and services are considered a single combined performance obligation.

As of June 30, 2018, the total transaction price of $41.7 million comprises the option fee of $15.0 million and the estimated variable consideration of $26.7 million related to reimbursement from Celgene for the manufacturing services during development. The total transaction price has been allocated to the performance obligations identified based on a relative SSP basis. The Company estimated the SSP of the license after considering potential future cash flows under the license. The Company then discounted these probability-weighted cash flows to their present value. The Company estimated the SSP of each of the research and development services and manufacturing services to be provided based on the Company's estimated cost of providing the services plus an applicable profit margin commensurate with observable market data for similar services.

None of the clinical or regulatory milestones have been included in the transaction price, as all milestone amounts are fully constrained. As part of its evaluation of the constraint, the Company considered numerous factors, including the fact that achievement of the milestones is outside the control of the Company and contingent upon the future success of its clinical trials, the licensee's efforts, and the receipt of regulatory approval. Any consideration related to sales-based milestones (including royalties) will be recognized when the related sales occur as these amounts have been determined to relate predominantly to the license granted to Celgene and therefore are recognized at the later of when the performance obligation is satisfied, or the related sales occur. The Company will re-evaluate the transaction price, including is estimated variable consideration included in the transaction price and all constrained amounts, in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

bb21217 research and development services

The Company allocated $5.4 million of the transaction price to the research and development services. The Company will satisfy this performance obligation as the research and development services are performed. The Company determined that the period of performance of the research and development services was two years through projected initial Phase I clinical study substantial completion, or through September 2019. The Company recognizes revenue related to research and development services performed using an input method by calculating costs incurred at each period end relative to total costs expected to be incurred.

The Company recognized revenue related to bb21217 research and development services for Celgene of $0.7 million and $1.4 million for the three and six months ended June 30, 2018, respectively. During the three and six months ended June 30, 2017, the Company did not recognize any revenue under the bb21217 License Agreement.

As of June 30, 2018, the aggregate amount of the transaction price allocated to the bb21217 research and development services performance obligation that are unsatisfied, or partially unsatisfied, and deferred is $3.6 million, which the Company expects to recognize through September 2019 as research and development services are performed.

bb21217 license and manufacturing services

The Company will satisfy its performance obligation related to the manufacture of vectors and associated payload for incorporation into bb21217 through development as the bb21217 manufacturing services are performed. As of June 30, 2018, the manufacturing services for bb21217 had not yet commenced. Therefore, no revenue has been recognized for the combined unit of accounting for the three and six months ended June 30, 2018 and 2017.

The aggregate amount of the transaction price allocated to the combined performance obligation, which consists of the bb21217 license and manufacturing services, is $36.2 million. The Company does not expect that recognition will begin in the next twelve months and has therefore classified deferred revenue associated with the combined performance obligation as deferred revenue, net of current portion on its consolidated balance sheet. The Company had $9.8 million remaining deferred revenue as of June 30, 2018 associated with the combined performance obligation consisting of the bb21217 license and manufacturing services.

Contract assets and liabilities

The Company receives payments from Celgene based on billing schedules established in each contract. Up-front payments and fees are recorded as deferred revenue upon receipt or when due until such time as the Company satisfies its performance obligations under these arrangements. A contract asset is a conditional right to consideration in exchange for goods or services that the Company has transferred to a customer. Amounts are recorded as accounts receivable when the Company's right to consideration is unconditional.

The following table presents changes in the balances of the Company's Celgene receivables and contract liabilities during the six months ended June 30, 2018:

For the six months ended June 30, 2018 (in thousands)	Balance at beginning of period under Topic 606	Additions	Deductions	Balance at end of period under Topic 606
Receivables	$ 4,635	$ 1,641	(6,276)	$—
Contract liabilities:				
Payable included in accrued expenses	$ —	$ 2,824	$ —	$2,824
Deferred revenue	$ 76,812	—	(21,589)	$55,223

The change in the receivables balance for the six months ended June 30, 2018 is primarily driven by cash collected from Celgene for the amounts owed to the Company for the satisfaction of vector manufacturing services performed under the collaboration to date. As of June 30, 2018, the Company does not have a receivable given that any amounts owed to the Company through June 30, 2018 were collected in the period and Celgene's U.S. development costs incurred in the second quarter of 2018 for which bluebird is responsible are in excess of the Company's U.S. development costs that Celgene is responsible for. The decrease in deferred revenue during the six months ended June 30, 2018 is primarily driven by revenue recognized for the combined performance obligation consisting of the bb2121 license and manufacturing services.

To date, there have been no impairment losses recognized on any receivables arising from the Company's contracts with customers.

During the six months ended June 30, 2018, $21.6 million of the deferred revenue balance at the beginning of the period was recognized as gross revenues.

9. License and royalty revenue

Novartis Pharma AG

On April 26, 2017, the Company entered into a worldwide license agreement with Novartis Pharma AG, or Novartis. Under the terms of the agreement, Novartis non-exclusively licensed certain patent rights related to lentiviral vector technology to develop and commercialize CAR T cell therapies for oncology, including Kymriah (formerly known as CTL019), Novartis's anti-CD19 CAR T therapy. At contract inception, financial terms of the agreement included a $7.5 million payment upon execution, $7.5 million of potential future milestone payments associated with regulatory approvals, and $1.1 million of payments for each subsequently licensed product, as well as low single digit royalty payments on net sales of covered products. In August 2017, Novartis received FDA approval for Kymriah and paid the Company $2.5 million as a result of the achievement of a related milestone.

Given this arrangement is within the scope of Topic 606, the Company assessed this arrangement in accordance with Topic 606 and concluded that at the date of contract inception, only one performance obligation, consisting of the license which was satisfied at contract inception, was identified. Accordingly, the nonrefundable license fee of $7.5 million was recognized as revenue upon contract execution in the second quarter of 2017 and the $2.5 million regulatory milestone was recognized as revenue upon milestone achievement, also in the second quarter of 2017, given there were no other unsatisfied performance obligations in the arrangement. This accounting conclusion was unchanged from its historical treatment under ASC 605. Because the single performance obligation was previously satisfied, all regulatory milestones will be recognized as revenue in full in the period in which the associated milestone is achieved. Regulatory approvals are not within the Company's control or the licensee's control and are generally not considered probable of being achieved until those approvals are received. As such, these milestones are constrained and excluded from the transaction price until such time as regulatory approvals are received.

The Company began recognizing royalty revenue from sales of Kymriah in the fourth quarter of 2017. As the license was deemed to be the predominant item to which the royalties relate, the Company recognizes royalties from the sales of Kymriah when the related sales occur. For the three and six months ended June 30, 2018, the Company recognized royalty revenue of $0.4 million and $0.7 million, respectively. The Company did not recognize royalty revenue in the comparative periods in the prior year given that Kymriah was approved for commercial sale in the second half of 2017.

The associated cost of license and royalty revenue for the three and six months ended June 30, 2018 was less than $0.1 million in both periods. For the three and six months ended June 30, 2017, the cost of license and royalty revenue was $0.3 million.

Orchard Therapeutics Limited (formerly GlaxoSmithKline Intellectual Property Development Limited)

On April 28, 2017, the Company entered into a worldwide license agreement with GlaxoSmithKline Intellectual Property Development Limited, or GSK. Under the terms of the agreement, GSK non-exclusively licensed certain patent rights related to lentiviral vector technology to develop and commercialize gene therapies for Wiscott-Aldrich syndrome and metachromatic leukodystrophy, two rare genetic diseases. Financial terms of the agreement include a nonrefundable upfront payment of $3.0 million as well as $1.3 million of potential milestone payments for each marketing authorization for each indication in any country as well as low single digit royalties on net sales of covered products. This license agreement was assigned by GSK to Orchard Therapeutics Limited, effective as of April 11, 2018.

Given this arrangement is within the scope of Topic 606, the Company assessed this arrangement in accordance with Topic 606 and concluded that at the date of contract inception, only one performance obligation, consisting of the license which was satisfied at contract inception, was identified. Accordingly, the entire nonrefundable license fee of $3.0 million was recognized as revenue upon contract execution in the second quarter of 2017 given there were no other unsatisfied performance obligations in the arrangement. This accounting conclusion was unchanged from its historical treatment under ASC 605. Because the single performance obligation was previously satisfied, all regulatory milestones will be recognized as revenue in full in the period in which the associated milestone is achieved. Regulatory approvals are not within the Company's control or the licensee's control and are generally not considered probable of being achieved until those approvals are received. As such, these milestones are constrained and excluded from the transaction price until such time as regulatory approvals are received. During the three and six months ended June 30, 2017, the Company recognized revenue of $3.0 million upon delivery of the license, as there were no other undelivered elements in the arrangements. There was no revenue recognized under this arrangement in the three and six months ended June 30, 2018.

For the three and six months ended June 30, 2017 the cost of license and royalty revenue was $0.1 million. Given there was no revenue recognized under this arrangement in the three and six months ended June 30, 2018, there was no associated cost of license and royalty revenue.

10. Equity

On December 15, 2017, the Company sold 3.2 million shares of common stock (excluding any shares sold pursuant to an overallotment option granted to the underwriters in connection with the offering) through an underwritten public offering at a price of $185.00 per share for aggregate net proceeds of $569.8 million. In January 2018, the Company sold 0.3 million shares of common stock pursuant to the partial exercise of an overallotment option granted to the underwriters in connection with the December 2017 underwritten public offering at a price of $185.00 per share for aggregate net proceeds of $48.7 million.

In July 2018, the Company sold 3.9 million shares of common stock (inclusive of shares sold pursuant to an overallotment option granted to the underwriters in connection with the offering) through an underwritten public offering at a price of $162.50 per share for aggregate net proceeds of $600.6 million.

11. Stock-based compensation

In January 2018 and 2017, the number of shares of common stock available for issuance under the 2013 Stock Option and Incentive Plan ("2013 Plan") was increased by approximately 2.0 million and 1.6 million shares, respectively, as a result of the automatic increase provision of the 2013 Plan. As of June 30, 2018, the total number of shares of common stock available for issuance under the 2013 Plan was approximately 1.8 million.

Stock-based compensation expense

The Company recognized stock-based compensation expense totaling $28.1 million and $51.1 million for the three and six months ended June 30, 2018, respectively. The Company recognized stock-based compensation expense totaling $13.5 million and $25.0 million for the three and six months ended June 30, 2017, respectively. Stock-based compensation expense by award type included within the condensed consolidated statements of operations and comprehensive loss was as follows (in thousands):

	For the three months ended		For the six months ended	
	June 30,		June 30,	
	2018	2017	2018	2017
Stock options	$20,932	$10,764	$38,227	$20,107
Restricted stock units	6,953	2,636	12,494	4,592
Employee stock purchase plan	171	89	330	272
	$28,056	$13,489	$51,051	$24,971

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

	For the three months ended		For the six months ended	
	June 30,		June 30,	
	2018	2017	2018	2017
Research and development	$14,196	$6,797	$25,820	$12,451
General and administrative	13,860	6,692	25,231	12,520
	$28,056	$13,489	$51,051	$24,971

In February 2018, the Company issued restricted stock units with service and performance conditions to employees, approximately 0.2 million of which are outstanding as of June 30, 2018 and none of which vested during the three or six months ended June 30, 2018. Vesting of these awards is contingent on the occurrence of a certain regulatory milestone event and fulfillment of any remaining service condition. As a result, the related compensation cost will be

first recognized as expense if and when achievement of the regulatory milestone is considered probable. These awards were modified in the second quarter of 2018 as a result of the adoption of a broad-based employee plan. The Company did not recognize any expense during the three or six months ended June 30, 2018 related to these awards and may recognize up to $40.4 million in stock-based compensation expense related to these awards upon achievement of the performance condition and subject to the service based condition.

As of June 30, 2018, the Company had $298.5 million of unrecognized stock-based compensation expense related to unvested stock options, restricted stock units and the employee stock purchase plan, which is expected to be recognized over a weighted-average period of 3.1 years, exclusive of any potential future stock-based compensation expense that may be recognized on any of the Company's outstanding performance-based awards for which the performance conditions were deemed not probable of achievement as of June 30, 2018.

Stock option activity

The following table summarizes the stock option activity under the Company's equity award plans:

	Shares (in thousands)	Weighted-average exercise price per share
Outstanding at December 31, 2017	3,755	$ 67.91
Granted	1,220	$ 198.41
Exercised	(426)	$ 59.45
Canceled or forfeited	(44)	$ 120.49
Outstanding at June 30, 2018	4,505	$ 103.55
Exercisable at June 30, 2018	1,954	$ 56.65
Vested and expected to vest at June 30, 2018	4,497	$ 103.61

During the six months ended June 30, 2018, 0.4 million shares of common stock were exercised, resulting in total proceeds to the Company of $25.3 million. In accordance with the Company's equity award plans, the shares were issued from a pool of shares reserved for issuance under the equity award plans.

Restricted stock unit activity

The following table summarizes the restricted stock unit activity under the Company's equity award plans:

	Shares (in thousands)	Weighted-average grant date fair value
Unvested balance at December 31, 2017	477	$ 80.72
Granted	575	$ 201.53
Vested	(107)	$ 77.53
Forfeited	(14)	$ 142.86
Unvested balance at June 30, 2018	931	$ 154.73

Refer above for discussion of the performance-based restricted stock units granted in February 2018, which are included in the table above.

Employee stock purchase plan

On June 3, 2013, the Company adopted its 2013 Employee Stock Purchase Plan ("2013 ESPP"), which authorized the initial issuance of up to a total of 238,000 shares of the Company's common stock to participating employees. During the six months ended June 30, 2018 and 2017, 9,055 shares and 11,079 shares of common stock were issued under the 2013 ESPP, respectively.

12. 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.

On December 22, 2017, the SEC staff issued Staff Accounting Bulletin No. 118, Income Tax Accounting Implications of the Tax Cuts and Jobs Act ("SAB 118"), which allows the recording of provisional amounts during a measurement period not to extend beyond one year of the enactment date. In accordance with SAB 118, the Company determined a provisional amount for the impact on its prior year deferred tax assets and valuation allowance in its prior year financial statements. The Company has not updated the provisional amounts and expects to complete the final assessment of the impact within the measurement period.

13. Net loss per share

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

	For the three and six months ended June 30,	
	2018	2017
Outstanding stock options	4,505	4,191
Restricted stock units	931	460
ESPP shares	5	11
	5,441	4,662

14. Subsequent events

As discussed in Note 10, “Equity,” in July 2018, the Company sold 3.9 million shares of common stock (inclusive of shares sold pursuant to an overallotment option granted to the underwriters in connection with the offering) through an underwritten public offering at a price of $162.50 per share for aggregate net proceeds of approximately $600.6 million.

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 21, 2018.

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

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

The following information and any forward-looking statements should be considered in light of factors discussed elsewhere in this Quarterly Report on Form 10-Q, including those risks identified under Part II, Item 1A. Risk Factors.

We caution readers not to place undue reliance on any forward-looking statements made by us, which speak only as of the date they are made. We disclaim any obligation, except as specifically required by law and the rules of the SEC, to publicly update or revise any such statements to reflect any change in our expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.

Overview

We are a clinical-stage biotechnology company committed to developing potentially transformative gene therapies for severe genetic diseases and cancer. 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. Our clinical programs in severe genetic diseases include our LentiGlobin® product candidate to treat transfusion-dependent -thalassemia, or TDT, and to treat severe sickle cell disease, or severe SCD, and our Lenti-D™ product candidate to treat cerebral adrenoleukodystrophy, or CALD, a rare hereditary neurological disorder. Our programs in oncology are built upon our leadership in lentiviral gene delivery and T cell engineering, with a focus on developing novel T cell-based immunotherapies, including chimeric antigen receptor (CAR) and T cell receptor (TCR) T cell therapies. bb2121 and bb21217, our product candidates in oncology, are CAR T cell product candidates for the treatment of multiple myeloma. We are co-developing and co-promoting the bb2121 product candidate in the United States with Celgene Corporation, or Celgene, and we have exclusively licensed to Celgene the development and commercialization rights for the bb2121 product candidate outside of the United States. We have exclusively licensed the development and commercialization rights for the bb21217 product candidate to Celgene, with an option to elect to co-develop and co-promote bb21217 within the U.S.

We are developing our LentiGlobin product candidate with the goal of filing for regulatory approval in the US and EU for different genotypes of TDT and for severe SCD. Both TDT and severe SCD are rare, hereditary blood disorders that often lead to severe anemia and shortened lifespans. We completed a Phase I/II study of our LentiGlobin product candidate in the United States, Australia, and Thailand for the treatment of subjects with TDT, called the Northstar Study (HGB-204). We are conducting the following clinical studies of our LentiGlobin product candidate: a single-center Phase I/II study in France of our LentiGlobin product candidate for the treatment of subjects with TDT or severe SCD (HGB-205); a multi-site, international, Phase III study for the treatment of subjects with TDT and a non-$^{0}/^{0}$ genotype, called the Northstar-2 Study (HGB-207); a multi-site, international, Phase III study for the treatment of subjects with TDT and a $^{0}/^{0}$ genotype, called the Northstar 3 Study (HGB-212); and a multi-site Phase I study in the United States for the treatment of subjects with severe SCD (HGB-206). We have achieved our enrollment target for the adult and adolescent cohort in the Northstar-2 Study. We anticipate a potential first conditional approval in the EU of our LentiGlobin product candidate for the treatment of adult and adolescent patients with TDT and a non- $^{0}/^{0}$ genotype in 2019. We are also engaged with the U.S. Food and Drug Administration, or FDA, and the EMA in discussions regarding our proposed development plans for LentiGlobin in severe SCD.

We are developing our Lenti-D product candidate with the goal of filing for regulatory approval in the US and EU for CALD, a rare, hereditary neurological disorder that is often fatal. We are conducting a multi-site, international, Phase II/III clinical study of our Lenti-D™ product candidate, called the Starbeam Study (ALD-102), for the treatment of subjects with CALD. Seventeen subjects were treated with our Lenti-D product candidate in the initial cohort of the Starbeam Study, and we are enrolling up to thirteen additional subjects in an expansion cohort of this study. We are also conducting an observational study of subjects with CALD treated by allogeneic hematopoietic stem-cell transplant referred to as the ALD-103 study. If our Lenti-D product candidate shows a sufficiently compelling treatment effect, and pending further discussion with regulatory authorities, the results from the Starbeam study could potentially form the basis of a BLA and a Marketing Authorization Application, or MAA, submission in the United States and European Union, respectively. We anticipate a potential first approval of our Lenti-D product candidate for the treatment of patients with CALD in 2020.

We are developing, in collaboration with Celgene, our bb2121 and bb21217 product candidates with the goal of filing for regulatory approval in multiple myeloma on a global basis. bb2121 is the lead product candidate arising from our multi-year collaboration with Celgene, for the discovery, development and commercialization of CAR T cell therapies targeting B-cell maturation antigen, or BCMA. In March 2018 we entered into an agreement with Celgene to co-develop and co-promote bb2121 in the United States, in which both parties will share equally in costs and profits. The FDA has granted Breakthrough Therapy designation and the EMA has granted PRIME eligibility to the bb2121 product candidate for relapsed/refractory multiple myeloma. Celgene is conducting a multi-site Phase I clinical study in the United States of the bb2121 product candidate for the treatment of subjects with relapsed/ refractory multiple myeloma (CRB-401), and a multi-site Phase II clinical study in the United States and Europe of the bb2121 product candidate for the treatment of subjects with relapsed/refractory multiple myeloma. Celgene has announced plans to initiate an international Phase III study of bb2121 in third line multiple myeloma in 2018. We and Celgene anticipate a potential approval of the bb2121 product candidate for the treatment of relapsed/ refractory multiple myeloma in 2020, although the parties no longer expect to submit a BLA with the FDA in 2019.

In September 2017, we initiated a Phase I clinical study of bb21217, the second anti-BCMA product candidate arising from our collaboration with Celgene, and Celgene exercised its option to obtain an exclusive worldwide license to develop and commercialize bb21217. We currently expect we will exercise our option to co-develop and co-promote bb21217 within the U.S. The FDA has granted Orphan Drug status to both bb2121 and bb21217 product candidates for the treatment of patients with relapsed/refractory multiple myeloma.

As of June 30, 2018, we had cash, cash equivalents and marketable securities of approximately $1.46 billion. In July 2018, we sold 3.9 million shares of common stock (inclusive of shares sold pursuant to an overallotment option granted to the underwriters in connection with the offering) through an underwritten public offering at a price of $162.50 per share for aggregate net proceeds of $600.6 million. As a result, we expect that our existing cash, cash equivalents and marketable securities will be sufficient to fund our current operations into 2022.

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

We have never been profitable and have incurred net losses in each year since inception. Our net loss was $146.0 million and $261.1 million for the three and six months ended June 30, 2018, respectively, and our accumulated deficit was $1.2 billion as of June 30, 2018. Substantially all of our net losses resulted from costs incurred in

connection with our research and development programs and from general and administrative costs associated with our operations. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. We expect our expenses will increase substantially in connection with our ongoing and planned activities, as we:

- conduct clinical studies for our LentiGlobin, Lenti-D product candidates, as well as to fund our share of the costs of clinical studies for the bb2121 and bb21217 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 establish the infrastructure necessary to support 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 currently 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. If we seek to obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses as we prepare for product sales, marketing, manufacturing, and distribution. Accordingly, we will seek to fund our operations through public or private equity or debt financings, strategic collaborations, or other sources. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. Our failure to raise capital or enter into such other arrangements as and when needed would have a negative impact on our financial condition and our ability to develop our products.

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

Financial operations overview

Revenues

To date, we have not generated any revenues from the sale of products. Our revenues have been derived from collaboration arrangements, out-licensing arrangements, research fees, and grant revenues. Effective January 1, 2018, we adopted Accounting Standards Codification (“ASC”), Topic 606, Revenue from Contracts with Customers (“Topic 606”), using the modified retrospective transition method.

Collaboration revenue is generated exclusively from our collaboration arrangement with Celgene. The terms of the arrangement with respect to bb2121 contain multiple promised goods or services, which include at inception: (i) research and development services, (ii) a license to bb2121, and (iii) manufacture of vectors and associated payload for incorporation into bb2121 under the license. As of September 2017, the collaboration also includes the following promised goods or services with respect to bb21217: (i) research and development services, (ii) a license to bb21217, and (iii) manufacture of vectors and associated payload for incorporation into bb21217 under the license. In March 2018, we entered into an agreement with Celgene to co-develop and co-promote bb2121 in which both parties will share equally in U.S. costs and profits. Collaboration revenue is recognized as the performance obligations are satisfied.

We analyze our collaboration arrangements to assess whether they are within the scope of ASC 808, Collaborative Arrangements (“ASC 808”) to determine whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities. This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For collaboration arrangements within the scope of ASC 808, we first determine which elements of the collaboration are deemed to be within the scope of ASC 808 and those that are more reflective of a vendor-customer relationship and therefore within the scope of Topic 606. For elements of collaboration arrangements that are accounted for pursuant to ASC 808, an appropriate recognition

method is determined and applied consistently, generally by analogy to Topic 606. Amounts that are owed to collaboration partners are recognized as an offset to collaboration revenues as such amounts are incurred by the collaboration partner. Where amounts owed to a collaboration partner exceed our collaboration revenues in a quarterly period, such amounts in excess are classified as research and development expense. For those elements of the arrangement that are accounted for pursuant to Topic 606, we apply the five-step model prescribed in Topic 606.

Nonrefundable license fees are recognized as revenue upon delivery of the license provided there are no unsatisfied performance obligations in the arrangement. License revenue has historically been generated from our out-license agreements with Novartis Pharma AG, or Novartis, and GlaxoSmithKline Intellectual Property Development Limited, or GSK. The license agreement with GSK was assigned by GSK to Orchard Therapeutics Limited, or Orchard, effective as of April 11, 2018. Under our out-licensing agreements we may also recognize revenue from potential future milestone payments and royalties.

For arrangements with licenses of intellectual property that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, we recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which the royalty has been allocated has been satisfied.

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;
- reimbursable costs to our partners for collaborative activities;
- facilities, depreciation, and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, information technology, insurance, and other supplies in support of research and development activities;
- costs associated with our research platform and preclinical 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, any of which could mean a significant change in the costs and timing associated with the development of our product candidates 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.

We plan to increase our research and development expenses for the foreseeable future as we continue to advance the development of our Lenti-D, LentiGlobin, and bb21217 product candidates, conduct research and development activities in oncology, fund our share of the costs of development of the bb2121 product candidate in collaboration with Celgene, and continue the research and development of product candidates using our gene editing technology platform. Our research and development expenses include expenses associated with the following activities:

- Starbeam Study (ALD-102) – We are conducting a Phase II/III clinical study in the United States, England and France to examine the safety and efficacy of our Lenti-D product candidate in the treatment of subjects with CALD.
- HGB-205 Study – We are conducting a Phase I/II clinical study in France to study the safety and efficacy of our LentiGlobin product candidate in the treatment of subjects with TDT and of subjects with severe SCD.
- HGB-206 Study – We are conducting a Phase I clinical study in the United States to study the safety and efficacy of our LentiGlobin product candidate in the treatment of subjects with severe SCD.
- Northstar-2 Study (HGB-207) – We are conducting a Phase III study at multiple sites internationally to examine the safety and efficacy of our LentiGlobin product candidate in the treatment of subjects with TDT and a non-$^{0}/^{0}$ genotype.
- Northstar-3 Study (HGB-212) – We are conducting a Phase III study at multiple sites internationally to examine the safety and efficacy of our LentiGlobin product candidate in the treatment of subjects with TDT and a $^{0}/^{0}$ genotype.

- CRB-402 study – We are conducting a Phase I clinical study of our bb21217 product candidate, our next-generation anti-BCMA product candidate in the treatment of subjects with relapsed/refractory multiple myeloma.
- Clinical studies for the bb2121 product candidate – Celgene is conducting a Phase I clinical study in the United States to study the safety and efficacy of the bb2121 product candidate in the treatment of subjects with relapsed/refractory multiple myeloma, and a Phase II clinical study in the United States and Europe to study the safety and efficacy of the bb2121 product candidate in the treatment of subjects with relapsed/ refractory multiple myeloma. We share the costs of these clinical studies with Celgene.
- 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, 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 other research and development expenses in the table below:

	For the three months ended		For the six months ended	
	June 30,		June 30,	
	2018	2017	2018	2017
	(in thousands)		(in thousands)	
LentiGlobin	$35,765	$23,159	$68,562	$43,668
Lenti-D	9,243	3,702	15,440	7,686
bb2121	19,770	8,513	32,035	14,564
bb21217	3,507	—	6,777	—
Pre-clinical programs	9,672	6,639	20,831	11,222
Total direct research and development expense	77,957	42,013	143,645	77,140
Employee-and contractor-related expenses	7,719	5,245	14,944	9,663
Stock-based compensation expense	14,196	6,797	25,820	12,451
Platform-related expenses	6,727	3,995	11,399	7,618
Facility expenses	7,730	5,695	15,403	11,687
Other expenses	685	146	912	360
Total other research and development expenses	37,057	21,878	68,478	41,779
Total research and development expense	$115,014	$63,891	$212,123	$118,919

The costs associated with our bb21217 program were included in pre-clinical programs until the third quarter of 2017 when we initiated the first clinical study of bb21217.

General and administrative expenses

General and administrative expenses consist primarily of salaries and related costs for personnel, including stock-based compensation and travel expenses for our employees in executive, operational, finance, legal, business development, commercial, information technology, and human resource functions. Other general and administrative expenses include facility-related costs, professional fees for accounting, tax, legal and consulting 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 the potential commercialization of our product candidates. Additionally, 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.

Cost of license and royalty revenue

Cost of license and royalty revenue represents expense associated with amounts owed to third party licensors as a result of revenue recognized under our out-license arrangements with Novartis and Orchard.

We anticipate that our cost of license and royalty revenue will increase in the future contingent upon the achievement of regulatory milestones by Novartis or Orchard. Additionally, we anticipate that our cost of license and royalty revenue will increase in the future as we expect to continue to recognize royalty revenue related to Novartis' commercial sale of Kymriah.

Change in fair value of contingent consideration

On June 30, 2014, we acquired Pregenen. 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.

As of June 30, 2018, there are $120.0 million in future contingent cash payments, of which $20.1 million relates to clinical milestones and $99.9 million relates to commercial milestones. We estimate future contingent cash payments have a fair value of $3.0 million as of June 30, 2018, all of which is classified as a non-current liability on our condensed consolidated balance sheet.

Interest income (expense), net

Interest income (expense), net consists primarily of interest expense on the financing obligation for our headquarters at 60 Binney Street in Cambridge, Massachusetts, and interest income earned on investments.

Other income (expense), net

Other income (expense), net consists primarily of losses on disposal of assets and gains and losses on foreign currency.

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 expected business and operational changes, sensitivity and volatility associated with the assumptions used in developing estimates, and whether historical trends are expected to be representative of future trends. 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, 2018, 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, 2017, which was filed with the SEC on February 21, 2018, except as otherwise described below.

Revenue recognition

Effective January 1, 2018, we adopted Accounting Standards Codification ("ASC"), Topic 606, Revenue from Contracts with Customers ("Topic 606"), using the modified retrospective transition method. Under this method, we have recognized the cumulative effect of the adoption as an adjustment to the opening balance of accumulated deficit in the current period condensed consolidated balance sheet. We have not revised our consolidated financial statements for

prior periods. This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as collaboration arrangements and leases.

Under Topic 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of Topic 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price, including variable consideration, if any; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. We only apply the five-step model to contracts when it is probable that the entity will collect the consideration to which it is entitled in exchange for the goods or services it transfers to the customer.

Once a contract is determined to be within the scope of Topic 606, we assess the goods or services promised within each contract and determine those that are performance obligations. Arrangements that include rights to additional goods or services that are exercisable at a customer's discretion are generally considered options. We assess if these options provide a material right to the customer and if so, they are considered performance obligations. The exercise of a material right is accounted for as a contract modification for accounting purposes.

We assess whether each promised good or service is distinct for the purpose of identifying the performance obligations in the contract. This assessment involves subjective determinations and requires management to make judgments about the individual promised goods or services and whether such are separable from the other aspects of the contractual relationship. Promised goods and services are considered distinct provided that: (i) the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer (that is, the good or service is capable of being distinct) and (ii) the entity's promise to transfer the good or service to the customer is separately identifiable from other promises in the contract (that is, the promise to transfer the good or service is distinct within the context of the contract). In assessing whether a promised good or service is distinct, we consider factors such as the research, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. We also consider the intended benefit of the contract in assessing whether a promised good or service is separately identifiable from other promises in the contract. If a promised good or service is not distinct, an entity is required to combine that good or service with other promised goods or services until it identifies a bundle of goods or services that is distinct.

The transaction price is then determined and allocated to the identified performance obligations in proportion to their standalone selling prices ("SSP") on a relative SSP basis. SSP is determined at contract inception and is not updated to reflect changes between contract inception and when the performance obligations are satisfied. Determining the SSP for performance obligations requires significant judgment. In developing the SSP for a performance obligation, we consider applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. We validate the SSP for performance obligations by evaluating whether changes in the key assumptions used to determine the SSP will have a significant effect on the allocation of arrangement consideration between multiple performance obligations.

If the consideration promised in a contract includes a variable amount, we estimate the amount of consideration to which it will be entitled in exchange for transferring the promised goods or services to a customer. We determine the amount of variable consideration by using the expected value method or the most likely amount method. We include the unconstrained amount of estimated variable consideration in the transaction price. The amount included in the transaction price is constrained to the amount for which it is probable that a significant reversal of cumulative revenue recognized will not occur. At the end of each subsequent reporting period, we re-evaluate the estimated variable consideration included in the transaction price and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis in the period of adjustment.

If an arrangement includes development and regulatory milestone payments, we evaluate whether the milestones are considered probable of being reached and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our control or the licensee's control, such as regulatory approvals, are generally not considered probable of being achieved until those approvals are received.

In determining the transaction price, we adjust consideration for the effects of the time value of money if the timing of payments provides us with a significant benefit of financing. We do not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the licensees and the transfer of the promised goods or services to the licensees will be one year or less. We assessed each of our revenue generating arrangements in order to determine whether a significant financing component exists and concluded that a significant financing component does not exist in any of our arrangements.

We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) each performance obligation is satisfied, either at a point in time or over time, and if over time

recognition is based on the use of an output or input method.

Collaboration revenue

To date, collaboration revenue has been exclusively generated from our collaboration arrangement with Celgene, which was originally entered into in March 2013 and was subsequently amended in June 2015, as further described in Note 8, “Collaboration revenue”.

We analyze our collaboration arrangements to assess whether they are within the scope of ASC 808, Collaborative Arrangements (“ASC 808”) to determine whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities. This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For collaboration arrangements within the scope of ASC 808 that contain multiple elements, we first determine which elements of the collaboration are deemed to be within the scope of ASC 808 and those that are more reflective of a vendor-customer

relationship and therefore within the scope of Topic 606. For elements of collaboration arrangements that are accounted for pursuant to ASC 808, an appropriate recognition method is determined and applied consistently, generally by analogy to Topic 606. Amounts that are owed to collaboration partners are recognized as an offset to collaboration revenues as such amounts are incurred by the collaboration partner. Where amounts owed to a collaboration partner exceed our collaboration revenues in each quarterly period, such amounts are classified as research and development expense. For those elements of the arrangement that are accounted for pursuant to Topic 606, we apply the five-step model described above.

License and royalty revenue

We enter into out-licensing agreements that are within the scope of Topic 606. We do not have any material license arrangements that contain more than one performance obligation. The terms of such out-license agreements include the license of functional intellectual property, given the functionality of the intellectual property is not expected to change substantially as a result of the licensor's ongoing activities, and typically include payment of one or more of the following: non-refundable up-front license fees; development and regulatory milestone payments and milestone payments based on the level of sales; and royalties on net sales of licensed products. Nonrefundable up-front license fees are recognized as revenue at a point in time when the licensed intellectual property is made available for the customer's use and benefit, which is generally at the inception of the arrangement. Milestone fees, which are a type of variable consideration, are recognized as revenue to the extent that it is probable that a significant reversal will not occur. For arrangements with licenses of intellectual property that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, we recognize royalty revenue and sales-based milestones at the later of (i) when the related sales occur, or (ii) when the performance obligation to which the royalty has been allocated has been satisfied.

Impact of Topic 606 adoption

As a result of adopting Topic 606, we recorded a $29.4 million adjustment to the opening balance of accumulated deficit in the first quarter of 2018 primarily as a result of the accounting for the up-front consideration received in March 2013 in connection with the collaboration arrangement with Celgene under ASC 605-25 versus Topic 606. Refer below for a summary of the amount by which each financial statement line item was affected the impact of the cumulative adjustment:

	Impact of Topic 606 Adoption on Condensed Consolidated Balance Sheet as of January 1, 2018		
(in thousands)	As reported under Topic 606	Adjustments	Balances without adoption of Topic 606
Deferred revenue, current portion	$45,344	$ 19,670	$ 25,674
Deferred revenue, net of current portion	$31,468	$ 9,705	$ 21,763
Accumulated deficit	$(943,183)	$ (29,375)	$ (913,808)

The amount by which each financial statement line item is affected in the current reporting period by Topic 606 as compared with the guidance that was in effect prior to adoption is disclosed below.

	Impact of Topic 606 Adoption on Condensed Consolidated Balance Sheet as of June 30, 2018		
(in thousands)	As reported under Topic 606	Adjustments	Balances without adoption of Topic 606
Deferred revenue, current portion	$27,323	$ 12,010	$ 15,313
Deferred revenue, net of current portion	$27,900	$ 8,545	$ 19,355
Accumulated deficit	$(1,204,303)	$ (20,555)	$ (1,183,748)

	Impact of Topic 606 Adoption on Condensed Consolidated Statement of Operations and Comprehensive Loss for the Three Months Ended June 30, 2018		
(in thousands, except per share data)	As reported under Topic 606	Adjustments	Balances without adoption of Topic 606
Collaboration revenue	$7,437	$ 887	$ 6,550
Research and development expense	$115,014	$ (1,800)	$ 116,814
Net loss	$(145,996)	$ 2,687	$ (148,683)
Net loss per share - basic and diluted:	$(2.91)	$ 0.05	$ (2.96)

	Impact of Topic 606 Adoption on Condensed Consolidated Statement of Operations and Comprehensive Loss for the Six Months Ended June 30, 2018		
(in thousands, except per share data)	As reported under Topic 606	Adjustments	Balances without adoption of Topic 606
Collaboration revenue	$23,045	$ 7,020	$ 16,025
Research and development expense	$212,123	$ (1,800)	$ 213,923
Net loss	$(261,120)	$ 8,820	$ (269,940)
Net loss per share - basic and diluted:	$(5.22)	$ 0.17	$ (5.39)

	Impact of Topic 606 Adoption on Condensed Consolidated Statement of Cash Flows for the Six Months Ended June 30, 2018		
(in thousands)	As reported under Topic 606	Adjustments	Balances without adoption of Topic 606
Net loss	$(261,120)	$ 8,820	$ (269,940)

Changes in deferred revenue	$(21,589)	$ (8,820)	$ (12,769)

Results of Operations

Comparison of the three months ended June 30, 2018 and 2017:

	For the three months ended June 30,		
	2018	2017	Change
	(in thousands)		
Revenue:			
Collaboration revenue	$7,437	$6,146	$1,291
License and royalty revenue	414	10,570	(10,156)
Total revenues	7,851	16,716	(8,865)
Operating expenses:			
Research and development	115,014	63,891	51,123
General and administrative	41,168	21,197	19,971
Cost of license and royalty revenue	21	420	(399)
Change in fair value of contingent consideration	262	(970)	1,232
Total operating expenses	156,465	84,538	71,927
Loss from operations	(148,614)	(67,822)	80,792
Interest income (expense), net	2,436	(2,242)	(4,678)
Other income (expense), net	182	(834)	(1,016)
Loss before income taxes	(145,996)	(70,898)	75,098
Net loss	$(145,996)	$(70,898)	$75,098

Revenues. Total revenue was $7.9 million for the three months ended June 30, 2018, compared to $16.7 million for the three months ended June 30, 2017. The decrease of $8.9 million was primarily attributable to license revenue from Novartis in the prior period.

Research and development expenses. Research and development expenses were $115.0 million for the three months ended June 30, 2018, compared to $63.9 million for the three months ended June 30, 2017. The overall increase of $51.1 million was primarily attributable to the following:

- $18.3 million of increased costs incurred for material production, laboratory expenses, and collaboration research;
- $15.5 million of increased employee compensation, benefit, and other headcount related expenses, of which $7.4 million is stock based compensation expense, primarily due to an increase in headcount to support overall growth;
- $6.6 million of license and milestone fees (exclusive of any costs recorded in cost of license and royalty revenue) primarily driven by milestones triggered by the first patient treated in the Phase 2 clinical study of bb2121, which is run by our collaborative partner, Celgene, as well as milestones owed to other collaborators as a result of certain clinical events occurring in the second quarter of 2018;
- $4.6 million of professional and consulting fees;
- $3.9 million of increased clinical trial related costs necessary to support the advancement of our clinical and pre-clinical programs; and
- $2.0 million of increased facility related costs.

General and administrative expenses. General and administrative expenses were $41.2 million for the three months ended June 30, 2018, compared to $21.2 million for the three months ended June 30, 2017. The increase of $20.0 million was primarily attributable to $12.7 million of increased employee compensation, benefit, and other headcount related expenses, of which $7.2 million is stock based compensation expense, primarily due to an increase in headcount to support overall growth. In addition, the overall increase is driven by increased market research costs of $4.0 million and increased professional and consulting fees of $3.1 million.

Cost of license and royalty revenue. Cost of license and royalty revenue was less than $0.1 million for the three months ended June 30, 2018, compared to $0.4 million for the three months ended June 30, 2017. The decrease is attributable to decreased license and royalty revenue in the same periods.

Change in fair value of contingent consideration. The change in fair value of contingent consideration is driven by changes in assumptions related to estimated milestone achievement dates and probabilities of achievement.

Interest income (expense), net. The change in interest income, net was primarily related to interest income earned on investments, offset by interest expense on the financing obligation for our headquarters at 60 Binney Street in Cambridge, Massachusetts. The increase in interest income is primarily driven by an increase in marketable securities held by us as a result of the deployment of cash received in connection with our prior common stock offerings as well as increased interest rates.

Other income (expense), net. The change in other income (expense), net was primarily related to gains and losses on foreign currency.

Comparison of the six months ended June 30, 2018 and 2017:

	For the six months ended June 30,		
	2018	2017	Change
	(in thousands)		
Revenues:			
Collaboration revenue	$23,045	$12,978	$10,067
License and royalty revenue	763	10,570	(9,807)
Total revenues	23,808	23,548	260
Operating expenses:			
Research and development	212,123	118,919	93,204
General and administrative	76,094	41,481	34,613
Cost of license revenue	36	420	(384)
Change in fair value of contingent consideration	796	463	333
Total operating expenses	289,049	161,283	127,766
Loss from operations	(265,241)	(137,735)	127,506
Interest income (expense), net	3,824	(687)	(4,511)
Other income (expense), net	297	(1,189)	(1,486)
Loss before income taxes	(261,120)	(139,611)	121,509
Net loss	$(261,120)	$(139,611)	$121,509

Revenues. Total revenue was $23.8 million for the six months ended June 30, 2018, compared to $23.5 million for the six months ended June 30, 2017. The increase of $0.3 million was primarily attributable to an increase in collaboration revenue for the bb2121 license and manufacturing services under our agreement with Celgene, offset by a decrease in license and royalty revenue.

Research and development expenses. Research and development expenses were $212.1 million for the six months ended June 30, 2018, compared to $118.9 million for the six months ended June 30, 2017. The increase of $93.2 million was primarily attributable to the following:

- $39.1 million of increased costs incurred for material production, laboratory expenses, and collaboration research;
- $29.1 million of increased employee compensation, benefit, and other headcount related expenses, of which $13.4 million is stock based compensation expense, primarily due to an increase in headcount to support overall growth;
- $10.0 million of license and milestone fees (exclusive of any costs recorded in cost of license and royalty revenue) primarily driven by milestones triggered by the first patient treated in the Phase 2 clinical study of bb2121 which is run by our collaborative partner, Celgene, as well as milestones owed to other collaborators as a result of certain clinical events occurring in the second quarter of 2018;
- $6.6 million of increased clinical trial related costs necessary to support the advancement of our clinical and pre-clinical programs;
- $4.6 million of increased professional and consulting fees; and
- $3.7 million of increased facility related expenses.

General and administrative expenses. General and administrative expenses were $76.1 million for the six months ended June 30, 2018, compared to $41.5 million for the six months ended June 30, 2017. The increase of $34.6 million was primarily attributable to $23.3 million of increased employee compensation, benefit, and other headcount related expenses, of which $12.7 million is stock based compensation expense, primarily due to an increase in headcount to support overall growth. In addition, the overall increase is driven by increased market research costs of $5.7 million and increased professional and consulting fees of $5.0 million.

Cost of license and royalty revenue. Cost of license and royalty revenue was less than $0.1 million for the six months ended June 30, 2018, compared to $0.4 million for the six months ended June 30, 2017. The decrease is attributable to decreased license and royalty revenue in the same periods.

Change in fair value of contingent consideration. The change in fair value of contingent consideration is driven by changes in assumptions related to estimated milestone achievement dates and probabilities of achievement.

Interest income (expense), net. The change in interest income, net was primarily related to interest income earned on investments, offset by interest expense on the financing obligation for our headquarters at 60 Binney Street in Cambridge, Massachusetts. The increase in interest income is primarily driven by an increase in marketable securities held by us as a result of the deployment of cash received in connection with our prior common stock offerings as well as increased interest rates.

Other income (expense), net. The change in other income (expense), net was primarily related to gains and losses on foreign currency.

Liquidity and Capital Resources

As of June 30, 2018, we had cash, cash equivalents and marketable securities of approximately $1.46 billion. In July 2018, we sold 3.9 million shares of common stock (inclusive of shares sold pursuant to an overallotment option granted to the underwriters in connection with the offering) through an underwritten public offering at a price of $162.50 per share for aggregate net proceeds of $600.6 million. As a result, we expect cash, cash equivalents and marketable securities to fund our planned operations into 2022.

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, 2018, our funds are primarily held in U.S. Treasury securities, U.S. government agency securities, certificates of deposit and money market accounts.

We have incurred losses and cumulative negative cash flows from operations since our inception in April 1992, and as of June 30, 2018 we had an accumulated deficit of $1.2 billion. 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.

Sources of Liquidity

Cash Flows

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

	For the six months ended June 30,	
	2018	2017
	(in thousands)	
Net cash used in operating activities	$(209,222)	$(128,837)
Net cash (used in) provided by investing activities	(292,212)	54,561
Net cash provided by financing activities	76,978	481,723
Net (decrease) increase in cash, cash equivalents and restricted cash	$(424,456)	$407,447

Cash Flows from Operating Activities. The $80.4 million increase in cash used in operating activities for the six months ended June 30, 2018 compared to the six months ended June 30, 2017 was partially due to the increase in net loss during this period of $121.5 million, which was driven by increased payroll and payroll-related expenses and spending on our clinical and pre-clinical stage programs to support overall growth. Cash used in operating activities was also driven by changes in operating assets and liabilities.

Cash Flows from Investing Activities. The $346.8 million increase in cash used by investing activities for the six months ended June 30, 2018 was primarily due to an increase of $572.4 million in cash used to purchase marketable securities, offset by an increase of $206.8 million in proceeds received from the maturity of marketable securities and a decrease of $18.8 million in cash used to purchase property, plant and equipment when compared to the six months ended June 30, 2017.

Cash Flows from Financing Activities. The $404.7 million decrease in cash provided by financing activities was primarily driven by a decrease of $388.1 million in proceeds from the public offering of common stock, net of issuance costs, and a decrease of $33.3 million in the reimbursement of tenant improvements under our financing lease obligation, offset by an increase of $17.0 million in proceeds from the issuance of common stock, in the six months ended June 30, 2018 compared to the six months ended June 30, 2017.

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 21, 2018.

Off-Balance Sheet Arrangements

As of June 30, 2018, 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, 2018 and December 31, 2017, we had cash, cash equivalents and marketable securities of $1.46 billion and $1.61 billion, respectively, primarily invested in U.S. government agency securities and treasuries, federally insured certificates of deposit and money market accounts invested in 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, 2018, the net fair value of our interest-sensitive marketable securities would have resulted in a hypothetical decline of approximately $8.1 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, 2018, 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, 2018, 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, 2018 there were 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, 2018, 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 21, 2018.

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. Only a few gene therapy products have been approved in the United States and European Union, or EU.

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

In addition, the clinical study requirements of the U.S. Food and Drug Administration, or FDA, the European Medicines Agency, or EMA, and other regulatory agencies and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other, better known or more extensively studied pharmaceutical or other product candidates. Currently, only a few gene therapy products have been approved in the Western world, including Orchard's Strimvelis and also Spark's gene therapy product, which received approval from the FDA in 2017. Novartis's and Gilead's CAR-T therapies both received approval from the FDA in 2017. Given the few precedents of approved gene therapy products, it is difficult to determine how long it will take or how much it will cost to obtain regulatory

approvals for our product candidates in the United States, the EU or other jurisdictions. Approvals by the EMA and the European Commission may not be indicative of what the FDA may require for approval.

Regulatory requirements governing gene and cell therapy products have evolved and may continue to change in the future. For example, on July 11, 2018, the FDA released draft guidance documents intended to reflect recent advances in the field, and to update the framework for the development, review and approval of gene therapies. These draft guidance documents pertain to the development of gene therapies for the treatment of specific disease categories, including rare diseases, and to manufacturing and long-term follow up issues relevant to gene therapy, among other topics. Furthermore, the FDA has established the Office of Cellular, Tissue and Gene Therapies within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. Gene therapy clinical studies conducted at institutions that receive funding for recombinant DNA research from the U.S. National Institutes of Health, or NIH, are also subject to review by the NIH Office of Biotechnology Activities' Recombinant DNA Advisory Committee, or RAC. Although the FDA decides whether individual gene therapy protocols may proceed, the RAC review process can impede the initiation of a clinical study, even if the FDA has reviewed the study and approved its initiation. Clinical trial sites in the United States that receive NIH funding for research involving recombinant or synthetic nucleic acid molecules are required to follow RAC

recommendations, or risk losing NIH funding for such research or needing NIH pre-approval before conducting such research. In addition, the FDA can put an investigational new drug application, or IND, on clinical hold if the information in an IND is not sufficient to assess the risks in pediatric patients. Before a clinical study can begin at any institution, that institution's institutional review board, or IRB, and its Institutional Biosafety Committee will have to review the proposed clinical study to assess the safety of the study. Moreover, serious adverse events or developments in clinical trials of gene therapy product candidates conducted by others may cause the FDA or other regulatory bodies to initiate a clinical hold on our clinical trials or otherwise change the requirements for approval of any of our product candidates.

These regulatory review agencies, committees and advisory groups and the new requirements and guidelines they promulgate may lengthen the regulatory review process, require us to perform additional or larger studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates or lead to significant post-approval studies, limitations or restrictions. As we advance our product candidates, we will be required to consult with these regulatory and advisory groups and comply with applicable requirements and guidelines. If we fail to do so, we may be required to delay or discontinue development of our product candidates. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenue to maintain our business.

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

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

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

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

In particular, each of the conditions for which we plan to evaluate our current hematopoietic stem cell, or HSC, product candidates are rare genetic disorders with limited patient pools from which to draw for clinical studies.

Further, because newborn screening for CALD is not widely adopted, and it can be difficult to diagnose CALD in the absence of a genetic screen, we may have difficulty finding patients who are eligible to participate in our study. The eligibility criteria of our clinical studies will further limit the pool of available study participants. Additionally, the process of finding and diagnosing patients may prove costly. Finally, our treatment process requires that the procurement of autologous cells from subjects be conducted where the cells can be shipped to a transduction facility within the required timelines, as the HSCs and T cells, in the case of our oncology product candidate, have limited viability following harvest.

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

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

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

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

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

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

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

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

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

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

Initial success in our ongoing clinical studies may not be indicative of results obtained when these studies are completed. Furthermore, success in early clinical studies may not be indicative of results obtained in later studies.

Our product candidates first initiated evaluation in human clinical studies in 2013, and we may experience unexpected results in the future. Results from previous or ongoing studies are not necessarily predictive of our future clinical study results, and initial or interim results may not continue or be confirmed upon completion of the study. There is limited data concerning long-term safety and efficacy following treatment with our gene therapy and T cell-based product candidates. These data, or other positive data, may not continue or occur for these subjects or for any future subjects in our ongoing or future clinical studies, and may not be repeated or observed in ongoing or future studies involving our product candidates. For instance, while patients with TDT or severe SCD who have been treated with our LentiGlobin product candidate may experience a reduction or temporary elimination of transfusion support, there can be no assurance that they will not require transfusion support in the future. Similarly, patients with relapsed/refractory multiple myeloma who have been treated with the bb2121 or the bb21217 product candidate may experience disease progression. Furthermore, our product candidates may also fail to show the desired safety and efficacy in later stages of clinical development despite having successfully advanced through initial clinical studies. There can be no assurance that any of these studies will ultimately be successful or support further clinical advancement or regulatory approval of our product candidates.

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

Patients with different genotypes of TDT may experience different outcomes from treatment with our product candidates, which may result in the delay of our clinical development and commercialization plans.

Initial results from our clinical studies of LentiGlobin suggest that patients with TDT and a non-$^{0}/^{0}$ genotype experienced better outcomes to treatment with our LentiGlobin product candidate than patients with TDT and a $^{0}/^{0}$ genotype. Consequently, we expect to seek FDA approval of our LentiGlobin product candidate initially for the treatment of patients with TDT and a non-$^{0}/^{0}$ genotype. In order to support an application for FDA approval of our LentiGlobin product candidate in patients with TDT and a $^{0}/^{0}$ genotype, we initiated the HGB-212 study, but we do not know if or when our LentiGlobin product candidate may be commercially available to patients with all genotypes.

* The results from our Starbeam Study may not be sufficiently robust to support the submission of marketing approval for our Lenti-D product candidate.

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

The Starbeam Study was not designed to achieve a statistically significant efficacy determination. Rather, we anticipate that the safety and efficacy of our Lenti-D product candidate will be evaluated in light of the data collected in our observational ALD-103 study. We expect that the FDA will assess the totality of the safety and efficacy data from our CALD clinical studies in reviewing any future BLA submission for our Lenti-D product candidate. Based on this assessment, the FDA may require that we conduct additional clinical studies prior to submitting or approving a BLA for this indication.

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

We cannot be certain that our Northstar-2 Study in patients with TDT and a non-$^0/^0$ genotype, or our Northstar-3 Study in patients with TDT and a $^0/^0$ genotype, together with data from our Northstar Study and HGB-205 study, will be sufficient to form the basis for a BLA submission for our LentiGlobin product candidate.

In general, the FDA requires the successful completion of two pivotal trials to support approval of a BLA, but in certain circumstances, will approve a BLA based on only one pivotal trial. If successful, we believe the results from our ongoing Northstar-2 Study, together with data from our Northstar Study and ongoing HGB-205 study, could be sufficient to form the basis for a BLA submission for our LentiGlobin product candidate to treat adult and adolescent patients with TDT and a non-$^0/^0$ genotype. In addition, if successful, we believe the results from our Northstar-3 Study, together with data from our Northstar Study and ongoing Northstar-2 Study, could be sufficient to form the basis for a BLA supplement submission for our LentiGlobin product candidate to treat patients with TDT and a $^0/^0$ genotype. However, it should be noted that our ability to submit and obtain approval of a BLA is ultimately an FDA review decision, which will be dependent upon the data available at such time, and the available data may not be sufficiently robust from a safety and/or efficacy perspective to support the submission or approval of a BLA. Depending on the outcome of these ongoing clinical studies, the FDA may require that we conduct additional or larger pivotal trials before we can submit or obtain approval for a BLA for our LentiGlobin product candidate for the treatment of TDT.

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

The EMA Adaptive Pathways pilot 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 through iterative extension of the indication, 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 the use in of medicinal product in patients. Based on our discussions with the EMA, we believe that we may be able to seek conditional approval for our LentiGlobin product candidate, with our refined manufacturing process, for the treatment of adult and adolescent subjects with TDT and a non- $^{0}/_{0}$ genotype on the basis of the totality of the clinical data from our ongoing studies with LentiGlobin. For efficacy, we believe that the Northstar Study and supportive ongoing HGB-205 study, together with the data available from our ongoing Northstar-2 Study and our long-term follow-up study LTF-303, could support the filing of a marketing authorization application in the European Union. This plan is contingent upon all of the studies conducted in patients with TDT with the LentiGlobin product candidate demonstrating sufficient efficacy and safety, and in particular, transfusion independence and reduction in transfusion requirements, for efficacy analyses in the Northstar, HGB-205 and Northstar-2 studies.

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

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

The manufacturing processes for our lentiviral vectors and our product candidates are complex. We have developed and have implemented an improved manufacturing process of our LentiGlobin drug product that is being administered in our Northstar-2 Study in patients with TDT and a non-$^{0}/^{0}$ genotype, our amended ongoing HGB-206 study in patients with severe SCD, and our Northstar-3 Study in patients with TDT and a $^{0}/^{0}$ genotype. The LentiGlobin drug product manufactured using the improved manufacturing process may not lead to similar or improved efficacy or safety results in subjects, as compared to the LentiGlobin drug product used in the Northstar Study, the ongoing HGB-205 study, or the HGB-206 study under the original protocol.

As we develop a commercial-scale manufacturing process for our LentiGlobin and Lenti-D product candidates, we are implementing improvements to the manufacturing process for both producing our lentiviral vectors and for our product candidates on a continual basis. In some circumstances, changes in the manufacturing process may require us to perform additional comparability studies or to collect additional clinical data from patients prior to undertaking additional clinical studies or filing for regulatory approval. These requirements may lead to delays in our clinical development and commercialization plans.

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

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

These well-publicized adverse events led to the development of new viral vectors, such as lentiviral vectors, with improved safety profiles and also the requirement of enhanced safety monitoring in gene therapy clinical trials, including periodic analyses of the therapy’s genetic insertion sites. In published studies, lentiviral vectors have demonstrated an improved safety profile over gamma-retroviral vectors, with no disclosed events of gene therapy-related adverse events, which we believe is due to a number of factors including the tendency of these vectors to integrate within genes rather than in areas that control gene expression, as well as their lack of strong viral

enhancers. However, it should be noted that in our Phase I/II study (the LG001 Study) of autologous HSCs transduced ex vivo using an earlier generation of our LentiGlobin vector, called HPV569, we initially observed in one subject that a disproportionate number of the cells expressing our functional gene had the same insertion site. Tests showed that this partial clonal dominance contained an insertion of the functional gene in the HMGA2 gene that persisted for a period of two to three years. Although there was some initial concern that the observed clonal dominance might represent a pre-leukemic event, there have been no adverse clinical consequences of this event, or any signs of cancer, in over seven years since the observation was made. The presence of the HMGA2 clone has steadily declined in this subject over time to the point that it is no longer the most common clone observed in this subject.

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

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

The bb2121 and bb21217 product candidates are chimeric antigen receptor, or CAR, T cell-based immunotherapies. In previous and ongoing clinical studies involving CAR T cell products, many subjects experienced side effects such as neurotoxicity and cytokine release syndrome, which have in some cases resulted in clinical holds in ongoing clinical trials of CAR T product candidates. There have been life threatening events related to severe neurotoxicity and cytokine release syndrome, requiring intense medical intervention such as intubation or pressor support, and in several cases, resulted in death. Severe neurotoxicity is a condition that is currently defined clinically by cerebral edema, confusion, drowsiness, speech impairment, tremors, seizures, or other central nervous system side effects, when such side effects are serious enough to lead to intensive care. In some cases, severe neurotoxicity was thought to be associated with the use of certain lymphodepletion regimens used prior to the administration of the CAR T cell products. Cytokine release syndrome is a condition that is currently defined clinically by certain symptoms related to the release of cytokines, which can include fever, chills, low blood pressure, when such side effects are serious enough to lead to intensive care with mechanical ventilation or significant vasopressor support. The exact cause or causes of cytokine release syndrome and severe neurotoxicity in connection with treatment of CAR T cell products is not fully understood at this time. In addition, subjects have experienced other adverse events in these studies, such as a reduction in the number of blood cells (in the form of neutropenia, thrombocytopenia, anemia or other cytopenias), febrile neutropenia, chemical laboratory abnormalities (including elevated liver enzymes), and renal failure.

Undesirable side effects caused by the bb2121 or bb21217 product candidate, other CAR T product candidates targeting BCMA, or our other T cell-based immunotherapy product candidates, could cause us or regulatory authorities to interrupt, delay or halt clinical studies and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign regulatory authorities. Results of our studies could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Treatment-related side effects could also affect patient recruitment or the ability of enrolled subjects to complete the studies or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff, as toxicities resulting from T cell-based immunotherapies are not normally encountered in the general patient population and by medical personnel. We expect to have to train medical personnel regarding our T cell-based immunotherapy product candidates to understand their side effects for both our planned clinical trials and upon any commercialization of any T cell-based immunotherapy product candidates. Inadequate training in recognizing or managing the potential side effects of T cell-based immunotherapy product candidates could result in patient deaths. Any of these occurrences may harm our business, financial condition and prospects significantly.

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

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

that are necessary or desirable for the successful commercialization of our treatment candidates. For example, the development of our product candidates for pediatric use is an important part of our current business strategy, and if we are unable to obtain regulatory approval for the desired age ranges, our business may suffer.

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

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

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

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

- issue a warning letter asserting that we are in violation of the law;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical studies;
- refuse to approve a pending marketing application, such as a BLA or supplements to a BLA submitted by us;
- seize product; or
- refuse to allow us to enter into supply contracts, including government contracts.

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

Risks related to our reliance on third parties

We expect to rely on third parties to conduct some or all aspects of our viral 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 viral vector production, drug 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, and that our viral vectors and drug products are manufactured in accordance with GMP as applied in the relevant jurisdictions.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines, conduct our studies in accordance with regulatory requirements or our stated study plans and protocols, or manufacture our viral vectors and drug products in accordance with GMP, we will not be able to complete, or may be delayed in completing, the preclinical and clinical studies and manufacturing process validation activities required to support future IND, MAA 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 are dependent on Celgene for the successful development and commercialization of bb2121 and bb21217. If Celgene does not devote sufficient resources to the development of bb2121 and bb21217, is unsuccessful in its efforts, or chooses to terminate its agreements with us, our business will be materially harmed.

We are co-developing and co-promoting the bb2121 product candidate in the United States with Celgene under our amended and restated co-development and co-promotion agreement with Celgene, or the bb2121 CCPS. Under the bb2121 CCPS, we and Celgene share the obligation to develop and commercialize the bb2121 product candidate in the United States, and we will be solely dependent on Celgene to develop and commercialize bb2121 outside of the United States.

In addition, we have exclusively licensed to Celgene the right to develop and commercialize the bb21217 product candidate, and we retain an option to co-develop and co-promote bb21217 in the United States under our license agreement and collaboration agreement with Celgene. With respect to bb21217, we are responsible for completing the ongoing CRB-402 study, but Celgene is responsible for further clinical development and commercialization costs, unless we choose to exercise our option to co-develop and co-promote bb21217 in the United States. If we exercise our option to co-develop and co-promote bb21217 in the United States, we and Celgene will share the obligation to develop and commercialize bb21217 in the United States, and we will be solely dependent on Celgene to develop and commercialize bb21217 outside of the United States.

In our partnership with Celgene, Celgene is obligated to use commercially reasonable efforts to develop and commercialize bb2121 and bb21217. Celgene may determine however, that it is commercially reasonable to develop and commercialize a next-generation product candidate, rather than continue the development of bb2121 and bb21217. Alternatively, Celgene may determine that it is not commercially reasonable to continue development of any product candidates that arise from our collaboration. These outcomes may occur for many reasons, including internal business reasons, results from clinical trials or because of unfavorable regulatory feedback. Further, on review of the safety and efficacy data, the FDA may impose requirements on the clinical trial program that render such a program commercially nonviable. In addition, under our agreements with Celgene, Celgene may determine the development plan and activities for that product candidate. We may disagree with Celgene about the development strategy it employs, but we will have limited rights to impose our development strategy on Celgene. Similarly, Celgene may decide to seek regulatory approval for, and limit commercialization of, bb2121 or bb21217 to narrower indications than we would pursue. More broadly, if Celgene elects to discontinue the development of bb2121 or bb21217, we may be unable to advance the product candidate ourselves. We would also be prevented from developing or commercializing another CAR T cell-based product candidate that targets BCMA outside of our collaboration with Celgene.

This partnership may not be scientifically or commercially successful for us due to a number of important factors, including the following:

- Celgene has wide discretion in determining the efforts and resources that it will apply to its partnership with us. The timing and amount of any development milestones, and downstream commercial profits, milestones and royalties that we may receive under such partnership will depend on, among other things, Celgene's efforts, allocation of resources and successful development and commercialization of bb2121, bb21217 and other product candidates that are the subject of its collaboration with us.
- Celgene may develop and commercialize, either alone or with others, products that are similar to or competitive with bb2121, bb21217 and other product candidates that are the subject of its collaboration with us. For example, Celgene is currently commercializing certain of its existing products, including lenalidomide and pomalidomide, for certain patients with relapsed/refractory multiple myeloma and is also developing JCAR-H125, another CAR-T product candidate targeting BCMA that it obtained through its acquisition of Juno Therapeutics, Inc. in March 2018.
- Celgene may terminate its partnership with us without cause and for circumstances outside of our control, which could make it difficult for us to attract new strategic partners or adversely affect how we are perceived in scientific and financial communities.
- Celgene may develop or commercialize our product candidates in such a way as to elicit litigation that could jeopardize or invalidate our intellectual property rights or expose us to potential liability.
- Celgene may not comply with all applicable regulatory requirements, or may fail to report safety data in accordance with all applicable regulatory requirements.
- If Celgene were to breach its arrangements with us, we may need to enforce our right to terminate the agreement in legal proceedings, which could be costly and cause delay in our ability to receive rights back to the relevant product candidates. If we were to terminate an agreement with Celgene due to Celgene's breach or Celgene terminated the agreement without cause, the development and commercialization of bb2121 or bb21217 product candidates that are

the subject of its collaboration with us could be delayed, curtailed or terminated because we may not have sufficient financial resources or capabilities to continue development and commercialization of these product candidates on our own if we choose not to, or are unable to, enter into a new collaboration for these product candidates.

- Celgene may enter into one or more transactions with third parties, including a merger, consolidation, reorganization, sale of substantial assets, sale of substantial stock or other change in control, which could divert the attention of its management and adversely affect Celgene's ability to retain and motivate key personnel who are important to the continued development of the programs under the strategic partnership with us. In addition, the third-party to any such transaction could determine to reprioritize Celgene's development programs such that Celgene ceases to diligently pursue the development of our programs and/or cause the respective collaboration with us to terminate.

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, as well as on third parties to administer our products to patients when and if our products are introduced into market. Any performance failure on the part of these third parties 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 $261.1 million for the six months ended June 30, 2018. As of June 30, 2018, we had an accumulated deficit of $1.2 billion.

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, including the bb2121 product candidate that we are co-developing with Celgene;
- expand the scope of our current clinical studies for our product candidates, including the bb2121 product candidate that we are co-developing with Celgene;
- initiate additional preclinical, clinical or other studies for our oncology product candidates;
- further develop the manufacturing process for our vectors or our product candidates;
    - change or add additional manufacturers or suppliers;
- seek regulatory and marketing approvals for our product candidates that successfully complete clinical studies;
- seek to identify and validate additional product candidates;
- acquire or in-license other product candidates and technologies;
- make milestone or other payments under any license agreements or our Stock Purchase Agreement with the former equityholders of Pregenen;
- maintain, protect and expand our intellectual property portfolio;
- establish a sales, marketing and distribution infrastructure in the United States and Europe to commercialize any products for which we may obtain marketing approval;
- attract and retain skilled personnel;
- build additional infrastructure to support our operations as a public company and our product development and planned future commercialization efforts, including manufacturing capacity at third-party manufacturers or potentially our own manufacturing facility; 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.

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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 private and governmental payors;
- obtaining market acceptance and adoption 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.

We expect to continue to incur significant expenditures for the foreseeable future, and we expect these expenditures to increase as we prepare for any potential commercial launch. Our expenses could increase beyond expectations if we are required by the FDA, the EMA, or other regulatory agencies, domestic or foreign, to perform clinical and other studies in addition to those that we currently anticipate. Even if 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, which costs may increase with any increased competition. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations.

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

We are currently advancing the LentiGlobin, Lenti-D, bb2121 and bb21217 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, 2018, our cash, cash equivalents and marketable securities were $1.46 billion. In July 2018, we sold 3.9 million shares of common stock (inclusive of shares sold pursuant to an overallotment option granted to the underwriters in connection with the offering) through an underwritten public offering at a price of $162.50 per share for aggregate net proceeds of $600.6 million. As a result, we expect that our existing cash, cash equivalents, and marketable securities will be sufficient to fund our current operations into 2022. 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 a mix of internal and third-party manufacturers to produce our vector, product candidates and other key materials, but we are still in the process of building out our internal capacity and also have not entered into binding agreements with all of the manufacturers needed to support commercialization. Additionally, neither we nor these manufacturers 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 reliable manufacturing capabilities for commercial quantities of our viral vectors or established transduction facilities in all of the desired commercialization regions to support commercialization of our products. Although we intend to rely on a mix of internal and third-party manufacturers for commercialization, we are still in the process of building out our internal capacity and also have not entered into binding agreements with all of the manufacturers needed to support our planned commercialization activities, and may not be able to timely or successfully build out our internal capacity, or negotiate binding agreements at commercially reasonable terms.

No manufacturer currently has the experience or ability to produce our vectors or drug product candidates at commercial levels. We are currently developing a commercial-scale manufacturing process for our LentiGlobin and Lenti-D product candidates, which we are transferring 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 we or our manufacturing partners do not obtain such regulatory approvals, our commercialization efforts will be harmed.

Additionally, since the HSCs and T cells 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 or successfully and timely develop our internal capacity, if we or 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. Furthermore, if we or our third-party manufacturers are unable to produce the necessary quantities of viral vectors or our product candidates in quantities, quality requirements, or within the time frames that we need to support our commercialization activities, it may result in delays in our development plans or increased capital expenditures.

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 us or 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.

Although we expect to begin building out our field team, we have no sales or distribution experience and only early capabilities for marketing and market access, and expect to invest significant financial and management resources to establish these capabilities. If we are unable to establish sales and distribution capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate any revenues.

Although we expect to begin building out our field team, we have no sales or distribution experience and only early capabilities for marketing and market access. To successfully commercialize any products that may result from our development programs, we will need to develop these capabilities in the United States, Europe and other regions, 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 a significant 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 for severe genetic and rare diseases and in the field of T cell-based immunotherapy, 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 in the areas of severe genetic diseases include Bellicum Pharmaceuticals, Inc., Acceleron Pharma, Inc. through their collaboration with Celgene Corporation, Orchard Therapeutics, Ltd. following their acquisition from GlaxoSmithKline of the product candidates and collaboration with TIGET, Sangamo BioSciences, Inc., through their collaboration with Sanofi, Novartis AG, Global Blood Therapeutics Inc., CRISPR Therapeutics AG, through their collaboration with Vertex Pharmaceuticals Incorporated, and in the area of anti-BCMA CAR-T therapies, Janssen Pharmaceuticals, Inc., through its collaboration with Nanjing Legend Biotech, Poseida Therapeutics Inc., Gilead Sciences, Inc., following their acquisition of Kite Pharma, Inc., Novartis AG, Adaptimmune Therapeutics plc, and Celgene Corporation following their acquisition of Juno Therapeutics, Inc. 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, manufacturing capabilities, 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 pathway could allow competitors to reference data from biological products already approved after 12 years from the time of approval. 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 our 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. For instance, UniQure encountered challenges in commercializing Glybera, the first approved gene therapy in Europe, and announced in 2017 that it will not seek renewal of Glybera's marketing authorization in Europe when it expired in October 2017, due to limited use since it was approved in 2012, and forecasted patient demand. Our efforts to educate the marketplace may require more resources than are required by the conventional technologies marketed by our competitors.

We intend to market our products outside of the United States, and we will be subject to the risks of doing business outside of the United States.

Because we intend to market our product candidates, if approved, outside of the United States, our business is subject to risks associated with doing business outside of the United States. Accordingly, our business and financial results in the future could be adversely affected due to a variety of factors, including:

- efforts to develop an international sales, marketing and distribution organization may increase our expenses, divert our management's attention from the acquisition or development of product candidates or cause us to forgo profitable licensing opportunities in these geographies;
- changes in a specific country's or region's political and cultural climate or economic condition;
- unexpected changes in foreign laws and regulatory requirements;
- difficulty of effective enforcement of contractual provisions in local jurisdictions;
- inadequate intellectual property protection in foreign countries;
- trade-protection measures, import or export licensing requirements such as Export Administration Regulations promulgated by the U.S. Department of Commerce and fines, penalties or suspension or revocation of export privileges;
- the effects of applicable foreign tax structures and potentially adverse tax consequences; and
- significant adverse changes in foreign currency exchange rates.

In addition to FDA and related regulatory requirements in the United States and abroad, we are subject to extensive additional federal, state and foreign anti-bribery regulation, which include the U.S. Foreign Corrupt Practices Act, the U.K. Bribery Act, and similar laws in other countries outside of the United States. We have developed and implemented a corporate compliance program based on what we believe are current best practices in the pharmaceutical industry for companies similar to ours, but we cannot guarantee that we, our employees, our consultants or our third-party contractors are or will be in compliance with all federal, state and foreign regulations regarding bribery and corruption. Moreover, our partners and third party contractors located outside the United States may have inadequate compliance programs or may fail to respect the laws and guidance of the territories in which they operate. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could also have an adverse effect on our business, financial condition and results of operations

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. In addition, because our CAR and TCR T cell product candidates represent new approaches to the treatment of cancer, we cannot accurately estimate the potential revenue. 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, certain countries, including a number of member states of the European Union, set prices and reimbursement for pharmaceutical products, or medicinal products, as they are commonly referred to in the European Union, with limited participation from the marketing authorization holders. We cannot be sure that such prices and reimbursement will be acceptable to us or our collaborators. If the regulatory authorities in these foreign jurisdictions set prices or reimbursement levels that are not commercially attractive for us or our collaborators, our revenues from sales by us or our collaborators, and the potential profitability of our drug products, in those countries would be negatively affected. An increasing number of countries are taking initiatives to attempt to reduce large budget deficits by focusing cost-cutting efforts on pharmaceuticals for their state-run health care systems. These international price control efforts have impacted all regions of the world, but have been most drastic in the European Union. Additionally, some countries require approval of the sale price of a product before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then may experience delays in the reimbursement approval of our product or be subject to price regulations that would delay our commercial launch of the product, possibly for lengthy time periods, which could negatively impact the revenues we are able to generate from the sale of the product in that particular country.

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.

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

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

In addition, other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. On August 2, 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation’s automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers up to 2% per fiscal year. On January 2, 2013, then President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, delayed for another two months the budget cuts mandated by these sequestration provisions of the Budget Control Act of 2011. On March 1, 2013, the President signed an executive order implementing sequestration, and on April 1, 2013, the 2% Medicare payment reductions went into effect. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures. For each state that does not choose to expand its Medicaid program, there may be fewer insured patients

overall, which could impact the sales, business and financial condition of manufacturers of branded prescription drugs or other therapies. Where patients receive insurance coverage under any of the new options made available through the Affordable Care Act, the possibility exists that manufacturers may be required to pay Medicaid rebates on that resulting drug utilization, a decision that could impact manufacturer revenues. Some of the provisions of the Affordable Care Act have yet to be fully implemented, while certain provisions have been subject to judicial and Congressional challenges. In January 2017, Congress voted to adopt a budget resolution for fiscal year 2017, that while not a law, is widely viewed as the first step toward the passage of legislation that would repeal certain aspects of the Affordable Care Act. Further, on January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the Affordable Care Act to waive, defer, grant exemptions from, or delay the implementation of any provision of the Affordable Care Act that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. Congress also could consider subsequent legislation to replace elements of the Affordable Care Act that are repealed. With the new Administration and Congress, there will likely be additional administrative or legislative changes, including modification, repeal, or replacement of all, or certain provisions of, the Affordable Care Act. However, it remains to be seen whether new legislation modifying the Affordable Care Act is enacted and, if so, precisely what the new legislation will provide, when it will be enacted and what impact it will have on the availability of healthcare and containing or lowering the cost of healthcare. The implications of a potential repeal and/or replacement of the Affordable Care Act, for our and our partners' business and financial condition, if any, are not yet clear.

The delivery of healthcare in the European Union, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to commercialize any products for which we obtain marketing approval.

We cannot predict what healthcare reform initiatives may be adopted in the future. Further federal, state and foreign legislative and regulatory developments are likely, and we expect ongoing initiatives to increase pressure on drug pricing. Such reforms could have an adverse effect on anticipated revenues from product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop product candidates.

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.

The market opportunities for our T cell-based immunotherapy product candidates may be limited to those patients who are ineligible for or have failed prior treatments and may be small.

The FDA often approves new therapies initially only for use in patients with relapsed or refractory advanced disease. We expect to initially seek approval of our T cell-based product candidates in cancer in this context. Subsequently, for those products that prove to be sufficiently beneficial, if any, we would expect to seek approval in earlier lines of treatment and potentially as a first line therapy, but there is no guarantee that our product candidates, even if approved, would be approved for earlier lines of therapy, and, prior to any such approvals, we may have to conduct additional clinical trials.

Our projections of both the number of people who have the cancers we may be targeting, as well as the subset of people with these cancers in a position to receive second or third line therapy, and who have the potential to benefit from treatment with our product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations, or market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these cancers. The number of patients may turn out to be lower than expected. Additionally, the potentially addressable patient population for our product candidates may be limited or may not be amenable to treatment with our product candidates. Even if we obtain significant market share for our product candidates, because the potential target populations are small, we may never achieve profitability without obtaining regulatory approval for additional indications.

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.

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, 2018, we had 600 full-time employees. As our business 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 the LentiGlobin, Lenti-D, bb2121 and bb21217 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 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.

Comprehensive Tax Reform Legislation Could Adversely Affect Our Business And Financial Condition.

On December 22, 2017, the “Tax Cuts and Jobs Act” (TCJA) was enacted. The TCJA significantly reforms the Internal Revenue Code of 1986, as amended (the “Code”). The TCJA, among other things, includes changes to U.S. federal tax rates, imposes significant additional limitations on the deductibility of interest and net operating loss carryforwards, allows for the expensing of capital expenditures, and puts into effect the migration from a “worldwide” system of taxation to a territorial system. Our net deferred tax assets and liabilities have been revalued at the newly enacted U.S. corporate tax rate, and the impact of the reduction to our deferred tax assets and associated valuation allowance was recognized in 2017. We continue to examine the impact this tax reform legislation may have on our business. The impact of this tax reform is uncertain and could be adverse.

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.

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions, ex parte reexaminations, post-grant review, and inter partes review proceedings before the U.S. Patent and Trademark Office, or U.S. PTO, and corresponding foreign patent offices. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are pursuing development candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods

for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire. Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, including combination therapy, the holders of any such patents may be able to block our ability to develop and commercialize the applicable product candidate unless we obtained a license or until such patent expires. In either case, such a license may not be available on commercially reasonable terms or at all.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

We may not be successful in obtaining or maintaining necessary rights to gene therapy product components and processes for our development pipeline through acquisitions and in-licenses.

Presently we have rights to the intellectual property, through licenses from third parties and under patents that we own, to develop our gene therapy product candidates. Because our programs may involve additional product candidates that may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license or use these proprietary rights. In addition, our product candidates may require specific formulations to work effectively and efficiently and these rights may be held by others. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities.

For example, we sometimes collaborate with U.S. and foreign academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution’s rights in technology resulting from the collaboration. Regardless of such right of first negotiation for intellectual property, we may be unable to negotiate a license within the specified time frame or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment. If we are unable to successfully obtain rights to required third-party intellectual property rights, our business, financial condition and prospects for growth could suffer.

If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We are a party to a number of intellectual property license agreements that are important to our business and expect to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose, various diligence, milestone payment, royalty and other obligations on us. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we would not be able to market products covered by the license.

We may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we have done so from time to time. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could harm our business significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our current product candidates or future products, resulting in either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties.

In many cases, patent prosecution of our licensed technology is controlled solely by the licensor. If our licensors fail to obtain and maintain patent or other protection for the proprietary intellectual property we license from them, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, and our competitors

could market competing products using the intellectual property. In certain cases, we control the prosecution of patents resulting from licensed technology. In the event we breach any of our obligations related to such prosecution, we may incur significant liability to our licensing partners. Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues and is complicated by the rapid pace of scientific discovery in our industry. Disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;

- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming and unsuccessful.

Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid, is unenforceable and/or is not infringed, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

Interference proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

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

Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law, including provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. The U.S. PTO is currently developing regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, were enacted March 16, 2013. However, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

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

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

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

We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property. We have had in the past, and we may also have to in the future, ownership disputes arising, for example, from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

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

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

Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court.

If we or one of our licensing partners initiated legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including patent eligible subject matter, lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the U.S. PTO, or made a misleading statement, during prosecution. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post grant review, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection would have a material adverse impact on our business.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involve both technological and legal complexity, and is therefore obtaining and enforcing biotechnology patents is costly, time-consuming and inherently uncertain. In addition, the United States has recently enacted and is currently implementing wide-ranging patent reform legislation. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts, and the U.S. PTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

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

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal

and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

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

Risks related to ownership of our common stock

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

Companies trading in the stock market in general, and The NASDAQ Global Select Market in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and biotechnology and pharmaceutical industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance.

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

- adverse results or delays in preclinical or clinical studies;
- reports of adverse events in other gene therapy products or clinical studies of such products;
- inability to obtain additional funding;
- any delay in filing an IND, MAA or BLA for any of our product candidates and any adverse development or perceived adverse development with respect to the FDA's review of that IND, MAA or BLA;
- failure to develop successfully and commercialize our product candidates;
- failure to maintain our existing strategic collaborations or enter into new collaborations;
- failure by us or our licensors and strategic collaboration partners to prosecute, maintain or enforce our intellectual property rights;
- changes in laws or regulations applicable to future products;
- inability to obtain adequate product supply for our product candidates or the inability to do so at acceptable prices;
- adverse regulatory decisions;
- introduction of new products, services or technologies by our competitors;
- failure to meet or exceed financial projections we may provide to the public;
- failure to meet or exceed the financial projections of the investment community;
- the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;

- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us, our strategic collaboration partner or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;

- additions or departures of key scientific or management personnel;
- significant lawsuits, including patent or stockholder litigation;
- changes in the market valuations of similar companies;
- sales of our common stock by us or our stockholders in the future; and
- trading volume of our common stock.

Actual or potential sales of our common stock by our employees, including our executive officers, pursuant to pre-arranged stock trading plans could cause our stock price to fall or prevent it from increasing for numerous reasons, and actual or potential sales by such persons could be viewed negatively by other investors.

In accordance with the guidelines specified under Rule 10b5-1 of the Securities Exchange Act of 1934, as amended, and our policies regarding stock transactions, a number of our employees, including executive officers and members of our board of directors, have adopted and may continue to adopt stock trading plans pursuant to which they have arranged to sell shares of our common stock from time to time in the future. Generally, sales under such plans by our executive officers and directors require public filings. Actual or potential sales of our common stock by such persons could cause the price of our common stock to fall or prevent it from increasing for numerous reasons.

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

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

Pursuant to our 2013 Stock Option and Incentive Plan, or the 2013 Plan, our management is authorized to grant stock options and other equity-based awards to our employees, directors and consultants. The number of shares available for future grant under the 2013 Plan automatically increases each year by up to 4% of all shares of our capital stock outstanding as of December 31 of the prior calendar year, subject to the ability of our board of directors or compensation committee to take action to reduce the size of the increase in any given year. Currently, we plan to register the increased number of shares available for issuance under the 2013 Plan each year. If our board of directors or compensation committee elects to increase the number of shares available for future grant by the maximum amount each year, our stockholders may experience additional dilution, which could cause our stock price to fall. We also have an Employee Stock Purchase Plan and any shares of common stock purchased pursuant to that plan will also cause dilution.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and pharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management’s attention and resources, which could harm our business.

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

Under Section 382 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an “ownership change,” generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the

corporation's ability to use its pre-change net operating loss carryforwards, or NOLs, and other pre-change tax attributes (such as research tax credits) to offset its post-change income may be limited. We have completed several financings since our inception which we believe have resulted in a change in control as defined by IRC Section 382. We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership. As a result, if we earn net taxable income, our ability to use our pre-change net operating loss carryforwards to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. The TCJA also reduced the corporate income tax rate to 21%, from a prior rate of 35%. This may cause a reduction in the economic benefit of our NOLs and other deferred tax assets available to us. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.

We have never declared or paid any cash dividends on our common stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock.

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

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

- authorize "blank check" preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;
- create a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our board of directors, the chairperson of our board of directors, our chief executive officer or our president;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- provide that our directors may be removed only for cause;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- specify that no stockholder is permitted to cumulate votes at any election of directors;
- expressly authorize our board of directors to modify, alter or repeal our amended and restated by-laws; and
- require supermajority votes of the holders of our common stock to amend specified provisions of our amended and restated certificate of incorporation and amended and restated by-laws.

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

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

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

Item 2. Unregistered Sales of Equity Securities and Uses of Proceeds

None

Item 3. Defaults Upon Senior Securities

None

Item 4. Mine Safety Disclosures

None

Item 5. Other Information

Our policy governing transactions in our securities by our directors, officers, and employees permits our officers, directors and certain other persons to enter into trading plans complying with Rule 10b5-1 under the Securities Exchange Act of 1934, as amended. We have been advised that certain of our officers (including David Davidson (Chief Medical Officer), Philip Gregory (Chief Scientific Officer), Susanna High (Chief Operating Officer), and Jeffrey Walsh (Chief Financial & Strategy Officer)), and certain of our directors (including James Mandell) have entered into trading plans covering periods after the date of this Quarterly Report on Form 10-Q in accordance with Rule 10b5-1 and our policy governing transactions in our securities. Generally, under these trading plans, the individual relinquishes control over the transactions once the trading plan is put into place. Accordingly, sales under these plans may occur at any time, including possibly before, simultaneously with, or immediately after significant events involving our company. We do not undertake to report Rule 10b5-1 trading plans that may be adopted by any officers or directors in the future, or to report any modifications or termination of any publicly announced trading plan, except to the extent required by law.

Item 6. Exhibits

The exhibits filed as part of this Quarterly Report on Form 10-Q are set forth in the Exhibit Index below, which is incorporated herein by reference.

Exhibit Index

Exhibit Number	Exhibit Title	Incorporated by Reference Form	File no.	Exhibit	Filing Date
2.1	Stock Purchase Agreement by and between the Registrant and Precision Genome Engineering, Inc.	8-K	001-35966	2.1	June 30, 2014
3.1	Amended and Restated Certificate of Incorporation of the Registrant	8-K	001-35966	3.1	June 24, 2013
3.2	Amended and Restated By-laws of the Registrant	8-K	001-35966	3.2	June 24, 2013
3.3	Amendment No. 1 to Amended and Restated By-laws of the Registrant	8-K	001-35966	3.1	February 11, 2016
4.1	Specimen Common Stock Certificate	S-1/A	333-188605	4.1	June 4, 2013
4.2	Amended and Restated Investors' Rights Agreement, dated as of July 23, 2012, by and among the Registrant and the Investors listed therein.	S-1	333-188605	4.5	May 14, 2013
4.3	Amendment to Amended and Restated Investors' Rights Agreement, dated as of July 8, 2014, by and among the Registrant and the Investors listed therein.	10-Q	001-35966	4.6	August 12, 2014
10.1#	Second Amended and Restated 2002 Employee, Director and Consultant Plan, as amended, and forms of award agreement thereunder	S-1	333-188605	10.1	May 14, 2013
10.2#	2010 Stock Option and Grant Plan, as amended, and forms of award agreement thereunder	S-1	333-188605	10.2	May 14, 2013
10.3#	2013 Stock Option and Incentive Plan and forms of award agreement thereunder	S-1/A	333-188605	10.3	June 4, 2013
10.4	Form of Indemnification Agreement between the Registrant and each of its Executive Officers and Directors	S-1	333-188605	10.4	May 14, 2013
10.5	Amended and Restated Lease Agreement, dated May 18, 2007, by and between the Registrant and Rivertech Associates II, LLC, as amended	10-Q	001-35966	10.1	November 14, 2013
10.6†	Patent License Agreement, dated December 11, 1996, by and between the Registrant (formerly known as Genetix	S-1	333-188605	10.6	May 14, 2013

	Pharmaceuticals Inc., successor-in-interest to Innogene Pharmaceuticals Inc.) and Massachusetts Institute of Technology, as amended				
10.7†	Fourth Amendment to Patent License Agreement, dated October 28, 2016, by and between the Registrant and Massachusetts Institute of Technology	10-K	001-35966	10.7	February 22, 2017
10.8†	Patent and Know-How License Agreement No. 07554F30, dated May 14, 2009, by and between the Registrant (formerly known as Genetix Pharmaceuticals Inc.) and INSERM-TRANSFERT, as amended	S-1	333-188605	10.7	May 14, 2013
10.9†	License Agreement, dated September 13, 2011, by and between the Registrant and Institut Pasteur, as amended	S-1	333-188605	10.8	May 14, 2013
10.10†	Amendment No. 3 to License Agreement, dated September 10, 2013, by and between the Registrant and Institut Pasteur	10-Q	001-35966	10.2	November 14, 2013
10.11†	Amendment No. 4 to License Agreement, dated April 1, 2015, by and between the Registrant and Institut Pasteur	10-Q	001-35966	10.10	May 6, 2015
10.12†	License Agreement, dated December 7, 2011, by and between the Registrant and Research Development Foundation	S-1	333-188605	10.9	May 14, 2013

Exhibit Number	Exhibit Title	Incorporated by Reference			
		Form	File no.	Exhibit	Filing Date
10.13†	Novation Agreement, dated April 2, 2012, by and between the Registrant and The Board of Trustees of the Leland Stanford Junior University	S-1	333-188605	10.10	May 14, 2013
10.14†	Master Collaboration Agreement by and between the Registrant and Celgene Corporation, dated March 19, 2013	S-1	333-188605	10.11	May 14, 2013
10.15†	Amended and Restated Master Collaboration Agreement by and between the Registrant and Celgene Corporation, dated June 3, 2015	10-Q	001-35966	10.14	August 7, 2015
10.16	Amendment No. 1 to Amended and Restated Master Collaboration Agreement by and between the Registrant and Celgene Corporation, dated February 17, 2016	10-Q	001-35966	10.15	May 4, 2016
10.17	Amendment No. 2 to Amended and Restated Master Collaboration Agreement by and between the Registrant and Celgene Corporation, dated September 28, 2017	10-Q	001-35966	10.17	November 1, 2017
10.18†	Amended and Restated License Agreement by and between the Registrant and Celgene Corporation, dated February 16, 2016	10-Q/A	001-35966	10.16	November 2, 2016
10.19†	Amended and Restated License Agreement by and between the Registrant and Celgene Corporation, dated September 28, 2017	10-Q	001-35966	10.19	November 1, 2017
10.20†	Amended and Restated Co-Development, Co-Promote and Profit Share Agreement by and between the Registrant and Celgene Corporation and Celgene European Investment Company LLC, dated March 26, 2018	10-Q	001-35966	10.20	May 2, 2018
10.21†	License Agreement by and between the Registrant and Biogen Idec MA Inc., dated August 13, 2014	10-Q/A	001-35966	10.17	November 2, 2016
10.22†	Letter Agreement by and between the Registrant and Biogen MA Inc., dated September 29, 2017	10-Q	001-35966	10.21	November 1, 2017
10.23†	Exclusive Patent License Agreement by and between the Registrant and the National Institutes of Health, dated August 31, 2015	10-Q/A	001-35966	10.18	November 2, 2016
10.24#	Amended and Restated Employment Agreement by and between the Registrant and Nick Leschly	S-1/A	333-188605	10.12	June 4, 2013

10.25#	Amended and Restated Employment Agreement by and between the Registrant and Jeffrey T. Walsh	S-1/A	333-188605	10.13	June 4, 2013
10.26#	Amended and Restated Employment Agreement by and between the Registrant and Mitch Finer	S-1/A	333-188605	10.14	June 4, 2013
10.27#	Transitional Services and Separation Agreement by and between the Registrant and Mitch Finer	10-Q	001-35966	10.17	May 6, 2015
10.28#	Amended and Restated Employment Agreement by and between the Registrant and David M. Davidson, M.D.	S-1/A	333-188605	10.15	June 4, 2013
10.29#	Employment Agreement, dated February 3, 2014, by and between the Registrant and Jason F. Cole	10-Q	001-35966	10.18	May 13, 2014
10.30#	Amendment to Employment Agreement, dated March 7, 2016, by and between the Registrant and Jason F. Cole	10-Q	001-35966	10.25	May 4, 2016
10.31#	Amendment No. 2 to Employment Agreement, dated November 3, 2016, by and between the Registrant and Jason F. Cole	10-K	001-35966	10.27	February 22, 2017
10.32#	Employment Agreement, dated October 20, 2014, by and between the Registrant and James DeTore	8-K	001-35966	10.1	November 10, 2014

Exhibit Number	Exhibit Title	Incorporated by Reference Form	File no.	Exhibit	Filing Date
10.33#	Separation Agreement, dated February 24, 2016, by and between the Registrant and James DeTore	10-Q	001-35966	10.27	May 4, 2016
10.34#	Employment Agreement, dated May 30, 2015, by and between the Registrant and Philip D. Gregory	10-Q	001-35966	10.21	August 7, 2015
10.35#	Amendment to Employment Agreement, dated November 3, 2016, by and between the Registrant and Philip D. Gregory	10-K	001-35966	10.31	February 22, 2017
10.36#	Employment Agreement, dated November 23, 2016, by and between the Registrant and Susanna High	10-K	001-35966	10.32	February 22, 2017
10.37#	Offer Letter, dated October 14, 2013, by and between the Registrant and Eric Sullivan	10-Q	001-35966	10.19	May 13, 2014
10.38#	2013 Employee Stock Purchase Plan	S-1/A	333-188605	10.17	June 4, 2013
10.39#	First Amendment of the Bluebird Bio, Inc. 2013 Employee Stock Purchase Plan	10-K	001-35966	10.38	February 21, 2018
10.40#	Offer Letter, dated November 16, 2017, by and between the Registrant and Kory Wentworth	10-K	001-35966	10.39	February 21, 2018
10.41#	Executive Cash Incentive Bonus Plan	S-1	333-188605	10.18	May 14, 2013
10.42	Lease, dated June 3, 2013, by and between the Registrant and 150 Second Street, LLC, as amended	S-1/A	333-188605	10.19	June 4, 2013
10.43	Lease Amendment, dated November 15, 2013, by and between the Registrant and 150 Second Street, LLC, as amended	10-K	001-35966	10.19	March 5, 2014
10.44	Lease Amendment, dated June 9, 2014, by and between the Registrant and 150 Second Street, LLC, as amended	10-Q	001-35966	10.24	August 12, 2014
10.45	Consent to Assignment, dated September 30, 2016, by and among the Registrant, ARE-MA Region No. 50, LLC, and Foundation Medicine, Inc.	10-Q	001-35966	10.35	November 2, 2016
10.46	Assignment and Assumption of Lease, dated September 30, 2016, by and between the Registrant and Foundation Medicine, Inc.	10-Q	001-35966	10.36	November 2, 2016
10.47		10-Q	001-35966	10.29	

	Lease, dated June 29, 2015, by and between the Registrant and ARE-MA Region No. 38, LLC				August 7, 2015
10.48†	Lease, dated September 21, 2015, by and between the Registrant and ARE-MA Region No. 40 LLC	10-Q	001-35966	10.30	November 5, 2015
10.49	First Amendment to Lease, dated June 21, 2016, by and between the Registrant and ARE-MA Region No. 40 LLC	10-Q	001-35966	10.37	August 3, 2016
10.50	Second Amendment to Lease, dated November 14, 2016, by and between the Registrant and ARE-MA Region No. 40 LLC	10-K	001-35966	10.44	February 22, 2017
10.51	Termination of Lease, dated February 10, 2017, by and between the Registrant and ARE-MA Region No. 38, LLC	10-K	001-35966	10.45	February 22, 2017
31.1	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	—	—	—	Filed herewith
31.2	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	—	—	—	Filed herewith

Exhibit Number	Exhibit Title	Incorporated by Reference Form	File no.	Exhibit	Filing Date
32.1	Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	—	—	—	Furnished herewith
101	The following materials from the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2018, formatted in XBRL (eXtensible Business Reporting Language): (i) Condensed Consolidated Balance Sheets, (ii) Condensed Consolidated Statements of Operations and Comprehensive Loss, (iii) Condensed Consolidated Statements of Cash Flows and (iv) Notes to Condensed Consolidated Financial Statements.	—	—	—	Filed herewith

†Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment and this exhibit has been submitted separately to the SEC.

#Indicates a management contract or any compensatory plan, contract or arrangement.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

bluebird bio, Inc.

Date: August 2, 2018 By: /s/ Nick Leschly

Nick Leschly

President, Chief Executive Officer and Director (Principal Executive Officer and Duly Authorized Officer)

Date: August 2, 2018 By: /s/ Jeffrey Walsh

Jeffrey Walsh

Chief Financial and Strategy Officer (Principal Financial Officer and Duly Authorized Officer)