bluebird bio, Inc.
Form 10-Q
May 03, 2019
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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 March 31, 2019

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 every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes No

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, 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	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

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.01 par value per share	BLUE	The NASDAQ Global Select Market LLC

As of April 26, 2019, there were 55,123,256 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 March 31, 2019	As of December 31, 2018
Assets		
Current Assets:		
Cash and cash equivalents	$221,738	$402,579
Marketable securities	1,100,079	982,725
Prepaid expenses	23,766	19,762
Receivables and other current assets	19,449	13,931
Total current assets	1,365,032	1,418,997
Marketable securities	408,949	506,123
Property, plant and equipment, net	114,030	246,622
Intangible assets, net	12,228	13,169
Goodwill	13,128	13,128
Operating lease right-of-use assets	184,618	—
Restricted cash and other non-current assets	40,630	44,805
Total assets	$2,138,615	$2,242,844
Liabilities and Stockholders' Equity		
Current Liabilities:		
Accounts payable	$30,241	$17,831
Accrued expenses and other current liabilities	76,152	99,393
Operating lease liability, current portion	17,566	—
Deferred revenue, current portion	11,490	18,602
Collaboration research advancement, current portion	11,242	10,605
Total current liabilities	146,691	146,431
Deferred revenue, net of current portion	14,777	16,338
Collaboration research advancement, net of current portion	30,746	33,349
Contingent consideration	5,526	5,230
Operating lease liability, net of current portion	168,200	—
Financing lease obligation, net of current portion	—	153,319
Other non-current liabilities	576	3,107
Total liabilities	366,516	357,774
Commitments and contingencies (Note 8)		

Stockholders' Equity:		
Preferred stock, $0.01 par value, 5,000 shares authorized; 0 shares issued and outstanding at March 31, 2019 and December 31, 2018	—	—
Common stock, $0.01 par value, 125,000 shares authorized; 55,069 and 54,738 shares issued and outstanding at March 31, 2019 and December 31, 2018, respectively	551	547
Additional paid-in capital	3,430,030	3,386,958
Accumulated other comprehensive loss	(1,792)	(3,627)
Accumulated deficit	(1,656,690)	(1,498,808)
Total stockholders' equity	1,772,099	1,885,070
Total liabilities and stockholders' equity	$2,138,615	$2,242,844

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 March 31,	
	2019	2018
Revenue:		
Collaboration revenue	$11,177	$15,608
License and royalty revenue	1,294	349
Total revenues	12,471	15,957
Operating expenses:		
Research and development	122,640	97,109
General and administrative	60,279	34,926
Cost of license and royalty revenue	430	17
Change in fair value of contingent consideration	296	534
Total operating expenses	183,645	132,586
Loss from operations	(171,174)	(116,629)
Interest income, net	10,102	1,388
Other (expense) income, net	(3,389)	115
Loss before income taxes	(164,461)	(115,126)
Income tax benefit	15	—
Net loss	$(164,446)	$(115,126)
Net loss per share - basic and diluted:	$(2.99)	$(2.31)
Weighted-average number of common shares used in computing net loss per share - basic and diluted:	54,957	49,923
Other comprehensive income (loss):		
Other comprehensive income (loss), net of tax expense of $0.4 million and $0.0 million for the three months ended March 31, 2019 and 2018, respectively	1,835	(844)
Total other comprehensive income (loss)	1,835	(844)
Comprehensive loss	$(162,611)	$(115,970)

See accompanying notes to unaudited condensed consolidated financial statements.

bluebird bio, Inc.

Condensed Consolidated Statements of Stockholders' Equity

(unaudited)

(in thousands)

	Common stock Shares	Amount	Additional paid-in capital	Accumulated other comprehensive loss	Accumulated deficit	Total stockholders' equity
Balances at December 31, 2018	54,738	$ 547	$3,386,958	$ (3,627)	$(1,498,808)	$ 1,885,070
Adjustment to beginning accumulated deficit from adoption of ASU 2016-02	—	—	—	—	6,564	6,564
Vesting of restricted stock units	131	2	(2)	—	—	—
Exercise of stock options	189	2	9,502	—	—	9,504
Purchase of common stock under ESPP	11	—	1,231	—	—	1,231
Stock-based compensation	—	—	32,341	—	—	32,341
Other comprehensive income	—	—	—	1,835	—	1,835
Net loss	—	—	—	—	(164,446)	(164,446)
Balances at March 31, 2019	55,069	$ 551	$3,430,030	$ (1,792)	$(1,656,690)	$ 1,772,099

	Common stock Shares	Amount	Additional paid-in capital	Accumulated other comprehensive loss	Accumulated deficit	Total stockholders' equity
Balances at December 31, 2017	49,406	$ 494	$2,540,951	$ (4,205)	$(913,808)	$ 1,623,432
Adjustment to beginning accumulated deficit from adoption of ASU 2014-09	—	—	—	—	(29,375)	(29,375)
Vesting of restricted stock units	74	1	(1)	—	—	—
Issuance of common stock upon public offering, net of issuance costs of $2,563	277	3	48,698	—	—	48,701
Exercise of stock options	301	3	19,727	—	—	19,730
Purchase of common stock under ESPP	9	—	687	—	—	687
Stock-based compensation	—	—	22,995	—	—	22,995
Other comprehensive loss	—	—	—	(844)	—	(844)
Net loss	—	—	—	—	(115,126)	(115,126)
Balances at March 31, 2018	50,067	$ 501	$2,633,057	$ (5,049)	$(1,058,308)	$ 1,570,201

See accompanying notes to unaudited condensed consolidated financial statements.

bluebird bio, Inc.

Condensed Consolidated Statements of Cash Flows

(unaudited)

(in thousands)

	For the three months ended March 31,	
	2019	2018
Cash flows from operating activities:		
Net loss	$(164,446)	$(115,126)
Adjustments to reconcile net loss to net cash used in operating activities:		
Change in fair value of contingent consideration	296	534
Depreciation and amortization	3,783	4,020
Stock-based compensation expense	32,341	22,995
Unrealized loss on equity securities	3,085	—
Other non-cash items	(3,456)	2,403
Changes in operating assets and liabilities:		
Prepaid expenses and other assets	(12,793)	(13,486)
Operating lease right-of-use assets	5,374	—
Accounts payable	10,590	(737)
Accrued expenses and other liabilities	(21,514)	4,541
Operating lease liabilities	3,224	—
Deferred revenue	(8,672)	(13,966)
Collaboration research advancement	(1,966)	—
Net cash used in operating activities	(154,154)	(108,822)
Cash flows from investing activities:		
Purchase of property, plant and equipment	(19,321)	(7,452)
Purchases of marketable securities	(381,735)	(402,413)
Proceeds from maturities of marketable securities	364,143	145,140
Net cash used in investing activities	(36,913)	(264,725)
Cash flows from financing activities:		
Proceeds from public offering of common stock, net of issuance costs	—	48,701
Reimbursement of assets under financing lease obligation	—	3,098
Payments on financing lease obligation	—	(106)
Proceeds from exercise of stock options and ESPP contributions	10,223	19,984
Net cash provided by financing activities	10,223	71,677
Decrease in cash, cash equivalents and restricted cash	(180,844)	(301,870)
Cash, cash equivalents and restricted cash at beginning of period	417,099	772,268
Cash, cash equivalents and restricted cash at end of period	$236,255	$470,398
Supplemental cash flow disclosures from investing and financing activities:		
Purchases of property, plant and equipment included in accounts payable and accrued expenses	$9,302	$2,817
Assets acquired under operating lease obligation	$5,500	$—

Tenant improvements included in receivables and other current assets	$8,009	$14
Restricted cash included in receivables and other current assets	$100	$100
Restricted cash included in restricted cash and other non-current assets	$14,417	$13,763

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 programs in severe genetic diseases include ZYNTEGLO™ (autologous CD34+ cells encoding A-T87Q-globin gene) as a treatment for transfusion-dependent -thalassemia, or TDT; its LentiGlobin® product candidate as a treatment for sickle cell disease, or SCD; and its Lenti-D™ product candidate as a treatment for cerebral adrenoleukodystrophy, or CALD. In the second half of 2018, the Company filed a marketing authorization application with the European Medicines Agency, or EMA, for ZYNTEGLO (formerly referred to as LentiGlobin for TDT) for the treatment of patients 12 years and older with TDT who do not have a 0/0 genotype, for whom hematopoietic stem cell (HSC) transplantation is appropriate but a human leukocyte-matched related HSC donor is not available. In March 2019, the Committee for Medicinal Products for Human Use of the EMA adopted a positive opinion recommending conditional marketing authorization for ZYNTEGLO in Europe. Assuming that the application is conditionally approved, the Company expects to begin commercializing and generating product revenues in the second half of 2019. The Company's programs in oncology are focused on developing novel T cell-based immunotherapies, including chimeric antigen receptor (CAR) and T cell receptor (TCR) T cell therapies. Idecabtagene vicleucel, or ide-cel (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. Please refer to Note 9, "Collaborative arrangements" for further discussion of the Company's collaboration with Celgene.

As of March 31, 2019, the Company had cash, cash equivalents and marketable securities of $1.73 billion. Although the Company has incurred recurring losses and expects to continue to incur losses for the foreseeable future, the Company expects that its existing cash, cash equivalents and marketable securities will be sufficient to fund current planned 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 March 31, 2019 and 2018.

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 condensed consolidated financial statements should be read in conjunction with the audited consolidated financial statements as of and for the year ended December 31, 2018, 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, 2019.

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. 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.

Significant accounting policies

The significant accounting policies used in preparation of these condensed consolidated financial statements for the three months ended March 31, 2019 are consistent with those discussed in Note 2 to the consolidated financial statements in the Company's 2018 Annual Report on Form 10-K, except as noted below with respect to the Company's lease accounting policies and as noted within the "Recent accounting pronouncements – Recently adopted" section below.

Leases

Effective January 1, 2019, the Company adopted ASU 2016-02, Leases (Topic 842), ("ASU 2016-02" or "ASC 842"), using the required modified retrospective approach and utilizing the effective date as its date of initial application. As a result, prior periods are presented in accordance with the previous guidance in ASC 840, Leases ("ASC 840").

At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the unique facts and circumstances present in the arrangement. Leases with a term greater than one year are recognized on the balance sheet as right-of-use assets and short-term and long-term lease liabilities, as applicable. The Company does not have material financing leases.

Operating lease liabilities and their corresponding right-of-use assets are initially recorded based on the present value of lease payments over the expected remaining lease term. Certain adjustments to the right-of-use asset may be required for items such as incentives received. The interest rate implicit in lease contracts is typically not readily determinable. As a result, the Company utilizes its incremental borrowing rate to discount lease payments, which reflects the fixed rate at which the Company could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, in a similar economic environment. To estimate its incremental borrowing rate, a credit rating applicable to the Company is estimated using a synthetic credit rating analysis since the Company does not currently have a rating agency-based credit rating. Prospectively, the Company will adjust the right-of-use assets for straight-line rent expense or any incentives received and remeasure the lease liability at the net present value using the same incremental borrowing rate that was in effect as of the lease commencement or transition date.

The Company has elected not to recognize leases with an original term of one year or less on the balance sheet. The Company typically only includes an initial lease term in its assessment of a lease arrangement. Options to renew a lease are not included in the Company's assessment unless there is reasonable certainty that the Company will renew.

ASC 842 transition practical expedients and application of transition provisions to leases at the transition date

The Company elected the following practical expedients, which must be elected as a package and applied consistently to all of its leases at the transition date (including those for which the entity is a lessee or a lessor): i) the Company did not reassess whether any expired or existing contracts are or contain leases; ii) the Company did not reassess the lease classification for any expired or existing leases (that is, all existing leases that were classified as operating leases in accordance with ASC 840 are classified as operating leases, and all existing leases that were classified as capital leases in accordance with ASC 840 are classified as finance leases); and iii) the Company did not reassess initial direct costs for any existing leases.

For leases that existed prior to the date of initial application of ASC 842 (which were previously classified as operating leases), a lessee may elect to use either the total lease term measured at lease inception under ASC 840 or the remaining lease term as of the date of initial application of ASC 842 in determining the period for which to measure its incremental borrowing rate. In transition to ASC 842, the Company utilized the remaining lease term of its leases in determining the appropriate incremental borrowing rates.

Application of ASC 842 policy elections to leases post adoption

The Company has made certain policy elections to apply to its leases executed post adoption, or subsequent to January 1, 2019, as further described below.

In accordance with ASC 842, components of a lease should be split into three categories: lease components, non-lease components, and non-components. The fixed and in-substance fixed contract consideration (including any consideration related to non-components) must be allocated based on the respective relative fair values to the lease components and non-lease components.

Entities may elect not to separate lease and non-lease components. Rather, entities would account for each lease component and related non-lease component together as a single lease component. The Company has elected to account for lease and non-lease components together as a single lease component for all underlying assets and allocate all of the contract consideration to the lease component only.

ASC 842 allows for the use of judgment in determining whether the assumed lease term is for a major part of the remaining economic life of the underlying asset and whether the present value of lease payments represents substantially all of the fair value of the underlying asset. The Company applies the bright line thresholds referenced in ASC 842-10-55-2 to assist in evaluating leases for appropriate classification. The aforementioned bright lines are applied consistently to the Company’s entire portfolio of leases.

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, right-of-use assets and lease liabilities, contingent consideration, stock-based compensation expense, accrued expenses, revenue and income taxes.

Recent accounting pronouncements

Recently adopted

ASU No. 2016-02, Leases (Topic 842), ASU No. 2018-10 Codification Improvements to Topic 842, Leases, ASU No. 2018-11, Leases (Topic 842): Targeted Improvements, and ASU No. 2019-01 Leases (Topic 842): Codification Improvements

In February 2016, the FASB issued ASU 2016-02, as amended, which superseded the lease accounting requirements in ASC 840 and created ASC 842. ASC 842 requires a lessee to recognize assets and liabilities on the balance sheet for most 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.

Effective January 1, 2019, the Company adopted ASU 2016-02, using the required modified retrospective approach and utilizing the effective date as its date of initial application. As a result, prior periods are presented in accordance with the previous guidance in ASC 840.

The adoption of this standard resulted in the recognition of operating lease right-of-use assets and operating lease liabilities of $184.4 million and $177.0 million, respectively, on the Company's condensed consolidated balance sheet relating to its leases for its corporate headquarters at 60 Binney Street in Cambridge, Massachusetts (the "60 Binney Street Lease"), its office and laboratory space in Seattle, Washington, its office space in Zug, Switzerland, and its embedded leases associated with certain of the Company's contract manufacturing agreements. The application of the standard's transition guidance required the de-recognition of the 60 Binney Street Lease building asset, financing lease obligation, current portion, and financing lease obligation, net of current portion in the amounts of $149.3 million, $1.4 million, and $153.3 million, respectively, as well as certain other adjustments to related account balances. In adopting ASU 2016-02, the Company recorded a total one-time adjustment of $6.6 million to the opening balance of accumulated deficit in the first quarter of 2019 primarily relating to the de-recognition of the 60 Binney Street Lease building asset finance lease obligation.

As a result of adopting ASU 2016-02, the Company recorded an increase to deferred tax assets and deferred tax liabilities of $5.3 million and $7.1 million, respectively. The $1.8 million net increase to deferred tax liabilities and an offsetting valuation allowance adjustment was recorded through the accumulated deficit, such that there was no tax impact on the Company's condensed consolidated financial statements as a result of adoption.

ASU No. 2017-08, Receivables – Nonrefundable Fees and Other Costs (Topic 310-20): Premium Amortization on Purchased Callable Debt Securities

In April 2017, the FASB issued ASU 2017-08, Receivables – Nonrefundable Fees and Other Costs (Topic 310-20): Premium Amortization on Purchased Callable Debt Securities ("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 Company adopted this standard on January 1, 2019 and it did not have a material impact on the Company's financial position or results of operations upon adoption.

ASU No. 2018-02, Income Statement - Reporting Comprehensive Income (Topic 220): Reclassification of Certain Tax Effects from Accumulated Other Comprehensive Income

In February 2018, the FASB issued ASU 2018-02, Income Statement - Reporting Comprehensive Income (Topic 220): Reclassification of Certain Tax Effects from Accumulated Other Comprehensive Income. 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 Company adopted this standard on January 1, 2019 and it did not have a material impact on the Company's financial position and results of operations upon adoption.

Not yet adopted

ASU No. 2016-13, Financial Instruments – Credit Losses (Topic 362): Measurement of Credit Losses on Financial Statements

In June 2016, the FASB issued ASU 2016-13, Financial Instruments – Credit Losses (Topic 362): Measurement of Credit Losses on Financial Statements. The new standard requires that expected credit losses relating to financial assets measured on an amortized cost basis and available-for-sale debt securities be recorded through an allowance for credit losses. It also limits the amount of credit losses to be recognized for available-for-sale debt securities to the amount by which carrying value exceeds fair value and also requires the reversal of previously recognized credit losses if fair value increases. The new standard will be effective beginning January 1, 2020 and early adoption is permitted with measurement dates on or after January 1, 2019. 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 No. 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 No. 2018-13, Fair Value Measurement (Topic 820): Disclosure Framework – Changes to the Disclosure Requirements for Fair Value Measurement

In August 2018, the FASB issued ASU 2018-13, Fair Value Measurement (Topic 820): Disclosure Framework – Changes to the Disclosure Requirements for Fair Value Measurement, ("ASU 2018-13"). The new standard removes certain disclosures, modifies certain disclosures and adds additional disclosures related to fair value measurement. The new standard will be effective beginning January 1, 2020 and early adoption is permitted. The Company is currently evaluating the potential impact ASU 2018-13 may have on its disclosures upon adoption.

ASU No. 2018-15, Intangibles-Goodwill and Other - Internal-Use Software (Subtopic 350-40): Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract

In August 2018, the FASB issued ASU 2018-15, Intangibles-Goodwill and Other-Internal-Use Software (Subtopic 350-40): Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract, ("ASU 2018-15"). The amendments in this update align the requirements for capitalizing implementation costs incurred in a hosting arrangement that is a service contract with the requirements for capitalizing implementation costs incurred to develop or obtain internal-use software (and hosting arrangements that include an internal-use software license). The accounting for the service element of a hosting arrangement that is a service contract is not affected by the amendments in this update. The new standard will be effective beginning January 1, 2020 and early adoption is permitted. The amendments in this update should be applied either retrospectively or prospectively to all implementation costs incurred after the date of adoption. The Company is currently evaluating the potential impact ASU 2018-15 may have on its financial position and results of operations upon adoption.

ASU No. 2018-18, Collaborative Arrangements (Topic 808): Clarifying the Interaction between Topic 808 and Topic 606

In November 2018, the FASB issued ASU 2018-18, Collaborative Arrangements (Topic 808): Clarifying the Interaction between Topic 808 and Topic 606, ("ASU 2018-18"). The amendments in this update clarify that certain transactions between collaborative arrangement participants should be accounted for as revenue when the collaborative arrangement participant is a customer in the context of a unit of account and precludes recognizing as revenue consideration received from a collaborative arrangement participant if the participant is not a customer. The new standard will be effective beginning January 1, 2020 and early adoption is permitted. The Company is currently evaluating the potential impact ASU 2018-18 may have on its financial position and results of operations upon adoption.

3. Marketable securities

The following table summarizes the marketable securities held at March 31, 2019 and December 31, 2018 (in thousands):

Description	Amortized cost / Cost	Unrealized gains	Unrealized losses	Fair value
March 31, 2019				
U.S. government agency securities and treasuries	$1,357,641	$ 1,604	$ (1,400)	$1,357,845
Certificates of deposit	5,960	—	—	5,960
Corporate bonds	83,536	81	(19)	83,598
Commercial paper	42,542	—	—	42,542
Equity securities	20,017	—	(934)	19,083
Total	$1,509,696	$ 1,685	$ (2,353)	$1,509,028
December 31, 2018				
U.S. government agency securities and treasuries	$1,459,649	$ 963	$ (3,011)	$1,457,601

Certificates of deposit	9,080	—	—	9,080
Equity securities	20,017	2,150	—	22,167
Total	$1,488,746	$ 3,113	$ (3,011)	$1,488,848

No available-for-sale debt securities held as of March 31, 2019 or December 31, 2018 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 March 31, 2019 and December 31, 2018 (in thousands):

Description	Total	Quoted prices in active markets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)
March 31, 2019				
Assets:				
Cash and cash equivalents	$221,738	$214,346	$7,392	$ —
Marketable securities:				
U.S. government agency securities and treasuries	1,357,845	—	1,357,845	—
Certificates of deposit	5,960	—	5,960	—
Commercial paper	42,542	—	42,542	—
Corporate bonds	83,598	—	83,598	—
Equity securities	19,083	19,083	—	—
Total assets	$1,730,766	$233,429	$1,497,337	$ —
Liabilities:				
Contingent consideration	$5,526	$—	$—	$ 5,526
Total liabilities	$5,526	$—	$—	$ 5,526
December 31, 2018				
Assets:				
Cash and cash equivalents	$402,579	$348,638	$53,941	$ —
Marketable securities:				
U.S. government agency securities and treasuries	1,457,601	—	1,457,601	—
Certificates of deposit	9,080	—	9,080	—
Equity securities	22,167	22,167	—	—
Total assets	$1,891,427	$370,805	$1,520,622	$ —
Liabilities:				
Contingent consideration	$5,230	$—	$—	$ 5,230
Total liabilities	$5,230	$—	$—	$ 5,230

Cash and cash equivalents

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 March 31, 2019, cash and cash equivalents comprise funds in cash, money market accounts, and commercial paper. As of December 31, 2018, cash and cash equivalents comprise funds in cash, U.S. treasury securities, U.S. government agency securities, and money market accounts.

Marketable securities

Marketable securities classified as Level 2 within the valuation hierarchy generally consist of certificates of deposit, U.S. treasury securities and government agency securities, corporate bonds, and commercial paper. 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.

The amortized cost of available-for-sale debt securities is adjusted for amortization of premiums and accretion of discounts to the earliest call date for premiums or to maturity for discounts. At March 31, 2019 and December 31, 2018, the balance in the Company's accumulated other comprehensive loss was composed primarily of activity related to the Company's available-for-sale debt securities. There were no material realized gains or losses recognized on the sale or maturity of available-for-sale securities during the three months ended March 31, 2019 or 2018, 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 March 31, 2019 and December 31, 2018 was $189.2 million and $787.5 million, respectively. As of March 31, 2019 and December 31, 2018, there were $411.6 million and $315.3 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 March 31, 2019 and December 31, 2018 was $0.1 million and $0.9 million, respectively. The aggregate unrealized loss on securities held by the Company for more than twelve months as of March 31, 2019 and December 31, 2018 was $1.3 million and $2.1 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 March 31, 2019 and December 31, 2018.

The Company holds equity securities with an aggregate fair value of $19.1 million and $22.2 million as of March 31, 2019 and December 31, 2018, respectively, within short-term marketable securities on its condensed consolidated balance sheet. The Company has recorded a $3.1 million unrealized loss during the three months ended March 31, 2019 related to its equity securities, which is included in other (expense) income, net on the condensed consolidated statements of operations and comprehensive loss.

Contingent consideration

In connection with its prior acquisition of Precision Genome Engineering, Inc. ("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 14.3% to 15.2%. 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

	three months ended March 31, 2019
Beginning balance	$ 5,230
Additions	—
Changes in fair value	296
Payments	—
Ending balance	$ 5,526

Please refer to Note 8, “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 March 31, 2019	As of December 31, 2018
Land	$1,210	$ 1,210
Building	14,913	180,094
Computer equipment and software	6,474	6,365
Office equipment	5,788	5,584
Laboratory equipment	39,442	35,693
Leasehold improvements	12,325	183
Construction-in-progress	60,766	46,669
Total property, plant and equipment	140,918	275,798
Less accumulated depreciation and amortization	(26,888)	(29,176)
Property, plant and equipment, net	$114,030	$ 246,622

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 therapies. Construction-in-progress as of March 31, 2019 and December 31, 2018 includes $47.1 million and $40.4 million, respectively, related to the North Carolina manufacturing facility. During the three months ended March 31, 2019, the Company placed an additional $2.7 million of the North Carolina manufacturing facility into service and began to depreciate the assets. Total building assets placed into service related to the North Carolina manufacturing facility as of March 31, 2019 and December 31, 2018 were $14.9 million and $12.2 million, respectively.

60 Binney Street Lease

As a result of the adoption of ASU 2016-02, the Company de-recognized $156.0 million of the building asset and $6.7 million of accumulated depreciation related to its corporate headquarters at 60 Binney Street. Prior to the adoption of ASU 2016-02, the Company classified leasehold improvements associated with the 60 Binney Street building as building. Subsequent to the adoption of ASU 2016-02, the leasehold improvements associated with the 60 Binney Street building are classified as leasehold improvements. Please refer to Note 2, "Basis of presentation, principles of consolidation and significant accounting policies" and Note 7, "Leases" for further information.

6. Accrued expenses and other current liabilities

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

	As of March 31, 2019	As of December 31, 2018
Employee compensation	$ 16,404	$ 28,567
Accrued manufacturing costs	12,125	21,618
Accrued clinical and contract research organization costs	14,724	11,891
Accrued license and milestone fees	323	7,739
Accrued professional fees	1,906	1,830
Financing lease obligation, current portion	—	1,424
Other	30,670	26,324
Total accrued expenses and other current liabilities	$ 76,152	$ 99,393

7. Leases

The Company leases certain office and laboratory space. Additionally, the Company has embedded leases at contract manufacturing organizations.

Embedded operating leases

On June 3, 2016, the Company entered into a manufacturing agreement for the future commercial production of the Company's ZYNTEGLO, LentiGlobin, and Lenti-D drug products 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 paid $12.0 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. Construction was completed in March 2018 and beginning in April 2018 the Company pays $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 in prior periods that this agreement contained an embedded lease under ASC 840 as the suites are designated for the Company's exclusive use during the term of the agreement. The Company concluded that it was not the deemed owner during construction nor was it a capital lease under ASC 840. As a result, in prior periods the Company accounted for the agreement as an operating lease under ASC 840 and recognized straight-line rent expense over the non-cancellable term of the embedded lease. As part of its adoption of ASC 842, effective January 1, 2019, the Company carried forward its existing lease classification under ASC 840. Additionally, the Company recorded a right-of-use asset and lease liability for this operating lease on the effective date and is recognizing rent expense on a straight-line basis throughout the remaining term of the embedded lease.

The Company's other embedded leases are not material to the condensed consolidated financial statements.

60 Binney Street Lease

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"), which is now the Company's corporate headquarters. Under the terms of the 60 Binney Street Lease, starting on October 1, 2016, the Company leases approximately 253,108 square feet of office and laboratory space at $72.50 per square foot per year, or $18.4 million per year in base rent, which is subject to scheduled annual rent increases of 1.75% plus certain

operating expenses and taxes. The Company currently maintains a $13.8 million collateralized letter of credit and, 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. Pursuant to a work letter entered into in connection with the 60 Binney Street Lease, the landlord contributed an aggregate of $42.4 million toward the cost of construction and tenant improvements for the Building.

The Company has occupied the Building beginning on March 27, 2017 and the 60 Binney Street Lease will continue until March 31, 2027. The Company has the option to extend the 60 Binney Street Lease for two successive five-year terms. The Company is accounting for this lease under ASC 842 using its initial 10-year term through March 31, 2027 and will reassess the lease term on a quarterly basis.

Due to the Company’s involvement 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, among other items, the Company was deemed for accounting purposes to be the owner of the Building during the construction period, per ASC 840. Accordingly, under ASC 840, construction costs that were incurred by the landlord directly or indirectly through reimbursement to the Company as part of its tenant improvement allowance were recorded as an asset in Property, plant and equipment, net on the Company’s 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 under ASC 840. 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 portion of the building in service over a useful life of 40 years and incurred interest expense related to the financing obligation.

As part of its adoption of ASC 842, the Company de-recognized the building asset and corresponding financing obligation recorded on the Company's consolidated balance sheets as of December 31, 2018, in accordance with the ASC 842 transition guidance. In applying the ASC 842 transition guidance, the Company classified this lease as an operating lease and recorded a right-of-use asset of $127.3 million and lease liability of $125.8 million on the effective date. The Company is recognizing rent expense on a straight-line basis throughout the remaining term of the lease.

Summary of all lease costs recognized under ASC 842

The following table contains a summary of the lease costs recognized under ASC 842 and other information pertaining to the Company's operating leases for the three months ended March 31, 2019:

Operating leases (in thousands)	For the three months ended March 31, 2019
Lease cost (1)	
Operating lease cost	$ 8,483
Total lease cost	$ 8,483
Other information	
Operating cash flows used for operating leases	$ 7,946
Weighted average remaining lease term	7.7 years
Weighted average discount rate	6.64 %

(1) Short-term lease costs and variable lease costs incurred by the Company for the three months ended March 31, 2019 were immaterial.

As of March 31, 2019, future minimum commitments under ASC 842 under the Company's operating leases were as follows:

Maturity of lease liabilities (in thousands)	As of March 31, 2019
2019 (excluding the three months ended March 31, 2019)	$21,286

2020	32,093
2021	32,480
2022	27,632
2023	28,033
2024 and thereafter	98,151
Total lease payments	239,675
Less: imputed interest	(53,909)
Total operating lease liabilities	$185,766

The above table excludes $18.0 million of legally binding minimum lease payments for leases executed but not yet commenced as of March 31, 2019. Please refer to Note 14, “Subsequent events” for discussion of a sublease agreement which was executed in April 2019.

8. Commitments and contingencies

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 March 31, 2019 and December 31, 2018 or royalties on future sales of specified products, which includes the collaboration agreement entered into with Regeneron Pharmaceuticals, Inc. (“Regeneron”) in August 2018. 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 in the event of termination to be based on the timing of the termination and the terms of the agreement. Please refer to Note 9, “Collaborative arrangements,” for further information on the collaboration agreement with Regeneron.

We may be obligated to make future development, regulatory and commercial milestone payments and royalty payments on future sales of specified products associated with our collaboration and license agreements. Payments under these agreements generally become due and payable upon achievement of such milestones or sales. When the achievement of these milestones or sales have occurred, such contingencies are recorded in the Company’s financial statements.

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

9. Collaborative arrangements

To date, the Company’s collaboration revenue has been exclusively generated from its collaboration arrangements with Celgene Corporation and Regeneron, each as further described below.

Celgene

Celgene Original Collaboration Agreement

On March 19, 2013, the Company entered into a Master Collaboration Agreement (the "Celgene 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 (the "Sublicense Agreement") with Celgene pursuant to which the Company obtained a sublicense to certain intellectual property from Celgene, originating under Celgene's license from Baylor College of Medicine, for use in the collaboration.

Under the terms of the Celgene Collaboration Agreement, the Company received a $75.0 million up-front, non-refundable cash payment. The Company was responsible for conducting discovery, research and development activities through completion of phase 1 clinical studies, if any, during the initial term of the Celgene 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 Celgene 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.

Celgene Amended Collaboration Agreement

On June 3, 2015, the Company and Celgene amended and restated the Celgene Collaboration Agreement (the "Amended Celgene Collaboration Agreement"). Under the Amended Celgene Collaboration Agreement, the parties narrowed the focus of the collaboration to exclusively work on anti- B-cell maturation antigen ("BCMA") product candidates for a new three-year term that ended in June 2018. In connection with the Amended Celgene Collaboration Agreement, the Company received an up-front, one-time, non-refundable, non-creditable payment of $25.0 million to fund research and development under the collaboration. The collaboration is governed by the JSC. Under the terms of the Amended Celgene Collaboration Agreement, for up to two product candidates selected for development under the collaboration, the Company was responsible for conducting and funding all research and development activities performed up through completion of the initial phase 1 clinical study of such product candidates.

On a product candidate-by-product candidate basis, up through a specified period following enrollment of the first patient in an initial phase 1 clinical study for such product candidate (the "Option Period"), the Company had 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.

Celgene Ide-cel License Agreement

On February 10, 2016, Celgene exercised its option to obtain an exclusive worldwide license to develop and commercialize ide-cel, the first product candidate under the Amended Celgene Collaboration Agreement, pursuant to an executed license agreement ("Ide-cel License Agreement") entered into by the parties on February 16, 2016 and paid to the Company the associated $10.0 million option fee. Pursuant to the Ide-cel License Agreement, Celgene was responsible for development and related funding of ide-cel after the substantial completion of the phase 1 clinical trial. The Company was responsible for the manufacture of vector and associated payload throughout development and upon Celgene's request, throughout commercialization, the costs of which were reimbursable by Celgene in accordance with the terms of the Amended and Restated Co-Development, Co-Promote and Profit Share Agreement, as further described below. Celgene was responsible for the manufacture of drug product throughout development and commercialization.

Celgene Ide-cel Co-Development, Co-Promote and Profit Share Agreement

On March 28, 2018, the Company elected to co-develop and co-promote ide-cel within the U.S. pursuant to the execution of the Amended and Restated Co-Development, Co-Promote and Profit Share Agreement ("Ide-cel CCPS"), which replaced the Ide-cel License Agreement. The responsibilities of the parties remain unchanged from those under the Ide-cel License Agreement, however, the Company will share equally in all profits and losses relating to developing, commercializing and manufacturing ide-cel within the U.S. and has the right to participate in the development and promotion of ide-cel in the U.S. Celgene is responsible for the costs incurred to manufacture vector and associated payload for use outside of the U.S., plus a markup. Under the Ide-cel CCPS, the Company may receive up to $70.0 million in development milestone payments for the first indication to be addressed by ide-cel, with the ability to obtain additional milestone payments for a second indication and modified licensed products. In addition, to the extent ide-cel is commercialized, the Company is 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.

Celgene 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 Celgene 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 1 clinical trial. The Company is responsible for the manufacture of vector and associated payload throughout development and upon Celgene's request, throughout commercialization. Expenses incurred by the Company associated with these activities are fully reimbursable by Celgene at cost plus a mark-up. Throughout both development and commercialization, Celgene is responsible for the manufacture of drug product.

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 on-going phase 1 clinical 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. Celgene would be responsible for the costs incurred to manufacture vector and associated payload for use outside of the U.S., plus a markup. 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 – Ide-cel

ASC Topic 606, Revenue From Contracts With Customers ("Topic 606"), allows 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, ide-cel, under the arrangement was considered a material right at the time the Amended Celgene 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. In making this determination, the Company also considered the option price relative to the value of the underlying license. Celgene's exercise of this material right in February 2016 was determined to represent a contract modification and represents the last contract modification prior to the adoption of Topic 606. As a result, the Celgene Collaboration Agreement, Amended Celgene Collaboration Agreement, and Ide-cel CCPS 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 due primarily to the significant uncertainty regarding whether any additional product candidates would be identified under the Amended Celgene Collaboration Agreement. 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 ide-cel, and (iii) manufacture of vectors and associated payload for incorporation into ide-cel 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 that time Celgene had 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 given that Celgene can benefit from the research and development services on their own and such services are distinct within the context of the contract. Thus, such services are considered to be a separate performance obligation. The Company concluded that the license to ide-cel 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.

Ide-cel transaction price

The following tables summarize the total transaction price, the allocation of the total transaction price to the identified performance obligations under the arrangement, and the amount of the transaction price unsatisfied as of March 31, 2019:

(in thousands)

	Ide-cel transaction price as of March 31, 2019
Up-front non-refundable payment - Celgene Collaboration Agreement	$ 75,000
Up-front non-refundable payment - Amended Celgene Collaboration Agreement	25,000
Ide-cel license fee - Ide-cel License Agreement	10,000
Estimated variable consideration	84,664
	$ 194,664

(in thousands)	Allocation of transaction price to performance obligations	Transaction price unsatisfied as of March 31, 2019
Ide-cel research and development services	$ 38,438	$ —
Ide-cel license and manufacturing services	156,226	32,821
	$ 194,664	$ 32,821

The estimated variable consideration of $84.7 million relates 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 standalone selling price ("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.

All of the clinical and regulatory milestones are fully constrained and are excluded from the transaction price. 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 clinical trials, the licensee's efforts, or 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 re-evaluates the transaction price, including its estimated variable consideration included in the transaction price and all constrained amounts, at each reporting period and as uncertain events are resolved or other changes in circumstances occur.

Ide-cel research and development services

The Company allocated $38.4 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 1 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 fully satisfied this performance obligation during the second quarter of 2018, any changes to the total transaction price following the completion of this performance obligation in May 2018 will be allocated to the performance obligations under the arrangement based on a relative SSP basis and therefore the allocation of any changes to the total transaction price may impact the revenue recognized for this performance obligation in the period of change.

The following table summarizes the revenue recognized, or revenue adjustment recorded, related to the ide-cel research and development services for the three months ended March 31, 2019 and 2018:

	For the three months ended March 31,	
(in thousands)	2019	2018
Ide-cel research and development services revenue (revenue adjustment)	$(209)	$2,183
	$(209)	$2,183

Ide-cel license and manufacturing services

The Company allocated $156.2 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 ide-cel.

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 collaboration revenue for its U.S. manufacturing services by analogy to Topic 606. The portion of Celgene's U.S. development costs that the Company 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 ide-cel, including expected demand from Celgene, and the costs associated with the manufacture of vectors and associated payload for incorporation into ide-cel. 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 ide-cel 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.

The following table summarizes the net collaboration revenue recognized or expense incurred related to the combined performance obligation for the license and vector manufacturing of ide-cel in the U.S. for the three months ended March 31, 2019, and 2018:

Ide-cel license and manufacturing services - U.S.	For the three months ended March 31,	
(in thousands)	2019	2018
ASC 808 ide-cel license and manufacturing revenue - U.S. (1)	$—	$3,761
ASC 808 ide-cel license and manufacturing research and development expense - U.S. (1)	$(3,244)	$—

(1) As noted above, the calculation of collaboration revenue or research and development expense to be recognized for the Company's combined performance obligation for its license and vector manufacturing of ide-cel in the U.S. is performed on a quarterly basis. The calculation is independent of previous activity, which may result in fluctuations between revenue and expense recognition period over period, depending on the varying extent of effort performed by each party during the period.

Revenue related to the combined unit of accounting for the non-US license and vector manufacturing services is accounted for in accordance with Topic 606. The following table summarizes the revenue recognized related to the combined unit of accounting for the ide-cel non-US license and vector manufacturing services for the three months ended March 31, 2019, and 2018:

Ide-cel license and manufacturing services - outside of U.S.	For the three months ended March 31,	
(in thousands)	2019	2018
ASC 606 license and manufacturing revenue - outside of U.S.	$9,064	$8,942

As of March 31, 2019, the aggregate amount of the transaction price allocated to the combined performance obligation, which consists of the ide-cel license and manufacturing services, that is unsatisfied, or partially unsatisfied, is $32.8 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. As of March 31, 2019 and December 31,

2018, the Company had $15.0 million and $23.0 million, respectively, of deferred revenue associated with the combined performance obligation consisting of the ide-cel 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 Celgene 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 given that Celgene can benefit from the research and development services on their own and such services are distinct within the context of the contract. Thus, such services are considered to be a separate performance obligation. Similar to ide-cel, 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.

bb21217 transaction price

The following tables summarize the total transaction price, the allocation of the total transaction price to the identified performance obligations under the arrangement, and the amount of the transaction price unsatisfied as of March 31, 2019:

(in thousands)	bb21217 transaction price as of March 31, 2019
bb21217 license fee - bb21217 License Agreement	$ 15,000
Estimated variable consideration	26,687
	$ 41,687

(in thousands)	Allocation of transaction price to performance obligations	Transaction price unsatisfied as of March 31, 2019
bb21217 research and development services	$ 5,444	$ 1,118
bb21217 license and manufacturing services	36,243	36,243
	$ 41,687	$ 37,361

The estimated variable consideration of $26.7 million relates 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.

All of the clinical and regulatory milestones are fully constrained and are excluded from the transaction price. 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, or 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 re-evaluates the transaction price, including its estimated variable consideration included in the transaction price and all constrained amounts, 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 1 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 following table summarizes the revenue recognized related to the bb21217 research and development services for the three months ended March 31, 2019, and 2018:

	For the three months ended March 31,	
(in thousands)	2019	2018
bb21217 research and development services revenue	$721	$721
	$721	$721

As of March 31, 2019, and December 31, 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 $1.1 million and $1.8 million, respectively, 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 March 31, 2019, the manufacturing services for bb21217 had not yet commenced. Therefore, no amounts have been recognized for the combined performance obligation in the consolidate statement of operations for the three months ended March 31, 2019, and 2018.

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 of remaining deferred revenue as of March 31, 2019 and December 31, 2018 associated with the combined performance obligation consisting of the bb21217 license and manufacturing services.

Contract assets and liabilities – ide-cel and bb21217

The Company receives payments from its collaborative partners 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 three months ended March 31, 2019:

(in thousands)	Balance at beginning of period	Additions	Deductions	Balance at end of period
Receivables	$ 6,528	$ —	$ (2,705)	$ 3,823
Contract liabilities:				
Deferred revenue	$ 34,939	$ —	$ (8,671)	$ 26,268

The change in the receivables balance for the three months ended March 31, 2019 is primarily driven by Celgene's U.S. development costs incurred in the first quarter of 2019 for which the Company is responsible are in excess of the Company's U.S. development costs for which Celgene is responsible. As of March 31, 2019, the Company has a receivable given that the Company's U.S. development costs incurred in the fourth quarter of 2018 for which Celgene is responsible are in excess of Celgene's U.S. development costs for which the Company is responsible, and no cash

was collected from Celgene related to the fourth quarter's costs as of March 31, 2019.

The decrease in deferred revenue during the three months ended March 31, 2019 is primarily driven by amounts recognized for the combined performance obligation consisting of the ide-cel license and manufacturing services. During the three months ended March 31, 2019, $8.7 million of the deferred revenue balance at the beginning of the period was released from deferred revenue, of which $3.6 million was recognized as collaboration revenue and $5.1 million was recorded as contra-research and development expense.

Regeneron

Regeneron Collaboration Agreement

On August 3, 2018, the Company entered into a Collaboration Agreement (the "Regeneron Collaboration Agreement") with Regeneron pursuant to which the parties will apply their respective technology platforms to the discovery, development, and commercialization of novel immune cell therapies for cancer. On August 24, 2018, following the completion of required regulatory reviews, the Regeneron Collaboration Agreement became effective. Under the terms of the agreement, the parties will leverage Regeneron's proprietary platform technologies for the discovery and characterization of fully human antibodies, as well as T cell receptors directed against tumor-specific proteins and peptides and the Company will contribute its field-leading expertise in gene therapy.

In accordance with the Regeneron Collaboration Agreement, the parties jointly selected six initial targets and intend to equally share the costs of research up to the point of submitting an IND application for a potential gene therapy product directed to a particular target. Additional targets may be selected during the five-year research collaboration term as agreed to by the parties.

Regeneron will accrue a certain number of option rights exercisable against targets as the parties reach certain milestones under the terms of the agreement. Upon the acceptance of an IND for the first product candidate directed to a target, Regeneron will have the right to exercise an option for co-development/co-commercialization of product candidates directed to such target on a worldwide or applicable opt-in territory basis, with certain exceptions. Where Regeneron chooses to opt-in, the parties will share equally in the costs of development and commercialization, and will share equally in any profits or losses therefrom in applicable opt-in territories. Outside of the applicable opt-in territories, the target becomes a licensed target and Regeneron would be eligible to receive, with respect to any resulting product, milestone payments of up to $130.0 million per product and royalties on net sales outside of the applicable opt-in territories at a rate ranging from the mid-single digits to low-double digits. Where Regeneron does not exercise its option, or does not have an option to a target, the target would also become a licensed target.

Either party may terminate a given research program directed to a particular target for convenience, and the other party may elect to continue such research program at its expense, receiving applicable cross-licenses. The terminating party will receive licensed product royalties and milestone payments on the potential applicable gene therapy products. Where the Company terminates a given research program for convenience, and Regeneron elects to continue such research program, the parties will enter into a transitional services agreement. Under certain conditions, following its opt-in, Regeneron may terminate a given collaboration program and the Company may elect to continue the development and commercialization of the applicable potential gene therapy products as licensed products.

Regeneron Share Purchase Agreement

A Share Purchase Agreement (“SPA”) was entered into by the parties on August 3, 2018. On August 24, 2018, the closing date of the transaction, the Company issued Regeneron 0.4 million shares of the Company’s common stock, subject to certain restrictions, for $238.10 per share, or $100.0 million in the aggregate. The purchase price represents $63.0 million worth of common stock plus a $37.0 million premium, which represents a collaboration research advancement, or credit to be applied to Regeneron’s initial 50 percent funding obligation for collaboration research, after which the collaborators will continue to fund ongoing research equally. The collaboration research advancement only applies to pre-IND research activities and is not refundable or creditable against post-IND research activities for any programs where Regeneron exercises their opt-in rights.

Accounting analysis – Regeneron

At the commencement of the arrangement, two units of accounting were identified, which are the issuance of 420,000 of the Company’s common shares and joint research activities during the five year research collaboration term. The Company determined the total transaction price to be $100.0 million, which comprises $54.5 million attributed to the equity sold to Regeneron and $45.5 million attributed to the joint research activities. In determining the fair value of the common stock at closing, the Company considered the closing price of the common stock on the closing date of the transaction and included a lack of marketability discount because Regeneron received shares subject to certain restrictions.

The Company analyzed the joint research activities to assess whether they fall within the scope of ASC 808, and will reassess this throughout the life of the arrangement based on changes in the roles and responsibilities of the parties. Based on the terms of the arrangement as outlined above, for the collaboration research performed prior to submission of an IND application for a potential gene therapy product, both parties are deemed to be active participants in the

collaboration. Both parties are performing research and development activities and will share equally in these costs through IND. Additionally, Regeneron and the Company are exposed to significant risks and rewards dependent on the commercial success of any product candidates that may result from the collaboration. As such, the collaboration arrangement is deemed to be within the scope of ASC 808.

The $45.5 million attributed to the joint research activities includes the $37.0 million creditable against amounts owed to the Company by Regeneron. The collaboration research advancement will be reduced over time for amounts due to the Company by Regeneron as a result of the parties agreeing to share in the costs of collaboration research equally. The remainder of the amount attributed to the joint research activities will be recognized over the five-year research collaboration term.

Consistent with its collaboration accounting policy, the Company will recognize collaboration revenue or research and development expense related to the joint research activities in future periods depending on the amounts incurred by each party in a given reporting period. That is, if the Company's research costs incurred exceed those research costs incurred by Regeneron in a given quarter, the Company will record collaboration revenue and reduce the original $37.0 million advance by the amount due from Regeneron until such advancement is fully utilized, after which the Company would record an amount due from Regeneron. If Regeneron's research costs incurred exceed those research costs incurred by the Company in a given quarter, the Company will record research and development expense and record a liability for the amount due to Regeneron.

The Company recognized $2.0 million of collaboration revenue from the Regeneron Collaboration Agreement during the three months ended March 31, 2019. The Company did not recognize any collaboration revenue, or research and development expense, from the Regeneron Collaboration Agreement during the three months ended March 31, 2018.

10. Equity

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 2019 and 2018, the number of shares of common stock available for issuance under the 2013 Stock Option and Incentive Plan ("2013 Plan") was increased by approximately 2.2 million and 2.0 million shares, respectively, as a result of the automatic increase provision of the 2013 Plan. As of March 31, 2019, the total number of shares of common stock available for issuance under the 2013 Plan was approximately 2.4 million.

Stock-based compensation expense

The Company recognized stock-based compensation expense totaling $32.3 million and $23.0 million for the three months ended March 31, 2019 and 2018, 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

	March 31,	
	2019	2018
Stock options	$23,183	$17,295
Restricted stock units	8,881	5,541
Employee stock purchase plan	277	159
	$32,341	$22,995

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	
	March 31,	
	2019	2018
Research and development	$15,516	$11,624
General and administrative	16,825	11,371
	$32,341	$22,995

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 March 31, 2019 and none of which vested during the three months ended March 31, 2019. 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 has not recognized any expense related to these awards and may recognize up to $36.2 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 March 31, 2019, the Company had $375.6 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 3.0 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 March 31, 2019.

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, 2018	4,643	$ 108.56
Granted	1,085	$ 135.53
Exercised	(189)	$ 50.31
Canceled, forfeited, or expired	(155)	$ 136.45
Outstanding at March 31, 2019	5,384	$ 115.84
Exercisable at March 31, 2019	2,372	$ 82.62
Vested and expected to vest at March 31, 2019	5,382	$ 115.85

During the three months ended March 31, 2019, 0.2 million shares of common stock were exercised, resulting in total proceeds to the Company of $9.5 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, 2018	931	$ 155.99
Granted	368	$ 135.70
Vested	(131)	$ 131.06
Forfeited	(40)	$ 149.31
Unvested balance at March 31, 2019	1,128	$ 152.49

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 0.2 million shares of the Company’s common stock to participating employees. During each of the three months ended March 31, 2019 and 2018, less than 0.1 million shares of common stock were issued under the 2013 ESPP.

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.

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 months ended March 31,	
	2019	2018
Outstanding stock options	5,384	4,446
Restricted stock units	1,128	920
ESPP shares	15	6
	6,527	5,372

14. Subsequent events

In April 2019, the Company entered into a sublease agreement for office space located at 50 Binney Street in Cambridge, Massachusetts (the "50 Binney Street Sublease") to supplement the Company's corporate headquarters located at 60 Binney Street in Cambridge, Massachusetts. Under the terms of the 50 Binney Street Sublease, the Company will lease 267,278 square feet of office space for $99.95 per square foot, or $26.7 million per year in base rent subject to certain operating expenses, taxes and annual rent increases. The Company anticipates the lease will commence on July 1, 2021 and end on December 31, 2030, unless the Company earlier occupies the premises or other conditions specified in the 50 Binney Street Sublease occur. The sublessor has the right to postpone the commencement date until January 1, 2022 by providing not less than nine months' prior written notice to the Company. Upon signing the 50 Binney Street Sublease, the Company executed a $40.1 million cash-collateralized letter of credit, which may be reduced in the future subject to the terms of the 50 Binney Street Sublease and certain reduction requirements specified therein. Payments will commence at the earlier of (i) the date which is 90 days following the commencement date and (ii) the date the Company takes occupancy of all or any portion of the premises.

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, 2019.

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 therapeutic potential in a variety of indications. 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 programs in severe genetic diseases include our ZYNTEGLO™ (autologous CD34+ cells encoding $^{A\text{-}T87Q}$-globin gene) product candidate as a treatment for transfusion-dependent -thalassemia, or TDT, our LentiGlobin® product candidate as a treatment for severe sickle cell disease, or SCD, and our Lenti-D™ product candidate as a treatment for cerebral adrenoleukodystrophy, or CALD. 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. Our product candidates in oncology, idecabtagene vicleucel, or ide-cel (bb2121), and bb21217, are CAR T cell product candidates for the treatment of multiple myeloma.

In March 2019, we announced that the Committee for Medicinal Products for Human Use of the European Medicines Agency, or EMA, has adopted a positive opinion recommending conditional marketing authorization for ZYNTEGLO

(formerly referred to as LentiGlobin for TDT) for the treatment of patients 12 years and older with TDT who do not have a $^{0}/^{0}$ genotype, for whom hematopoietic stem cell (HSC) transplantation is appropriate but a human leukocyte-matched related HSC donor is not available. We expect to launch ZYNTEGLO in Europe, and begin to generate product revenues, assuming that we receive conditional approval, in 2019. We plan to file a biologics license application, or BLA, in the United States in 2019 for the use of ZYNTEGLO in the treatment of adult and adolescent patients with TDT who do not have a $^{0}/^{0}$ genotype. 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 SCD, with a potential first submission for regulatory approval in 2022.

Based on our discussions with the FDA and EMA, we believe that we may be able to seek approval for our Lenti-D product candidate for the treatment of patients with CALD on the basis of our clinical data from our ongoing Starbeam study, and the ongoing ALD-103 observational study. We anticipate a potential first submission for regulatory approval of our Lenti-D product candidate for the treatment of patients with CALD in 2020.

In collaboration with Celgene Corporation, or Celgene, we are developing ide-cel and the bb21217 product candidate as treatments for multiple myeloma, a hematologic malignancy that develops in the bone marrow and is fatal if untreated. We are co-developing and co-promoting ide-cel in the United States with Celgene and we have exclusively licensed to Celgene the development and commercialization rights for ide-cel outside of the United States. We and Celgene anticipate the first potential approval of ide-cel as a treatment for relapsed and refractory multiple myeloma in 2020. We have exclusively licensed the development and commercialization rights for the bb21217 product candidate to Celgene, with an option for us to elect to co-develop and co-promote bb21217 within the United States.

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.

As of March 31, 2019, we had cash, cash equivalents and marketable securities of approximately $1.73 billion. We have never been profitable and have incurred net losses in each year since inception. Our net loss was $164.4 million for the three months ended March 31, 2019, and our accumulated deficit was $1.66 billion as of March 31, 2019. 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 ZYNTEGLO, LentiGlobin, Lenti-D product candidates, as well as to fund our share of the costs of clinical studies for ide-cel and the bb21217 product candidate;
- increase research and development-related activities for the discovery and development of product candidates in severe genetic diseases and oncology;
- continue our research and development efforts internally and through our collaborations with external partners, such as with Regeneron;
- manufacture clinical study materials and establish the infrastructure necessary to support and develop large-scale manufacturing capabilities;
- seek regulatory approval for our product candidates;
- add personnel to support our product development and commercialization efforts; and
- increase activities leading up to the potential commercial launch of ZYNTEGLO.

We do not expect to generate revenue from product sales until the second half of 2019, assuming we receive marketing approval for ZYNTEGLO. While we are in the process of completing construction and qualification of our internal lentiviral vector manufacturing capacity, currently 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. As 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.

To date, collaboration revenue has been primarily generated from our collaboration arrangement with Celgene. The terms of the arrangement with respect to ide-cel contain multiple promised goods or services, which include at inception: (i) research and development services, (ii) a license to ide-cel, and (iii) manufacture of vectors and associated payload for incorporation into ide-cel under the license. As of September 2017, the collaboration also included 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 ide-cel 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 paid to us 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 Orchard Therapeutics Limited, or Orchard. 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;
- milestones and upfront license payments;
- 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 ZYNTEGLO, LentiGlobin, Lenti-D, and bb21217 product candidates, conduct research and development activities in severe genetic diseases and oncology, fund our share of the costs of development of the ide-cel 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:

- Northstar-2 Study (HGB-207) – a multi-site, international phase 3 study to examine the safety and efficacy of ZYNTEGLO in the treatment of patients with TDT and a non-$^{0}/^{0}$ genotype.
- Northstar-3 Study (HGB-212) – a multi-site, international phase 3 study to examine the safety and efficacy of ZYNTEGLO in the treatment of patients with TDT and a $^{0}/^{0}$ genotype or an IVS-I-110 mutation.
- HGB-205 study – a single-center phase 1/2 study in France to study the safety and efficacy of ZYNTEGLO in the treatment of patients with TDT and of patients with SCD.
- HGB-206 study – a multi-site phase 1/2 study in the United States to study the safety and efficacy of ZYNTEGLO in the treatment of patients with SCD.
- Our planned HGB-210 study – our planned multi-site, international phase 3 study of patients with SCD and a history of vaso-occlusive events. We plan to initiate this study in 2019.
- Starbeam Study (ALD-102) – a multi-site, international phase 2/3 study to examine the safety and efficacy of our Lenti-D product candidate in the treatment of patients with CALD.
- Our ALD-104 study – our multi-site, international phase 3 study to examine the safety and efficacy of our Lenti-D product candidate after myeloablative conditioning using busulfan and fludarabine in the treatment of patients with CALD. The first patient in this study was treated in April 2019.
- CRB-401 study – an open label, single-arm, multi-center, phase 1 study to examine the safety and efficacy of ide-cel in the treatment of patients with relapsed and refractory multiple myeloma.
- KarMMA (MM-001) study – an open label, single-arm, multi-center phase 2 study to examine the efficacy and safety of ide-cel in the treatment of patients with relapsed and refractory multiple myeloma.
- CRB-402 study – an open label, single-arm, multicenter, phase 1 study to examine the safety and efficacy of the bb21217 product candidate in the treatment of patients with relapsed and refractory multiple myeloma.
- Additional clinical studies for the development of ide-cel, including: KarMMa-2 (MM-002), a multi-cohort, open-label, multicenter phase 2 study to examine the safety and efficacy of ide-cel in the treatment of patients with relapsed and refractory multiple myeloma and in high-risk multiple myeloma; KarMMa-3 (MM-003), a multicenter, randomized, open-label phase 3 study comparing the efficacy and safety of ide-cel versus standard triplet regimens in patients with relapsed and refractory multiple myeloma; and a planned multi-center phase 2 study to examine the safety and efficacy of ide-cel in the treatment of patients with newly-diagnosed multiple myeloma.

- We will continue to manufacture clinical study materials in support of our clinical studies.

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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 March 31,	
	2019	2018
	(in thousands)	
LentiGlobin (including ZYNTEGLO)	$31,846	$32,797
Lenti-D	8,686	6,197
Ide-cel	19,791	12,265
bb21217	4,486	3,270
Pre-clinical programs	11,329	11,159
Total direct research and development expense	76,138	65,688
Employee-and contractor-related expenses	10,518	7,225
Stock-based compensation expense	15,516	11,624
Platform-related expenses	4,627	4,672
Facility expenses	14,619	7,673
Other expenses	1,222	227
Total other research and development expenses	46,502	31,421
Total research and development expense	$122,640	$97,109

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 tisagenlecleucel.

Change in fair value of contingent consideration

On June 30, 2014, we acquired Precision Genome Engineering, Inc., or 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 March 31, 2019, 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 $5.5 million as of March 31, 2019, all of which is classified as a non-current liability on our unaudited condensed consolidated balance sheet.

Interest income, net

Interest income, net consists primarily of interest income earned on investments and, for the three months ended March 31, 2018, interest expense on the financing lease obligation for our headquarters at 60 Binney Street in Cambridge, Massachusetts. Upon adoption of ASU 2016-02, Leases (Topic 842), ("ASU 2016-02" or "ASC 842"), we de-recognized the financing lease obligation. Please refer to Note 2, "Basis of presentation, principles of consolidation and significant accounting policies" and Note 7, "Leases" in the Notes to Condensed Consolidated Financial Statements (unaudited) for further information.

Other (expense) income, net

Other (expense) income, net consists primarily of losses on equity securities held by us, 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 three months ended March 31, 2019, 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, 2018, which was filed with the SEC on February 21, 2019, except as otherwise described in Note 2, "Basis of presentation, principles of consolidation and significant accounting policies" in the Notes to Condensed Consolidated Financial Statements (unaudited).

Results of Operations

Comparison of the three months ended March 31, 2019 and 2018:

	For the three months ended March 31,		
	2019	2018	Change
	(in thousands)		
Revenue:			
Collaboration revenue	$11,177	$15,608	$(4,431)
License and royalty revenue	1,294	349	945
Total revenues	12,471	15,957	(3,486)
Operating expenses:			
Research and development	122,640	97,109	25,531
General and administrative	60,279	34,926	25,353
Cost of license and royalty revenue	430	17	413
Change in fair value of contingent consideration	296	534	(238)
Total operating expenses	183,645	132,586	51,059
Loss from operations	(171,174)	(116,629)	(54,545)
Interest income (expense), net	10,102	1,388	8,714
Other (expense) income, net	(3,389)	115	(3,504)
Loss before income taxes	(164,461)	(115,126)	(49,335)
Income tax (expense) benefit	15	—	15
Net loss	$(164,446)	$(115,126)	$(49,320)

Revenues. Total revenue was $12.5 million for the three months ended March 31, 2019, compared to $16.0 million for the three months ended March 31, 2018. The decrease of $3.5 million was primarily attributable to a decrease in collaboration revenue for the ide-cel license and manufacturing services under our agreement with Celgene, offset by an increase in license and royalty revenue.

Research and development expenses. Research and development expenses were $122.6 million for the three months ended March 31, 2019, compared to $97.1 million for the three months ended March 31, 2018. The overall increase of $25.5 million was primarily attributable to the following:

- $12.8 million of increased employee compensation, benefit, and other headcount related expenses, of which $3.9 million is stock based compensation expense, primarily due to an increase in headcount to support overall growth;
- $8.8 million of increased costs incurred for laboratory expenses, non-clinical expenses, and collaboration research;
- $6.9 million of increased facility related costs, primarily from rent expense incurred as a result of the adoption of ASU 2016-02; and
- $2.2 million of increased professional and consulting fees.

These increased costs were offset by:

- $3.2 million of decreased license and milestone fees;
- $1.4 million of decreased material production costs; and

- $1.3 million of decreased clinical trial related costs.

General and administrative expenses. General and administrative expenses were $60.3 million for the three months ended March 31, 2019, compared to $34.9 million for the three months ended March 31, 2018. The increase of $25.4 million was primarily attributable to the following:

- $13.9 million of increased employee compensation, benefit, and other headcount related expenses, of which $5.5 million is stock based compensation expense, primarily due to an increase in headcount to support overall growth;
- $6.7 million of increased professional and consulting fees;
- $4.3 million of increased market research costs; and
- $1.9 million of increased office supplies and software licenses.

These increased costs were offset by decreased facility related costs of $1.5 million.

Interest income, net. The change in interest income (expense), net was primarily related to interest income earned on investments, as well as a decrease in interest expense incurred due to the de-recognition of the financing lease obligation associated with our corporate headquarters at 60 Binney Street related to the adoption of ASU 2016-02 on January 1, 2019.

Other (expense) income, net. The change in other (expense) income, net was primarily related to unrealized losses on equity securities.

Liquidity and Capital Resources

As of March 31, 2019, we had cash, cash equivalents and marketable securities of approximately $1.73 billion. We expect that our existing cash, cash equivalents and marketable securities will be sufficient to fund our current 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 March 31, 2019, our funds are primarily held in U.S. treasury securities, U.S. government agency securities, certificates of deposit, corporate bonds, commercial paper and money market accounts.

We have incurred losses and cumulative negative cash flows from operations since our inception in April 1992, and as of March 31, 2019 we had an accumulated deficit of $1.66 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 three months ended March 31,	
	2019	2018
	(in thousands)	
Net cash used in operating activities	$(154,154)	$(108,822)
Net cash used in investing activities	(36,913)	(264,725)
Net cash provided by financing activities	10,223	71,677
Net decrease in cash, cash equivalents and restricted cash	$(180,844)	$(301,870)

Cash Flows from Operating Activities. The $45.3 million increase in cash used in operating activities for the three months ended March 31, 2019 compared to the three months ended March 31, 2018 was partially due to the increase in net loss during this period of $49.3 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 $227.8 million decrease in cash used in investing activities for the three months ended March 31, 2019 was primarily due to an increase of $219.0 million in proceeds received from the maturity of marketable securities and a decrease in cash used to purchase marketable securities of $20.7 million, offset by an increase of $11.9 million in cash used to purchase property, plant and equipment, primarily related to the facility in Durham, North Carolina, compared to the three months ended March 31, 2018.

Cash Flows from Financing Activities. The $61.5 million decrease in cash provided by financing activities was primarily driven by a decrease in proceeds from public offering of common stock of $48.7 million, as well as a decrease in proceeds from issuance of common stock to employees of $9.8 million in the three months ended March 31, 2019 compared to the three months ended March 31, 2018.

Contractual Obligations and Commitments

Except for the subsequent event described in Note 14 to the Condensed Consolidated Financial Statements (unaudited), 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, 2019.

Off-Balance Sheet Arrangements

As of March 31, 2019, 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 March 31, 2019 and December 31, 2018, we had cash, cash equivalents and marketable securities of $1.73 billion and $1.89 billion, respectively, primarily invested in U.S. government agency securities and treasuries, federally insured certificates of deposit, corporate bonds, commercial paper 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 March 31, 2019, the net fair value of our interest-sensitive marketable securities would have resulted in a hypothetical decline of approximately $9.5 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 March 31, 2019, 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 March 31, 2019, our disclosure controls and procedures were effective at the

reasonable assurance level.

Changes in Internal Control over Financial Reporting

During the quarter ended March 31, 2019, we implemented certain internal controls in connection with our adoption of ASU 2016-02, Leases (Topic 842). There were no other changes in our internal control over financial reporting during the first quarter of 2019, 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 March 31, 2019, 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 Form 10-K filed with the Securities and Exchange Commission, or the SEC, on February 21, 2019.

Risks related to the 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.

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, a limited number of gene therapy products, including CAR T therapies, have been approved by the FDA, the EMA and the European Commission. 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 European Union 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 the development of gene therapy products have changed frequently and may continue to change in the future. The FDA has established the Office of Tissues and Advanced Therapies within the Center for Biologics Evaluation and Research (CBER), to consolidate the review of gene therapy and related products, and to advise the CBER on its review. Before a clinical study can begin at any institution, that institution's 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.

Success in early clinical studies may not be indicative of results obtained in later studies.

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 patients or for any future patients 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 who have been treated with ZYNTEGLO may experience a reduction of or independence from transfusion support following successful engraftment, there can be no assurance that they will not require transfusion support in the future. Similarly, patients with relapsed and refractory multiple myeloma who have been treated with ide-cel or the bb21217 product candidate may experience disease progression. We have experienced unexpected results in the past, and we may experience unexpected results in the future. For instance, initial results from our clinical studies of ZYNGEGLO suggested that patients with TDT who do not have a $^{0}/^{0}$ genotype experienced better outcomes to treatment than patients with TDT who have a $^{0}/^{0}$ genotype. Consequently, we are seeking conditional approval in the European Union, and we expect to seek FDA approval in the United States, of ZYNTEGLO initially for the treatment of patients with TDT who do not have a $^{0}/^{0}$ genotype. In order to support an application for FDA approval of ZYNTEGLO in patients with TDT who have a $^{0}/^{0}$ genotype, we initiated the HGB-212 study, but we do not know if or when ZYNTEGLO may be commercially available to patients with all genotypes. 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.

*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.

In March 2019, we announced that the Committee for Medicinal Products for Human Use of the EMA adopted a positive opinion recommending conditional marketing authorization of ZYNTEGLO for the treatment of patients 12

years and older with TDT who do not have a $^0/^0$ genotype, for whom HSC transplantation is appropriate but a human leukocyte-matched related HSC donor is not available. Whether ZYNTEGLO receives conditional approval will ultimately be determined at the discretion of the European Commission, and will be dependent upon the data available, which may not be sufficiently robust from a safety and/or efficacy perspective to support conditional approval. Even if conditional approval is obtained, the conditions to be imposed on us under this program are unknown and will be imposed at the time of any such conditional approval.

In 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 ZYNTEGLO to treat adult and adolescent patients with TDT who do not have a $^0/^0$ 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 ZYNTEGLO to treat patients with TDT who have a $^0/^0$ genotype. However, it should be noted that our ability to submit and obtain approval of a BLA is ultimately an FDA review decision, which will be dependent upon the data available at such time, and the available data may not be sufficiently robust from a safety and/or efficacy perspective to support the submission or approval of a BLA. Depending on the outcome of these 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 ZYNTEGLO for the treatment of TDT.

Based on our discussions with the FDA and EMA, we believe that we may be able to seek approval for our Lenti-D product candidate for the treatment of patients with CALD on the basis of the clinical data from our ongoing Starbeam study, and the ongoing ALD-103 observational study. Our regulatory submission plans are contingent upon our Lenti-D product candidate demonstrating sufficient efficacy and safety in the Starbeam study. Whether our Lenti-D product candidate is eligible for approval will ultimately be determined at the discretion of the FDA and 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 approval. Depending on the outcome of our ongoing studies, the FDA in the United States and EMA and European Commission in the European Union may require that we conduct additional or larger clinical trials before our Lenti-D product candidate is eligible for approval.

In the development of our LentiGlobin product candidate for the treatment of patients with SCD, we are exploring efficacy endpoints based on $^{A\text{-}T87Q}$ expression and total hemoglobin, and the relationship such endpoints have with clinical outcomes. Our development plans in the United States are contingent upon our LentiGlobin product candidate demonstrating sufficient efficacy and safety in the ongoing HGB-206 study and planned HGB-210 study. Whether our LentiGlobin product candidate is eligible for approval will ultimately be determined at the discretion of the FDA 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 approval. For instance, the FDA may not accept $^{A\text{-}T87Q}$ expression and total hemoglobin as surrogate endpoints for other SCD clinical outcomes such as frequency of vaso-occlusive events. Depending on the outcome of our ongoing and planned studies, the FDA may require that we conduct additional or larger clinical trials before our LentiGlobin product candidate is eligible for approval for the treatment of patients with SCD. In addition, we are engaged with the EMA in discussions regarding our proposed development plans for LentiGlobin in SCD in Europe, and we cannot be certain that our HGB-206 study and planned HGB-210 study will be sufficient to form the basis for an initial MAA submission in Europe for the treatment of patients with SCD.

Based on our discussions with the FDA, we and Celgene believe that we may be able to seek approval for ide-cel for the treatment of patients with relapsed and refractory multiple myeloma on the basis of the clinical data from our ongoing CRB-401 and KarMMA studies. Our regulatory submission plans are contingent upon ide-cel demonstrating sufficient efficacy and safety in these studies. Whether ide-cel is eligible for approval will ultimately be determined at the discretion of the FDA, 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 approval. Depending on the outcome of our ongoing studies, the FDA may require that we conduct additional or larger clinical trials before ide-cel is eligible for approval.

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

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

- delays in reaching a consensus with regulatory agencies on study design;
- delays in obtaining required institutional review board, or IRB, or Institutional Ethics Committee approval at each clinical study site;
- 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;
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failure by our third-party clinical research organizations, or 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.

Furthermore, 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 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. The conditions for which we plan to evaluate our current product candidates in severe genetic diseases are rare disorders with limited patient pools from which to draw for clinical studies. The eligibility criteria of our clinical studies will further limit the pool of available study participants, and the process of finding and diagnosing patients may prove costly. Patients may be unwilling to participate in our 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. We have experienced delays in some of our clinical studies in the past, and we may experience similar delays in the future.

Any inability to successfully complete preclinical and clinical development could result in additional costs to us or impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties. In addition, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional studies to demonstrate comparability of our modified product candidates to earlier versions.

Clinical study delays could also shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

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

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

Treatment with our gene therapy product candidates involves chemotherapy and myeloablative treatments, which can cause side effects or adverse events that are unrelated to our product candidates, but may still impact the perception of the potential benefits of our product candidates and 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.

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. In published studies, lentiviral vectors have demonstrated an improved safety profile over gamma-retroviral vectors used

in early gene therapy studies, 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 a phase 1/2 study of HPV569, which utilized an earlier generation lentiviral vector of the vector used in ZYNTEGLO and LentiGlobin, 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.

Patients receiving T cell-based immunotherapies, such as our oncology product candidates ide-cel and bb21217, may experience serious adverse events, including neurotoxicity and cytokine release syndrome. If our product candidates are revealed to have high and unacceptable severity and/or prevalence of side effects or unexpected characteristics, their clinical development, regulatory approval, and commercial potential will be negatively impacted, which will significantly harm our business, financial condition and prospects.

Ide-cel and the bb21217 product candidate are chimeric antigen receptor, or CAR, T cell-based immunotherapies. In previous and ongoing clinical studies involving CAR T cell products, including those involving ide-cel and the bb21217 product candidate, patients experienced side effects such as neurotoxicity and cytokine release syndrome. There have been life threatening events related to severe neurotoxicity and cytokine release syndrome, requiring intense medical intervention such as intubation or pressor support, and in several cases, resulted in death. Severe neurotoxicity is a condition that is currently defined clinically by cerebral edema, confusion, drowsiness, speech impairment, tremors, seizures, or other central nervous system side effects, when such side effects are serious enough to lead to intensive care. In some cases, severe neurotoxicity was thought to be associated with the use of certain lymphodepletion regimens used prior to the administration of the CAR T cell products. Cytokine release syndrome is a condition that is currently defined clinically by certain symptoms related to the release of cytokines, which can include fever, chills, low blood pressure, when such side effects are serious enough to lead to intensive care with mechanical ventilation or significant vasopressor support. The exact cause or causes of cytokine release syndrome and severe neurotoxicity in connection with treatment of CAR T cell products is not fully understood at this time. In addition, patients 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 ide-cel or the 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. In some cases, side effects such as neurotoxicity or cytokine release syndrome have resulted in clinical holds of ongoing clinical trials and/or discontinuation of the development of the product candidate. 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 patients 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. Medical personnel may need additional training regarding T cell-based immunotherapy product candidates to understand their side effects. Inadequate training in recognizing or failure to effectively manage 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 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.

*The United Kingdom's decision to withdraw from the European Union could result in increased regulatory and legal complexity, which may make it more difficult for us to do business in Europe and impose additional challenges in securing regulatory approval of our product candidates in Europe.

Negotiations for the United Kingdom's exit from the European Union, or Brexit, has caused political and economic uncertainty, including in the regulatory framework applicable to our operations and potential products, and this uncertainty may persist for years. Brexit could, among other outcomes, disrupt the free movement of goods, services and people between the United Kingdom and the European Union, and result in increased legal and regulatory complexities, as well as potential higher costs of conducting business in Europe. For instance, preparations for Brexit has resulted in the decision to move the EMA from the United Kingdom to the Netherlands, with operations beginning in the Netherlands in March 2019.

The cumulative effects of the disruption to the regulatory framework may add considerably to the development lead time to marketing authorization and commercialization of products in the European Union and/or the United Kingdom. It is possible that there will be increased regulatory complexities which can disrupt the timing of our clinical trials and regulatory approvals. In addition, changes in, and legal uncertainty with regard to, national and international laws and regulations may present difficulties for our clinical and regulatory strategy. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenues and achieve and sustain profitability. In particular, we cannot predict whether, or the extent to which, Brexit will affect the timing for the potential commercialization plans of our product candidates in the United Kingdom in 2019 and beyond.

Risks related to our reliance on third parties

We expect to rely on third parties to conduct some or all aspects of our lentiviral 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 lentiviral 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 manufacturing, 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 lentiviral 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 lentiviral 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, or to support commercialization of our products, if approved. Many of our agreements with these third parties contain termination provisions that allow these third parties to terminate their relationships with us at any time. If we need to enter into alternative arrangements, our product development and commercialization activities could be delayed.

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.

We may be forced to manufacture lentiviral vector and drug product candidates ourselves, for which we may not have the capabilities or resources, or enter into an agreement with a different manufacturer, which we may not be able to do on reasonable terms, if at all. In some cases, the technical skills required to manufacture our lentiviral vector or drug product candidates may be unique or proprietary to the original manufacturer, and we may have difficulty or there may be contractual restrictions prohibiting us from, transferring such skills to a back-up or alternate supplier, or we may be unable to transfer such skills at all. 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.

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 revenues.

*We are dependent on Celgene for the successful development and commercialization of ide-cel and bb21217. If Celgene does not devote sufficient resources to the development of ide-cel 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 ide-cel in the United States with Celgene under our amended and restated co-development and co-promotion agreement with Celgene, or the Ide-cel CCPS. Under the Ide-cel CCPS, we and Celgene share the obligation to develop and commercialize ide-cel in the United States, and we will be solely dependent on Celgene to develop and commercialize ide-cel 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 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 ide-cel and bb21217. Celgene may determine however, that it is commercially reasonable to de-prioritize or discontinue the development of ide-cel and bb21217. These outcomes may occur for many reasons, including internal business reasons (including due to the existence of other Celgene programs that are potentially competitive with ide-cel and bb21217), 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 has certain decision-making rights in determining the development and commercialization plans 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, ide-cel or bb21217 to narrower indications than we would pursue. More broadly, if Celgene elects to discontinue the development of ide-cel 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 ide-cel, 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 ide-cel, 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 and 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 ide-cel 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. In January 2019, Celgene and Bristol-Myers Squibb Company, or BMS, announced that they have entered into a definitive merger agreement under which BMS will acquire Celgene. The transaction has been approved by the stockholders of Celgene and BMS, and is expected to be completed in the third quarter of 2019. The acquisition of Celgene by BMS may result in organizational and personnel changes, shifts in business focus or other developments that may have a material adverse effect on our collaboration with Celgene. There is no guarantee that BMS will place the same emphasis on the collaboration or on the development and commercialization of the ide-cel or bb21217 product candidates.

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 and other regulatory authorities' 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. 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 and other regulatory authorities may require us to perform additional clinical studies before approving any marketing applications.

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.

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 incurred net losses in each year since our inception in 1992, including net losses of $164.4 million for the three months ended March 31, 2019. As of March 31, 2019, we had an accumulated deficit of $1.66 billion. The amount of our future net losses will depend, in part, on the rate of our future expenditures and our ability to generate revenues. We have devoted significant financial resources to research and development, including our clinical and preclinical development activities, which we expect to continue for the foreseeable future. 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. We do not expect to generate any product revenues until the second half of 2019, assuming we receive marketing approval for ZYNTEGLO in the European Union for the treatment of adult and adolescent patients with TDT who do not have a $^{0}/^{0}$ genotype. 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. In addition, to the extent payment for our products is subject to outcomes-based arrangements over time, the total payments received from product sales may vary, our cash collection of future payments and revenues assumptions from product sales will be at risk, and the timing of revenue recognition may not correspond to the timing of cash collection.

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 ide-cel, which we are co-developing with Celgene;
- establish capabilities to support our planned commercialization efforts, including establishing a sales, marketing and distribution infrastructure in the United States and Europe, and commercialize any products for which we may obtain marketing approval;
- obtain, build and expand manufacturing capacity, including capacity at third-party manufacturers and our own manufacturing facility;
- initiate additional research, preclinical, clinical or other programs as we seek to identify and validate additional product candidates;
- acquire or in-license other product candidates and technologies;
- maintain, protect and expand our intellectual property portfolio;
- attract and retain skilled personnel; and
- experience any delays or encounter issues with any of the above.

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

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

Our ability to generate revenues 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. 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 commercial 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 field-based team, 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 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 ZYNTEGLO in TDT, LentiGlobin in SCD, Lenti-D in CALD, and ide-cel and bb21217 in multiple myeloma, 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 March 31, 2019, our cash, cash equivalents and marketable securities were $1.73 billion. We expect that our existing cash, cash equivalents, and marketable securities will be sufficient to fund our current planned 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 rely on a complex supply chain for our product candidates. The manufacture and delivery of our engineered autologous gene therapy product presents significant challenges for us, and we may not be able to produce our vector and products at the quality, quantities, locations or timing needed to support commercialization. In addition, we may encounter challenges with engaging or coordinating with qualified treatment centers needed to support commercialization.

In order to develop our product candidates, apply for regulatory approvals and commercialize our products if approved, we will need to develop, contract for, or otherwise arrange for the necessary manufacturing capabilities. We currently rely on third parties to manufacture the vector and the drug product candidate that we require for any clinical trials that we initiate. Although we intend to rely on a mix of internal and third-party manufacturers to support our planned commercialization efforts, we are still in the process of completing construction and qualification of our internal capacity and we have not secured commercial-scale manufacturing capacity in all of the regions where we intend to commercialize our potential products. By building our own internal manufacturing facility, we have incurred substantial expenditures and expect to incur significant additional expenditures in the future. In addition, there are many risks inherent in the construction of a new facility that could result in delays and additional costs, including the need to obtain access to necessary equipment and third-party technology, if any. Also, we have had to, and will continue to, hire and train qualified employees to staff our manufacturing facility. We may not be able to timely or successfully build out our internal capacity or negotiate binding agreements at commercially reasonable terms with third-party manufacturers.

The manufacture of our lentiviral vector and drug product candidates is complex and requires significant expertise. Manufacturers of cell therapy products often encounter difficulties in production, particularly in scaling out and validating initial production, and ensuring that the product meets required specifications. These problems include difficulties with production costs and yields, quality control, including stability of the product, quality assurance testing, operator error, shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. We cannot make any assurances that these problems will not occur in the future, or that we will be able to resolve or address problems that occur in a timely manner or with available funds. Furthermore, our cost of goods development is at an early stage. The actual cost to manufacture our lentiviral vector and drug product candidates could be greater than we expect and could materially and adversely affect the commercial viability of our product candidates. If we or such third-party manufacturers are unable to produce the necessary quantities of lentiviral vector 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.

Additionally, since the HSCs and T cells have a limited window of stability following procurement from the subject, we must establish 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 establish additional transduction facilities that can replicate our transduction process in order to address those patient populations. 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.

Our commercial plan is to engage apheresis centers in our key launch regions as qualified treatment centers for the collection of patient HSCs and infusion of the drug product once manufactured. To ensure that the qualified treatment centers are prepared to collect patient HSCs and to ship them to our transduction facilities in accordance with our specifications and regulatory requirements, we plan to train and conduct quality certifications of each center as part of engagement. We intend for these qualified treatment centers to be the first and last points on our complex supply chain to reach patients in the commercial setting. We may not be able engage qualified treatment centers in all of the regions in our commercial launch strategy, or we may encounter other challenges or delays in engaging qualified treatment centers. We may fail to manage the logistics of collecting and shipping patient material to the manufacturing site and shipping the product candidate back to the patient. Logistical and shipment delays and problems caused by us, our vendors other factors not in our control, such as weather, could prevent or delay the delivery of products to patients. If our qualified treatment centers fail to perform satisfactorily, we may suffer reputational, operational, and business harm. We anticipate having to maintain a complex chain of identity and chain of custody with respect to patient material as it moves through the manufacturing process, from the qualified treatment center to the transduction facility, and back to the patient. Failure to maintain chain of identity and chain of custody could adverse patient outcomes, loss of product or regulatory action.

Although we are continuing to build 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 are continuing to build out our field team in anticipation of our potential first commercial launch in Europe in 2019, 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. If our competitors obtain orphan drug exclusivity for products that regulatory authorities determine constitute the same drug and treat the same indications as our product candidates, we may not be able to have competing products approved by the applicable regulatory authority for a significant period of time.

We are engaged in gene therapy for severe genetic diseases and cancer, 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. 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, safer, 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. For additional information regarding our competition, see “Item 1. Business—Competition” in our Annual Report on Form 10-K.

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. Generally, if a product candidate with an orphan drug designation receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period marketing exclusivity, which precludes the FDA or the European Commission from approving another marketing application for a product that constitutes the same drug treating the same indication for that marketing exclusivity period, except in limited circumstances. If another sponsor receives such approval before we do (regardless of our orphan drug designation), we will be precluded from receiving marketing approval for our product for the exclusivity period for the applicable indication.

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. 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;
- requirements or limitations imposed by a specific country or region on potential qualified treatment centers or other aspects of commercialization applicable to autologous gene therapies such as ours;
- 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. 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 additional uncertainty related to pricing and reimbursement for our product candidates. 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 our gene therapy products. In addition, because our therapies represent new treatment approaches, the estimation of potential revenues will be complex. 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 that are potential one-time treatments. 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, or HHS, 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. 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 with the reimbursement experienced by the initial gene therapies to receive marketing authorization may 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.

Furthermore, because our target patient populations are relatively small, the pricing and reimbursement of our product candidates, if approved, must be adequate to cover the costs to treat and support the treatment of patients. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell our product candidates will be adversely affected. We have proposed novel payment models, including outcomes-based arrangements with payments over time, to assist with realizing the value and sharing the risk of a potential one-time treatment, such as ZYNTEGLO. While we are engaged in discussions with potential payors, there is no assurance that any payors will adopt these payment models. These payment models may not be sufficient for payors to grant coverage, and if we are unable to obtain adequate coverage for our products, the adoption of our products may be limited. In addition, to the extent reimbursement for our products is subject to outcomes-based arrangements, the total payments received from product sales may vary, our cash collection of future payments and revenue assumptions from product sales will be at risk, and the timing of revenue recognition may not correspond to the timing of cash collection. Moreover, the administration of our products require procedures for the collection of HSCs from the patient, followed by chemotherapy and myeloablative treatments, before infusion of the engineered cell therapy product. The manner and level at which reimbursement is provided for these services is also important. Inadequate reimbursement for such services may lead to physician resistance and adversely affect our ability to market or sell our products. These factors could affect our ability to successfully commercialize our products and generate revenues, which would adversely impact our business, financial condition, results of operations and prospects.

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

The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval of our product candidates or any future product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product for which we obtain marketing approval. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

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 changed 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, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, 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 a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (70% commencing January 1, 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer’s outpatient drugs to be covered under Medicare Part D.

Since January 2017, the Trump administration has signed two Executive Orders designed to delay the implementation of certain provisions of the Affordable Care Act or otherwise circumvent some of the requirements for health insurance mandated by the Affordable Care Act. One Executive Order directs 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 or regulatory burden on states, individuals,

healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. The second Executive Order terminates the cost-sharing subsidies that reimburse insurers under the Affordable Care Act. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in Affordable Care Act risk corridor payments to third-party payors who argued were owed to them. The effects of this gap in reimbursement on third-party payors, the viability of the Affordable Care Act marketplace, providers, and potentially our business, are not yet known.

In July 2018, the CMS published a final rule permitting further collections and payments to and from certain Affordable Care Act-qualified health plans and health insurance issuers under the Affordable Care Act risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. In addition, CMS has recently published a final rule that would give states greater flexibility, starting in 2020, in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the Affordable Care Act for plans sold through such marketplaces. On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, or the Texas District Court Judge, ruled that the individual mandate is a critical and inseverable feature of the Affordable Care Act, and therefore, because it was repealed as part of the Tax Cuts and Jobs Act of 2017, the remaining provisions of the Affordable Care Act are invalid as well. While the Trump Administration and CMS have both stated that the ruling will have no immediate effect, and on December 30, 2018 the Texas District Court Judge issued an order staying the judgment pending appeal, it is unclear how this decision, subsequent appeals and other efforts to repeal and replace the Affordable Care Act will impact the Affordable Care Act and our business.

Since its enactment, some of the provisions of the Affordable Care Act have yet to be fully implemented, while certain provisions have been subject to judicial, congressional, or executive challenges. As a result, there have been delays in the implementation of, and action taken to repeal or replace, certain aspects of the Affordable Care Act. The U.S. Supreme Court has upheld certain key aspects of the legislation, including a tax-based shared responsibility payment imposed on certain individuals who fail to maintain qualifying health coverage for all or part of a year or pay a penalty, which is commonly known as the "individual mandate." However, as a result of tax reform legislation passed in December 2017, the individual mandate has been eliminated effective January 1, 2019. On January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain Affordable Care Act-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. The Bipartisan Budget Act of 2018, or the BBA, among other things, amends the Affordable Care Act, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole."

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. In August 2011, President Obama signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee on Deficit Reduction did not achieve a targeted deficit reduction, which triggered the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of, on average, 2% per fiscal year through 2025 unless Congress takes additional action. These reductions were extended through 2027 under the BBA. In January 2013, the American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Additionally, the Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. The U.S. Department of Health and Human Services, or HHS, has already started the process of soliciting feedback on some of these measures and, at the same time, is immediately implementing others under its existing authority. For example, in September 2018, CMS announced that it will allow Medicare Advantage Plans the option to use step therapy for Part B drugs beginning January 1, 2019, and in October 2018, CMS proposed a new rule that would require direct-to-consumer television advertisements of prescription drugs and biological products, for which payment is available through or under Medicare or Medicaid, to include in the advertisement the Wholesale Acquisition Cost, or list price, of that drug or biological product. Although a number of these, and other proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures,

and, in some cases, designed to encourage importation from other countries and bulk purchasing.

We expect that the healthcare reform measures that have been adopted and may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product and could seriously harm our future revenues. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private third-party payors.

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.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our product. Such reforms could have an adverse effect on anticipated revenue 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.

If the market opportunities for our product candidates are smaller than we believe they are, and if we are not able to successfully identify patients and achieve significant market share, our revenues may be adversely affected and our business may suffer.

We focus our research and product development on treatments for severe genetic diseases and cancer. 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 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 diseases. The number of patients may turn out to be lower or more difficult to identify than expected. For instance, 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 would benefit from treatment from our Lenti-D product candidate. Additionally, the potentially addressable patient population for our product candidates may be limited or may not be amenable to treatment with our product candidates. For instance, we are initially seeking approval of ZYNTEGLO for the treatment of patients with TDT who do not have a $^{0}/^{0}$ genotype. We do not have any assurance whether or when ZYNTEGLO may be commercially available to patients with all genotypes of TDT.

Even if we obtain significant market share for our product candidates within an approved indication, because the potential target populations for our product candidates are small, we may never achieve profitability without obtaining regulatory approval for additional indications. For instance, in the field of cancer, 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.

Any of these factors may negatively affect our ability to generate revenues from sales of our product and our ability to achieve and maintain profitability, and as a consequence, our business may suffer.

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, including gene editing technologies, is unsafe or unethical, and research activities and adverse events in the field, even if not ultimately attributable to us our or our product candidates 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. 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.

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.

As we evolve from a U.S.-based company primarily involved in discovery, pre-clinical research and clinical development into a company that develops and commercializes multiple drugs with an international presence, we will need to expand our organization and we may experience difficulties in managing this growth, which could disrupt our operations.

We filed our first application for marketing authorization in 2018 and are preparing for a potential commercial launch in 2019, which we hope will be the first of a sequence of marketing approvals and commercial launches for multiple products across multiple geographies. As we advance multiple product candidates through late-stage clinical research and plan submissions for marketing authorizations, we are expanding our operations in the United States and Europe. As of March 31, 2019, we had 827 full-time employees. As we pursue our development and commercialization strategy, we expect to expand our full-time employee base and to hire more consultants and contractors in the United States and Europe. This expected growth may place a strain on our administrative and operational infrastructure. As a result, 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.

We may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties, reputational harm, and diminished profits and future earnings.

In the United States, the research, manufacturing, distribution, sale, and promotion of drugs and biologic products are subject to regulation by various federal, state, and local authorities in addition to FDA, including CMS, other divisions of the HHS, (e.g., the Office of Inspector General), the United States Department of Justice offices of the United States Attorney, the Federal Trade Commission and state and local governments. Our operations are directly, or indirectly through our prescribers, customers and purchasers, subject to various federal and state fraud and abuse laws and regulations, including, without limitation, the federal Anti-Kickback Statute, the federal civil and criminal False Claims Act and Physician Payments Sunshine Act and regulations and equivalent provisions in other countries. These laws apply to, among other things, our proposed sales, marketing and educational programs. In addition, we may be subject to patient privacy laws by both the federal government and the states in which we conduct our business.

State and federal regulatory and enforcement agencies continue actively to investigate violations of health care laws and regulations, and the United States Congress continues to strengthen the arsenal of enforcement tools. Most recently, the Bipartisan Budget Act of 2018 increased the criminal and civil penalties that can be imposed for violating certain federal health care laws, including the Anti-Kickback Statute. Enforcement agencies also continue to pursue novel theories of liability under these laws. In particular, government agencies have recently increased regulatory scrutiny and enforcement activity with respect to programs supported or sponsored by pharmaceutical companies, including reimbursement and co-pay support, funding of independent charitable foundations and other programs that offer benefits for patients. Several investigations into these programs have resulted in significant civil and criminal settlements.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. If our operations are found to be in violation of any of the laws described above or any other government regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government health care programs, such as Medicare and Medicaid, imprisonment and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. 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 harm our financial condition and divert the attention of our management from operating our business.

In the European Union, interactions between pharmaceutical companies, healthcare professionals, and patients are also governed by strict laws, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct in the individual EU member states. The provision of benefits or advantages to healthcare professionals to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is prohibited in the European Union. Also, direct-to-consumer advertising of prescription-only medicinal products is prohibited at the European Union level and in the individual member states. In addition, the UK Bribery Act applies to any company incorporated in or "carrying on business" in the UK, irrespective of where in the world the alleged bribery activity occurs, which could have implications for our interactions with physicians both in and outside of the UK. Infringement of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain European Union member states must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual European Union member states. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the European Union member states. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

EU member states, Switzerland and other countries have also adopted data protection laws and regulations, which impose significant compliance obligations. In the European Union, the collection and use of personal health data is currently governed by the provisions of the General Data Protection Regulation, or the GDPR. The GDPR, together with the national legislation of the individual EU member states governing the processing of personal data, impose strict obligations and restrictions on the ability to collect, analyze and transfer personal data, including health data from clinical trials and adverse event reporting. In particular, these obligations and restrictions concern the consent of the individuals to whom the personal data relates, the information provided to the individuals for the consent to be considered valid, the transfer of personal data out of the European Economic Area, security breach notifications, the use of third-party processors in connection with the processing of the personal data, confidentiality of the personal data, as well as substantial potential fines for breaches of the data protection obligations. Data protection authorities from the different EU member states may interpret the GDPR and national laws differently and impose additional requirements, which add to the complexity of processing personal data in the European Union. The GDPR also

imposes strict rules on the transfer of personal data to countries outside the European Union, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR is a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with any activities falling within the scope of the GDPR.

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 patients 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.

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. Our research programs, including our oncology research programs, may fail to identify other potential product candidates for clinical development for a number of reasons. We 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.

The increasing use of social media platforms presents new risks and challenges.

Social media is increasingly being used to communicate about our clinical development programs and the diseases our product candidates are being developed to treat. We intend to utilize appropriate social media in connection with our commercialization efforts following approval of our product candidates. Social media practices in the biopharmaceutical industry continue to evolve and regulations relating to such use are not always clear. This evolution creates uncertainty and risk of noncompliance with regulations applicable to our business. For example, patients may use social media channels to report an alleged adverse event. When such disclosures occur, there is a risk that we fail to monitor and comply with applicable adverse event reporting obligations, or we may not be able to defend our business or the public's legitimate interests in the face of the political and market pressures generated by social media due to restrictions on what we may say about our investigational products. There is also a risk of inappropriate disclosure of sensitive information or negative or inaccurate posts or comments about us on any social networking website, or a risk that a post on a social networking website by any of our employees may be construed as inappropriate promotion. If any of these events were to occur or we otherwise fail to comply with applicable regulations, we could incur liability, face regulatory actions, or incur other harm to our business.

Our computer systems, or those of our third-party collaborators, service providers, contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product candidates' development programs and have a material adverse effect on our reputation, business, financial condition or results of operations.

Our computer systems and those of our current or future third-party collaborators, service providers, contractors and consultants may fail and are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. The size and complexity of our information technology systems, and those of our collaborators, service providers, contractors and consultants, and the large amounts of information stored on those systems make those systems vulnerable to service interruptions, security breaches, or other failures, resulting from inadvertent or intentional actions by our employees or those of third-party business partners, or from cyber-attacks by malicious third parties. Attacks on information technology systems are increasing in their frequency, levels of persistence, sophistication and intensity, and they are being conducted by increasingly sophisticated and organized groups and individuals with a wide range of motives and expertise. In addition to extracting sensitive information, such attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. The prevalent use of mobile devices also increases the risk of data security incidents. If we experience a material system failure, accident or security breach that causes interruptions in our operations or the operations of third-party collaborators, service providers, contractors and consultants, it could result in significant reputational, financial, legal, regulatory, business or operational harm. For example, the loss of

clinical trial data for our product candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications or other data or applications relating to our technology or product candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of our product candidates could be delayed. We also rely on third-party service providers for aspects of our internal control over financial reporting and such service providers may experience a material system failure or fail to carry out their obligations in other respects, which may impact our ability to produce accurate and timely financial statements, thus harming our operating results, our ability to operate our business, and our investors' view of us. In addition, our liability insurance may not be sufficient in type or amount to cover us against claims related to material failures, security breaches, cyberattacks and other related breaches.

Any failure or perceived failure by us or any third-party collaborators, service providers, contractors or consultants to comply with our privacy, confidentiality, data security or similar obligations to third parties, or any data security incidents or other security breaches that result in the unauthorized access, release or transfer of sensitive information, including personally identifiable information, may result in governmental investigations, enforcement actions, regulatory fines, litigation or public statements against us, could cause third parties to lose trust in us or could result in claims by third parties asserting that we have breached our privacy, confidentiality, data security or similar obligations, any of which could have a material adverse effect on our reputation, business, financial condition or results of operations. Moreover, data security incidents and other security breaches can be difficult to detect, and any delay in identifying them may lead to increased harm. While we have implemented data security measures intended to protect our information technology systems and infrastructure, there can be no assurance that such measures will successfully prevent service interruptions or data security incidents.

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 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.

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 successfully manage the commercial launch of our product candidates following regulatory approval, including failure to manage our supply chain operations in the coordination and delivery of drug product to patients at qualified treatment centers;
- failure to obtain sufficient pricing and reimbursement for our product candidates from private and governmental payors;
- failure to obtain market acceptance and adoption of our product;

- 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. 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

Purchases of Equity Securities by the Issuer

We repurchased the following shares of our common stock in the periods set forth in the table below:

Period	Total Number of Shares (or Units) Purchased	Average Price Paid per Share (or Unit)	Total Number of Shares (or Units) Purchased as Part of Publicly Announced Plan or Program	Maximum (or Approximate Dollar Value) of Shares (or Units) that May Yet Be Purchased Under the Plans or Programs
March 1 – March 31, 2019 (a)	115	$150.82	—	—

(a) Our 2013 Stock Option and Incentive Plan permits participants to use the fair market value of our common stock they own to pay for the exercise of stock options ("stock swap method"). In connection with the exercise of a stock option to purchase 432 shares of our common stock at an exercise price of $39.89 per share, an optionee tendered 115 shares of our common stock held by the optionee in consideration of the full aggregate exercise price in accordance with the terms of the option and the Option Plan. The shares used under the stock swap method are included in the total number of shares purchased in the table above

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), Jason Cole (Chief Operating and Legal Officer), Jeffrey Walsh (Chief Strategy Officer) and Kory Wentworth (Vice President, Finance and Treasurer)), 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†	Patent License Agreement, dated December 11, 1996, by and between the Registrant (formerly known as Genetix Pharmaceuticals Inc., successor-in-interest to Innogene Pharmaceuticals Inc.) and Massachusetts Institute of Technology, as amended	S-1	333-188605	10.6	May 14, 2013

10.6†	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
10.7†	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
10.8†	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
10.9†	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
10.10†	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
10.11†	License Agreement, dated December 7, 2011, by and between the Registrant and Research Development Foundation	S-1	333-188605	10.9	May 14, 2013
10.12†	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

Exhibit Number	Exhibit Title	Incorporated by Reference Form	File no.	Exhibit	Filing Date
10.13†	Master Collaboration Agreement by and between the Registrant and Celgene Corporation, dated March 19, 2013	S-1	333-188605	10.11	May 14, 2013
10.14†	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
10.15	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
10.16	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
10.17†	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
10.18†	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
10.19†	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
10.20†	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
10.21†	Letter Agreement by and between the Registrant and Biogen MA Inc., dated September 29, 2017	10-Q	001-35966	10.21	November 1, 2017
10.22†	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
10.23†	License Agreement, dated December 23, 2015, by and between the Registrant and SIRION Biotech GmbH	10-K	001-35966	10.23	February 21, 2019
10.24†	Toll Manufacturing and Service Agreement, dated November 18, 2016 by and between the Registrant and APCETH	10-K	001-35966	10.24	February 21,

	Biopharma GmbH				2019
10.25†	Clinical and Commercial Supply Agreement – Viral Vector Product, dated November 27, 2017, by and between the Registrant and SAFC Carlsbad, Inc.	10-K	001-35966	10.25	February 21, 2019
10.26#	Amended and Restated Employment Agreement by and between the Registrant and Nick Leschly	S-1/A	333-188605	10.12	June 4, 2013
10.27#	Amended and Restated Employment Agreement by and between the Registrant and Jeffrey T. Walsh	S-1/A	333-188605	10.13	June 4, 2013
10.28#	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 May 30, 2015, by and between the Registrant and Philip D. Gregory	10-Q	001-35966	10.21	August 7, 2015

Exhibit Number	Exhibit Title	Incorporated by Reference Form	File no.	Exhibit	Filing Date
10.33#	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
10.34#	2013 Employee Stock Purchase Plan	S-1/A	333-188605	10.17	June 4, 2013
10.35#	First Amendment of the Bluebird Bio, Inc. 2013 Employee Stock Purchase Plan	10-K	001-35966	10.38	February 21, 2018
10.36#	Offer Letter, dated November 16, 2017, by and between the Registrant and Kory Wentworth	10-K	001-35966	10.39	February 21, 2018
10.37#	Executive Cash Incentive Bonus Plan	S-1	333-188605	10.18	May 14, 2013
10.38#	Employment Agreement, dated December 18, 2018, by and between the Registrant and William (“Chip”) Baird	8-K	001-35966	10.1	February 11, 2019
10.39†	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
10.40	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
10.41	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
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
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 March 31,	—	—	—	Filed herewith

	2019, 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 Stockholders' Equity, (iv) Condensed Consolidated Statements of Cash Flows and (v) Notes to Condensed Consolidated Financial Statements.

†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: May 2, 2019 By: /s/ Nick Leschly

Nick Leschly

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

Date: May 2, 2019 By: /s/ Chip Baird

Chip Baird

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