UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

FORM 10-Q

(Mark One)

☒ **QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the quarterly period ended June 30, 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 Cambridge, Massachusetts	**02142**
(Address of Principal Executive Offices)	**(Zip Code)**

(339) 499-9300
(Registrant's Telephone Number, Including Area Code)

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

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

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 ☒

As of July 25, 2019, there were 55,269,239 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,” “seek,” “should,” “target,” “would,” or the negative of these words or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

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

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

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

bluebird bio, Inc.

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PART I. FINANCIAL INFORMATION

Item 1. Financial Statements

bluebird bio, Inc.

Condensed Consolidated Balance Sheets
(unaudited)
(in thousands, except par value amounts)

	As of June 30, 2019	As of December 31, 2018
Assets		
Current Assets:		
Cash and cash equivalents	$ 280,995	$ 402,579
Marketable securities	972,885	982,725
Prepaid expenses	25,427	19,762
Receivables and other current assets	21,473	13,931
Total current assets	1,300,780	1,418,997
Marketable securities	287,922	506,123
Property, plant and equipment, net	129,135	246,622
Intangible assets, net	16,480	13,169
Goodwill	13,128	13,128
Operating lease right-of-use assets	190,979	—
Restricted cash and other non-current assets	84,920	44,805
Total assets	$ 2,023,344	$ 2,242,844
Liabilities and Stockholders' Equity		
Current Liabilities:		
Accounts payable	$ 29,458	$ 17,831
Accrued expenses and other current liabilities	91,105	99,393
Operating lease liability, current portion	18,872	—
Deferred revenue, current portion	9,484	18,602
Collaboration research advancement, current portion	13,190	10,605
Total current liabilities	162,109	146,431
Deferred revenue, net of current portion	13,739	16,338
Collaboration research advancement, net of current portion	28,333	33,349
Contingent consideration	5,740	5,230
Operating lease liability, net of current portion	175,350	—
Financing lease obligation, net of current portion	—	153,319
Other non-current liabilities	1,699	3,107
Total liabilities	386,970	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 June 30, 2019 and December 31, 2018	—	—
Common stock, $0.01 par value, 125,000 shares authorized; 55,228 and 54,738 shares issued and outstanding at June 30, 2019 and December 31, 2018, respectively	553	547
Additional paid-in capital	3,489,112	3,386,958
Accumulated other comprehensive loss	(819)	(3,627)
Accumulated deficit	(1,852,472)	(1,498,808)
Total stockholders' equity	1,636,374	1,885,070
Total liabilities and stockholders' equity	$ 2,023,344	$ 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 June 30,		For the six months ended June 30,	
	2019	2018	2019	2018
Revenue:				
Collaboration revenue	$ 11,558	$ 7,437	$ 22,735	$ 23,045
License and royalty revenue	1,738	414	3,032	763
Total revenues	13,296	7,851	25,767	23,808
Operating expenses:				
Research and development	146,540	115,014	269,180	212,123
General and administrative	68,631	41,168	128,910	76,094
Cost of license and royalty revenue	613	21	1,043	36
Change in fair value of contingent consideration	214	262	510	796
Total operating expenses	215,998	156,465	399,643	289,049
Loss from operations	(202,702)	(148,614)	(373,876)	(265,241)
Interest income, net	9,387	2,436	19,489	3,824
Other (expense) income, net	(2,936)	182	(6,325)	297
Loss before income taxes	(196,251)	(145,996)	(360,712)	(261,120)
Income tax benefit	469	—	484	—
Net loss	$ (195,782)	$ (145,996)	$ (360,228)	$ (261,120)
Net loss per share - basic and diluted:	$ (3.55)	$ (2.91)	$ (6.54)	$ (5.22)
Weighted-average number of common shares used in computing net loss per share - basic and diluted:	55,165	50,153	55,062	50,038
Other comprehensive income (loss):				
Other comprehensive income (loss), net of tax expense of $0.8 million and $0.0 million for the three months ended June 30, 2019 and 2018, respectively, and $1.3 million and $0.0 million for the six months ended June 30, 2019 and 2018, respectively	973	(345)	2,808	(1,189)
Total other comprehensive income (loss)	973	(345)	2,808	(1,189)
Comprehensive loss	$ (194,809)	$ (146,341)	$ (357,420)	$ (262,309)

See accompanying notes to unaudited condensed consolidated financial statements.

bluebird bio, Inc.

Condensed Consolidated Statements of Stockholders' Equity
(unaudited)
(in thousands)

	Common stock		Additional paid-in capital	Accumulated other comprehensive loss	Accumulated deficit	Total stockholders' equity
	Shares	Amount				
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
Vesting of restricted stock units	66	1	(1)	—	—	—
Exercise of stock options	93	1	3,972	—	—	3,973
Stock-based compensation	—	—	55,111	—	—	55,111
Other comprehensive income	—	—	—	973	—	973
Net loss	—	—	—	—	(195,782)	(195,782)
Balances at June 30, 2019	55,228	$ 553	$ 3,489,112	$ (819)	$ (1,852,472)	$ 1,636,374

	Common stock		Additional paid-in capital	Accumulated other comprehensive loss	Accumulated deficit	Total stockholders' equity
	Shares	Amount				
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
Vesting of restricted stock units	33	—	—	—	—	—
Exercise of stock options	125	1	5,616	—	—	5,617
Stock-based compensation	—	—	28,056	—	—	28,056
Other comprehensive loss	—	—	—	(345)	—	(345)
Net loss	—	—	—	—	(145,996)	(145,996)
Balances at June 30, 2018	50,225	502	2,666,729	(5,394)	(1,204,303)	1,457,534

See accompanying notes to unaudited condensed consolidated financial statements.

bluebird bio, Inc.

Condensed Consolidated Statements of Cash Flows
(unaudited)
(in thousands)

	For the six months ended June 30,	
	2019	2018
Cash flows from operating activities:		
Net loss	$ (360,228)	$ (261,120)
Adjustments to reconcile net loss to net cash used in operating activities:		
Change in fair value of contingent consideration	510	796
Depreciation and amortization	7,831	8,199
Stock-based compensation expense	87,452	51,051
Unrealized loss on equity securities	6,184	—
Other non-cash items	(7,064)	2,834
Changes in operating assets and liabilities:		
Prepaid expenses and other assets	(20,694)	(3,279)
Operating lease right-of-use assets	11,037	—
Accounts payable	6,652	4,097
Accrued expenses and other liabilities	(9,301)	9,789
Operating lease liabilities	(259)	—
Deferred revenue	(11,716)	(21,589)
Collaboration research advancement	(2,431)	—
Net cash used in operating activities	(292,027)	(209,222)
Cash flows from investing activities:		
Purchase of property, plant and equipment	(37,925)	(20,689)
Purchases of marketable securities	(471,365)	(689,163)
Proceeds from maturities of marketable securities	704,803	417,640
Net cash provided by (used in) investing activities	195,513	(292,212)
Cash flows from financing activities:		
Proceeds from public offering of common stock, net of issuance costs	—	48,702
Reimbursement of assets under financing lease obligation	—	3,098
Payments on financing lease obligation	—	(446)
Proceeds from exercise of stock options and ESPP contributions	15,004	25,624
Net cash provided by financing activities	15,004	76,978
Decrease in cash, cash equivalents and restricted cash	(81,510)	(424,456)
Cash, cash equivalents and restricted cash at beginning of period	417,099	772,268
Cash, cash equivalents and restricted cash at end of period	$ 335,589	$ 347,812
Reconciliation of cash, cash equivalents and restricted cash:		
Cash and cash equivalents	$ 280,995	$ 333,949
Restricted cash included in receivables and other current assets	$ 100	$ 100
Restricted cash included in restricted cash and other non-current assets	$ 54,494	$ 13,763
Total cash, cash equivalents and restricted cash	$ 335,589	$ 347,812
Supplemental cash flow disclosures from investing and financing activities:		
Purchases of property, plant and equipment included in accounts payable and accrued expenses	$ 8,869	$ 7,815
Assets acquired under operating lease obligation	$ 17,489	$ —

See accompanying notes to unaudited condensed consolidated financial statements.

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 is a biotechnology company committed to researching, developing and commercializing potentially transformative gene therapies for 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 $\beta^{A\text{-}T87Q}$-globin gene) gene therapy as a treatment for transfusion-dependent β-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. 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 (formerly referred to as 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.

In June 2019, the Company received conditional marketing authorization from the European Commission 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 β^0/β^0 genotype, for whom hematopoietic stem cell (HSC) transplantation is appropriate but a human leukocyte-matched related HSC donor is not available. Through June 30, 2019, the Company had not generated any revenue from product sales and had not capitalized any inventory costs related to the production of ZYNTEGLO.

As of June 30, 2019, the Company had cash, cash equivalents and marketable securities of $1.54 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 June 30, 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.

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 and six months ended June 30, 2019 are consistent with those discussed in Note 2 to the consolidated financial statements included 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: future undiscounted cash flows and subsequent fair value estimates, as appropriate, used to assess potential and measure any impairment of long-lived assets, including goodwill and intangible assets, and the measurement of 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 one year or less, as part of which a lessee can make an accounting policy election not to recognize lease assets and lease liabilities for those leases. 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 at adoption 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 as of January 1, 2019 primarily relating to the de-recognition of the 60 Binney Street Lease building asset and related 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 as of January 1, 2019, 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, ASU No. 2019-05 Financial Instruments – Credit Losses (Topic 326): Targeted Transition Relief

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 targeted transition relief standard allows filers an option to irrevocably elect the fair value option of ASC 825-10, Financial Instruments-Overall, applied on an instrument-by-instrument basis for eligible instruments. The new standard will be effective beginning January 1, 2020. The Company is currently evaluating the potential impact ASU 2016-13, and related updates, will have on its financial position and 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 the Company plans to early adopt the provisions of this ASU for purposes of performing its annual goodwill impairment test for 2019 during the fourth quarter of 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. 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. 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. 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. The Company is currently evaluating the potential impact ASU 2018-18 may have on its financial position and results of operations upon adoption.

ASU No. 2019-04, Codification Improvements to Topic 326, Financial Instruments – Credit Losses, Topic 815, Derivatives and Hedging, and Topic 825, Financial Instruments

In April 2019, the FASB issued ASU 2019-04, *Codification Improvements to Topic 326, Financial Instruments – Credit Losses, Topic 815, Derivatives and Hedging, and Topic 825, Financial Instruments, ("ASU 2019-04").* This update provides clarifications for three topics related to financial instruments accounting, some of which apply to the Company. The amendments in this update will be effective beginning January 1, 2020. The adoption of ASU 2019-04 is not expected to have a material impact on the Company's financial position or results of operations upon adoption.

3. Marketable securities

The following table summarizes the marketable securities held at June 30, 2019 and December 31, 2018 (in thousands):

Description	Amortized cost / Cost	Unrealized gains	Unrealized losses	Fair value
June 30, 2019				
U.S. government agency securities and treasuries	$ 1,060,606	$ 3,084	$ (519)	$ 1,063,171
Certificates of deposit	4,520	—	—	4,520
Corporate bonds	113,820	633	(12)	114,441
Commercial paper	62,692	—	—	62,692
Equity securities	20,017	—	(4,034)	15,983
Total	$ 1,261,655	$ 3,717	$ (4,565)	$ 1,260,807
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 June 30, 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 June 30, 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)
June 30, 2019				
Assets:				
Cash and cash equivalents	$ 280,995	$ 280,995	$ —	$ —
Marketable securities:				
U.S. government agency securities and treasuries	1,063,171	—	1,063,171	—
Certificates of deposit	4,520	—	4,520	—
Commercial paper	62,692	—	62,692	—
Corporate bonds	114,441	—	114,441	—
Equity securities	15,983	15,983	—	—
Total assets	$ 1,541,802	$ 296,978	$ 1,244,824	$ —
Liabilities:				
Contingent consideration	$ 5,740	$ —	$ —	$ 5,740
Total liabilities	$ 5,740	$ —	$ —	$ 5,740
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 June 30, 2019, cash and cash equivalents comprise funds in cash and money market accounts. 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 June 30, 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 and six months ended June 30, 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 June 30, 2019 and December 31, 2018 was $52.4 million and $787.5 million, respectively. As of June 30, 2019 and December 31, 2018, there were $229.2 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 June 30, 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 June 30, 2019 and December 31, 2018 was $0.5 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 June 30, 2019 and December 31, 2018.

The Company holds equity securities with an aggregate fair value of $16.0 million and $22.2 million as of June 30, 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 and $6.2 million unrealized loss during the three and six months ended June 30, 2019, respectively, 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 14.2% to 15.0%. Significant increases or decreases in any of the probabilities of success would result in a significantly higher or lower fair value measurement, respectively. Significant increases or decreases in the other inputs would result in a significantly lower or higher fair value measurement, respectively.

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

	For the six months ended June 30, 2019
Beginning balance	$ 5,230
Additions	—
Changes in fair value	510
Payments	—
Ending balance	$ 5,740

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 June 30, 2019	As of December 31, 2018
Land	$ 1,210	$ 1,210
Building	14,913	180,094
Computer equipment and software	6,518	6,365
Office equipment	6,308	5,584
Laboratory equipment	40,953	35,693
Leasehold improvements	21,598	183
Construction-in-progress	67,470	46,669
Total property, plant and equipment	158,970	275,798
Less accumulated depreciation and amortization	(29,835)	(29,176)
Property, plant and equipment, net	$ 129,135	$ 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 June 30, 2019 and December 31, 2018 includes $63.7 million and $40.4 million, respectively, related to the North Carolina manufacturing facility.

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 assets. Subsequent to the adoption of ASU 2016-02, the leasehold improvements owned by the Company 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 June 30, 2019	As of December 31, 2018
Employee compensation	$ 22,638	$ 28,567
Accrued manufacturing costs	20,497	21,618
Accrued clinical and contract research organization costs	16,035	11,891
Accrued property, plant, and equipment	6,113	5,451
Accrued license and milestone fees	1,690	7,739
Accrued professional fees	1,497	1,830
Financing lease obligation, current portion	—	1,424
Other	22,635	20,873
Total accrued expenses and other current liabilities	$ 91,105	$ 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 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.

50 Binney Street Sublease

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 of approximately 3%. The lease will commence when the space is available for use by the Company, which is anticipated to be 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. The $40.1 million of cash collateralizing the letter of credit is classified as Restricted cash and other non-current assets on the Company's condensed consolidated balance sheets. 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. In connection with the execution of the 50 Binney Street Sublease, the Company also entered into a Purchase Agreement for furniture and equipment (the "Furniture Purchase Agreement") located on the premises upon lease commencement. Upon execution of the Furniture Purchase Agreement, the Company made an upfront payment of $7.5 million, all of which was recorded within Restricted cash and other non-current assets on the Company's condensed consolidated balance sheets as of June 30, 2019.

The Company will assess the lease classification of the 50 Binney Street Sublease and commence recognition of the associated rent expense upon lease commencement.

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 and six months ended June 30, 2019:

Operating leases (in thousands)	**For the three months ended June 30, 2019**	**For the six months ended June 30, 2019**
Lease cost (1)		
Operating lease cost	$ 8,917	$ 17,400
Total lease cost	$ 8,917	$ 17,400
Other information		
Operating cash flows used for operating leases		$ 13,237
Weighted average remaining lease term		7.7 years
Weighted average discount rate		6.17%

(1) Short-term lease costs and variable lease costs incurred by the Company for the three and six months ended June 30, 2019 were immaterial.

As of June 30, 2019, future minimum commitments under ASC 842 under the Company's operating leases were as follows:

Maturity of lease liabilities (in thousands)	As of June 30, 2019
2019 (excluding the six months ended June 30, 2019)	$ 17,031
2020	33,780
2021	34,215
2022	29,417
2023	29,869
2024 and thereafter	108,687
Total lease payments	252,999
Less: imputed interest	(58,777)
Total operating lease liabilities	$ 194,222

The above table excludes legally binding minimum lease payments for leases executed but not yet commenced as of June 30, 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 that may be met in subsequent periods 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.

The Company may be obligated to make future development, regulatory and commercial milestone payments and royalty payments on future sales of specified products associated with its 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, the corresponding amounts are recognized 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 a total of $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 the second quarter of 2019, a $10.0 million development milestone was achieved such that as of June 30, 2019, the total remaining potential development milestones on the first indication of ide-cel is $60.0 million. 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 represented an option to acquire additional goods and services that is not representative of a material right. In addition, as of the February 2016 contract modification date, Celgene had not exercised its option to purchase any commercial vector. Accordingly, the manufacture of commercial vector was not considered to be a performance obligation at that 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 June 30, 2019:

(in thousands)	Ide-cel transaction price as of June 30, 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
Ide-cel development milestone	10,000
Estimated variable consideration	87,189
	$ 207,189

(in thousands)	Allocation of transaction price to performance obligations	Transaction price unsatisfied as of June 30, 2019
Ide-cel research and development services	$ 40,912	$ —
Ide-cel license and manufacturing services	166,277	26,723
	$ 207,189	$ 26,723

The estimated variable consideration of $87.2 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 which have not been met as of period end 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 $40.9 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 and six months ended June 30, 2019 and 2018:

	For the three months ended June 30,		For the six months ended June 30,	
(in thousands)	2019	2018	2019	2018
Ide-cel research and development services revenue	$ 2,473	$ 953	$ 2,264	$ 3,136
	$ 2,473	$ 953	$ 2,264	$ 3,136

Ide-cel license and manufacturing services

The Company allocated $166.3 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 for the joint ide-cel development efforts in the U.S. under ASC 808, including revenue or expense related to the combined performance obligation for the license and vector manufacturing of ide-cel for development in the U.S., for the three and six months ended June 30, 2019, and 2018:

	For the three months ended June 30,		For the six months ended June 30,	
(in thousands)	2019	2018	2019	2018
ASC 808 ide-cel revenue - U.S. (1)	$ —	$ —	$ —	$ 3,761
ASC 808 ide-cel research and development expense - U.S. (1)	$ (1,065)	$ (3,349)	$ (4,309)	$ (3,349)

(1) As noted above, the calculation of collaboration revenue or research and development expense to be recognized for joint ide-cel development efforts 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 and six months ended June 30, 2019, and 2018:

	For the three months ended June 30,		For the six months ended June 30,	
(in thousands)	2019	2018	2019	2018
ASC 606 ide-cel license and manufacturing revenue - outside of U.S.	$ 7,899	$ 5,764	$ 16,963	$ 14,706

As of June 30, 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 $26.7 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 June 30, 2019 and December 31, 2018, the Company had $12.7 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 June 30, 2019:

(in thousands)	bb21217 transaction price as of June 30, 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 June 30, 2019
bb21217 research and development services	$ 5,444	$ 721
bb21217 license and manufacturing services	36,243	36,243
	$ 41,687	$ 36,964

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 and six months ended June 30, 2019, and 2018:

	For the three months ended June 30,		For the six months ended June 30,	
(in thousands)	**2019**	**2018**	**2019**	**2018**
bb21217 research and development services revenue	$ 721	$ 721	$ 1,442	$ 1,442
	$ 721	$ 721	$ 1,442	$ 1,442

As of June 30, 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 $0.7 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 June 30, 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 and six months ended June 30, 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 June 30, 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 six months ended June 30, 2019:

(in thousands)	Balance at beginning of period	Additions	Deductions	Balance at end of period
Receivables	$ 6,528	$ 10,450	$ (6,528)	$ 10,450
Contract liabilities:				
Payable included in accrued expenses	$ —	$ 3,781	$ —	$ 3,781
Deferred revenue	$ 34,939	$ 10,000	$ (21,716)	$ 23,223

The increase in the receivables balance for the six months ended June 30, 2019 is primarily driven by amounts owed to the Company for a development milestone that was achieved in the second quarter of 2019, offset by amounts collected from Celgene in the period and amounts owed to Celgene under the Ide-cel CCPS.

The decrease in deferred revenue during the six months ended June 30, 2019 is primarily driven by amounts recognized for the combined performance obligation consisting of the ide-cel license and manufacturing services. During the six months ended June 30, 2019, $21.7 million of the deferred revenue balance at the beginning of the period was released from deferred revenue, of which $10.0 million was recognized as collaboration revenue and $11.7 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. A target would also become a licensed target in the event Regeneron does not have an option to such target, or Regeneron does not exercise its option with respect to such 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 0.4 million shares of the Company's common stock 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. As of June 30, 2019 and December 31, 2018, the Company has $41.5 million and $44.0 million, respectively, of the collaboration research advancement remaining to be recognized.

The Company recognized $0.5 million and $2.5 million of collaboration revenue from the Regeneron Collaboration Agreement during the three and six months ended June 30, 2019, respectively. The Company did not recognize any collaboration revenue, or research and development expense, from the Regeneron Collaboration Agreement during the three and six months ended June 30, 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 June 30, 2019, the total number of shares of common stock available for issuance under the 2013 Plan was approximately 2.2 million.

Stock-based compensation expense

The Company recognized stock-based compensation expense totaling $55.1 million and $87.5 million for the three and six months ended June 30, 2019, respectively. The Company recognized stock-based compensation expense totaling $28.1 million and $51.1 million for the three and six months ended June 30, 2018, respectively. Stock-based compensation expense by award type included within the condensed consolidated statements of operations and comprehensive loss was as follows:

	For the three months ended June 30,		For the six months ended June 30,	
(in thousands)	**2019**	**2018**	**2019**	**2018**
Stock options	$ 24,800	$ 20,932	$ 47,983	$ 38,227
Restricted stock units	30,012	6,953	38,893	12,494
Employee stock purchase plan	299	171	576	330
	$ 55,111	$ 28,056	$ 87,452	$ 51,051

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

	For the three months ended June 30,		For the six months ended June 30,	
(in thousands)	**2019**	**2018**	**2019**	**2018**
Research and development	$ 29,694	$ 14,196	$ 45,210	$ 25,820
General and administrative	25,417	13,860	42,242	25,231
	$ 55,111	$ 28,056	$ 87,452	$ 51,051

In February 2018, the Company issued restricted stock units with service and performance conditions to employees, approximately 0.2 million of which are outstanding as of June 30, 2019. Vesting of these awards is contingent on the occurrence of a certain regulatory milestone event which was achieved in June 2019 and fulfillment of any remaining service condition. The Company began recognizing expense for these awards in the second quarter of 2019 when achievement of the regulatory milestone was deemed probable. The Company recognized $20.1 million of expense related to these awards in the second quarter of 2019 and will continue to recognize stock-based compensation expense related to these awards through June 2021 when the final tranche of the awards vest.

As of June 30, 2019, the Company had $372.4 million of unrecognized stock-based compensation expense related to unvested stock options, restricted stock units, performance-based restricted stock units, and the employee stock purchase plan, which is expected to be recognized over a weighted-average period of 2.8 years.

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	1,266	$ 136.17
Exercised	(282)	$ 47.80
Canceled, forfeited, or expired	(234)	$ 129.85
Outstanding at June 30, 2019	5,393	$ 117.30
Exercisable at June 30, 2019	2,520	$ 88.94
Vested and expected to vest at June 30, 2019	5,393	$ 117.30

During the six months ended June 30, 2019, 0.3 million shares of common stock were exercised, resulting in total proceeds to the Company of $13.5 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	438	$ 136.32
Vested	(197)	$ 142.82
Forfeited	(69)	$ 153.94
Unvested balance at June 30, 2019	1,103	$ 150.67

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 six months ended June 30, 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. The tax benefit recorded during the three and six months ended June 30, 2019 is due to the deferred tax benefit for which an offsetting tax expense is recognized in other comprehensive income (loss), partially reduced by state and foreign income taxes.

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:

	For the three and six months ended June 30,	
(in thousands)	**2019**	**2018**
Outstanding stock options	5,393	4,505
Restricted stock units	1,103	931
ESPP shares	15	5
	6,511	5,441

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 biotechnology company committed to researching, developing and commercializing 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. In June 2019, we received conditional marketing authorization from the European Commission for ZYNTEGLO™ (autologous CD34+ cells encoding $\beta^{A\text{-}T87Q}$-globin gene) gene therapy as a treatment for adult and adolescent patients with transfusion-dependent β-thalassemia, or TDT, and a non-β^0/β^0 genotype, for whom hematopoietic stem cell (HSC) transplantation is appropriate but a human leukocyte antigen (HLA)-matched related HSC donor is not available. Our other programs in severe genetic diseases include 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.

We are commercializing ZYNTEGLO in the European Union and expect to begin to generate product revenue in early 2020. In the second half of 2019, we plan to initiate a rolling submission for regulatory approval of ZYNTEGLO in the United States for the treatment of adult and adolescent patients with TDT who do not have a β^0/β^0 genotype. We are engaged with the U.S. Food and Drug Administration, or FDA, and the European Medicines Agency, or EMA, in discussions regarding our proposed development plans for ZYNTEGLO in patients with TDT and a β^0/β^0 genotype. We are also engaged with the FDA and 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 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 June 30, 2019, we had cash, cash equivalents and marketable securities of approximately $1.54 billion. We have never been profitable and have incurred net losses in each year since inception. Our net loss was $195.8 million and $360.2 million for the three and six months ended June 30, 2019, respectively, and our accumulated deficit was $1.85 billion as of June 30, 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 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 ZYNTEGLO, and our LentiGlobin and Lenti-D product candidates, as well as to fund our share of the costs of clinical studies for ide-cel and bb21217;
- 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 commercial launch of ZYNTEGLO in multiple markets.

We do not expect to generate revenue from product sales until early 2020. 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 our product candidates and begin to commercialize ZYNTEGLO, we expect to incur significant commercialization expenses as we prepare for product sales, marketing, manufacturing, and distribution. Accordingly until we generate significant revenues from product sales, 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 not succeed in achieving regulatory approval for all 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 ZYNTEGLO and our 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 ide-cel 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-β^0/β^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 β^0/β^0 genotype or an IVS-I-110 mutation.
- HGB-206 study – a multi-site phase 1/2 study in the United States to study the safety and efficacy of LentiGlobin in the treatment of patients with SCD.
- HGB-210 study – our planned multi-site, international phase 3 study of LentiGlobin in patients with SCD and a history of vaso-occlusive events. We plan to initiate this study in the second half of 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.
- 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 incur costs related to the manufacture of clinical study materials in support of our clinical studies.
- Academic collaborations for early pipeline activities, including investigator-initiated proof-of-concept clinical trials.

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 June 30,		For the six months ended June 30,	
	2019	2018	2019	2018
	(in thousands)		(in thousands)	
LentiGlobin (including ZYNTEGLO)(1)	$ 28,291	$ 35,765	$ 60,136	$ 68,562
Lenti-D	12,011	9,243	20,697	15,440
Ide-cel	24,406	19,770	44,197	32,035
bb21217	6,031	3,507	10,517	6,777
Pre-clinical programs	9,871	9,672	21,200	20,831
Total direct research and development expense	80,610	77,957	156,747	143,645
Employee-and contractor-related expenses	12,203	7,719	22,721	14,944
Stock-based compensation expense	29,694	14,196	45,210	25,820
Platform-related expenses	6,209	6,727	10,836	11,399
Facility expenses	16,458	7,730	31,077	15,403
Other expenses	1,366	685	2,589	912
Total other research and development expenses	65,930	37,057	112,433	68,478
Total research and development expense	$ 146,540	$ 115,014	$ 269,180	$ 212,123

(1) Following our receipt of conditional approval for the marketing authorization of ZYNTEGLO by the European Commission in June 2019, all manufacturing costs associated with the production of LentiGlobin produced for use in the commercial sale of ZYNTEGLO in the European Union will be evaluated for capitalization as inventory on our condensed consolidated balance sheets. As of June 30, 2019, no costs have been capitalized.

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 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 June 30, 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 $5.7 million as of June 30, 2019, all of which are classified as a non-current liability on our condensed consolidated balance sheet.

Interest income, net

Interest income, net consists primarily of interest income earned on investments and, for the three and six months ended June 30, 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 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 six months ended June 30, 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.

Results of Operations

Comparison of the three months ended June 30, 2019 and 2018:

	For the three months ended June 30,		
	2019	2018	Change
	(in thousands)		
Revenue:			
Collaboration revenue	$ 11,558	$ 7,437	$ 4,121
License and royalty revenue	1,738	414	1,324
Total revenues	13,296	7,851	5,445
Operating expenses:			
Research and development	146,540	115,014	31,526
General and administrative	68,631	41,168	27,463
Cost of license and royalty revenue	613	21	592
Change in fair value of contingent consideration	214	262	(48)
Total operating expenses	215,998	156,465	59,533
Loss from operations	(202,702)	(148,614)	(54,088)
Interest income, net	9,387	2,436	6,951
Other (expense) income, net	(2,936)	182	(3,118)
Loss before income taxes	(196,251)	(145,996)	(50,255)
Income tax benefit	469	—	469
Net loss	$ (195,782)	$ (145,996)	$ (49,786)

Revenues. Total revenue was $13.3 million for the three months ended June 30, 2019, compared to $7.9 million for the three months ended June 30, 2018. The increase of $5.4 million was primarily attributable to an increase in collaboration revenue for the ide-cel license and manufacturing services under our agreement with Celgene as well as an increase in license and royalty revenue.

Research and development expenses. Research and development expenses were $146.5 million for the three months ended June 30, 2019, compared to $115.0 million for the three months ended June 30, 2018. The overall increase of $31.5 million was primarily attributable to the following:

- $25.8 million of increased employee compensation, benefit, and other headcount related expenses, which is primarily driven by an increase in headcount to support overall growth and an increase of $15.5 million in stock-based compensation expense. Refer to Note 11, *"Stock-based compensation"*, in the Notes to Condensed Consolidated Financial Statements for discussion of stock-based compensation expense recognized on the performance-based restricted stock units;
- $9.7 million of increased IT and facility related costs, which includes the impact of adopting ASU 2016-02; and
- $5.0 million of increased material production costs.

These increased costs were offset by $5.5 million of decreased license and milestone fees and $3.4 million of decreased clinical trial related costs.

General and administrative expenses. General and administrative expenses were $68.6 million for the three months ended June 30, 2019, compared to $41.2 million for the three months ended June 30, 2018. The increase of $27.4 million was primarily attributable to the following:

- $22.4 million of increased employee compensation, benefit, and other headcount related expenses, which is primarily driven by an increase in headcount to support overall growth and an increase of $11.6 million in stock-based compensation expense. Refer to Note 11,*"Stock-based compensation"*, in the Notes to Condensed Consolidated Financial Statements for discussion of stock-based compensation expense recognized on the performance-based restricted stock units; and
- $6.1 million of increased consulting fees and market research costs.

Interest income, net. The change in interest income, 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 changes in fair value of equity securities.

Comparison of the six months ended June 30, 2019 and 2018:

	For the six months ended June 30,		
	2019	2018	Change
	(in thousands)		
Revenues:			
Collaboration revenue	$ 22,735	$ 23,045	$ (310)
License and royalty revenue	3,032	763	2,269
Total revenues	25,767	23,808	1,959
Operating expenses:			
Research and development	269,180	212,123	57,057
General and administrative	128,910	76,094	52,816
Cost of license and royalty revenue	1,043	36	1,007
Change in fair value of contingent consideration	510	796	(286)
Total operating expenses	399,643	289,049	110,594
Loss from operations	(373,876)	(265,241)	108,635
Interest income, net	19,489	3,824	(15,665)
Other (expense) income, net	(6,325)	297	6,622
Loss before income taxes	(360,712)	(261,120)	99,592
Income tax benefit	484	—	484
Net loss	$ (360,228)	$ (261,120)	$ 99,108

Revenues. Total revenue was $25.8 million for the six months ended June 30, 2019, compared to $23.8 million for the six months ended June 30, 2018. The increase of $2.0 million was primarily attributable to an increase in license and royalty revenue.

Research and development expenses. Research and development expenses were $269.2 million for the six months ended June 30, 2019, compared to $212.1 million for the six months ended June 30, 2018. The overall increase of $57.1 million was primarily attributable to the following:

- $38.7 million of increased employee compensation, benefit, and other headcount related expenses, which is primarily driven by an increase in headcount to support overall growth and an increase of $19.4 million in stock-based compensation expense. Refer to Note 11, *"Stock-based compensation"*, in the Notes to Condensed Consolidated Financial Statements for discussion of stock-based compensation expense recognized on the performance-based restricted stock units;
- $16.6 million of increased IT and facility related costs, which includes the impact of adopting ASU 2016-02; and
- $12.4 million of increased costs incurred for laboratory expenses, material production, and collaboration research.

These increased costs were offset by $8.8 million of decreased license and milestone fees and $4.8 million of decreased clinical trial related costs.

General and administrative expenses. General and administrative expenses were $128.9 million for the six months ended June 30, 2019, compared to $76.1 million for the six months ended June 30, 2018. The increase of $52.8 million was primarily attributable to the following:

- $36.3 million of increased employee compensation, benefit, and other headcount related expenses, which is primarily driven by an increase in headcount to support overall growth and an increase of $17.0 million in stock-based compensation expense. Refer to Note 11, *"Stock-based compensation"*, in the Notes to Condensed Consolidated Financial Statements for discussion of stock-based compensation expense recognized on the performance-based restricted stock units; and
- $17.1 million of increased consulting fees and market research costs.

Interest income, net. The change in interest income, 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 changes in fair value on equity securities.

Liquidity and Capital Resources

As of June 30, 2019, we had cash, cash equivalents and marketable securities of approximately $1.54 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 June 30, 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 June 30, 2019 we had an accumulated deficit of $1.85 billion. We anticipate that we will continue to incur losses for at least the next several years. We expect that our research and development and general and administrative expenses will continue to increase and, as a result, we will need additional capital to fund our operations, which we may raise through public or private equity or debt financings, strategic collaborations, or other sources.

Sources of Liquidity

Cash Flows

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

	For the six months ended June 30,	
	2019	**2018**
	(in thousands)	
Net cash used in operating activities	$ (292,027)	$ (209,222)
Net cash provided by (used in) investing activities	195,513	(292,212)
Net cash provided by financing activities	15,004	76,978
Net decrease in cash, cash equivalents and restricted cash	$ (81,510)	$ (424,456)

Cash Flows from Operating Activities. The $82.8 million increase in cash used in operating activities for the six months ended June 30, 2019 compared to the six months ended June 30, 2018 was partially due to the increase in net loss during this period of $99.1 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 $487.7 million change in cash provided by (used in) investing activities for the six months ended June 30, 2019 was primarily due to an increase of $287.2 million in proceeds received from the maturity of marketable securities and a decrease in cash used to purchase marketable securities of $217.8 million, offset by an increase of $17.2 million in cash used to purchase property, plant and equipment, primarily related to the facility in Durham, North Carolina, compared to the six months ended June 30, 2018.

Cash Flows from Financing Activities. The $62.0 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 $10.6 million in the six months ended June 30, 2019 compared to the six months ended June 30, 2018.

Contractual Obligations and Commitments

There have been no material changes to our contractual obligations and commitments as included in our Annual Report on Form 10-K, which was filed with the SEC on February 21, 2019.

Off-Balance Sheet Arrangements

As of June 30, 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 June 30, 2019 and December 31, 2018, we had cash, cash equivalents and marketable securities of $1.54 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 June 30, 2019, the net fair value of our interest-sensitive marketable securities would have resulted in a hypothetical decline of approximately $7.0 million.

Item 4. Controls and Procedures

Management's Evaluation of our Disclosure Controls and Procedures

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

As of June 30, 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 June 30, 2019, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Control over Financial Reporting

During the quarter ended June 30, 2019 there were no changes in our internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15(d)-15(f) promulgated under the Securities Exchange Act of 1934, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II. OTHER INFORMATION

Item 1. Legal Proceedings

In the ordinary course of business, we are from time to time involved in lawsuits, claims, investigations, proceedings, and threats of litigation relating to intellectual property, commercial arrangements, employment and other matters. While the outcome of these proceedings and claims cannot be predicted with certainty, as of June 30, 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 commercialization

We have limited experience as a commercial company and the marketing and sale of ZYNTEGLO or future products may be unsuccessful or less successful than anticipated.

We are beginning to commercialize ZYNTEGLO in the European Union as a treatment for adult and adolescent patients with TDT and a non-β^0/β^0 genotype, following our receipt of conditional marketing approval by the European Commission in June 2019. We have limited experience as a commercial company and there is limited information about our ability to overcome many of the risks and uncertainties encountered by companies commercializing products in the biopharmaceutical industry. We also have several programs in late-stage clinical development. To execute our business plan, in addition to successfully marketing and selling ZYNTEGLO, we will need to successfully:

- establish and maintain our relationships with qualified treatment centers who will be treating the patients who receive our product and any future products;
- obtain adequate pricing and reimbursement for ZYNTEGLO and any future products;
- gain regulatory acceptance for the development and commercialization of the product candidates in our pipeline;
- develop and maintain successful strategic alliances; and
- manage our spending as costs and expenses increase due to clinical trials, marketing approvals, and commercialization.

If we are not successful in accomplishing these objectives, we may not be able to develop product candidates, commercialize ZYNTEGLO or any future products, raise capital, expand our business, or continue our operations.

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

The commercial success of ZYNTEGLO and of any future products will depend in part on the medical community, patients, and third-party or governmental payors accepting gene therapy products in general, and ZYNTEGLO and any future products in particular, as medically useful, cost-effective, and safe. ZYNTEGLO and any other products that we may 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 ZYNTEGLO and of any future products 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 and any future products 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 product and any future products;
- publicity concerning our product, any future 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 our products 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. Any of these factors may cause ZYNTEGLO, or any future products, to be unsuccessful or less successful than anticipated.

If the market opportunities for our product or any future products 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 or any future products, 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 would benefit from treatment from our Lenti-D product candidate. Additionally, the potentially addressable patient population for our product and any future products may be limited or may not be amenable to treatment with our products. For instance, we received conditional marketing approval in Europe of ZYNTEGLO for the treatment of patients with TDT who do not have a β^0/β^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 a product within an approved indication, because the potential target populations for our product and for the product candidates in our pipeline are small, we may never achieve profitability without obtaining marketing 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 any future products and our ability to achieve and maintain profitability and, as a consequence, our business may suffer.

We rely on a complex supply chain for ZYNTEGLO and 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 product 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 commercialize ZYNTEGLO and any future products, 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 for the commercial setting and for any clinical trials that we initiate. Although we intend to eventually rely on a mix of internal and third-party manufacturers to support our 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 ZYNTEGLO or future 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 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 could be greater than we expect and could materially and adversely affect the commercial viability of our product and any future products. If we or such third-party manufacturers are unable to produce the necessary quantities of lentiviral vector and our drug product, 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 product and any future products may be materially harmed. Furthermore, if we or our third-party manufacturers are unable to produce our viral vectors or our drug products in quantities, in accordance with quality requirements, or within the time frames that we need to support our development and commercialization activities, it may result in delays in our 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 and 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 agreements for the commercial supply for all 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 and any future products. Currently, we rely on third-party contract manufacturers in the United States and Europe to produce drug product for commercialization and 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 drug product back to the patient. Logistical and shipment delays and problems caused by us, our vendors, and other factors not in our control, such as weather, could prevent or delay the delivery of product 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 result in adverse patient outcomes, loss of product or regulatory action.

Although we are continuing to build out our commercial capabilities, we have no prior sales or distribution experience and limited capabilities for marketing and market access. We expect to invest significant financial and management resources to establish these capabilities and infrastructure to support commercial operations. If we are unable to establish these commercial capabilities and infrastructure or to enter into agreements with third parties to market and sell our product or any future products, we may be unable to generate sufficient revenue to sustain our business.

Although we are continuing to build out our field team as part of our first commercial launch in Europe, we have no prior sales or distribution experience and limited capabilities for marketing and market access. To successfully commercialize ZYNTEGLO and any other products that may result from our development programs, we will need to develop these capabilities and further expand our infrastructure to support commercial operations in the United States, Europe and other regions, either on our own or with others. Commercializing an autologous gene therapy such as ZYNTEGLO is resource-intensive and will require substantial investment in commercial capabilities. 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 these functions, including marketing and sales functions, we may be unable to compete successfully against these more established companies. Furthermore, a significant proportion of the patient populations for ZYNTEGLO and our potential products lies outside of the United States and Europe. We may not be able to establish our global capabilities and infrastructure in a timely manner or at all. The cost of establishing such capabilities and infrastructure may not be justifiable in light of the potential revenues generated by any particular product and/or in

any specific geographic region. We currently expect to rely heavily on third parties to launch and market ZYNTEGLO and our potential products in certain geographies, if approved. We may enter into collaborations with third parties to utilize their mature marketing and distribution capabilities, but we may be unable to enter into agreements on favorable terms, if at all. If our future collaborative partners do not commit sufficient resources to commercialize ZYNTEGLO or our future products, if any, and we are unable to develop the necessary commercial and manufacturing capabilities on our own, we may be unable to generate sufficient product revenue to sustain our business.

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 to offer therapeutic benefit in a single administration, we face additional uncertainty related to pricing and reimbursement for our product. Failure to obtain or maintain adequate coverage and reimbursement for any new or current product 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 gene therapy products. In addition, because our therapies represent new treatment approaches, the estimation of potential revenues will be complex. Sales of our product and any future products will depend substantially, both domestically and abroad, on the extent to which the costs of our product and any future products 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 or any future products. 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 product and any future 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 or any future products. We expect to experience pricing pressures in connection with the sale of our product and any future products, 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 and any future products 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 and any future products 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 product or any future products, the adoption of our

product or any future products may be limited. In addition, to the extent reimbursement for our product 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 requires 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 product. These factors could affect our ability to successfully commercialize our product and any future products and generate revenues, which would adversely impact our business, financial condition, results of operations and prospects.

Risks related to the research and development of our product candidates

**** We cannot predict when or if we will obtain marketing approval to commercialize our product candidates, and the marketing approval of our product and any future products may ultimately be for more narrow indications than we expect.***

Before obtaining marketing approval from regulatory authorities for the commercialization 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. 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. 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;
- 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;
- 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, the timing of our clinical studies depends on the speed at which we can recruit eligible patients to participate in testing our product candidates. 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 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. We have experienced delays in some of our clinical studies in the past, and we may experience similar delays in the future. In addition, if we make manufacturing or formulation changes to our product or product candidates, we may need to conduct additional studies to demonstrate comparability of the modified versions to earlier versions.

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 SCD who have been treated with LentiGlobin may experience a reduction of vaso-occlusive events following successful engraftment, there can be no assurance that they will not experience vaso-occlusive events 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 β^0/β^0 genotype experienced better outcomes to treatment than patients with TDT who have a β^0/β^0 genotype. Consequently, we received 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 β^0/β^0 genotype. In order to support an application for marketing approval of ZYNTEGLO in patients with TDT who have a β^0/β^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 marketing approval of our product candidates.

Even if our product candidates demonstrate safety and efficacy in clinical studies, regulatory delays or rejections may be encountered as a result of many factors, including changes in regulatory policy during the period of product development. 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 marketing approval for the desired age ranges, our business may suffer. Furthermore, approvals by the EMA and the European Commission may not be indicative of what the FDA may require for approval.

In general, the FDA requires the successful completion of two pivotal trials to support approval of a biologics licensing application, or 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 β^0/β^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 β^0/β^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 adult and adolescent patients with TDT who do not have a β^0/β^0 genotype.

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 $\beta^{A\text{-}T87Q}$ 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 $\beta^{A\text{-}T87Q}$ 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 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 and any future products. 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 or any future products, 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 products that we may develop, or achieve patent protection, marketing approval, product commercialization and market penetration earlier than us. Additionally, technologies developed by our competitors may render our potential products 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 marketing 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 ZYNTEGLO and 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 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.

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, including our gene editing platforms. Our research programs in oncology and severe genetic diseases 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. 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. If any of these events occur, we may be forced to abandon our research, development or commercialization efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations.

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.

**** 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, and the commercial potential of our product and any future products will be materially and negatively impacted.***

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 in TDT and LentiGlobin in SCD, 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, or in the commercial setting. 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, and we may be unable to continue to commercialize our approved product.

Additionally, our product and any future products 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. Furthermore, treatment with our gene therapy product and product candidates involve chemotherapy or myeloablative treatments, which can cause side effects or adverse events that are unrelated to our product and product candidates but may still impact the perception of the potential benefits of our product and any future products and the success of our clinical studies. Any of these events could impair our ability to commercialize our product and any future products and the commercial potential of our products will be materially and negatively impacted.

Patients receiving T cell-based immunotherapies, such as ide-cel and the bb21217 product candidate, 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, marketing 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 marketing 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.

Negative public opinion and increased regulatory scrutiny of gene therapy and genetic research may damage public perception of our product and any future products or adversely affect our ability to conduct our business or obtain and maintain marketing approvals for our product and 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 or our product or product candidates, could result in increased governmental regulation, unfavorable public perception, challenges in recruiting patients to participate in our clinical studies, potential regulatory delays in the testing or approval of our potential products, stricter labeling requirements for those product candidates that are approved, and a decrease in demand for any such product. 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 approved products.

Risks related to our reliance on third parties

****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 one or both of the programs that render them 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 the programs. 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 marketing 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 had 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 BMS has announced that the transaction is expected to be completed at the end of 2019 or the beginning of 2020. 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 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, including manufacturing in the commercial context.

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 products 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 products 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 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 marketing approval, or impact our ability to successfully commercialize our product or any 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 product and product candidates. 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 and 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 and 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 marketing 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 marketing approval of our product and potential products. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our 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 marketing 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 and any future products, 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 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 marketing 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 drug product, 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 have incurred net losses in each year since our inception in 1992, including net losses of $360.2 million for the six months ended June 30, 2019. As of June 30, 2019, we had an accumulated deficit of $1.85 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 early 2020 from ZYNTEGLO in the European Union for the treatment of adult and adolescent patients with TDT who do not have a β^0/β^0 genotype. Following marketing approval, our future revenues will depend upon the size of any markets in which our product and any future products have received approval, and our ability to achieve sufficient market acceptance, reimbursement from third-party payors and adequate market share for our product and any future products in those markets.

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

- continue our research and preclinical and clinical development of our product candidates, including ide-cel, which we are co-developing with Celgene;
- establish capabilities to support our commercialization efforts, including establishing a sales, marketing and distribution infrastructure in the United States and Europe, and to commercialize ZYNTEGLO and any other 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 and any future products. Our ability to generate 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 drug products;
- 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 for our product candidates and commercial demand for any approved product;
- launching and commercializing any approved product, 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 any approved product from private and governmental payors;
- obtaining market acceptance and adoption of any approved product and gene therapy as a viable treatment option;
- addressing any competing technological and market developments;
- 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 commercialize ZYNTEGLO in the European Union, which costs may increase with any increased competition. Our expenses could increase beyond expectations if we are required by the FDA, the EMA, or other regulatory agencies, domestic or foreign, to perform clinical and other studies in addition to those that we currently anticipate. Even if we are able to generate product revenues, 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 and commercializing gene therapy products is expensive, and we expect our research and development expenses and our commercialization expenses to increase substantially in connection with our ongoing activities, particularly as we advance our product candidates in clinical studies and begin to commercialize ZYNTEGLO in TDT in Europe.

As of June 30, 2019, our cash, cash equivalents and marketable securities were $1.54 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 marketing 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 approved product and 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.

If the estimates we make, or the assumptions on which we rely, in preparing our consolidated financial statements are incorrect, our actual results may vary from those reflected in our projections and accruals.

Our consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America, or GAAP. The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of our assets, liabilities, revenues and expenses, the amounts of charges accrued by us and related disclosure of contingent assets and liabilities. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. We cannot assure you, however, that our estimates, or the assumptions underlying them, will be correct. For example, we make estimates regarding the research and development budgets applicable to the programs subject to our strategic collaborations. If we are incorrect in these estimates, we may under- or over-state our collaboration revenue. We may be incorrect in our assumptions regarding the applicability of drug pricing programs and rebates that may be applicable to our product or any future products, which may result in our under- or over-estimating our anticipated product revenues especially as applicable laws and regulations governing pricing evolve over time. In addition, to the extent payment for our product or any future 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.

Further, from time to time we issue financial guidance relating to our expectations for our cash, cash equivalents and marketable debt securities available for operations, which guidance is based on estimates and the judgment of management. If, for any reason, our expenses differ materially from our guidance or we utilize our cash more quickly than anticipated, we may have to adjust our publicly announced financial guidance. If we fail to meet, or if we are required to change or update any element of, our publicly disclosed financial guidance or other expectations about our business, our stock price could decline.

Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or our guidance.

Our operating results are difficult to predict and will likely fluctuate from quarter to quarter and year to year. Due to the recent approval by the European Commission of ZYNTEGLO and the absence of historical sales data, our product sales will be difficult to predict from period to period.

In addition, we have entered into licensing and collaboration agreements with other companies that include research and development funding and milestone payments to us, and we expect that amounts earned from our collaboration agreements will continue to be an important source of our revenues. Accordingly, our revenues will also depend on research and development funding and the achievement of development and clinical milestones under our existing collaboration and license agreements, including, in particular, our collaborations with Celgene and Regeneron, as well as entering into potential new collaboration and license agreements. These payments may vary significantly from quarter to quarter and any such variance could cause a significant fluctuation in our operating results from one quarter to the next.

Further, changes in our operations, such as increased development, manufacturing and clinical trial expenses in connection with our expanding pipeline programs, or our undertaking of additional programs, or business activities, or entry into strategic transactions, including potential future acquisitions of products, technologies or businesses may also cause significant fluctuations in our expenses.

The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance. This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated revenue or earnings guidance we may provide.

Risks related to our business operations

We are commercializing ZYTENGLO outside of the United States, and therefore we will be subject to the risks of doing business outside of the United States.

Because we are commercializing ZYNTEGLO 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 commercial and supply chain 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.

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 received conditional marketing authorization for our first product in 2019 and are launching ZYNTEGLO to treat the first patient in the commercial setting in early 2020, 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 June 30, 2019, we had 929 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. 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. Recruiting and retaining qualified employees, consultants and advisors for our business, including scientific and technical personnel, will be critical to our success. 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. 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.

Even if we receive marketing approval for a product candidate, any approved product will remain subject to regulatory scrutiny.

Even if we obtain marketing approval in a jurisdiction, the regulatory authority may still impose significant restrictions on the indicated uses or marketing of any approved products such as ZYNTEGLO, 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 marketing approval for a product, 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 marketing 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 any approved product and generate revenues.

We are 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 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 approved product or product candidates harms patients, or is perceived to harm patients even when such harm is unrelated to our approved product or product candidates, our marketing 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 product or product candidates. There is a risk that our product or 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 develop our product candidates or commercialize any approved product; and
- decreased demand for any approved product.

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

Patients with the diseases targeted by our approved product and 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 approved product or 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 marketing approval for any approved product, 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 marketing approval process in other countries, or impact and limit the type of marketing approval our product candidates may receive or any approved product maintains. 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.

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 70% 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 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."

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.

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 ZYNTEGLO and any other 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 marketing approval and may affect our overall financial condition and ability to develop product candidates.

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

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

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

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

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

The 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 marketing 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 and commercialize our approved product. 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 the development of our product candidates or allow commercialization of our approved product, 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, approved product, 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 approved product or 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. 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 approved product and/or product candidates. Such a loss of patent protection would have a material adverse impact on our business.

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.

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 our product, product candidates or other gene therapy products, or in 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 ZYNTEGLO, or our product candidates following marketing 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 ZYNTEGLO or our product candidates from private and governmental payors;
- failure to obtain market acceptance and adoption of ZYNTEGLO or any other potential product following marketing approval;
- 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 ZYNTEGLO or 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

None

Item 3. Defaults Upon Senior Securities

None

Item 4. Mine Safety Disclosures

None

Item 5. Other Information

Our policy governing transactions in our securities by our directors, officers, and employees permits our officers, directors and certain other persons to enter into trading plans complying with Rule 10b5-1 under the Securities Exchange Act of 1934, as amended. We have been advised that certain of our officers (including David Davidson (Chief Medical Officer), Jeffrey Walsh (Chief Strategy Officer), Philip Gregory (Chief Scientific Officer), Jason Cole (Chief Operating and Legal Officer), and Kory Wentworth (Vice President, Finance and Treasurer)) 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

Exhibit Number	Exhibit Title	Incorporated by Reference			
		Form	File no.	Exhibit	Filing Date
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
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 Biopharma GmbH, as amended	—	—	—	Filed herewith
10.25††	Clinical and Commercial Supply Agreement – Viral Vector Product, dated November 27, 2017, by and between the Registrant and SAFC Carlsbad, Inc., as amended	—	—	—	Filed herewith

Exhibit Number	Exhibit Title	Incorporated by Reference			
		Form	File no.	Exhibit	Filing Date
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
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
10.42††	Sublease, dated April 16, 2019, by and between the Registrant and Aventis Inc.	—	—	—	Filed herewith
10.43	Amendment to Sublease, dated April 19, 2019, by and between the Registrant and Aventis Inc.	—	—	—	Filed herewith
31.1	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	—	—	—	Filed herewith
31.2	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	—	—	—	Filed herewith

Exhibit Number	Exhibit Title	Incorporated by Reference			
		Form	File no.	Exhibit	Filing Date
32.1	Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	—	—	—	Furnished herewith
101.INS	XBRL Instance Document – the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document.				
101.SCH	XBRL Taxonomy Extension Schema Document.	—	—	—	Filed herewith
101.CAL	XBRL Taxonomy Extension Calculation Document.	—	—	—	Filed herewith
101.DEF	XBRL Definition Linkbase Document.	—	—	—	Filed herewith
101.LAB	XBRL Taxonomy Extension Label Linkbase Document.	—	—	—	Filed herewith
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document.	—	—	—	Filed herewith
104	Cover Page Interactive Data File – Formatted as Inline XBRL with applicable taxonomy extension information contained in Exhibits 101.	—	—	—	Filed herewith

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

†† Portions of this exhibit (indicated by asterisks) have been omitted in accordance with the rules of the SEC.

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

SIGNATURES

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

bluebird bio, Inc.

Date: August 1, 2019

By: /s/ Nick Leschly
Nick Leschly
President, Chief Executive Officer and Director (Principal Executive Officer and Duly Authorized Officer)

Date: August 1, 2019

By: /s/ Chip Baird
Chip Baird
Chief Financial Officer (Principal Financial Officer and Duly Authorized Officer)

[***] INDICATES MATERIAL THAT HAS BEEN OMITTED BECAUSE IT IS BOTH (I) NOT MATERIAL, AND (II) WOULD LIKELY CAUSE COMPETITIVE HARM TO THE COMPANY IF PUBLICLY DISCLOSED.

Exhibit 10.24

EXECUTION VERSION

Toll Manufacturing and Service Agreement

by and between

bluebird bio, Inc.

and

APCETH Biopharma GmbH

November 18, 2016

Toll manufacturing and service AGREEMENT

Between

1. bluebird bio, Inc., a Delaware corporation with an office at 150 2nd Street, Third Floor, Cambridge, MA 02141, USA

- "**BBB**" -,

and

2. APCETH Biopharma GmbH, registered in the Commercial Register of the District Court of Munich under HR B 220566, with an office at Max-Lebsche-Platz 30, 81377 München, Germany

- "**APCETH**" -.

- BBB and APCETH shall also be referred to individually as "**Party**" and jointly as "**Parties**" –

and

3. Apceth GmbH & Co. KG, registered in the Commercial Register of the District Court of Munich under HR HRA91052, with an office at Max-Lebsche-Platz 30, 81377 München, Germany

[***] INDICATES MATERIAL THAT HAS BEEN OMITTED BECAUSE IT IS BOTH (I) NOT MATERIAL, AND (II) WOULD LIKELY CAUSE COMPETITIVE HARM TO THE COMPANY IF PUBLICLY DISCLOSED.

Index

Introduction

(A) APCETH is a company providing service solutions for the development and manufacture of cell-based therapies. APCETH operates a multi-client production facility located at Haidgraben 5, 85521 Ottobrunn, Germany (the "**Facility**").

(B) BBB is a pharmaceutical company dedicated to gene therapy product development for potential usage as a therapy in a number of disease areas.

(C) BBB and apceth GmbH & Co. KG, having an office at Max-Lebsche-Platz 30, 81377 München, Germany, entered into a "Development and Manufacturing Service Agreement" dated [***](the "**MSA**"), pursuant to which BBB has engaged apceth GmbH & Co. KG for the performance of certain services regarding the development and manufacture of BBB's gene therapy products, and on [***], BBB and apceth GmbH & Co. KG [***].

(D) [***].

(E) The Parties intend to extend the existing contractual service relationship between the Parties by entering into this "Toll Manufacturing and Service Agreement" (this "**Agreement**"), regarding the supply by APCETH to BBB of Product (as hereinafter defined).

(F) For the aforementioned purpose, the Parties have reached agreement on certain material terms summarized in a non-binding term sheet covering the envisaged terms of a Toll Manufacturing and Supply Agreement (the "**Term Sheet**"). This Agreement shall constitute the "Toll Manufacturing and Service Agreement" referenced in, and contemplated by, the Term Sheet.

(G) In addition, (1) the Parties wish to [***], and (2) the Parties wish to terminate the MSA, and all outstanding work orders thereto, effective upon the Effective Date (as hereinafter defined).

(H) [***].

Against this background the Parties agree:

1. DEFINITIONS

In this Agreement, the following terms with capitalized initial letter, including any grammatical variations, shall have the meanings as set forth below. Where the context so requires the singular includes the plural and vice versa; this applies in particular with respect to the Product:

1.1 "**Access Fee**" shall have the meaning as set forth in Section 11.1.

1.2 "**Affiliate**" shall mean, with respect to either BBB or APCETH, any corporation, company, partnership, limited liability company, business trust, incorporated association, joint stock company, joint venture and/or other organization or entity ("**Entity**") which controls, is controlled by or is under common control with BBB or APCETH, as the case may be. For purposes of this definition, "**control**" with respect to an Entity shall mean the possession, either directly or indirectly through one (1) or more intermediaries, of the power to direct or cause the direction of the management and policies of such Entity, whether through the majority ownership of voting securities entitled to elect the directors or management of such Entity, the actual power to elect or direct the management of such Entity, or by contract or otherwise.

1.3 "**Agreement**" shall mean this Toll Manufacturing and Supply Agreement including all Schedules incorporated by reference, and executed Work Orders entered into in accordance with the terms hereto.

1.4 "**APCETH Technology**" shall mean the Technology owned by or licensed to APCETH (a) existing prior to the Effective Date, or (b) developed or obtained by APCETH independently of this Agreement and without reliance of the Confidential Information of BBB.

1.5 "**APCETH Improvement Technology**" shall have the meaning as set forth in Section 14.3(c).

1.6 "**Applicable Laws**" shall mean (a) GMP, and (b) all other laws, rules and regulations that apply to the performance of either Party's obligations under this Agreement.

1.7 "**Batch**" shall mean the quantity of Product [***] and as may be further defined in the Specifications and Quality Agreement applicable to such Product, and the EU Good Manufacturing Practice Guideline.

1.8 "**Batch Record**" means the production record pertaining to a specific Batch of Product [***] that is specified in the applicable Work Order, the applicable Quality Agreement or otherwise mutually agreed to in writing by the quality representatives of the Parties.

1.9 "**BBB Technology**" shall mean the Technology owned by or licensed to BBB (a) existing prior to the Effective Date, or (b) developed or obtained by BBB independently of this Agreement and without reliance of the Confidential Information of APCETH. BBB Technology includes [***].

1.10 "**BBB New Technology**" shall have the meaning as set forth in Section 14.3(a).

1.11 "**Business Day**" shall mean any calendar day except Saturday, Sunday or any day on which commercial banks in Boston, Massachusetts or Munich, Bavaria are authorized or required by law to remain closed.

1.12 "**Clean Room**" shall mean [***].

1.13 "**Clinical Supply Phase**" shall have the meaning as set forth in Section 7.1.

1.14 "**Confidential Information**" shall have the meaning as set forth in Section 17.1.

1.15 "**Data Protection Laws**" shall have the meaning as set forth in Section 17.7.

1.16 "**Defect**" shall mean any deviation in the Batch delivered hereunder (in accordance with Section 5.2) from the quality owed pursuant to [***].

1.17 "**Delivery Schedule**" shall have the meaning as set forth in Section 5.4.

1.18 "**Discloser**" shall have the meaning as set forth in Section 17.1.

1.19 [***].

1.20 "**Effective Date**" shall have the meaning as set forth in Section 18.1.

1.21 [***].

1.22 "**Extension Date"** shall be [***].

1.23 "**Facility**" shall have the meaning as set forth in Recital A.

1.24 "**Forecast**" shall have the meaning as set forth in Section 5.3.

1.25 "**GMP**" or "**Good Manufacturing Practice**" shall mean [***].

1.26 [***].

1.27 "**IMPD**" shall mean Investigational Medicinal Product Dossier.

1.28 "**Insolvency Event**" shall mean, with respect to a Party, that such Party (a) has an involuntary petition in bankruptcy filed against it which is not challenged within [***] or dismissed within [***]; (b) seeks, consents to or does not contest the appointment of a receiver, custodian or trustee, preliminary insolvency administrator, insolvency administrator or of a similar appointee, for itself or for all or any part of its property; (c) files a petition seeking relief under the bankruptcy, insolvency, arrangement, reorganization or other debtor relief laws of any competent jurisdiction; (d) gives notice to any governmental or judicial body of insolvency or pending insolvency; (e) becomes "insolvent", i.e. illiquid and/or over indebted, as that term is defined under Applicable Laws; or (f) makes an assignment for the benefit of creditors or takes any other similar action for the protection or benefit of creditors.

1.29 "**Marketing Authorization**" shall mean the marketing authorizations submitted or granted, or expected to be submitted or granted, and required for the marketing and sale of the Product in the European Union, the European Economic Area, or any country within the European Union or the European Economic Area as of the Effective Date and as may join the European Union or the European Economic Area following the Effective Date.

1.30 "**Minimum Utilization Requirement**" shall have the meaning as set forth in Section 13.

1.31 "**MSA**" shall have the meaning as set forth in Recital C.

1.32 [***].

1.33 "**Patient Information**" shall have the meaning as set forth in Section 17.7.

1.34 "**Product**" shall mean the autologous cells transduced with a defined lentiviral vector suspended in cryopreservative solution in the final immediate container [***].

1.35 [***].

1.36 [***].

1.37 "**Production Scenario**" shall have the meaning as set forth in Section 4.2.

1.38 "**Production Year**" shall mean a period of twelve (12) consecutive months, commencing on the Supply Initiation Date, and each subsequent twelve (12) month period.

1.39 "**Qualified Person**" shall mean a qualified person in accordance with [***].

1.40 "**Quality Agreement**" shall mean an agreement between the Parties executed before the Effective Date, and amended from to time, determining the roles and responsibilities of the Parties in relation to the manufacture of the Product, as well as details, Specifications, quality requirements and other requirements (including but not limited to GMP) applicable to the Supplied Material and the manufacture of the Product by APCETH. The Quality Agreement shall be incorporated herein by reference.

1.41 "**Recipient**" shall have the meaning as set forth in Section 17.1.

1.42 [***].

1.43 "**Supplied Material Delivery Schedule**" shall have the meaning as set forth in Section 6.1.

1.44 "**Supplied Materials**" shall have the meaning as set forth in Section 6.1.

1.45 "**Supply Initiation Date**" shall be [***].

1.46 "**Technology"** shall mean any intellectual property right including (without limitation) patents, patent applications, supplementary protection certificates, utility models, database rights, rights in design topography and rights (whether or not any of these rights can be registered and including applications and the right to apply for registration of any such rights) and all data, inventions (whether or not patentable), documentation, regulatory submissions, specifications, know-how, trade secrets, methods, techniques, and all other intellectual property rights in the United States, Germany, and throughout the world, including Confidential Information.

1.47 **"Technology Transfer"** shall have the meaning as set forth in Section 14.5.

1.48 "**Term Sheet**" shall have the meaning as set forth in Recital F.

1.49 "**Third Party**" shall mean any person or Entity other than the Parties and their Affiliates.

1.50 "**Work Order**" shall mean the written order, executed from time to time, referencing this Agreement and setting forth each Party's responsibilities with respect to the performance of services under this Agreement. As each subsequent Work Order shall be incorporated by reference and made a part of this Agreement. The initial Work Orders under this Agreement are attached hereto as Appendices 1 through 3.

1.51 **"Work Order Fees"** shall have the meaning as set forth in Section 11.6.

2. SUBJECT OF THIS AGREEMENT AND ORDER OF PRECEDENCE

2.1 On the basis of the terms of this Agreement, APCETH shall provide services to BBB, as the Parties shall agree in an executed Work Order from time to time, including (a) the manufacture of Products in the Clean Rooms, and (b) any development services or technology transfer services. Work Orders covering the manufacture of Products as initially produced under this Agreement as set forth under Section 1.34, that utilize BBB's reserved production capacity in accordance with the terms and conditions of this Agreement shall not require the separate consent or signature of APCETH, and shall be invoiced by APCETH to BBB [***]. Work Orders covering development services, technology transfer services, or manufacture of Products other than such initially produced under this Agreement as set forth under

Section 1.34, such services shall be separately agreed to by the Parties on such executed Work Order and invoiced separately by APCETH to BBB. Such executed Work Orders (whether covering the manufacture of Product or otherwise) are essential parts of this Agreement and incorporated herein by reference. The Schedules attached to this Agreement are essential parts of this Agreement and incorporated herein by reference. In the event of contradictions or inconsistencies between this Agreement, its Schedules, including the applicable Quality Agreement, or any Work Order, the following order of precedence applies: (a) the main part of this Agreement, (b) the applicable Quality Agreement (including its attachments and references), (c) the applicable Work Order, and (d) the other Schedules; provided, however, the Quality Agreement shall prevail over the main part of this Agreement in matters of determining the Specifications and other quality or process requirements applicable to Product or its manufacture.

2.2 Any Affiliate of BBB (a "**BBB Affiliate**") may engage APCETH to perform services on behalf of itself or BBB, or another BBB Affiliate, and may utilize the reserved production capacity under Section 4.2 for the manufacture of Product, and may directly engage APCETH by executing a Work Order, provided that BBB shall have included each such Affiliates' manufacturing requirements to the Forecast in accordance with Section 5.3 and have indicated in such Forecast to which BBB Affiliate each such Batch is assigned. For such Work Orders covering the manufacture of Product, such BBB Affiliate (in the place of BBB) shall directly provide APCETH with the applicable Supplied Materials and shall take title of the resulting Batch directly from APCETH.

2.3 [***].

2.4 [***].

3. PROVISION OF CLEAN ROOMS

3.1 **Responsibility for the Set-Up.** APCETH shall make available and exclusively dedicate to BBB, unless provided for otherwise in Section 3.2 below, the Clean Rooms in the Facility for clinical and commercial supply of Products. The Clean Rooms shall be in accordance with the design and specifications as set forth in the Clean Room Specification attached to this Agreement as Schedule 1. The Clean Rooms shall be in a state ready for manufacture of the Product, which means fully equipped, maintained, validated and with a sufficient number of qualified and trained staff in accordance with BBB's reserved production capacity according to the elected Production Scenario as provided in Section 4.2. APCETH shall ensure that the Clean Rooms will meet all statutory and regulatory requirements applicable to clean rooms for pharmaceutical production, [***].

3.2 **Dates of provision.**

(a) **Availability of** [***]. Beginning on the Supply Initiation Date, APCETH shall [***].

(b) **Availability of** [***]. Beginning on the Extension Date, APCETH shall [***].

3.3 **Maintenance.** APCETH shall be responsible for properly maintaining the Clean Rooms. The Parties acknowledge and agree that, in order to enable APCETH to perform maintenance and/or validation activities in the Facility [***].

3.4 **Change of Clean Room Specifications**. All changes required of the Facility (e.g., due to regulatory changes, process changes requested by BBB, or the purchase of additional equipment required for Production Scenario II) in connection with the manufacturing of the Products shall be discussed by the Parties and the Parties shall agree in writing to any such expenses to be charged separately. For the avoidance of doubt, APCETH shall (a) implement any changes to the Facility having an actual or potential effect on the manufacture of the Product only with BBB's prior written approval, and (b) bear the costs of any changes to the Facility and/or the Clean Rooms requested by APCETH, if such changes are not based on any legal or regulatory requirements.

4. TERMS OF MANUFACTURE OF PRODUCT

4.1 **General.** APCETH shall manufacture the Product in accordance with (a) this Agreement, (b) the applicable Work Order, (c) the applicable Quality Agreement, including the applicable Specifications, (d) any IMPD of the respective country and/or the Marketing Authorizations applicable to the Product, (e) GMP, and (f) all other Applicable Laws.

4.2 **Capacity and Production Scenarios.** The reserved production capacity of the Clean Rooms, production shifts per calendar week and the minimum amount of Batches to be delivered by APCETH is determined by the Production Scenario elected by BBB ("**Production Scenario**"). The number of Batches to be delivered under a given Production Scenario is established with consideration to the anticipated [***] and the production process utilized as of the Effective Date for the Products initially produced under the Agreement, as attached hereto as Schedule 2. [***].

(a) [***].

(b) [***].

(c) [***].

(d) [***].

(e) **Process Improvements**. The Parties currently envisage to improve the manufacturing process for the Products in order to reduce processing times resulting in an increased output of Batches per calendar week. If the Parties mutually agree that the currently envisaged improved process has been successfully established at APCETH's Facility, (i) [***], and (ii) [***].

(f) [***].

4.3 **Subcontracting.** APCETH shall not subcontract any of the works or services to be performed by APCETH under this Agreement to its Affiliates or Third Parties without the prior written consent of BBB (not to be unreasonably withheld). Any consent given by BBB shall require that the agreements between APCETH and such Affiliates or Third Parties are made in writing and substantially correspond to the terms set forth in this Agreement. APCETH shall not be responsible for any delays of the works or services to be performed by APCETH under this Agreement resulting from BBB unreasonably withholding its consent to a subcontract under this Agreement. [***]. APCETH shall remain primarily liable for the performance of its obligations under this Agreement, shall be solely responsible for costs, expenses, damages, or losses of any nature arising out of such performance as if such performance had been provided by APCETH itself under this Agreement.

5. DELIVERY AND DELIVERY SCHEDULE

5.1 **Testing by APCETH.** Before delivery to BBB, or its designee, (a) each Batch manufactured under this Agreement shall be sampled and tested by APCETH against the Specifications, (b) APCETH shall review the Batch Records and (c) the Qualified Person of APCETH shall assess whether the manufacturing process has taken place in compliance with the Specifications and release such Batch for delivery to BBB, or its designee, all in accordance with the Quality Agreement. BBB may review the Batch Records for each Batch manufactured under this Agreement before release for delivery to BBB as set forth in the applicable Quality Agreement

5.2 **Terms of delivery**. The delivery of each Batch shall be [***].

5.3 **Forecasts.** At the beginning of each Production Year and [***] thereafter, APCETH shall provide to BBB a schedule setting out the anticipated [***] for a [***], which shall be binding upon the Parties. BBB shall provide APCETH with a [***] forecast ("**Forecast**") for its requirements of [***].

5.4 **Delivery Schedule**. The binding delivery dates for a Batch shall be determined in a delivery schedule [***].

5.5 **Incoming Controls; Determination of Defective Product.**

(a) Concurrently with delivery of a Batch, APCETH shall provide BBB with the delivery documents as required by the applicable Quality Agreement. In case of any disagreement between the Parties as to whether a Batch conforms to the Specifications, Section 5.5(c) applies.

(b) Without limiting BBB's rights under Section 5.5(a) above, upon receipt of a Batch at its final destination, BBB (itself or through the relevant BBB Affiliate or designated Third Party) shall [***].

(c) If there is a difference of opinions between the Parties on whether or not (i) a unit of Product or a Batch is Defective, or (ii) any Defect arose due to Defective Supplied Materials, the Parties shall compare and discuss all relevant existing test results. The quality assurance representatives of both Parties shall attempt in good faith try to resolve the discrepancy. If the Parties do not come to a consensus within [***], they shall agree upon a [***].

(d) Should a part of a Batch reveal a Defect, such Batch shall be deemed to be Defective as a whole. [***].

6. PROVISION OF SUPPLIED MATERIALS

6.1 **Supplied Materials**. BBB (itself or through the relevant BBB Affiliate) shall provide APCETH with the required starting material for the production of Product, including mobilized peripheral blood from patients and lentiviral vector as further specified in the Quality Agreement (the "**Supplied Materials**"). BBB shall provide APCETH with a proposed delivery schedule for Supplied Materials ("**Supplied Material Delivery Schedule**"), which shall be in accordance with the Forecast provided to APCETH and the present stock of released Supplied Material at APCETH. BBB and its Affiliates shall have the right to request in writing from APCETH on a [***] basis an account of its remaining stock of Supplied Material available for the production of Product.

6.2 **Retention of Title.** BBB shall at all times retain title to the Supplied Materials provided by it, and to the extent that any of the Supplied Material is processed (including through manufacturing of the Product), BBB shall be deemed to be the manufacturer of the processed material within the meaning of § 950 Civil Code (*Bürgerliches Gesetzbuch – BGB*) and shall immediately acquire ownership in such processed material. To the extent that BBB's Supplied Material is blended, combined or processed with other substances owned by APCETH, BBB shall immediately acquire co-ownership in such product and APCETH hereby assigns its co-ownership share to BBB. BBB hereby accepts such assignment. Where the Supplied Materials have not already been labelled by BBB, APCETH shall clearly label BBB's Supplied Material and any product derived from the Supplied Material as the property of BBB. For the avoidance of doubt, the labelling of a visual code that can be traced by APCETH's ERP systems (material management system) will be sufficient to fulfil such obligation. APCETH, at BBB's request, shall cooperate with BBB in securing and filing any necessary statements or documents to preserve and evidence BBB's ownership of and security interest in BBB's Supplied Material and any product derived from the Supplied Material in any jurisdiction as reasonably requested by BBB.

6.3 **Storage, Use and Handling.** APCETH shall store and handle the Supplied Material in accordance with the Quality Agreement and any written instructions by BBB. APCETH shall use such Supplied Materials only for manufacturing the Product in accordance with the terms of this Agreement and the Quality Agreement. APCETH undertakes not to sell or assign such Supplied Materials without BBB's prior written consent. APCETH shall not use the Product(s) and/or the Supplied Materials in any in vivo experiments on human subjects or otherwise use the Product and/or the Supplied Materials for any other purpose.

7. CLINICAL SUPPLY PHASE.

7.1 Until the first grant of Marketing Authorization for a Product in the European Union or the European Economic Area, the Clean Room(s) will be used exclusively for clinical supply of the Products ("**Clinical Supply Phase**"). During the Clinical Supply Phase, the following provisions shall apply notwithstanding anything to the contrary set forth in this Agreement:

(a) For scheduling purposes, BBB will share with APCETH at least [***] outlook on planning activities;

(b) With respect to the Forecast to be provided by BBB pursuant to the second sentence of Section 5.3, BBB shall provide a [***] forecast of its requirements of production shifts for clinical supply, which shall be binding upon the Parties;

(c) BBB shall inform APCETH on its filing strategy in the European Union and the European Economic Area for the application of the Marketing Authorization for each Product prior to the first grant of Marketing Authorization, including the envisaged timeline and the expected down-time of production until the commencement of the commercial supply. During the last [***] of such down-time leading to the commercial supply of the Product, the Parties shall agree on at least [***] to maintain the training status of APCETH's personnel and the readiness of the Facility;

(d) BBB shall inform APCETH in writing of the anticipated launch of the commercial supply of a Product at least [***] before such date, and no later than [***]; and

(e) APCETH shall obtain any required licenses for commercial manufacture of a Product before the submission by BBB of the application for Marketing Authorization of such Product, provided that BBB has timely provided APCETH with all relevant information and documentation required therefore, in particular the IMPD of the respective country or the Marketing Authorization of such Product.

7.2 Following the Clinical Supply Phase, BBB shall provide APCETH with information described in Section 7.1(d) for any Products prior to such Products' first grant of Marketing Authorization.

8. INFORMATION AND REGULATORY ASSISTANCE AND QUALITY CONTROL

8.1 **Information.** APCETH shall make available to BBB upon BBB's request, copies of all relevant documentation and information resulting from the manufacture and supply of Products in order to enable BBB to evaluate the status of the Product and to meet any statutory or regulatory requirements necessary for the Product, such documentation and information to include the date of manufacture and the Batch number, a summary of results of the in-process controls, quality control and release documentation, including a certificate of analysis and a certificate of compliance for the Product. BBB shall make available to APCETH the relevant sections of the approved IMPD of the respective country and/or Marketing Authorization for the Products and any updates thereof in a timely manner to meet any statutory or regulatory requirements for the manufacturing, quality control and release of the Product in the Clean Rooms.

8.2 **Regulatory Assistance.** APCETH shall provide commercially reasonable support for all regulatory activities related to the manufacture of the Product, including any updates to the CMC (Chemistry, Manufacturing, and Controls) part of the Marketing Authorization dossier and/or other documentation or information relevant for obtaining, updating and maintaining the Marketing Authorizations. APCETH is obliged to support and allow any pre-approval inspection of the Facility required by any competent governmental authority, or any "mock audit" as part of pre-approval preparations and protocol. APCETH may charge BBB for its regulatory assistance under this Section 8.2 at [***].

8.3 **Regulatory Inspections.** APCETH will permit BBB or its designees to be present and participate in any visit or inspection by any regulatory authority of the Facility which solely relates to any Product or the manufacturing process of the Product. For the avoidance of doubt, this shall not include any visit or inspection related to other products manufactured at APCETH or the general GMP inspection by the regulatory authority. APCETH shall notify BBB promptly if a regulatory authority requests permission to inspect any Clean Room made available to BBB as set forth in Section 3.2 and/or any of APCETH's records or documents related to APCETH's performance under this Agreement. Upon notification of an inspection, APCETH shall promptly notify BBB of the date and time of such inspection and allow BBB to assist in the preparation for such inspection by a regulatory authority. APCETH will provide [***] notice to BBB, or as may be otherwise provided in the Quality Agreement, if the purpose of any such visit or inspection relates to or might affect the manufacture of Product, provided that the visit or inspection was announced to APCETH in advance with sufficient notice. APCETH agrees to provide BBB with copies of all regulatory authority documentation including but not limited to correspondence, statements, warnings, enforcement actions, pleadings, summons, forms and records that APCETH receives as a result of or in anticipation of an inspection of the Clean Rooms. APCETH agrees to promptly notify BBB of any findings resulting from any inspection by a regulatory authority relating to the manufacture of Product, to take any necessary corrective action within the timelines set by the relevant authority within [***] and to provide copies of any relevant correspondence to BBB within [***] after submission, or as may be otherwise provided in the Quality Agreement.

8.4 **Audits.** APCETH shall, on reasonable prior notice unless stated otherwise by Applicable Laws, allow BBB and/or its designee(s) to perform quality audits in connection with the manufacture of the Product, at regular business hours and upon [***] prior notice, and otherwise permit BBB and/or its designee(s) (reasonably acceptable to APCETH) access to the Facility in accordance with the applicable provisions of the Quality Agreement.

8.5 **Permits.** APCETH shall obtain and maintain during the term of this Agreement, [***], any Facility-related or Clean Room-related regulatory approvals and any other permits necessary for the performance of the manufacturing services by APCETH under this Agreement, excluding the Marketing Authorizations and any other Product-specific approvals for which BBB shall be responsible at BBB`s expense. At BBB's request, APCETH shall provide BBB with copies of all granted regulatory approvals and any other permits and submissions to regulatory and/or other governmental authorities related to the manufacture of the Product.

8.6 **Product Complaints**. If either Party becomes aware of product complaint information related to the Products from its Affiliates or Third Parties, it shall forward this information to the other Party as soon as possible, however no later than [***] after receipt of the information, as further detailed in the Quality Agreement. Information on product complaints shall be forwarded as it has been received, without screening, selection or processing. APCETH shall cooperate with any reasonable requests received from BBB on any reply to any complainant.

8.7 **Product Recalls.** Each Party shall provide to the other Party within [***] any data or information that could result in a recall of the Product, in accordance with the procedure defined in the Quality Agreement. Any decision for a recall of Product will be taken by the Party as defined in the Quality Agreement, and the responsibility for any communication with Third Parties remain with BBB.

8.8 **Waste Disposal**. The generation, collection, storage, handling, transportation, movement and release of hazardous materials and waste generated in connection with the manufacture of Product will be the responsibility of APCETH at [***]. Without limiting any other applicable requirements, APCETH will prepare, execute and maintain, as the generator of waste, all licences, registrations, approvals, authorizations, notices, shipping documents and waste manifests required under Applicable Laws.

8.9 **Safety Procedures**. APCETH will be solely responsible for implementing and maintaining health and safety procedures for the performance of manufacturing activities and for the handling of any materials or hazardous waste used in or generated by such manufacturing activities. APCETH, in consultation with, BBB will develop safety and handling procedures for Product; provided, however, that BBB will have no responsibility for APCETH´s health and safety program.

8.10 **Quality Agreement**. All further provisions regarding audits and inspections, Product complaints and recall management are set forth in the Quality Agreement applicable to the Products. The Parties acknowledge and agree that no Products shall be manufactured under this Agreement until the applicable Quality Agreement is effective.

9. REMEDIES FOR DELAY OR DEFECTIVE PRODUCTS

9.1 **Provision of Clean Rooms.**

(a) In the event of APCETH's breach of Sections 3.1 through 3.3, APCETH shall [***].

(b) If such failure results in [***], BBB shall be entitled to:

(i) [***]

(ii) [***].

(c) [***].

9.2 **Defective Batch**

(a) In the event of a Defective Batch, [***]:

(i) [***]

(ii) [***].

(b) [***].

(c) BBB shall, at APCETH's reasonable discretion and following APCETH's reasonable instructions, either return or dispose of any Defective Batch under Section 9.2(a) or Batch suspected to contain a Defect under Section 9.2(b), and the Parties shall handle such Batches in accordance with the applicable Quality Agreement and in case of a Recall in accordance with Section 8.7.

(d) [***].

9.3 **Failure to Deliver**

(a) In the event a Batch is not released in accordance with the Delivery Schedule, [***].

(b) If a Batch is not released in accordance with the Delivery Schedule due to [***].

(c) [***].

10. REPRESENTATIONS, WARRANTIES AND COVENANTS

10.1 **APCETH Representations and Warranties.**

APCETH hereby represents and warrants to BBB by way of an independent warranty according to Article 311 Civil Code (*selbstständiges Garantieversprechen i. S. d. § 311 BGB*) that,

(a) APCETH has the full power and right to enter into this Agreement, and that there are no obligations, agreements, assignments, licenses, encumbrances or rights of any kind held by other parties, private or public, that are inconsistent with the provisions of this Agreement;

(b) APCETH is the lawful owner of the Facility;

(c) the Clean Rooms will be in accordance with the specifications as required by Section 3 and set forth in the Clean Room Specifications attached to this Agreement as Schedule 1;

(d) APCETH, to the best of its knowledge, it and its Affiliates, approved subcontractors, and each of their respective officers and directors, as applicable, and any person used by APCETH, and its Affiliates, subcontractors to perform services under this Agreement: (i) have not been debarred and are not subject to a pending debarment pursuant to Section 306 of the United States Food, Drug and Cosmetic Act, 21 U.S.C. § 335a; (ii) are not disqualified by any government or regulatory authorities from performing specific services, and are not subject to a pending disqualification proceeding; and (iii) have not been convicted of a criminal offense related to the provision of healthcare items or services, and are not subject to any such pending action. APCETH shall notify BBB immediately if APCETH, its Affiliates, or approved subcontractors, or any person used to perform services hereunder, or any of their respective officers or directors, as applicable, is subject to the foregoing, or if any action, suit, claim, investigation, or proceeding relating to the foregoing is pending, or to the best of APCETH's knowledge, is threatened;

(e) at the time of delivery to BBB, the Product will have been manufactured in accordance with this Agreement, the Quality Agreement (including the Specifications), the Marketing Authorizations, GMP and all other Applicable Laws and will be transferred free of any liens or encumbrances of any kind arising from the acts or omissions of APCETH, its Affiliates, or their respective agents; and

(f) to the best of APCETH's knowledge, the conduct and the provision of the Services (other than the use of BBB Technology or Supplied Materials) will not violate any patent, trade secret or other proprietary or intellectual property rights of any third party, and it will promptly notify BBB in writing should it become aware of any such violation or any claims asserting such violation.

10.2 **BBB Representations and Warranties.**

BBB hereby represents and warrants to BBB by way of an independent warranty according to Article 311 Civil Code (*selbstständiges Garantieversprechen i. S. d. § 311 BGB*) that BBB has the full power and right to enter into this Agreement and that there are no obligations, agreements, assignments, licenses, encumbrances or rights of any kind held by other parties, private or public, that are inconsistent with the provisions of this Agreement.

10.3 **Warranty Rights.**

The representations and warranties provided to BBB by APCETH according to Section 10.1 do not exclude or supersede BBB's warranty rights under Section 9.

11. PAYMENTS AND PAYMENT TERMS

11.1 **Access Fee**. As compensation for certain opportunity costs of APCETH, BBB shall pay to APCETH a one-time non-refundable access fee of Three Million (3,000,000) EUR ("**Access Fee**") in two instalments:

(a) [***]: Two Million (2,000,000) EUR; and

(b) [***]: One Million (1,000,000) EUR.

[***].

11.2 **Maintenance Fee**. Effective following the Supply Initiation Date, BBB shall pay to APCETH a maintenance fee to [***]. The Maintenance Fee for the [***] shall be [***], payable in [***]. Effective following the Extension Date, the [***] to be paid by BBB to APCETH shall amount to [***], payable in [***]; provided, however, that

(i) the applicable Maintenance Fee for the calendar year [***] shall be adjusted [***]; and

(ii) prior to BBB's exclusive access to [***], [***] of the Maintenance Fee shall be adjusted pro rata, [***].

11.3 **Production Fees.**

(a) The Production Fee for each Production Year shall represent the [***]. The following Production Fees applicable to each Production Scenario shall apply:

(i) [***]

(ii) [***]

(iii) [***]

(b) The Production Fee shall be due and payable in [***], and the Production Fee applicable [***].

11.4 **Adjustment**. APCETH may adjust the Maintenance Fee and the Production Fee in accordance with [***], by [***]; provided, however, in no event shall such an adjustment result in an increase of the Maintenance Fee or Production Fee by more than [***] during the [***] of this Agreement [***].

11.5 **Material Costs.** Costs for raw materials and third party laboratory costs necessary for the manufacture of Product as specified in the Quality Agreement shall be [***], provided that [***].

11.6 **Work Order Fees**. The completion of any Work Orders (other than for the manufacture of Product) and any other further ongoing work orders under the MSA for certain technology transfer and development works shall be performed under this Agreement and shall be charged separately ("**Work Order Fees**").

11.7 **Cumulative Payments**. Any amounts due and payable under this Section 11 are cumulative, except as otherwise explicitly provided.

11.8 **Invoice**. APCETH will invoice BBB [***]. Notwithstanding the foregoing, APCETH will not invoice BBB for a Batch [***]. Payment [***] will be due (i) [***] after receipt of invoice for any Access Fee payment in accordance with Section 11.1, and (ii) [***] after receipt of the invoice and reasonable supporting documentation (such as administrative requests from BBB's accounts payables) for all other payments under this Agreement.

11.9 **Payments**. BBB will make all payments pursuant to this Agreement by check or wire transfer to a bank account designated in writing by APCETH.

11.10 **Financial Records**.

(a) APCETH will keep accurate records of [***], and, upon the request of BBB, will permit BBB or its duly authorized agents to examine such records during normal business hours for the purpose of verifying the correctness of all such calculations.

(b) Furthermore, in the event that BBB is required to capitalize the Clean Rooms in accordance with U.S. Generally Accepted Accounting Principles and the Accounting Standards Codification 840-10 (and any applicable updates or successor accounting guidance promulgated by the Financial Accounting Standards Board), and solely for such purpose, APCETH shall provide to BBB, upon BBB's reasonable request, necessary information to account for this Agreement as a capital lease in BBB's financial statements. [***].

[***].

11.11 **Taxes**. Duty, sales, use or exercise taxes imposed by any governmental entity that apply to the manufacture, sale and delivery of Product will be borne by [***].

12. JOINT STEERING COMMITTEE

12.1 **Establishment.** The Parties will establish a steering committee to coordinate and supervise their activities under this Agreement (the "**Joint Steering Committee**" or "**JSC**"), and to facilitate communication between the Parties. The Joint Steering Committee will consist of an equal number of members of each Party. Each Party shall appoint [***] as members to the JSC. The members initially appointed by each Party are set out in Schedule 3, and each Party may change its members appointed to the JSC by written notice to the other Party upon [***] notice.

12.2 **Meetings.** The Joint Steering Committee shall meet regularly (in person or by teleconference) at such intervals as the Parties may agree, but no less frequently than [***]. Additionally, the JSC shall meet within [***] after receipt of a written request by one Party to the other Party to hold such a meeting.

12.3 **Authority.** The JSC shall be an advisory body only, for the coordination and supervision of the activities and the flow of information between the Parties, and shall not have the power to take any action under this Agreement, interpret, amend or modify this Agreement, or waive compliance therewith.

13. MINIMUM UTILIZATION

Prior to engaging a new Third Party manufacturer [***] ("**Minimum Utilization Requirement**"). Notwithstanding the foregoing, the Minimum Utilization Requirement shall not apply (i) [***], or (ii) [***].

14. INTELLECTUAL PROPERTY

14.1 **BBB Technology.** All rights to and interests in BBB Technology will remain solely in BBB, and no right or interest therein is transferred or granted to APCETH under this Agreement. APCETH acknowledges and agrees that it does not acquire a license or any other right to BBB Technology or BBB New Technology except for the limited purpose of performing its obligations under this Agreement, and that such limited, non-exclusive license will expire upon the completion of such obligations or the termination of this Agreement, whichever is the first to occur.

14.2 **APCETH Technology.** All rights to and interests in APCETH Technology will remain solely in APCETH and, except as otherwise set forth in this Agreement, no right or interest therein is transferred or granted to BBB under this Agreement. APCETH hereby grants a non-exclusive, worldwide, perpetual, irrevocable, transferable and sublicensable (through multiple tiers) license to BBB and BBB's Affiliates to use any APCETH Technology and APCETH Improvement Technology that APCETH incorporates into the manufacturing process of Product, solely to use, develop, manufacture or have manufactured Product, distribute, offer for sale, sell and otherwise dispose of Product, subject to the terms set forth in Section 14.5.

14.3 **New Technology.**

(a) Except as set forth herein, as between the Parties, BBB shall own all right, title and interest in and to any Technology that APCETH and/or any approved subcontractor of APCETH develops, conceives, invents, or first reduces to practice or makes, solely or jointly with BBB in the course of performing the obligations under this Agreement ("**BBB New Technology**"). Subject to Section 14.3(b) below, APCETH herewith assigns and transfers all rights and title in and to such BBB New Technology to BBB [***], and BBB hereby accepts such assignment and transfer. APCETH shall promptly disclose to BBB in writing all BBB New Technology.

(b) If an APCETH employee makes an invention under this Agreement constituting BBB New Technology, APCETH shall promptly inform BBB. If BBB wishes to obtain the related rights and titles to such BBB New Technology, BBB will inform APCETH accordingly and APCETH shall then claim such invention ("*Inanspruchnahme*") in accordance with the provisions of the German Employee Inventions Act ("*Arbeitnehmererfindungsgesetz*") and all rights in and title to such claimed inventions shall be part of the assignment and transfer of BBB New Technology to BBB in accordance with Section 14.3(a) above. The assignment and transfer of the rights in relation to such inventions shall be [***].

(c) Notwithstanding the foregoing, in the event that BBB makes use of any APCETH Technology or APCETH's Confidential Information in accordance with Section 14.2, BBB New Technology shall not include any Technology that is solely an improvement or enhancement of any APCETH Technology or APCETH's Confidential Information without reference to BBB Technology or BBB's Confidential Information (collectively, "**APCETH Improvement Technology**") and APCETH shall own all right, title and interest in and to any APCETH Improvement Technology. For clarity, APCETH Improvement Technology shall be [***].

(d) APCETH shall execute, and shall require its personnel as well as APCETH's approved subcontractors and their personnel involved in the performance of this Agreement to execute, any documents reasonably required to confirm BBB`s ownership of BBB New Technology, and any documents required to apply for, maintain and enforce any patent or other right in the BBB New Technology.

14.4 **Patent Filings.** BBB will have the exclusive right and option, but not the obligation, in its sole discretion, to prepare, file, prosecute, maintain and defend, at its sole expense, any patents that claim or cover the BBB New Technology.

14.5 **Technology Transfer.** Within [***] after the term of this Agreement, or in accordance with Section 19.1(c), APCETH shall, upon BBB's request, provide reasonable technology transfer assistance services to BBB in connection with the establishment of Product manufacturing capabilities at a Third Party contract manufacturer, as set forth in detail in this Section ("**Technology Transfer**"). In such case, APCETH shall promptly

(a) transfer to BBB and/or a Third Party designated by BBB all data and information necessary to transfer the manufacturing process, as further developed by APCETH, to any third party and to implement the manufacturing process (e.g. in-process control assays, standard operating procedures, and such), and

(b) furnish to BBB and/or such Third Party all reasonable assistance and personnel and answer all reasonable questions regarding the transfer of the manufacturing process; in each case, in order to allow BBB or such Third Party to replicate and implement the manufacturing process and to take over the manufacturing of the Product.

Without limiting the foregoing, APCETH will provide BBB and/or the Third Party designated by BBB with the following documentation: [***]. The Parties shall agree in good faith on a schedule and plan for affecting the Technology Transfer. For its assistance in the Technology Transfer, [***].

15. INSURANCE

15.1 APCETH shall secure and maintain in full force and effect throughout the term of this Agreement (and for at least [***] thereafter for claims made coverage) [***], the following minimum insurance coverage with financially sound and nationally reputable insurers [***]:

(a) [***];

(b) [***].

15.2 APCETH will at BBB's written request provide BBB with a certificate of insurance evidencing such coverage as required by Section 15.1. Where reasonably possible, APCETH will provide BBB with at least [***] advance written notice of any material change or cancellation in coverage or limits.

16. INDEMNIFICATION AND LIMITATION OF LIABILITY

16.1 **Indemnification of BBB**

APCETH will indemnify BBB, its Affiliates, and its and their respective directors, officers, employees, independent contractors, consultants and agents (the "**BBB Parties**"), and defend and hold each of them harmless, from and against any and all losses, damages, liabilities, costs and expenses (including reasonable lawyers' fees and expenses) in connection with any and all liability suits, investigations, claims or demands (collectively, "**Losses**") to the extent such Losses arise out of or result from any claim, lawsuit or other action or threat by a third party arising out of: (a) [***], or (b) [***].

16.2 **Indemnification of APCETH**

BBB will indemnify APCETH, its Affiliates, and its and their respective directors, officers, employees, independent contractors, consultants and agents (the "**APCETH Parties**"), and defend and hold each of them harmless, from and against any and all Losses to the extent such Losses arise out of or result from any claim, lawsuit or other action or threat by a Third Party arising out of: (a) [***], or (b) [***].

16.3 **Indemnification Procedure**

(a) An "**Indemnitor**" means the indemnifying Party pursuant to Section 16.1 or 16.2, as applicable. An "**Indemnitee**" means the Party that is being indemnified pursuant to Section 16.1 or 16.2, as applicable.

(b) An Indemnitee shall promptly notify the Indemnitor in writing of any claim, lawsuit or other action or threat of which it becomes aware for which the Indemnitor might be liable under Section 16.1 or 16.2, as applicable. The Indemnitee agrees to the control of such defense by the Indemnitor to the extent permissible under Applicable Laws. The Indemnitee shall cooperate fully with, and provide information to, Indemnitor and its legal representatives as reasonably requested in the investigation and defense of any claim, lawsuit or other action covered by this indemnification, all at the reasonable expense of the Indemnitor. The Indemnitee shall have the right, but not the obligation, to be represented by counsel of its own selection and expense; provided, however, that the Indemnitor will have final decision-making authority regarding all aspects of the defense of the claim, lawsuit, threat or other action.

(c) Neither Party will be responsible for, or be bound by, any settlement of any claim or suit made by the other Party without its prior written consent; provided, however, that the Indemnitee will not unreasonably withhold or delay such consent.

16.4 **Limitation of Liability**

(a) AS FAR AS LEGALLY PERMISSIBLE BY APPLICABLE LAWS, THE PARTIES' OBLIGATION TO INDEMNIFY PURSUANT TO SECTION 16.1 OR 16.2, AS APPLICABLE SHALL BE CAPPED AT [***].

(b) THE LIMITATIONS UNDER THIS SECTION 16.4 SHALL APPLY ACCORDINGLY FOR THE DIRECT LIABILITY OF ONE PARTY TO THE RESPECTIVE OTHER IN ALL CASES OTHER THAN FOR BREACH OF THE CONFIDENTIALITY AND NON-USE OBLIGATIONS IN SECTION 17; PROVIDED, THAT NEITHER PARTY WILL BE LIABLE UNDER ANY LEGAL THEORY (WHETHER TORT, CONTRACT OR OTHERWISE) FOR SPECIAL, INDIRECT, INCIDENTAL, CONSEQUENTIAL OR PUNITIVE DAMAGES ARISING OUT OF OR RELATED TO THIS AGREEMENT OR THE EXERCISE OF ITS RIGHTS HEREUNDER, INCLUDING LOST PROFITS ARISING FROM OR RELATING TO ANY BREACH OF THIS AGREEMENT, HOWEVER CAUSED, EVEN IF THE PARTY HAS BEEN ADVISED OF THE POSSIBILITY OF SUCH DAMAGES.

17. CONFIDENTIAL INFORMATION AND DATA PROTECTION

17.1 **Definition.** "**Confidential Information**" means any and all non-public scientific, technical, financial regulatory or business information, or data or trade secrets in whatever form (written, oral or visual) that is furnished or made available by one Party (the "**Discloser**") to the other (the "**Recipient**") or developed by either Party under this Agreement. For clarity, Confidential Information of a Party includes information of Affiliates or a Third Party that the Discloser has an obligation to keep confidential.

17.2 **Disclosure and Use Restriction.** Except as expressly provided herein, each Party agrees that for the term of the Agreement and [***] thereafter, each Party and its Affiliates will protect the Confidential Information of the other Party using the same degree of care it uses to protect its own confidential information but in any event no less than a reasonable degree of care, maintain as confidential, and not publish or otherwise disclose any Confidential Information of the other Party, except in accordance with Section 17.3 or 17.4. Neither Party will use Confidential Information of the other Party except as necessary to perform its obligations under this Agreement or to reasonably exercise its rights under this Agreement.

17.3 **Permitted Disclosure.** Recipient may provide Discloser's Confidential Information to its Affiliates, and to its and their directors, employees, consultants, independent contractors and agents; provided however, that (a) any such Affiliates, directors, employees, consultants, independent contractors and agents are bound by written obligations of confidentiality with respect to the Discloser's Confidential Information that are at least as restrictive as those set forth in this Agreement; (b) Recipient remains liable for the compliance of such Affiliates, directors, employees, consultants, independent contractors and agents with such obligations; and (c) such disclosure is only permitted to the extent necessary for a Party to carry out its obligations under this Agreement.

17.4 **Required Disclosure.** Recipient may also disclose Discloser´s Confidential Information to the extent ordered by a competent regulatory or governmental authority or court of competent jurisdiction, or if the Recipient is required to disclose the other Party's Confidential Information to comply with Applicable Laws, the rules of any stock exchange or listing entity, or to defend or prosecute litigation; provided that the Recipient notifies the Discloser prior to the Disclosure in writing, takes all reasonable and lawful actions to avoid or minimize the degree of such disclosure and cooperates reasonably with the Discloser in any efforts to seek a protective order.

17.5 **Exceptions.** Recipient's obligation of non-disclosure and non-use under this Agreement will not apply to any portion of Discloser's Confidential Information that Recipient can demonstrate, by appropriate evidence:

(a) is generally known to the public at the time of disclosure or becomes generally known through no wrongful act on the part of Recipient or its Affiliates;

(b) at the time of disclosure is already in possession of the Recipient or its Affiliates, other than as a result of Recipient's or its Affiliate's breach of any legal or contractual obligation;

(c) becomes known to or is lawfully provided to the Recipient or its Affiliates, without restriction as to confidentiality or use, by a source lawfully entitled to possession of such Confidential Information; or

(d) is independently developed by the Recipient or its Affiliates without use of or reference to the Discloser's Confidential Information.

17.6 **Return of Confidential Information.** Upon the effective date of the expiration or termination of this Agreement, Recipient agrees, except as otherwise provided in this Agreement, to return to Discloser all documentation or other tangible evidence or embodiment of Discloser's Confidential Information (including, if BBB is the Discloser, any Supplied Materials) and not to use such Confidential Information unless agreed otherwise. Notwithstanding the foregoing, Recipient may retain one archival copy of Discloser's Confidential Information in order to monitor Recipient's ongoing obligation of confidentiality and non-use under this Agreement and in compliance with sample retention protocols required by the Quality Agreement and GMP, as may be applicable; provided that such archival copy must be kept confidential in accordance with this Section 17 and segregated from Recipient's regular files.

17.7 **Data Protection**. Each of the Parties is, and shall be, in compliance with all Applicable Laws pertaining to patient personal information and patient health information, including data safety and data protection ("**Data Protection Laws**"). BBB shall not make patient personal information or patient health information available to APCETH which is not pseudonymized in accordance with applicable Data Protection Laws. Each of the Parties will treat all patient personal information and patient health information (in case of APCETH in pseudonymized form) as Confidential Information, in accordance with this Agreement. Each Party has implemented, and shall implement, in accordance with applicable privacy and security laws all policies, privacy notices, consent forms and administrative, physical and technological safeguards that reasonably and adequately protect the personal information and patient health information of patients, including the mobilized peripheral blood from patients ("**Patient Information**") created, received, maintained, or transmitted under this Agreement.

18. TERM AND TERMINATION

18.1 **Term of this Agreement.** The initial term of this Agreement shall commence on the Supply Initiation Date (the "**Effective Date**") and end after a period of five (5) years starting from the Supply Initiation Date.

18.2 **Renewal.** Following the initial term, this Agreement shall automatically renew for additional three (3) year terms, unless either Party provides the other Party with notice of non-renewal at least [***] prior to the end of the applicable term.

18.3 **Termination by either Party**

(a) Either Party may terminate this Agreement with immediate effect upon written notice to the other Party:

(i) for any material breach of this Agreement by the other Party, unless such breach is cured within [***] after the breaching Party receives written notice of such breach from the non-breaching Party; provided, however, that if such breach is not capable of being cured within such [***] period and the breaching Party has commenced and diligently continued actions to cure such breach within such [***] period, except in the case of a payment default, the cure period shall be extended to [***], so long as the breaching Party is making diligent efforts to do so; or

(ii) to the extent permitted under Applicable Laws, if an Insolvency Event occurs with respect to the other Party. In any event, when a Party first becomes aware of the likely occurrence of an Insolvency Event with regard to such Party, it shall promptly so notify the other Party in order to allow the other Party to protect its interests under this Agreement.

(b) [***]:

(i) [***]

(ii) [***].

18.4 **Termination by BBB**

BBB is entitled to terminate this Agreement:

(a) for convenience with at least (i) [***] prior written notice prior to [***], or (ii) twelve (12) months' prior written notice following [***];

(b) during the Clinical Supply Phase, with [***] prior written notice, in the event (i) [***], or (iii) [***]; or

(c) with immediate effect, if a Force Majeure Event has prevented APCETH's performance (in whole or substantial part) of this Agreement for a period of [***].

19. EFFECTS OF TERMINATION

19.1 **Termination Payment.**

(a) Upon termination by BBB according to Section 18.4(a), [***].

(b) Upon termination by BBB according to Section 18.4(b), [***]

(c) Upon termination by BBB due to a material breach of APCETH, [***].

(d) Upon termination by APCETH due to a material breach of BBB, [***].

19.2 **Technology Transfer.** After termination of this Agreement, APCETH shall, upon BBB's request, provide reasonable assistance in Technology Transfer services as set forth in Section 14.5.

19.3 **Return of Materials**. Upon termination of this Agreement, BBB may at its sole discretion as an alternative to the return of Confidential Information as set forth in Section 17.6, request in writing the destruction of any documents or remaining Supplied Materials and provide appropriate evidence of such destruction.

20. COMPLIANCE, ANTI-BRIBERY AND ANTI-CORRUPTION

Either Party shall act in full compliance with all Applicable Laws, including all applicable labor, tax and social insurance law and industrial safety regulations with regard to its employees involved in the performance of this Agreement. APCETH shall ensure by appropriate contractual arrangements and supervision that any approved subcontractors act in full compliance with the aforementioned Applicable Laws. APCETH agrees to comply with the reasonable, written instructions of BBB and/or its Affiliates with respect to the Applicable Laws relating to the import, export or re-export of the Supplied Materials and/or Product, provided that where APCETH complies with such instructions, BBB shall be responsible for the import, export or re-export of the Supplied Materials and/or Products.

20.1 **Representation and Warranty.** Either Party represents and warrants by way of an independent warranty (*selbstständiges Garantieversprechen i.S.d. § 311 (1) BGB*), that it, its owners, directors, officers, employees will act in full compliance with applicable anti-corruption laws and regulations, industry and professional codes of practice, including the U.S. Foreign Corrupt Practices Act and the UK Bribery Act. Without limiting the generality of the foregoing, either Party represents and warrants in particular that it and its owners, directors, officers, employees will not directly or indirectly in connection with the business of the other Party or with this Agreement:

(a) offer, promise, pay or arrange for payment or giving of a bribe or any benefit, advantage or anything of value to any public official, individual, entity or any other third party in exchange for an improper advantage in any form either directly or indirectly in order to fulfil, obtain or retain (a) regulatory permits like the building permit, (b) any kind of business including any commercial transaction to which the other Party is a party, or which is otherwise in connection with this Agreement, or (c) any other improper advantage;

(b) transfer anything of value to a public official without the prior approval of the other Party, regardless of whether or not such transfer might constitute a bribe;

(c) transfer anything of value to subcontractors, or any third party for the purpose of offering, promising, paying, receiving, soliciting, or arranging for the payment of, or reimbursing anyone for payment of, a bribe or a transaction of anything of value to a public official; or

(d) request, accept a promise of or receive any payment, benefit or advantage from any individual or entity for itself or for a third party in return for giving another person or entity unfair preferences in the procurement of goods or commercial or other services in connection with this Agreement.

20.2 **Reporting.** Either Party shall report any suspicion of past, current or potential violations of this Section 20 immediately to the other Party, to the extent permitted by Applicable Law. If a Party is in doubt whether a certain act violates its obligations under this Section, such Party shall contact the other Party and shall delay the decision before taking the action.

20.3 **Audit Right.** The audit rights of BBB under Section 8.4 and 11.10 encompass the relevant records ensuring compliance with this Section 20.

20.4 **Consequences of Violation**. Any uncured or incurable violation of this Section 20 shall constitute a material breach of this Agreement.

21. NOTICES

21.1 Unless otherwise expressly agreed in writing, all declarations or communications in connection with this Agreement, including the Schedules attached hereto and incorporated by reference, shall only be validly served if they are delivered in writing by registered mail, by internationally recognized expedited delivery service (receipt requested), or by fax (with written confirmation of receipt) to the following addresses for delivery of the Parties.

(a) For declarations or communications to be made to BBB:

bluebird bio Inc.

150 2nd Street, Cambridge, MA 02141,

Attention: Chief Legal Officer

with a copy to [***]

[***]

(b) For declarations or communications to be made to APCETH:

apceth Biopharma GmbH

Haidgraben 5

D-85521 Ottobrunn

Germany

Attention: Geschäftsführung

with a copy to [***]

[***]

21.2 Furthermore, the above addresses and fax numbers shall be applicable for the purpose of service until such time as one of the Parties informs the other(s) in writing of any change.

22. GOVERNING LAW, ARBITRATION

22.1 This Agreement and all claims and rights arising out of or in connection with this Agreement shall be exclusively governed by German law and shall be construed and enforced in accordance with German law without regard to its conflict of law provisions. The application of the United Nations Convention on Contracts for the International Sale of Goods (CISG) is excluded.

22.2 All disputes between the Parties and all disputes between BBB and apceth GmbH & Co KG arising out of or in connection with this Agreement, its completion or implementation shall be conclusively decided pursuant to the rules of arbitration of the International Chamber of Commerce (ICC), Paris, with the exclusion of recourse to the courts of law. The place of arbitration shall be Zurich, Switzerland. All disputes shall be decided by a single arbitrator. The arbitrator shall be appointed in accordance with the rules of arbitration of the International Chamber of Commerce (ICC), Paris.

23. FINAL PROVISIONS

23.1 **Assignment**. This Agreement shall be binding upon the successors and assigns of the Parties. Neither Party may assign or transfer this Agreement, in whole or in part, without the prior written consent of the other Party. Notwithstanding the foregoing, BBB may assign this Agreement (i) to its Affiliates, provided that BBB guarantees fulfilment of the obligations, including all payment obligations, of the assignee, and (ii) to a successor in interest by way of merger, acquisition, consolidation, or sale of all or substantially all of the business to which this Agreement relates. No assignment shall relieve any Party of responsibility for the performance of any obligation that accrued prior to the effective date of such assignment.

23.2 **Force Majeure**. Neither Party shall be in breach of this Agreement if there is any failure of performance under this Agreement (except for payment of any amounts due under this Agreement) occasioned by any reason beyond the reasonable control and without the fault or negligence of the Party affected thereby, including, without limitation, an fire, flood, act of government or state, war, civil commotion, insurrection, acts of terrorism, embargo, sabotage, prevention from or hindrance in obtaining energy or other utilities, a shortage of raw materials or other necessary components, labor disputes of whatever nature (a "**Force Majeure Event**"). Such excuse shall continue as long as the Force Majeure Event continues. Upon cessation of such Force Majeure Event, the affected Party shall promptly resume performance under this Agreement. A Party affected by a Force Majeure Event will give the other Party prompt written notice, to the extent possible, of the occurrence of any Force Majeure Event, the nature thereof, and the extent to which it will be unable to fully perform its obligations under this Agreement and will use commercially reasonable efforts to resume performance or mitigate the effects of the Force Majeure Event as quickly as practicable and to give the other Party prompt written notice when it is again fully able to perform such obligations.

23.3 **Headings.** Headings in this Agreement shall be for convenience only and shall not affect the interpretation of the Agreement.

23.4 **Severability.** If any provision of this Agreement is or becomes invalid, either as a whole or in part, this shall not affect the validity or enforceability of the remainder of the Agreement. The Parties agree to replace the invalid provision by a provision which serves the purposes of the Agreement as closely as possible. The same shall apply to any possible omission in this Agreement. If the defectiveness of a provision is based on the determination of a certain level of performance or a certain time (deadline or fixed date), the provision is deemed to have been agreed with the level or time which comes as close as legally possible to the original level or time.

23.5 **Survival.** The provisions of Sections 1, 6.2, 9, 14, 15, 16, 17, 19, 21, 22, and 23 shall survive the expiration or termination of this Agreement.

23.6 **Written Amendments and No Continuing Waiver:** Valid amendments or supplements to this Agreement must be made in writing (in the sense of sec. 126 German Civil Code), unless notarisation is prescribed by law, and shall expressly refer to this Agreement. The same shall apply to any agreement to deviate from or cancel this requirement of written form. The failure of any Party at any time or times to require the performance of this Agreement will in no manner affect its rights at a later time to enforce the same. No waiver by any Party of the breach of any term contained in this Agreement, whether by conduct or otherwise, in any one or more instances, will be deemed to be or construed as a further or continuing waiver of any such breach or the breach of any other term of this Agreement.

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bluebird bio, Inc.

/s/ Jason F. Cole

Name: Jason F. Cole

Title: Chief Legal Officer

Date: 28 Nov 2016

Apceth Biopharma GmbH

/s/ C. Guenther

Name: Dr. Christine Guenther

Title: CEO

Date: 18 Nov 2016

Apceth GmbH & Co. KG

/s/ C. Guenther

Name: Dr. Christine Guenther

Title: CEO

Date: 18 Nov 2016

List of Schedules

[***]

[***] INDICATES MATERIAL THAT HAS BEEN OMITTED BECAUSE IT IS BOTH (I) NOT MATERIAL, AND (II) WOULD LIKELY CAUSE COMPETITIVE HARM TO THE COMPANY IF PUBLICLY DISCLOSED.

AMENDMENT No. 1 TO THE TOLL MANUFACTURING AND SERVICE AGREEMENT

Amendment Agreement No. 1 (**"Amendment Agreement No. 1"**) to the Toll Manufacturing and Service Agreement shall become effective on November 16, 2018 and is entered into by and between:

bluebird bio Inc. ("BBB")
having its principal place of business at 60 Binney St., Cambridge, MA 02142, United States of America

and,

apceth Biopharma GmbH ("APCETH"),
having its principal place of business at Haidgraben 5, 85521 Ottobrunn, Germany.

BBB and APCETH hereinafter also each referred to as a **"Party"** and jointly as the **"Parties"**.

Whereas,

The Parties entered into a Toll Manufacturing and Service Agreement (**"TMSA"**) effective on January 1, 2017 regarding the clinical and commercial GMP-manufacturing of BBB's Products and related services by APCETH.

The Parties entered into an Addendum to the TMSA on May 21, 2018 regarding the European Union's General Data Protection Regulation.

The Parties now wish to make certain amendments to the TMSA as detailed herein in this Amendment Agreement No. 1.

NOW THEREFORE, the Parties agree as follow:

1. Section 16.2 - Indemnification of APCETH shall be replaced by:

"16.2 Indemnification of APCETH

BBB will indemnify APCETH, its Affiliates, its approved subcontractors and its and their respective directors, officers, employees, independent contractors, consultants and agents (the "APCETH Parties"), and defend and hold each of them harmless, from and against any and all Losses to the extent such Losses arise out of or result from any claim, lawsuit or other action or threat by a Third Party arising out of: [***]."

2. Furthermore, behind Section 16.4 lit. (b) a new Section 16.4 lit. (c) shall be added to the TMSA as follows:

"(c) NOTWITHSTANDING ANYTHING OF THE ABOVE, THE LIMITATIONS UNDER THIS SECTION 16.4 SHALL NOT APPLY TO [***]."

3. Except as expressly provided in this Amendment Agreement No. 1, all other terms, conditions and provisions of the MSA shall continue in full force and effect as provided therein.

[***] INDICATES MATERIAL THAT HAS BEEN OMITTED BECAUSE IT IS BOTH (I) NOT MATERIAL, AND (II) WOULD LIKELY CAUSE COMPETITIVE HARM TO THE COMPANY IF PUBLICLY DISCLOSED.

IN WITNESS WHEREOF, the Parties have caused this Amendment Agreement No. 1 to be executed and delivered by their respective duly authorized officers

bluebird bio Inc.

Cambridge, MA 19/11/2018
(Place, Date)

/s/ Jason Cole
Name: Jason Cole
Title: Chief Legal Officer

apceth Biopharma GmbH

Ottobrunn 16.11.2018
(Place, Date)

/s/ Dusan Kosijer
Name: Dusan Kosijer
Title: CFO

[***] INDICATES MATERIAL THAT HAS BEEN OMITTED BECAUSE IT IS BOTH (I) NOT MATERIAL, AND (II) WOULD LIKELY CAUSE COMPETITIVE HARM TO THE COMPANY IF PUBLICLY DISCLOSED.

[***] INDICATES MATERIAL THAT HAS BEEN OMITTED BECAUSE IT IS BOTH (I) NOT MATERIAL, AND (II) WOULD LIKELY CAUSE COMPETITIVE HARM TO THE COMPANY IF PUBLICLY DISCLOSED.

Exhibit 10.25

EXECUTION VERSION

Clinical and Commercial Supply Agreement

Viral Vector Product

by and between

bluebird bio, Inc.

and

SAFC Carlsbad, Inc.

November 27, 2017

CLINICAL AND COMMERCIAL SUPPLY AGREEMENT

VIRAL VECTOR PRODUCT

This Clinical and Commercial Supply Agreement (this "**Agreement**"), executed as of November 27, 2017 and effective as of January 1, 2018 (the "**Effective Date**"), is entered into by and between:

bluebird bio, Inc., a Delaware corporation, with a place of business located at 60 Binney Street, Cambridge, MA 02142 ("**Company**"), and

SAFC Carlsbad, Inc., a company incorporated under the laws of the State of California, USA, with its principal offices located at 6211 El Camino Real, Carlsbad, California, 92009 ("**SAFC**").

Company and SAFC are hereinafter sometimes referred to separately as a "**Party**" or together as the "**Parties**".

RECITALS

WHEREAS, Company is engaged in the development of its [***] (each, a "**Drug Product**" and collectively, the "**Drug Products**");

WHEREAS, SAFC develops and manufactures a broad range of viral vectors for viral and gene therapy related products that are active key ingredient(s) for use in biopharmaceutical development, clinical trials and commercial use;

WHEREAS, Company desires to engage SAFC to manufacture and supply the Vector Products (as defined herein) for use by Company in its manufacture, use and sale of its Drug Products;

WHEREAS, this Agreement is for the clinical and commercial manufacture and supply, and any and all related services, including but not limited to, Testing, Process Characterization and Process Performance Qualification (as such terms are defined herein);

WHEREAS, this Agreement supersedes and replaces that certain Production Service Agreement by and between the Parties dated October 30, 2008, as amended (the "**Prior Agreement**") and said Prior Agreement is terminated in its entirety as of the Effective Date; and

NOW, THEREFORE, in consideration of the above premises and the mutual covenants, obligations and agreements contained herein, the Parties hereby agree as follows:

1. Definitions and Interpretation

1.1 "**Affiliate**" means any entity directly or indirectly controlling, controlled by or under common control with either Party hereto. For purpose of this definition, "control" shall mean ownership of over fifty percent (50%) of the equity capital, the outstanding voting securities or other ownership interest of an entity, or the right to receive over fifty percent (50%) of the profits or earnings of an entity. In the case of non-stock organizations, the term "control" shall mean the power to control the distribution of profits.

1.2 "**Agreement**" means, collectively, this Agreement, its Exhibits, any Task Orders, Purchase Orders and any other documents incorporated herein by reference, including without limitation the Quality Agreement(s) (as hereinafter defined); provided, however, the Quality Agreement(s) may be amended and modified separately as a stand-alone document and not require amendment of this Agreement under those circumstances.

1.3 "**Batch**" means a specific quantity of Vector Product produced, tested and released from a single operation of the Manufacturing Process, as described in the Master Batch Record. A "Batch" may be any of the following types as further defined hereinafter and identified on the applicable Task Order [***].

1.4 "**Batch Record**" and "**Master Batch Record**" have the meanings assigned to such terms in the Quality Agreement.

1.5 "**Cell Bank**" means either a master cell bank or a working cell bank, whichever the case may be in its use.

1.6 "**Certificate of** [***]" means a certificate issued by [***].

1.7 "**CFR**" means the U.S. Code of Federal Regulations.

1.8 "**Clinical Batch**" means a Batch produced by SAFC under cGMP conditions and intended for use by Company for investigational purposes.

1.9 "**Commercial Batch**" means a Batch produced by SAFC under cGMP conditions after Company has obtained Regulatory Approval for Sale (as defined herein) of its Drug Product.

1.10 "**Confidential Information**" shall mean all technical, business and other information, whether tangible or intangible, including (without limitation) any and all data, techniques, discoveries, inventions, processes, know-how, patent applications, inventor certificates, trade secrets, methods of production and other confidential or proprietary information, that either Party or any Affiliate of a Party has ownership rights to (as either owner, licensee or sub-licensee), or may hereafter obtain ownership rights to, and discloses to the other Party. All Confidential Information disclosed by either Party or its Affiliates to the other Party or its Affiliates pursuant to the Prior Agreement shall be deemed to be the disclosing Party's Confidential Information hereunder. The Parties agree to either (a) clearly mark the term "Confidential Information" upon written Confidential Information, or (b) in the case of oral disclosure of Confidential Information, to confirm the confidential or proprietary nature of such Confidential Information in a writing prior to such disclosure or within [***] following such disclosure. Notwithstanding the foregoing, failure to mark or confirm in writing such Confidential Information does not constitute a designation of non-confidentiality when the confidential or proprietary nature would be reasonably recognized by the receiving Party based on the subject matter or type of information disclosed or the circumstances of disclosure, and such information shall be deemed Confidential Information hereunder.

1.11 "**Consumables**" means all single use, regularly replaced or reused materials that are required to perform the Manufacturing Process (including Resins but excluding Plasmid Stocks and Raw Materials).

1.12 "**Contract Year**" means each consecutive twelve (12) month period during the Term, beginning on January 1, 2018 and on each January 1 during the Term thereafter.

1.13 "**Current Good Manufacturing Practices**" or "**cGMP**" shall mean current good manufacturing practices applicable to the Manufacture of Vector Product, that are promulgated by any applicable governmental or regulatory authority, and as may be set forth in the Quality Agreement.

1.14 "**Deviation**" shall have the meaning set forth in the Quality Agreement.

1.15 "**EMA**" shall mean the European Medicines Agency of the European Union, and any successor(s) thereto.

1.16 "**Failure to Supply**" shall have the meaning set forth in Section 3.8(a) hereof.

1.17 "**FDA**" shall mean the United States Food and Drug Administration, and any successor thereto.

1.18 "**Manufacture**", "**Manufacturing**" or "**Manufactured**" means all activities related to the manufacturing of Vector Product, or any ingredient thereof to be undertaken by SAFC in accordance with the terms and conditions of this Agreement and the Quality Agreement, which may include manufacturing Vector Product or supplies for Company's commercial sale in and for its Drug Product(s), packaging Vector Product, in-process and final testing and release of Vector Product, or any component or ingredient thereof, quality assurance activities related to manufacturing and release of Vector Product and regulatory activities related to any of the foregoing, as may be more specifically identified in the Quality Agreement, the Specifications, and the applicable Purchase Order.

1.19 "**Manufacturing Facility**" means those parts of the manufacturing facility owned by SAFC Carlsbad, Inc., located at 6219 El Camino Real, Carlsbad, California, 92009, operated by SAFC, validated and made available in accordance with this Agreement.

1.20 "**Manufacturing Process**" shall mean the instructions, Specifications (as well as specifications for raw materials and excipients), formulae, procedures, tests and standards developed, established and mutually agreed in writing by the Parties for Manufacturing the Vector Product.

1.21 "**Materials Specification**" means a document detailing the specifications that are applicable for each Raw Material or Consumable, each as mutually approved in writing by the parties.

1.22 "**Minimum Lead Time**" shall have the meaning set forth in Section 3.3(b) hereof.

1.23 "**Minimum Purchase Commitment**" means Company's minimum binding purchase commitment to SAFC for a minimum number of Batches of Vector Product during a Contract Year, determined as set forth in Section 3.1(a).

1.24 "**Out of Specification**" or "**OOS**" shall have the meaning set forth in the Quality Agreement.

1.25 "**Plasmid Stocks**" means any Company proprietary plasmids or reference materials received by SAFC from Company.

1.26 "**Process Characterization Batch**" means a non-cGMP Batch produced by SAFC for the purposes of examination by the Parties as to proposed operational ranges and their individual and/or combined impact on product safety, integrity, strength, purity and quality in an effort to further define the process for commercial manufacturing of the Vector Product.

1.27 "**Process Performance Qualification Batch**" means a cGMP Batch produced by SAFC that confirms the process design and demonstrates consistency of operating within the allowed process parameter ranges.

1.28 "**Production Records**" means all Records (including Batch Records, Master Batch Records, and Specifications) and other documentation, including but not limited to databases or other work product generated by SAFC for Company during and in connection with the Services, whether recorded in writing, electronically, or otherwise.

1.29 "**Project**" means clearly identified portions within a fully-executed Task Order that sets forth specific Services.

1.30 "**Purchase Order**" means a document issued by Company to SAFC, which shall include such details as a description, quantities, and agreed upon prices for the Vector Product and/or Services for the applicable Task Order and serves as an ordering acknowledgement mechanism for financial management and invoicing.

1.31 "**Quality Agreement**" means the Quality Agreement between Company and SAFC attached hereto and incorporated herein by reference as Exhibit 1, and as may be amended in accordance with the terms of this Agreement.

1.32 "**Raw Materials**" means all components, reagents and solvents intended for use in the Manufacturing Process for the Vector Product, but excluding any Plasmid Stocks and Consumables, which meet the applicable Materials Specifications.

1.33 "**Regulations**" means any and all laws, rules and regulations applicable to the performance of the Services in the country in which (a) Services are performed, or (b) a regulatory filing including results of Services is intended to be filed. Regulations shall include, without limitation, and where and when applicable; (i) the United States Food, Drug, and Cosmetic Act, as amended and any and all rules, regulations and guidance promulgated thereunder, (ii) all applicable European Union, national and local laws, standards and guidelines, (iii) any and all rules and regulations of the Regulatory Agency or any other federal or state government agency related to the conduct of clinical research studies, and (iv) any applicable guidelines promulgated by the International Conference on Harmonization, including without limitation, the ICH Harmonized Tripartite Guidelines for Good Manufacturing Practice, (v) cGMP, and (vi) cGLP.

1.34 "**Regulatory Agency**" means (a) any regulatory or health authority in the United States or in other countries, including without limitation, the FDA and the EMA, (b) if applicable to a particular Task Order (as hereinafter defined), the relevant government regulatory authority or authorities in countries outside of the United States responsible for the conduct of clinical research studies and/or approval of pharmaceutical products, and (c) any other governmental regulatory authority or authorities identified in the Quality Agreement.

1.35 "**Regulatory Approval for Sale**" means with respect to a country or extra-national territory, any and all approvals (including Biologic License Applications and Marketing Authorization Applications), licenses, registrations or authorizations of any Regulatory Agency necessary in order to commercially distribute, sell or market a Drug Product in such country or some or all of such extra-national territory, including any pricing or reimbursement approvals that may be required in such country or some or all of such extra-national territory, and not including approvals for sale or distribution under compassionate use, named patient programs, or other expanded access programs.

1.36 "**Regulatory Filing**" means any or all correspondence or petitions, to Regulatory Agencies for the purpose of obtaining or maintaining the Regulatory Approval for Sale of Drug Product or the Manufacturing Process as required by statute, or modifying or supplementing existing filings and subsequent amendments and supplements thereto, including any foreign counterparts thereof and any other filings required by Regulatory Agencies relating to the Manufacture, testing, sale or distribution of Vector Product under this Agreement.

1.37 "**Resins**" means all chromatographic media intended to refine or purify the Vector Product, as specified in the Master Batch Record, all of which meet the applicable Materials Specifications.

1.38 "**Run Equivalent**" shall mean one Batch of Vector Product as counted against the Minimum Purchase Commitment, and the associated Batch production price excluding any Batch testing fees (refer to Exhibit 4, Table 1).

1.39 "**SAFC Technology**" means any and all SAFC confidential information, trade secrets and SAFC intellectual property and the like.

1.40 "**Services**" means the services to be performed by SAFC pursuant to a fully-executed Task Order under this Agreement.

1.41 "**Specifications**" shall mean Material, Manufacturing and Vector Product specifications set forth in Exhibit 2 hereto.

1.42 "**Task Order**" means a mutually agreed upon and executed in writing by the Parties that describes the Services to be performed by SAFC for Company, which specifies; (a) Project scope, (b) quantity, (c) delivery dates, (d) shipping instructions and addresses, (e) storage instructions, if any, (f) price and payment schedule, and (g) related Testing. A sample form of a Task Order is attached as Exhibit 3.

1.43 "**Technology Transfer to SAFC**" means the Services related to technology transfer of a Manufacturing Process by Company to SAFC, including any production preparatory, training or related support activities for [***].

1.44 "**Term**" shall have the meaning set forth in Section 10.1 hereof.

1.45 "**Testing**" means a scientific evaluation of the quality, safety and purity of Vector Product through assays performed by a qualified testing facility as more particularly described in a Task Order.

1.46 "**Third Party Supplier**" shall have the meaning set forth in Section 3.8(c)(ii) hereof.

1.47 "**Vector Product**" means the purified active biological ingredient in its final formulation in the applicable closure that results from the Manufacture by SAFC, whether clinical or commercial in nature and as more particularly described in the applicable Specification.

2. Manufacture and Supply of Vector Product

2.1 General Conditions of Supply. During the Term, SAFC shall Manufacture and supply Vector Product to Company, and Company shall purchase Vector Product from SAFC in such quantities as Company may order from time to time, subject to the limitations and requirements set forth herein. In consultation with Company, SAFC shall establish, update as necessary, and reserve sufficient qualitied personnel time, manufacturing resources, equipment and cGMP production capacity to enable SAFC to Manufacture Vector Product in accordance with SAFC's obligations under this Agreement. All Vector Product Manufactured hereunder shall be Manufactured solely by SAFC in suites exclusively dedicated to Company at the Manufacturing Facility. SAFC may not change the Manufacturing site, location or suites for Vector Product without the prior written approval of Company. SAFC shall perform all maintenance required on equipment within the Manufacturing Facility, including maintenance required according to the equipment manufacturer's specifications and maintenance required to ensure continued validation of the equipment to cGMP requirements.

2.2 Control of Plasmid Stocks and Cell Banks; Storage Services.

(a) SAFC shall maintain all portions of the Plasmid Stocks and Cell Bank that it receives from Company or Company's agents in safe and secure storage under its control in accordance with the storage guidelines set out in the Quality Agreement and/or Materials Specifications, and SAFC shall not transfer the Plasmid Stocks or Cell Bank to any SAFC Affiliate or to any third party that is not specifically authorized in advance and in writing by Company. SAFC shall comply with all applicable regulatory requirements relating to general safety in handling the Plasmid Stocks and Cell Bank. SAFC shall not use the Plasmid Stocks or Cell Bank for any purpose except as contemplated by this Agreement or as otherwise authorized in writing by Company, and in no event shall SAFC modify or attempt to modify the Plasmid Stocks or Cell Bank. Upon Company's written request, SAFC shall return all or portions of the Plasmid Stocks and Cell Bank to Company or its designee.

(b) Storage service fees for [***] shall be contained in an annual Task Order mutually agreed to by the Parties no less than [***] prior to the next Contract Year.

2.3 Standard of Performance. At all times during the Term, SAFC will perform the Services with due care, and in accordance with this Agreement, the Specifications, Quality Agreement and applicable laws and regulations, including and not limited to, Current Good Manufacturing Practices applicable to its facilities and to biologics, it being understood that an immaterial incident or deviation from such standards that does not affect the timing for Manufacture of a Batch (including its production, testing, or release), or delivery of a Batch, shall not by itself be deemed a breach of SAFC's obligations hereunder and that the parties will work together in good faith to resolve any such incident or deviation pursuant to the Quality Agreement.

2.4 Changes to Specifications and Process. The Specifications shall be amended only as agreed upon in writing by Company and SAFC; provided, however, that the Parties agree to cooperate to amend or supplement the Specifications to the extent reasonably necessary to comply with changes in applicable laws or regulations or the requirements of applicable Regulatory Agencies or as Company may reasonably request from time to time (provided such request is made in good faith). SAFC shall follow the change control procedures set forth in the Quality Agreement for any proposed changes in the Manufacturing Process. SAFC acknowledges that any such change(s) shall, in each case, comply with cGMP, this Agreement, all regulatory submissions, and the Quality Agreement. In the event such amendment (whether as a result of changes in applicable laws or regulations or the requirements of applicable Regulatory Agencies or at Company's reasonable and good faith request or otherwise) requires additional cost or schedule adjustments for the Manufacture of Vector Product hereunder, Company and SAFC shall agree in good faith on an equitable adjustment to price or schedule or both, as appropriate. Any such amended Specifications shall be reflected in and attached hereto as an amended and restated Exhibit 2.

2.5 Raw Materials and Consumables.

(a) Procurement. SAFC shall be responsible for the procurement of all [***] necessary for the Manufacture of Vector Product. SAFC shall use commercially reasonable efforts to procure all [***], consistent with and having regard to such matters as security and sources of supply, quality of product, volume requirements, terms and conditions of supply and the Manufacturing schedule. The Parties shall use their good faith efforts to identify and establish a list of [***] by [***] and update Exhibit 6, as attached hereto and incorporated herein.

(b) Compliance with Specifications. All [***] hereunder shall comply with the applicable Materials Specifications and the Master Batch Record.

(c) Alternate Sources of Supply. SAFC shall be responsible to establish a source or sources of supply for all [***] sufficient to ensure SAFC's ability to fulfil its obligations to Manufacture Vector Product hereunder in a timely and cost-effective manner, and in accordance with the Quality Agreement. [***].

(d) Sole-Sourced Raw Materials and Consumables. For any sole-sourced [***] that SAFC has provided proper notice to Company in accordance with Section 2.5(c)(i), [***].

(e) Vendor Audits. SAFC shall, conduct all necessary audits on vendors and suppliers of Raw Materials, Consumables and Resins to ensure that such vendors and suppliers comply with applicable regulatory and quality requirements.

(f) Inventory of Materials and Spare Parts. SAFC shall establish, update as necessary and implement, inventory management processes and procedures designed to ensure that SAFC is able to obtain, on a timely basis, all [***] necessary to Manufacture Vector Product hereunder. SAFC shall ensure that an inventory of spare parts for all equipment it uses to Manufacture Vector Product is maintained consistent with the manufacturers' recommendations.

(g) Storage and Use of Materials and Vector Product. SAFC shall ensure that all [***] that are in SAFC's control, as well as all Manufacturing Process intermediates and Vector Product in SAFC's control, are stored in accordance with the terms and conditions of the storage guidelines set out in the Quality Agreement, the Materials Specifications and/or the Master Batch Record (as applicable), or as otherwise mutually agreed to by SAFC and Company in writing.

2.6 Quality Control and Release. The quality control(s) and the release(s) of Vector Product (including documentation) shall be done by SAFC in accordance with the Quality Agreement. Pursuant to Section 4.3 below, Company shall have the right to reject Vector Product that does not meet the quality control and release testing requirements agreed upon by SAFC and Company in the Specifications.

2.7 Access to the Manufacturing Facility

(a) Inspections. Upon reasonable advance notice, and at mutually agreeable times and dates during normal business hours and in accordance with any requirements of the Quality Agreement, SAFC will permit Company representatives to visit the Manufacturing Facility, discuss the Services with appropriate officials of SAFC, and inspect Production Records, including but not limited to all data, relevant to the Services. Such Manufacturing Facility visits shall also be permitted during the data retention period described in the Quality Agreement, if any. Company will comply with any and all SAFC safety, security and confidentiality measures for the Manufacturing Facility and other related facilities.

(b) Person-In-Plant. In addition to the foregoing inspection right and audit right otherwise set forth herein, with [***] prior written notice to SAFC, Company may designate an individual from time to time in its discretion (the "**Person-In-Plant**"), who will be present in the Manufacturing Facility during operating hours and during active Manufacturing, to observe the testing and production phases of the Manufacturing Process, and to consult with SAFC. Company shall cause the Person-In-Plant to (i) not cause any disruption to SAFC's business activities and (ii) comply with SAFC's safety, security and confidentiality measures. The duration and activities for Person-In-Plant shall be pre-approved by SAFC in advance of scheduling and entry of such Person-In-Plant.

2.8 Documentation.

(a) General. Upon completion of Manufacture of each Batch of Vector Product, SAFC shall provide to Company the following documentation related to the Manufacturing of Vector Product in accordance with the Quality Agreement, as applicable: (i) a Certificate of [***], (ii) all Deviations, and (iii) the executed Batch Record.

(b) Confidential Records. The Master Batch Records and all documents referred to in Section 2.8(a) shall be Confidential Information of Company and shall not be used or disclosed by SAFC other than for the purposes of permitting SAFC to exercise its rights or fulfil its obligations under this Agreement (including but not limited to, the provision of the Master Batch Record and other documents to Company for quality review) and, where necessary, for disclosure to the relevant Regulatory Agencies in order to comply with regulatory requirements relating to the Manufacturing of Vector Product by SAFC.

(c) Retention of Documentation. All Production Records related to the Manufacturing of Vector Product shall be owned by Company and archived with SAFC after Manufacturing for a period as stated in the Quality Agreement.

2.9 Safety of Vector Product. In each case in accordance with the Quality Agreement: (i) each Party shall immediately notify the other Party of any unusual health or environmental occurrence relating to the Vector Product; and (ii) each Party shall advise the other Party immediately of any safety or toxicity problems of which it becomes aware regarding the Vector Product.

3. Purchase Commitment, Forecasts and Orders; Release, Delivery and Storage; Delay and Third Party Supplier

3.1 Minimum Purchase Commitment; Run Equivalents; Additional Batches and Manufacturing Capacity; Support Studies.

(a) During the Term, Company shall purchase the Minimum Purchase Commitment which shall be equal to [***]. In the event Company fails to purchase the Minimum Purchase Commitment [***]. Such payment requirement for the shortfall of Batches shall be invoiced [***].

(b) Notwithstanding Section 3.1(a), in any Contract Year in which [***].

(c) Company may request additional Batches beyond its Minimum Purchase Commitment, provided that Company makes such request upon written notice to SAFC [***].

(d) Company may request support studies related or unrelated to any Batches or Technology Transfer to SAFC under this Agreement, and such support studies shall be incremental to any Minimum Purchase Commitment and shall be under a separate and distinct Task Order outlining the scope of work and cost of such support studies.

3.2 Forecasts; Change of Vector Product.

(a) In advance of the Effective Date, Company shall determine and provide to SAFC, Company's initial Contract Year's forecast, which shall then be updated on a [***] basis. Each [***] update shall include a "rolling" [***] update that includes [***]. Subsequent Contract Year forecasts will be due [***]. Company may update the previous forecast more frequently than on a [***] basis. Forecasting shall not in any way change or affect Company's Minimum Purchase Commitment obligations.

(b) At Company's reasonable request in advance, SAFC will review with Company the inventory and lead times for major components of the Manufacturing Process. Company acknowledges and understands that any forecast will be used by SAFC for planning purposes (including raw material acquisitions and investment in equipment and other resources) in order to make available the production capacity required to Manufacture and supply the forecasted amounts of Vector Product within the time frames agreed to by both Parties.

(c) [***].

3.3 Initial Supply; Purchase Orders, Task Orders, Invoicing and Payment.

(a) To initiate SAFC's Manufacture and supply of Vector Product for the initial Contract Year, SAFC shall issue a Task Order for Company's review and execution and Company shall then, [***] prior to the first scheduled production start date issue a binding written Purchase Order for its purchase of Vector Product. Both the Task Order and the Purchase Order shall be in accordance with the Minimum Purchase Requirement and may include additional Batches as agreed upon pursuant to Section 3.1(c). The Parties acknowledge, recognize and agree that the Purchase Order is an ordering mechanism for proper financial management and invoicing between the Parties, and has not effect on the terms and conditions of this Agreement, which shall prevail in the event of any other terms and conditions contained in a Purchase Order.

(b) For each subsequent Contract Year following the initial Contract Year, a Task Order for the Contract Year shall be executed between the Parties in writing as above and Company shall issue to SAFC a Purchase Order [***] prior to the start of the Contract Year, or such shorter time period as may be agreed upon by the Parties in writing, for its purchase of Vector Product for such Contract Year. The minimum number of days between the date of a Purchase Order and the Manufacture start date of Vector Product under this Section 3.3(b) and Section 3.3(a) above shall be referred to hereinafter as the "**Minimum Lead Time**".

(c) Within [***] of receipt of a Purchase Order, SAFC shall notify Company in writing of its acceptance of the Purchase Order. If SAFC fails to respond within such [***] period, the Purchase Order shall be deemed accepted, but only to the extent that any amount ordered is not in excess of the Minimum Purchase Commitment and that the requested delivery date satisfies the Minimum Lead Time. SAFC, in its sole discretion, may refuse and reject a Purchase Order if the Purchase Order does not accurately reflect the agreed upon Task Order.

(d) If a Purchase Order exceeds the Minimum Purchase Commitment, or does not meet the Minimum Lead Time, SAFC, in its sole and absolute discretion, may (i) accept such Purchase Order, and/or (ii) adjust the price and other related terms taking into consideration the amount of the order that exceeds the Minimum Purchase Commitment and such shorter lead-time. In the event Company wishes not to proceed after such adjustments by SAFC, the Purchase Order shall be deemed to be rejected.

(e) Invoicing and Payment.

(i) [***].

(ii) [***].

(iii) [***].

3.4 Release of Vector Product.

(a) SAFC shall notify Company when (i) the Manufacture of each Batch of Vector Product is complete, including (ii) all Manufacturing records have been reviewed, (iii) all testing is completed, reviewed, and Vector Product meets Specifications, (iv) all Deviations have been adequately reviewed and approved, and (iv) Vector Product has been released by SAFC, as applicable and in accordance with the Quality Agreement.

(b) [***].

3.5 Delivery, Title and Risk of Loss. All Vector Product supplied by SAFC hereunder shall be supplied FCA SAFC's shipping point within the meaning of [***]. [***]. SAFC may only make delivery in installments with the prior approval of Company, and if approved, all such installments to be separately invoiced and paid for when due per invoice, without regard to subsequent deliveries. Delay in delivery of any approved installment shall not relieve Company of its obligations to accept any and all remaining deliveries.

3.6 Packaging. SAFC will preserve, package, handle, and pack all Vector Product so as to protect Vector Product from loss or damage, in conformance with the Specifications and the Quality Agreement.

3.7 Storage. SAFC shall hold all Vector Product under the storage conditions established pursuant to the Quality Agreement and in accordance with cGMP. SAFC, at its own cost, shall store Vector Product for a period not to exceed [***] after Vector Product has been released in accordance with Section 3.4 above. Any Vector Product held by SAFC beyond the time periods specified above shall be subject to storage charges at SAFC's current list prices or as mutually agreed to by the Parties in writing.

3.8 Delay and Third Party Supplier.

(a) If SAFC is or will be unable for any reason (including an event of Force Majeure under Section 12.18 hereof) to [***].

(b) [***]

(c) [***]

(i) [***]

(ii) [***]

(iii) [***]

(d) [***].

(e) For the sake of clarity, the remedies provided in this Section 3.8 and the timelines for the completion of any investigation under Section 3.8(b) do not affect (i) any other obligations of SAFC contained herein; (ii) Company's right to terminate pursuant to Section 10.2(a)(i); (iii) or any other remedies available to Company as provided herein.

4. General Manufacturing Requirements

4.1 Specifications. In the event of a conflict between the provisions of this Agreement and the provisions of the Quality Agreement, the provisions of the Quality Agreement shall prevail only for all quality related requirements, responsibilities and obligations, otherwise, this Agreement shall prevail. Neither Party shall make changes to the Production Records or the Specifications without the prior written approval of the other party which approval will not be unreasonably withheld. SAFC shall only make changes in the Standard Operating Procedures (SOPs), production equipment, production procedures, or testing methods existing as of the date of this Agreement which materially affect the Services in accordance with the provisions contained in the Quality Agreement. SAFC shall maintain all Production Records and other records as are necessary and appropriate to demonstrate compliance with the Regulations. Company shall be entitled to request SAFC to change the Specifications and the SOPs. SAFC shall use commercially reasonable efforts to accommodate such change; provided that Company will reimburse SAFC the reasonable and necessary costs SAFC incurs in making any such change; provided further that the parties shall engage in good faith negotiations to adjust the costs to reflect the increase or decrease of ongoing costs hereunder resulting from any such change; provided further that if the parties cannot reach agreement to adjust the costs pursuant to this Section 4.1 despite such good faith negotiations, then SAFC shall not be required to change the Specifications or SOPs as requested by Company.

4.2 Testing. If provided for in the applicable Task Order with respect to a Batch, SAFC shall test such Batch to ensure compliance with the Specifications.

4.3 Acceptance. Subject to Section 4.4 below, Company shall have a period of [***] from the date of its (or its designee's) receipt the Batch Record (which includes the Certificate of [***]) to reject in writing the Vector Product for nonconformity of such Batch with the Specifications. If no written notification is received by SAFC within the [***] period, such Batch is deemed accepted. If Company rejects such shipment in writing within the [***] time period, it shall promptly so notify SAFC and provide sufficient detail of the nonconformity, and the provisions of Section 5.2 below shall apply.

4.4 Latent Defects. If after accepting a shipment of Vector Product, Company subsequently discovers latent material defects [***].

4.5 Deviation Report. If during the Manufacture, including but not limited to the processing, storage, distribution, testing, transport, disposal or other handling, of Vector Product by SAFC an unexpected result arises that [***].

4.6 SAFC's costs shall not include Company's materials, which include but are not limited to cells, plasmids, equipment, raw materials, consumables or other materials.

5. Rejection, Defects and Non-Conforming Goods

5.1 Disagreement Concerning Fulfilment of Specifications. In the event of any disagreement between the Parties as to whether Vector Product conforms to the Quality Agreement, the applicable Specifications, or cGMP, the quality assurance representatives of the Parties will attempt in good faith to resolve any such disagreement and the Parties will follow their respective SOPs. If the foregoing discussions do not resolve the disagreement within [***] of Company's notice pursuant to Section 4.3 or 4.4, a representative sample of such Vector Product and/or relevant documentation will be submitted to an independent testing laboratory (in the case of an alleged failure to meet Specifications) and/or independent cGMP quality or regulatory consultant (in the case of an alleged failure to comply with cGMP), as appropriate, that are mutually agreed upon by the Parties for tests and final determination as to whether such Vector Product conforms with Specifications and/or cGMP quality standards. The laboratory must meet SAFC supplier qualification standards for cGMP test laboratory. The laboratory and consultant, as applicable, must be of recognized standing in the industry, and consent to the appointment of such laboratory and consultant will not be unreasonably withheld or delayed by either Party. Such laboratory will use the test methods contained in the applicable Specifications. The determination of conformance by such laboratory and/or cGMP consultant, as applicable, with respect to all or part of such Vector Product will be final and binding on the Parties, absent manifest error. The fees and expenses of the laboratory and/or consultant, as applicable, incurred in making such determination will be paid by the Party against whom the determination is made.

5.2 Remedies for Non-Conforming Product.

(a) If any Vector Product Manufactured by SAFC fails to conform to Specifications or cGMP (unless the non-conformity is attributable to Company's negligence or misconduct), SAFC shall [***]. Non-conforming Vector Product shall be disposed of in accordance with the Quality Agreement and at SAFC's expense (unless the non-conformity is attributable to Company's negligence or misconduct). If Company is directed to destroy non-conforming Vector Product, then Company shall provide SAFC a certificate certifying such destruction.

(b) Except as provided for pursuant to any Party's indemnification obligations for third party claims, the remedy described in this Section 5.2 shall be Company's sole remedy and SAFC's only liability for non-conforming Vector Product.

5.3 Deviations and OOS. SAFC and Company shall cooperate in the investigation and response to any Vector Product complaints concerning Deviations and OOS, all in accordance with the Quality Agreement.

6. Pricing; Terms of Payment and SAFC Performance Bonus

6.1 Currency. Except as otherwise expressly indicated, all references to "$" or to "dollars" in this Agreement shall be read as referring to the legal tender of the United States of America.

6.2 Pricing. The pricing for Vector Product Manufactured under this Agreement is set forth in the Price and Payment Schedule as more particularly described in Exhibit 4. [***]. All prices are quoted in United States Dollars.

6.3 Invoices and Payments. SAFC shall invoice Company per Section 3.3(e) and the Price and Payment Schedule in Exhibit 4. All payments made hereunder are due within [***] from the receipt of the SAFC invoice. Payments shall be made to SAFC in accordance with the instructions on the invoice. All payments hereunder shall be made in United States Dollars. In the event Company disputes an invoice or portion thereof, Company shall be required to do so in writing to SAFC within [***] from the receipt of such disputed invoice.

6.4 Overdue Payments. Company shall pay interest on all past-due amounts at a rate of interest equal to the lesser of [***] or the maximum rate permitted by applicable law.

6.5 Annual Price Adjustment. To reflect changes in the cost of labor and raw materials, SAFC may adjust the Batch production price each Contract Year of the Term following the initial Contract Year in accordance with the following: (a) SAFC shall provide Company with written notice of any [***]; (b) [***].

6.6 Taxes.

(a) If Company must withhold from any payment to SAFC under this Agreement any taxes required to be withheld by Company under the applicable laws of any country, state, territory or jurisdiction, such amount shall be paid to the appropriate taxing authorities. Upon request, Company shall provide SAFC with sufficient documentation of such withholding as is reasonably available to allow SAFC to verify such withholding and to document such tax withholdings for purposes of claiming tax credits and similar benefits.

(b) Any use tax, sales tax, excise tax, duty, custom, inspection or testing, or any other tax, fee or charge of any nature whatsoever imposed by any governmental authority, on or measured by the transaction between Company and SAFC, but excluding any tax payable on income, revenue, profits or capital of SAFC, shall be paid by Company in addition to any other amounts due hereunder. If SAFC recovers all or any portion of any tax, fee or charge paid by Company, SAFC shall credit Company with the amount recovered.

6.7 SAFC Performance Bonus. Company shall pay SAFC a performance bonus as more particularly described in Exhibit 4 (Section 3) ("**Performance Bonus**"). Such Performance Bonus shall be invoiced separately by SAFC to Company [***] of the end of the applicable Contract Year.

7. Recall, Warranties, Indemnification and Insurance

7.1 Recall.

(a) Company shall be responsible for making the determination and for conducting any recall of Drug Product, and SAFC shall co-operate with and give all reasonable and necessary assistance to Company in conducting any such recall to the extent it relates to Vector Product. Notwithstanding anything herein to the contrary, SAFC shall only bear the cost and expense of a recall directly resulting from [***]. In the event of such recall or similar action, each Party shall use commercially reasonable efforts to mitigate the costs associated therewith.

(b) In the case of a dispute as to the existence or level of non-conforming Vector Product in connection with a recall under Section 7.1(a) above, the matter shall be resolved in accordance with the procedures set forth in Section 5.1.

7.2 SAFC Representations and Warranties. SAFC hereby represents and warrants as follows:

(a) The execution, delivery and performance of this Agreement does not conflict with, violate or breach any agreement to which SAFC is a party or SAFC's constituent documents, and SAFC is not prohibited or limited by any law or agreement (to which it is a party) from entering into this Agreement and the performance of this Agreement will not create any conflict of interest with any other business or activity engaged in by SAFC;

(b) Vector Product shall be Manufactured and shipped in compliance with cGMP, the Master Batch Record, the Specifications, the Quality Agreement and all other applicable laws, rules and regulations;

(c) SAFC and its Affiliates, approved subcontractors and any person used by SAFC and its Affiliates and subcontractors to perform services under this Agreement (i) have not been debarred and are not the subject of a conviction described in Section 306 of the United States Food, Drug and Cosmetic Act, 21 U.S.C. § 335a; (ii) are not subject to any similar sanction by any government regulatory authority; and (iii) SAFC shall notify Company immediately in writing if SAFC, its Affiliates or any subcontractor or any person used to perform services hereunder, as applicable, is subject to the foregoing, or of any action, suit, claim, investigation or proceeding;

(d) All Vector Product delivered by SAFC hereunder will conform to the Quality Agreement and the Specifications; and

(e) SAFC will have obtained and maintained in effect all such approvals and permits as may be required under applicable laws, rules, regulations and requirements to operate the Manufacturing Facility for the purposes of Manufacturing Vector Product under the Quality Agreement and under this Agreement. SAFC shall make copies of such registrations and all related documents available for viewing by Company and its designees for inspection, upon prior reasonable request from Company.

7.3 Company Representations and Warranties. Company represents and warrants that the execution, delivery and performance of this Agreement does not conflict with, violate or breach any agreement to which Company is a party or Company's constituent documents; Company is not prohibited or limited by any law or agreement to which it is a party from entering into this Agreement; and the performance of this Agreement will not create any conflict with any other business or activity engaged in by Company.

7.4 Disclaimer. EXCEPT AS EXPRESSLY SET FORTH IN THIS AGREEMENT, THE PARTIES MAKE NO REPRESENTATIONS OR WARRANTIES OF ANY KIND WHATSOEVER, EITHER EXPRESS OR IMPLIED, WRITTEN OR ORAL, INCLUDING WITHOUT LIMITATION ANY IMPLIED WARRANTY OF MERCHANTABILITY, WARRANTY OF FITNESS FOR A PARTICULAR PURPOSE, OR WARRANTY OF NON-INFRINGEMENT, WHETHER ARISING BY LAW, COURSE OF DEALING, COURSE OF PERFORMANCE, USUAGE OF TRADE OR OTHERWISE, ALL OF WHICH ARE EXPRESSLY DISCLAIMED.

7.5 Company Indemnification. Subject to Section 12.5, Company shall indemnify, defend and hold harmless SAFC, its Affiliates and its or their directors, officers and employees from all actions, losses, demands, costs and liabilities arising from any third party claim (including reasonable attorneys' fees) to which SAFC is or may become subject insofar as they arise out of or are alleged or claimed to arise out of:

(a) [***];

(b) [***];

(c) [***];

(d) [***];

(e) [***];

(f) [***]; or

(g) [***];

(h) in each case except that Company shall have no obligation to indemnify, defend or hold harmless SAFC, its Affiliates and its or their directors, officers and employees for any negligent acts or omissions or willful misconduct by SAFC or its Affiliates and its or their directors, officers, employees, agents or permitted subcontractors associated with its obligations under this Agreement, or for any losses or claims whatsoever to the extent that SAFC has an obligation to indemnify Company with respect to such losses and claims pursuant to Section 7.6 below.

7.6 SAFC Indemnification. Subject to Section 12.5, SAFC shall indemnify, defend and hold harmless Company, its Affiliates and its or their directors, officers and employees from all actions, losses, demands, costs and liabilities arising from any third party claim (including reasonable attorney's fees) to which Company is or may become subject insofar as they arise out of or are alleged or claimed to arise out of:

(a) [***];

(b) [***];

(c) in each case except that SAFC shall have no obligation to indemnify, defend, or hold harmless Company, its Affiliates and its or their directors, officers and employees for any negligent acts or omissions or willful misconduct by Company or its Affiliates and its or their directors, officers, employees, agents or permitted subcontractors associated with its obligations under this Agreement, or for any losses or claims whatsoever to the extent that Company has an obligation to indemnify SAFC with respect to such losses and claims pursuant to Section 7.5 above.

7.7 Indemnification Procedure. Either Party intending to seek indemnification from the other Party under Sections 7.5 or 7.6 above, as the case may be, shall give the other Party prompt notice of any such claim or lawsuit (including a copy thereof) served upon it and shall fully cooperate with the other Party and its legal representatives in the investigation of any matter which is the subject of indemnification. Such Party seeking indemnification shall not unreasonably withhold its approval of the settlement of any claim, liability or action covered by the above indemnification provisions. Notwithstanding the foregoing, the failure to give timely notice to the indemnifying Party shall not release the indemnifying Party from any liability to the Party seeking indemnification to the extent the indemnifying Party is not prejudiced thereby.

7.8 Company Insurance. Without limiting its liability under this Agreement (except as may be otherwise expressly provided in this Agreement), during the Term and for five (5) years after the expiration or termination of this Agreement, Company shall obtain and maintain commercial general liability insurance of [***]. With respect to all insurance coverage required under this Section, (i) Company shall, promptly upon SAFC's request, furnish SAFC with certificates of insurance evidencing such insurance and (ii) all policies shall include provisions for at least [***] prior written notice of cancellation.

7.9 SAFC Insurance. Without limiting its liability under this Agreement (except as may be otherwise expressly provided in this Agreement), during the Term and for five (5) years after the expiration or termination of this Agreement, SAFC shall obtain and maintain the following minimum insurance coverages with financial sound and nationally reputable insurers: [***]. Company shall be named as an additional insured (except on policies for workers compensation and professional liability/ errors and omissions) and SAFC will provide Company with a certificate of insurance evidencing such coverages upon Company's written request. SAFC will provide Company with [***] advance written notice of any material change or cancellation in coverage or limits.

8. Regulatory Matters; Compliance with Laws

8.1 Regulation of Manufacturing Process. If Company, as the Sponsor under the FDA regulations who holds the investigational new drug application or biologics license application is required by the FDA (or the corresponding foreign equivalent required by the EMA or other Regulatory Agency), or any other Regulatory Agency to validate or re-validate Manufacturing Processes that will impact the Manufacturing of Vector Product, Company shall notify SAFC and consult with SAFC regarding the required activities. SAFC shall only be responsible for the costs of any such validation or re-validation if the validation or re-validation is required due to (i) the non-compliance of the Manufacturing Facility, or (ii) any acts, omissions or deficiencies with respect to the personnel, training or other items within SAFC's reasonable control; otherwise any and all such costs or expenses shall be the sole responsibility and obligation of Company.

8.2 Regulatory Testing Requirements. Should, during the course of conducting the Services, regulatory testing requirements covering the Vector Product change such that additional material expense would be incurred by SAFC to satisfy the terms of this Agreement, those expenses will be the responsibility and obligation of Company.

8.3 Correspondence. SAFC will notify Company (pursuant to the Quality Agreement) promptly upon receipt of any correspondence from a Regulatory Agency, which relates to the Vector Product. In addition, SAFC shall provide to the Regulatory Agencies all documents and information requested by such authority, and shall submit to all inquiries, audits and inspections by the Regulatory Agencies.

8.4 Compliance with Laws; Authorizations. In performing this Agreement, each Party shall (i) comply with all applicable laws and regulations and (ii) obtain all releases, licenses, permits or other authorization required by any governmental body or authority.

8.5 Regulatory Matters

(a) Records. SAFC shall maintain all records required by the Quality Agreement, or as otherwise agreed to in writing by SAFC and Company. SAFC agrees that, in response to any complaint, or in the defense by Company of any litigation, hearing, regulatory proceeding or investigation relating to Vector Product, SAFC shall use reasonable efforts to make available to Company during normal business hours and upon reasonable prior written notice, such SAFC employees and records reasonably necessary to permit the effective response to, defense of, or investigation of such matters, subject to appropriate confidentiality protections. If SAFC incurs costs or expenses with respect to the foregoing attributable to Company's negligence or willful misconduct, Company shall reimburse SAFC for reasonable costs and expenses incurred by SAFC.

(b) Complaints. Company shall have responsibility for reporting any complaints relating to Vector Product to Regulatory Agencies, including, but not limited to, complaints relating to the Manufacture of Vector Product in accordance with the Quality Agreement, or as otherwise agreed in writing by SAFC and Company. If SAFC incurs costs or expenses with respect to the foregoing attributable to Company's negligence or willful misconduct, Company shall reimburse SAFC for reasonable costs and expenses incurred by SAFC.

(c) Regulatory Communications and Correspondence. Any and all communications from and to Regulatory Authorities related to Vector Product or to the Manufacture of Vector Product at the Manufacturing Facility shall be handled in accordance with the Quality Agreement, or as otherwise agreed in writing by SAFC and Company.

(d) Regulatory Filings and Maintenance. SAFC shall prepare and maintain all Regulatory Filings and Manufacturing files, certificates, authorizations, data and other records that directly or indirectly pertain to the Manufacture of ABI, as further set forth in the Quality Agreement or as otherwise agreed in writing by SAFC and Company.

(e) Cooperation in Obtaining Government Approvals. As set forth in the Quality Agreement, or as otherwise agreed to in writing by SAFC and Company, at Company's request, SAFC shall provide Company with such existing documents and information (or copies thereof) held by SAFC to assist Company in securing and maintaining Regulatory Agency approvals for Vector Product. In addition, SAFC shall provide Company with such information as is reasonably requested in writing by Company relating to the Manufacturing Process, the Master Batch Record, SAFC services performed under this Agreement or other ABI-related documentation.

(f) Ownership of Regulatory Filings. Company shall be the sole owner of all Regulatory Filings and all governmental approvals obtained by Company from any Regulatory Agency with respect to Vector Product.

(g) Company Access to Manufacturing Data and Documentation. Company shall have full access to and the right to use and reference any, correspondence, facility and engineering records and diagrams, validation documentation, lot files, reports, analyses, regulatory requirements and any other data and documentation generated in connection with the Manufacturing activities conducted by SAFC hereunder, and SAFC shall provide Company with copies of the foregoing upon request.

9. Confidentiality; Intellectual Property License

9.1 Confidentiality Obligations of SAFC. In the course of the performance of this Agreement, Company may, from time to time, disclose Confidential Information of Company to SAFC or its Affiliates. Confidential Information of Company shall specifically include but not be limited to the Plasmids, Cell Banks, any documentation relating to the Manufacturing Process provided by Company to SAFC, all elements of the Manufacturing Process provided by Company to SAFC or acquired by Company from SAFC, Vector Product specific unit operations of the Manufacturing Process, the Vector Product, clinical data and information, business plans and regulatory and product strategies and information. Except as expressly permitted otherwise by the terms of this Agreement, SAFC shall: (i) maintain in confidence and not disclose the Confidential Information of Company to any third party, except on a need-to-know basis to SAFC's (or its Affiliates') employees and agents to the extent such disclosure is reasonably necessary in connection with SAFC's (or its Affiliates') activities as expressly authorized by this Agreement and upon obligations of confidentiality similar to those set forth herein; and (ii) not use or grant the use of the Confidential Information of Company for any purpose other than the performance of SAFC's obligations hereunder.

9.2 Confidentiality Obligations of Company. In the course of the performance of this Agreement, SAFC may, from time to time, disclose Confidential Information of SAFC to Company or its Affiliates. Except as expressly permitted otherwise by the terms of this Agreement, Company shall: (i) maintain in confidence and not disclose the Confidential Information of SAFC to any third party, except on a need-to-know basis to Company's (or its Affiliates') employees and agents to the extent such disclosure is reasonably necessary in connection with Company's (or its Affiliates') activities as expressly authorized by this Agreement and upon obligations of confidentiality similar to those set forth herein; and (ii) not use or grant the use of the Confidential Information of SAFC for any purpose other than the performance of Company's obligations hereunder.

9.3 Exceptions. The provisions of Sections 9.1 and 9.2 above shall not apply to any Confidential Information of the disclosing Party that can be shown by competent evidence by the receiving Party:

(a) To have been known to or in the possession of the receiving Party without any separate obligation of confidentiality before the date of its actual receipt from the disclosing Party;

(b) To be or to have become readily available to the public other than through any act or omission of any Party in breach of any confidentiality obligations owed to the disclosing Party;

(c) To have been disclosed to the receiving Party, other than under an obligation of confidentiality, by a third party which does not have an obligation to the disclosing Party not to disclose such information to others; or

(d) To have been subsequently independently developed by the receiving Party without use of or reference or access to the disclosing Party's Confidential Information.

9.4 License. During the Term, Company hereby grants to SAFC a royalty-free, non-exclusive license under any know-how, trade secrets, copyrights, designs, databases, discoveries, improvements and inventions (whether patentable or not) related to Vector Product or the Manufacture of Vector Product that are owned or controlled by Company and that are reasonably required for SAFC's performance of its obligations under this Agreement, but only for such purposes and only to the extent reasonably required for SAFC to perform its obligations under this Agreement.

9.5 Proprietary Rights.

(a) Except as expressly set forth in this Agreement each Party owns, and shall continue to own its existing intellectual property, without conferring any interests therein on the other Party. Nothing contained in this Agreement nor any disclosure or provision to SAFC of any Company Confidential Information or other Company information or items shall be deemed to transfer or grant to SAFC or any other person or entity any right to use or exploitation thereof nor to any right, title, interest, or license in, to or under any patent, patent application or other intellectual property, right or asset of Company (including without limitation, any Company Materials, cell banks, specimens, documentation, Production Records, Specifications, raw data, work product, improvements, discoveries, know-how, inventions and other insights), whether patentable or not.

(b) SAFC agrees that all data, information, documents, concepts, ideas, improvements and other insights, exclusive of Process Inventions (defined below), arising from SAFC's performance of its obligations under this Agreement (collectively "**Inventions**"), shall promptly be disclosed to Company in writing. SAFC agrees that all Inventions are the exclusive property of Company. SAFC hereby assigns to Company all right, title and interest, including copyrights and other intellectual property rights, in and to all Inventions which may be developed as a result of SAFC's performance of the Manufacturing, or by SAFC in the course of performing its obligations under this Agreement. SAFC will, at no cost to Company, execute (and will ensure that its employees will execute) any and all documents and, at Company's cost, do any and all things reasonably requested by Company to vest and perfect Company's interest in the Inventions.

(c) In performing the Manufacturing and in applying SAFC Technology to the Manufacture of the Vector Product, SAFC may develop ideas, know-how, inventions, techniques, improvements and other technology, whether or not patentable or copyrightable, and associated intellectual property that are of general applicability, or are applicable to the conduct of its business ("Process Inventions"). For the sake of clarity, ideas, know-how, inventions, techniques, improvements and other technology arising from the application of Company Confidential Information technology, or that relate exclusively to Vector Product or Manufacturing Process are Inventions and not Process Inventions.

(d) SAFC shall ensure that all of SAFC's employees, agents and authorized contractors are employed or engaged on terms consistent with this Section.

9.6 Company Materials. As between the Parties, Company shall own and retain all rights in and title to the biological materials described [***].

10. Term and Termination.

10.1 Term. The initial term this Agreement shall commence as of the Effective Date and shall continue in full force and effect [***] ("Initial Term"), unless earlier terminated as provided in Section 10.2. The Initial Term and any duly exercised extension to the Initial Term, may be referred to herein as the "Term".

10.2 Termination. Notwithstanding the provisions of Section 10.1 above,

(a) Either Party may terminate this Agreement as follows:

(i) Termination for Material Breach. Either Party may terminate this Agreement by written notice at a date set in the notice (allowing at least [***] for cure) in the event of a material breach of this Agreement by the other Party; provided that the breaching Party fails to cure such breach within [***] from the date of such notice, or if the nature of the breach is such as to reasonably require more than [***] to cure, the Party (1) fails to use diligent efforts to cure such material breach, or (2) fails to cure such material breach within an additional [***] period.

(ii) Insolvency. If either Party shall become insolvent or shall make or seek to make an arrangement with, or an assignment for the benefit of creditors, or if proceedings in voluntary or involuntary bankruptcy shall be instituted by, on behalf of or against such Party, that is not dismissed within [***], or if a receiver or trustee of such Party's assets shall be appointed, or bankruptcy proceedings begin, the other Party may terminate this Agreement, as may be permitted by the applicable laws, with immediate effect.

(iii) Force Majeure; No-Fault Termination. Either Party shall have the right to terminate this Agreement, upon providing written notice thereof to the other Party, such termination to be effective [***] from the effective date of such notice if, as a result of a Force Majeure Event, a Party is unable fully to perform its obligations under this Agreement for any consecutive period of [***], unless the Parties mutually agree in writing upon a shorter time period.

(b) Clinical Trial Failure. Prior to Company's first Drug Product to receive Regulatory Approval for Sale, Company may terminate this Agreement upon [***] written notice of a clinical trial for a Drug Product is terminated or if Regulatory Approval for Sale is not granted following Company's submission of an application for Regulatory Approval for Sale.

10.3 Rights and Obligations Upon Termination.

(a) Return of Inventory and Confidential Information. In the event of any termination or expiration, SAFC shall return to Company: (i) all Company property (at Company's expense, unless Company terminates this Agreement pursuant to Section 10.2(a)(i) or (iii), in which case such property shall be returned at SAFC's expense), except to the extent required to be retained by law or to comply with such Party's continuing obligations hereunder; and (ii) all Confidential Information of Company and shall make no further use of such Confidential Information without the prior written consent of Company. In the event of any termination or expiration of the Term, Company shall return to SAFC all Confidential Information of SAFC and shall make no further use of such Confidential Information without the prior written consent of SAFC; provided, however, that Company may retain a reasonable number of copies to exercise its rights under Section 9, but which shall remain subject to the obligations of non-use and confidentiality set forth in this Agreement.

(b) Payments. Termination of this Agreement shall not release either Party from the obligation to make payment of all amounts owing to the Party at the time of such termination. Upon termination of this Agreement by SAFC pursuant to Section 10.2, Company shall take delivery and pay for all Vector Product that is subject to an open Purchase Order, pay all monies due and owing pursuant to this Agreement and reimburse SAFC for its costs for all material, work in process, finished Vector Product and all other outstanding inventory (meaning all raw materials that are specifically required and purchased by SAFC for the Manufacture of the Vector Product) to the extent that such items were reasonably acquired by SAFC to meet its obligations hereunder in a timely manner, and make any such other payments to SAFC as required under this Agreement.

(c) Raw Materials and Consumables. Upon expiration or termination of this Agreement by Company, Company may elect (but shall have no obligation) to purchase from SAFC, at SAFC's actual cost, all remaining usable Raw Materials and Consumables paid for by SAFC for the Manufacture of Vector Product under this Agreement as of the date of expiration or termination, together with all appropriate documentation related to such quantities of Raw Materials and Consumables.

(d) Incomplete Task Orders. Upon termination or expiration of this Agreement, SAFC shall make all necessary arrangements to have any open and incomplete Task Orders completed or fulfilled by another contract manufacturer. SAFC's obligations pursuant to this Section 10.3(d) shall include a technology transfer as may be necessary to a new contract manufacturer selected by Company or Company itself, in accordance with the provisions of Section 3.8(iii); provided, however, unless this Agreement is terminated by Company pursuant to Section 10.2(a), Company shall bear any and all cost of such technology transfer.

11. Governing Law; Dispute Resolution

11.1 Governing Law. This Agreement shall be governed by, and interpreted and construed in accordance with, the laws of the State of Massachusetts, USA, without regard to its conflict of law provisions. The U.N. Convention on International Sales of Goods shall not apply to this Agreement.

11.2 Dispute Resolution; Venue. In the event that any dispute arises between the Parties out of or in connection with this Agreement, the Parties agree to use good faith efforts in an attempt to resolve such dispute, and if such dispute is not resolved within [***], each Party shall refer such dispute to each such Party's senior executive officer for further attempts to resolve such dispute for a period of [***]. Any legal action or proceeding concerning the validity, interpretation and enforcement of this Agreement, matters arising out of or related to this Agreement or its making, performance or breach, or related matters will be brought exclusively in the courts of the United States of America for the District of Massachusetts, sitting in Suffolk County, Massachusetts. All parties consent to the exclusive jurisdiction of those courts and waive any objection to the proprietary or convenience of such venue.

12. Miscellaneous

12.1 Termination of Prior Agreement, Transfer of Task Orders. Effective upon the Effective Date, the Parties hereby terminate the Prior Agreement in its entirety. Notwithstanding the foregoing, all outstanding task orders under the Prior Agreement and as more particularly listed and described in Exhibit 7, shall continue under this Agreement following the Effective Date (the "Transferred Task Orders"), and are hereby incorporated by reference as Task Orders hereunder as of the Effective Date; provided, however, the amounts payable for performance of Services provided pursuant to such Transferred Task Orders shall be in accordance with the amounts set forth on such Transferred Task Orders, and any Batches produced pursuant to such Transferred Task Orders shall not be considered or included for consideration of the Company's Minimum Purchase Commitment or SAFC's Performance Bonus.

12.2 Financial Records. SAFC will keep accurate financial records of all Services performed under this Agreement including invoice calculations. Company, at its own expense, have access to such financial records upon [***] prior written notice to SAFC, and upon mutually agreeable times and dates during SAFC's normal business hours for the sole purpose of verifying the correctness of such calculations. All information and materials made available to or otherwise obtained or prepared by or for Company in connection with such an audit shall be SAFC's Confidential Information. Company may not exercise this right more than once for any Contract Year. Furthermore, in the event that Company is required to capitalize the Manufacturing Facility in accordance with U.S. generally accepted accounting principles and the applicable accounting standards (and any applicable updates or successor accounting guidance promulgated by the Financial Accounting Standards Board), and solely for such purpose, SAFC shall cooperate with Company and shall provide to Company such information reasonably necessary to permit Company to account for this Agreement as a capital lease in Company's financial statements. Such information provided to Company shall be the Confidential Information of SAFC.

12.3 Publicity. Each party shall obtain the prior written approval of the other party, such approval not to be unreasonably withheld, to the content of any written publicity, news release or other public statement or announcement which includes the name of the other party and relates to this Agreement, prior to originating or releasing it. Each party shall advise the other as to whether or not any publicity, news release or other public statement or announcement is approved within [***] after the receipt of the text of the publicity, news release or other public statement or announcement, failing which it shall be deemed to be approved. If a party advises that it will not approve any publicity, news release or other public statement or announcement, the party that is refusing to approve shall provide the other party with reasons for the refusal. If either party is prevented from complying with the foregoing as a result of the requirements of a securities commission or other regulatory body, the parties shall not be considered to be in breach of this Section or of the confidentiality obligations set forth in Section 9, but shall use reasonable efforts to consult with and keep the other party informed, and shall use reasonable efforts to obtain a protective order.

12.4 Use of Names. SAFC shall not use the name of Company or the names of their employees, or representatives or Affiliates in any advertising materials or in any publication without prior written consent of Company. Company shall not use the name of SAFC or the names of their employees, or representatives or Affiliates in any advertising materials or in any publication without prior written consent of SAFC. Notwithstanding the foregoing, Company shall be entitled to identify SAFC as the source of Vector Product in any regulatory submission without SAFC's prior written consent.

12.5 Limitation of Liability and Damages.

(a) NEITHER PARTY SHALL BE LIABLE TO THE OTHER PARTY FOR INDIRECT, INCIDENTAL OR CONSEQUENTIAL DAMAGES (SUCH AS LOST PROFITS), EXCEPT FOR BREACH OF CONFIDENTIALITY OBLIGATIONS OR AS EXPRESSLY PROVIDED IN THIS AGREEMENT, OR ANY SPECIAL OR PUNITIVE DAMAGES ARISING OUT OF THE PERFORMANCE OF THIS AGREEMENT, WHETHER BASED ON CONTRACT, NEGLIGENCE, STRICT LIABILITY, OTHER TORT OR OTHERWISE AND REGARDLESS OF WHETHER ANY PARTY HAS BEEN ADVISED OF THE POSSIBILITY OF SUCH DAMAGES.

(b) THE MAXIMUM AGGREGATE LIABILITY OF SAFC AND ITS AFFILIATES TO COMPANY AND ITS AFFILIATES FOR ANY CAUSE OF ACTION (OR RELATED CAUSES OF ACTION) ARISING OUT OF OR RELATED TO THIS AGREEMENT AND/OR THE MANUFACTURE OR DELIVERY OF THE VECTOR PRODUCT [***] GIVING RISE TO THE LIABILITY.

(c) The foregoing limitations in above shall survive notwithstanding any failure of essential purpose of a limited remedy.

12.6 Assignment; Successors; Subcontractors; Third-Party Beneficiaries.

(a) Neither Party may assign or otherwise transfer any of its rights or obligations under this Agreement without the prior written consent of the other Party, which will not be unreasonably withheld, except that Company may assign, in whole or in part, without such consent any of its rights or obligations under this Agreement (i) to any Affiliate, provided that any such assignment to an Affiliate shall not relieve the assigning Party as the primary obligor hereunder, or (ii) in connection with the merger, consolidation or sale of the stock or substantially all of the assets of the assigning Party's business responsible for the performance of this Agreement.

(b) Subject to the preceding subsection (a), this Agreement will apply to, be binding in all respects upon, and inure to the benefit of the successors and permitted assigns of the Parties.

(c) SAFC shall not subcontract or otherwise delegate the performance of any of its obligations hereunder to a non-affiliated third party without the prior written approval of Company. If Company approves any subcontract, SAFC shall: (a) exercise reasonable diligence in the selection of such subcontractors, (b) fully qualify each subcontractor and (c) remain primarily liable for the performance of its obligations hereunder.

(d) Nothing expressed or referred to in this Agreement will be construed to give any person other than the Parties any legal or equitable right, remedy or claim under or with respect to this Agreement or any provision of this Agreement. This Agreement and all of its provisions and conditions are for the sole and exclusive benefit of the Parties to this Agreement and their successors and assigns.

12.7 Transactions Outside Scope of Agreement. Other than as expressly provided for otherwise in this Agreement, this Agreement shall in no way limit or restrict the ability of either Party or any Affiliate of such Party to offer its products or services to any other person.

12.8 No Transfer of Rights. No transfer, grant or license of rights under any patent or copyright or to any proprietary information or trade secret is made or is to be implied by this Agreement except as may be expressly stated otherwise herein.

12.9 Independent Contractors. The Parties undertake to carry out this Agreement as independent contractors. No franchise, partnership, joint venture or relationship of principal and agent is intended by this Agreement. Neither Party is authorized, in the name of or on behalf of the other Party, to incur any obligation, receive any benefit or right or otherwise bind the other Party. All employees, agents, representatives and contractors of a Party are solely those of such Party and no acts thereof will be binding upon the other Party.

12.10 Waiver. The failure or the delay of any Party hereto to enforce at any time any provision of this Agreement shall not be construed to be a waiver of such provision or of the right of such Party thereafter to enforce such provision. No waiver of any breach of this Agreement shall be held to constitute a waiver of any other or subsequent breach of this Agreement.

12.11 Severability. Should any provision of this Agreement become void or be cancelled, then the other provisions shall remain in full force and effect. If a provision of this Agreement should be void or should be declared void, then the Parties will attempt to replace it by another valid provision or will leave the provision unreplaced by mutual consent. Any provision of this Agreement held invalid or unenforceable only in part or degree will remain in full force and effect to the extent not held invalid or unenforceable.

12.12 Exhibits. All Exhibits attached hereto are hereby incorporated in and made a part of this Agreement as if fully set forth herein.

12.13 Entire Agreement. This Agreement, including all Exhibits, Task Orders, Purchase Orders hereto, contains the final, complete and exclusive agreement of the Parties relative to the subject matter hereof and supersedes all prior and contemporaneous understandings and agreements relating to its subject matter.

12.14 Amendment. This Agreement shall not be deemed or construed to be modified, amended, rescinded, cancelled or waived, in whole or in part, except by written amendment signed by the Parties hereto.

12.15 Notices. All notices, consents, waivers and other communications under this Agreement must be in writing and will be deemed to have been duly given when (i) delivered by hand (with written confirmation of receipt), (ii) sent by facsimile (with written confirmation of transmission), (iii) when received by the addressee if sent by registered or certified mail (return receipt requested) or if sent by an internationally recognized overnight delivery service, in each case to the appropriate addresses and facsimile numbers set forth below (or to such other addresses and facsimile numbers as a Party may designate by notice to the other Party):

If to Company:
bluebird bio, Inc.
60 Binney Street
Cambridge, MA 02142
Attention: Chief Legal Officer
With copy to: Chief Technology and Manufacturing Officer

All invoices to:
invoices@bluebirdbio.com

If to SAFC:
SAFC Carlsbad, Inc.
6211 El Camino Real
Carlsbad, CA 92009
Attention: General Manager

With a copy to:
EMD Millipore Corporation
400 Summit Drive
Burlington, MA 01803
Attention: General Counsel

12.17 Section Headings; Construction. The headings of Sections in this Agreement are provided for convenience only and will not affect its construction or interpretation. Unless otherwise expressly provided, the word "including" does not limit the preceding words or terms.

12.18 Force Majeure. Any events that are beyond the reasonable control of the Parties, such as fire, flood, war, strike, civil unrest, terrorism, natural catastrophes, government acts and regulations, national, international or sectoral financial crises and other cases of force majeure beyond a Party's control (a "Force Majeure Event"), will, except for Company's payment obligations hereunder, for the duration of the event as it affects the affected Party, suspend the obligations of the affected Party under this Agreement. As soon as there is an indication of an event of force majeure, the Party affected by it will advise the other Party within [***] or as soon as practical of the effect of such event on this Agreement and about the measures to be taken to mitigate such effect. The Parties are obligated to use reasonable efforts to mitigate damages and to resume the fulfilment of the contractual obligations as quickly as possible.

12.19 Expenses. Except as otherwise expressly provided in this Agreement, in the Exhibits hereto or in any agreement or other document expressly referenced herein and forming a part hereof, including the Quality Agreement, each Party to this Agreement will bear its respective expenses incurred in connection the performance of its obligations hereunder. In the event of termination of this Agreement, the obligation of each Party to pay its own expenses will be subject to any rights of a Party arising from a breach of this Agreement by the other.

12.20 Counterparts. This Agreement may be executed in one or more counterparts, each of which will be deemed to be an original copy of this Agreement and all of which, when taken together, will be deemed to constitute one and the same agreement.

12.21 Entire Agreement. This Agreement (including the Exhibits and executed Task Orders or Purchase Orders hereto) constitutes the entire agreement of the parties with respect to the subject matter hereof, and it supersedes all prior oral and written agreements, commitments or understandings with respect to the matters provided for herein, including without limitation the Prior Agreement, any Confidentiality Agreement and any other confidentiality agreement, memorandum of understanding, letter of intent or letter of agreement.

12.22 Survival. Neither expiration nor termination of this Agreement shall terminate those obligations and rights of the parties pursuant to this Agreement which by their terms are intended to survive and such provisions shall survive the expiration or termination of this Agreement. Without limiting the generality of the foregoing, the following provisions of this Agreement shall survive any expiration or termination hereof: Sections 2.8(b) and (c), 2.9, 7, 9.1, 9.2, 9.3, 9.5, 9.6, 10.3, 11, 12, and all definitions herein required to interpret the foregoing.

IN WITNESS WHEREOF, the Parties intending to be bound by the terms and conditions hereof have caused this Agreement to be signed effective as of the Effective Date by their duly authorized representatives.

SAFC CARLSBAD, INC.		**bluebird bio, Inc.**	
By:	/s/ Martha Rook	By:	/s/ Jason F. Cole
Name:	Martha Rook	Name:	Jason F. Cole
Title:	Head of Gene Editing and Novel Modalities	Title:	Chief Legal Officer

Index of Exhibits

Exhibit 1 – [***]

Exhibit 2 – [***]

Exhibit 3 – [***]

Exhibit 4 – [***]

Exhibit 5 – [***]

Exhibit 6 – [***]

Exhibit 7 – [***]

Amendment No. 1 to Clinical and Commercial Supply Agreement

This Amendment No. 1 to Clinical and Commercial Supply Agreement (this "**Amendment**") is made on January 7, 2019 ("**Amendment Effective Date**") by and between bluebird bio, Inc., a Delaware corporation ("**Company**"), and SAFC Carlsbad, Inc., a company incorporated under the laws of the State of California ("**SAFC**"). Reference is hereby made to that certain Clinical and Commercial Supply Agreement between Company and SAFC dated as of November 27, 2017, having an effective date of January 1, 2018 (as may be amended from time to time, the "**Agreement**"). Capitalized terms used but not otherwise defined herein shall have the meanings given to such terms in the Agreement.

NOW, THEREFORE, in consideration of the mutual covenants contained herein, and for other good and valuable consideration, the amount and sufficiency of which are hereby acknowledged, the Parties hereby agree as follows:

1. Section 3.3(b) of the Agreement is hereby amended by appending the following paragraphs, as paragraphs 3.3(b)(i) and 3.3(b)(ii), respectively:

   [***]

2. A new Section 12.23, **Data Privacy**, is hereby added to the Agreement as follows:

   Data Privacy. [***]

3. Exhibit F is hereby added to the Agreement as attached hereto.

This Amendment is binding upon and shall inure to the benefit of the Parties and their respective successors and assigns. The Agreement as modified by this Amendment is the entire agreement between the Parties with respect to the subject matter hereof and supersedes all prior and contemporaneous oral and written agreements and discussions. Except as expressly modified by this Amendment, all terms and provisions of the Agreement remain in full force and effect. In the event of a conflict between the terms and provisions of this Amendment and the Agreement, the terms and provisions of this Amendment shall control. This Amendment may be executed in any number of counterparts, each of which shall be deemed an original, but all of which when taken together shall constitute one and the same instrument.

[Remainder of the page is intentionally left blank]

IN WITNESS WHEREOF, the Parties have signed this Amendment as of the Amendment Effective Date.

SAFC CARLSBAD, INC.

By: /s/ Joan Haab 1/4/2019
Name: Joan Haab
Title: Site Head, Carlsbad Viral Vector Manufacturing

BLUEBIRD BIO, INC.

By: /s/ Jason Cole
Name: Jason Cole
Title: Chief Legal Officer

[***] INDICATES MATERIAL THAT HAS BEEN OMITTED BECAUSE IT IS BOTH (I) NOT MATERIAL, AND (II) WOULDLIKELY CAUSE COMPETITIVE HARM TO THE COMPANY IF PUBLICLY DISCLOSED.

EXHIBIT F

[***]

[***] INDICATES MATERIAL THAT HAS BEEN OMITTED BECAUSE IT IS BOTH (I) NOT MATERIAL, AND (II) WOULDLIKELY CAUSE COMPETITIVE HARM TO THE COMPANY IF PUBLICLY DISCLOSED.

[***] INDICATES MATERIAL THAT HAS BEEN OMITTED BECAUSE IT IS BOTH (I) NOT MATERIAL, AND (II) WOULD LIKELY CAUSE COMPETITIVE HARM TO THE COMPANY IF PUBLICLY DISCLOSED.

Exhibit 10.42

Sublease

THIS SUBLEASE (this "**Sublease**"), dated as of April 16, 2019 (the "**Effective Date**"), between AVENTIS INC., a Pennsylvania corporation, having an address at North American Legal Department, U.S. Corporate, 55 Corporate Drive, Mail Stop 55A-525A, Bridgewater, New Jersey 08807-0977 ("**Lessor**") and BLUEBIRD BIO, INC., a Delaware corporation, having an address at 60 Binney Street, Cambridge, Massachusetts 02142, Attn: General Counsel ("**Lessee**").

W I T N E S S E T H:

WHEREAS, by that certain Lease Agreement, dated as of March 25, 2015, as amended by that certain First Amendment to Lease, dated as of October 27, 2015, and as further amended by Agreement Regarding Early Access, Waiver and Related Matters, dated as of June 19, 2017, and as further amended by Second Amendment to Lease, dated as of June 30, 2018, and as further amended by Acknowledgment of Delivery and Rent Commencement Dates dated as of April 1, 2019 (as heretofore amended, the "**Prime Lease**"), by and between ARE-MA REGION NO. 40, LLC, a Delaware limited liability company ("**Prime Landlord**"), as landlord, and Sanofi US Services Inc, as tenant, Prime Landlord leased to Lessor certain premises located in the building located at 50 Binney Street, Cambridge, MA (the "**Building**") as such premises are more particularly described in the Prime Lease;

WHEREAS, Sanofi US Services Inc. assigned the Prime Lease to Lessor pursuant to that certain Assignment and Assumption of Lease, dated as of February 14, 2019, by and between Sanofi US Services Inc., as assignor, and Lessor, as assignee;

WHEREAS, Lessee desires to sublease from Lessor certain premises, consisting of the entire Premises under the Prime Lease, on the first through tenth floors of the Building, together with certain areas of the Garage (as defined in the Prime Lease) and all as identified on **Exhibit A** hereto (the "**Subleased Premises**"), containing approximately 267,278 rentable square feet in total, upon the terms, covenants and conditions hereinafter set forth.

NOW THEREFORE, for good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties hereto agree as follows:

1. Subleased Premises

1.01. Lessor hereby subleases to Lessee, and Lessee hereby subleases and hires from Lessor, the Subleased Premises for the term hereinafter stated on the terms and provisions hereinafter provided or incorporated in this Sublease by reference. Lessee shall have the right to use such common areas which are appurtenant to or service the Subleased Premises to the extent that such right has been granted to Lessor pursuant to the Prime Lease. Lessor represents and warrants to Lessee that (i) a true, correct and complete copy of the Prime Lease (excluding redacted terms not relevant to Lessee) is attached here as **Exhibit B**, (ii) the Prime Lease is in full force and effect, (iii) to Lessor's knowledge, Lessor is not in default under the Prime Lease, and (iv) Lessor has not received any notice from Prime Landlord that Lessor is in default under the Prime Lease.

1.02. Lessee has examined the Subleased Premises and is fully familiar with the physical condition thereof. Except as specifically set forth in this Sublease, Lessor has not made and does not make any representations or warranties as to such physical condition, the rentable area of the Subleased Premises, the use to which the Subleased Premises may be put, or any other matter or thing affecting or relating to the Subleased Premises, and Lessee hereby expressly agrees to accept the Subleased Premises in its "as-is" condition, subject to the terms and conditions of this Sublease. All understandings and agreements heretofore made between the parties hereto are merged in this Sublease which alone fully and completely expresses their agreement, and neither party is relying upon any statement, representation or warranty made by the other not embodied in this Sublease.

1.03. Lessee shall use and occupy the Subleased Premises solely for technical office use (which includes, as permitted uses and not accessory uses, research and development use, lab use and office use), with permitted accessory uses, all as such use may be permitted in the Prime Lease, and for no other purpose whatsoever.

2. Term, Prime Landlord Consent, Non-disturbance

2.01. The term (the "**Term**") of this Sublease shall commence on the later to occur of (i) the date Prime Landlord has consented to the subleasing contemplated hereby in accordance with Section 2.02 and (ii) the date Lessor has delivered the Premises to Lessee in accordance with Section 3.01 hereof (the "**Commencement Date**"), and shall expire at 11:59 pm on December 31, 2030 (the "**Expiration Date**").

2.02. This Sublease shall have no effect until Prime Landlord shall have given its written consent hereto in accordance with the terms of the Prime Lease. If Prime Landlord has not given its written consent to this Sublease for any reason whatsoever within one hundred twenty (120) days after the date of the execution and delivery of this Sublease by Lessor and Lessee and its delivery to Prime Landlord, then either party hereto may elect to cancel this Sublease by giving notice to the other party within sixty (60) days after the expiration of said one hundred twenty (120)-day period (unless such period shall be extended as hereinafter provided or otherwise by mutual agreement between Lessor and Lessee), but prior to the giving of said

consent by Prime Landlord to this Sublease. Lessor and Lessee each agree to use all reasonable efforts to obtain such consent. Lessee acknowledges that it will be required to execute and deliver such consent as a condition precedent to the execution thereof by Prime Landlord and Lessee agrees that it shall promptly execute and deliver to Lessor such consent provided the same does not impose material obligations or liabilities on Subtenant in addition to Subtenant's obligations and liabilities under this Sublease, or materially reduce Subtenant's rights as provided under this Sublease. If either party shall have given notice of termination to the other party in accordance with the provisions of this Section 2.02, then: (i) Lessor shall not be obligated to take any further action to obtain such consent, (ii) Lessor shall refund to Lessee the Security Deposit (as defined herein) and any additional sums paid in relation to this Sublease, all to the extent paid by Lessee and (iii) this Sublease shall thereupon be deemed null and void and of no further force and effect and neither of the parties hereto shall have any rights or claims against the other, except for those provisions which expressly survive the expiration or termination of this Sublease. Whether or not such consent is granted, Lessor shall pay the out of pocket fees and costs charged by Prime Landlord in connection with the request for its consent to this Sublease in accordance with the applicable provisions of the Prime Lease.

2.03. Except as permitted pursuant to Sections 19 (casualty) and 20 (condemnation) of the Prime Lease, Lessor shall not voluntarily cancel, terminate, amend the material terms of or surrender the Prime Lease without the prior written consent of Lessee, which consent may be withheld in Lessee's sole discretion, provided, that, Lessee shall not have any right to consent to any of the foregoing if (a) Prime Landlord accepts this Sublease as a direct lease between Prime Landlord and Lessee or (b) any such cancellation, termination, amendment or surrender would not have an adverse effect upon this Sublease. Notwithstanding anything contained herein, Lessor agrees not to exercise any extension, expansion or contraction options or any further rights contained in the redacted portions of the Prime Lease, without the written consent of Lessee, which may be withheld in its sole discretion. Lessor shall deliver to Lessee copies of all executed amendments to the Prime Lease, which copies may be redacted so as to remove from view any confidential information. Lessor shall not, without Lessee's prior written consent, cause a default under the Prime Lease that would permit the Prime Landlord to cancel or terminate or surrender the premises demised under the Prime Lease unless Prime Landlord has either agreed or will agree to recognize Lessee's rights under this Sublease from and after the date of such surrender or termination of the Prime Lease pursuant to a written agreement reasonably acceptable to Lessee. Lessor shall not take any action under the Prime Lease that would adversely impair the right of Lessee to use and occupy the Subleased Premises for the purposes and as provided under this Sublease. If the term of the Prime Lease is terminated for any reason prior to the Expiration Date, this Sublease shall thereupon terminate ipso facto without any liability of Lessor to Lessee by reason of such early termination unless such termination is due to (i) Lessor's violation of its express covenant set forth in this Section 2.03 or (ii) Lessor's default under the Prime Lease which default was not caused by Lessee. References in this Sublease to the "termination" of this Sublease include the Expiration Date and any earlier termination thereof pursuant to the provisions of this Sublease, the Prime Lease or by law. Except as otherwise expressly provided in this Sublease with respect to those obligations of Lessee which by their nature or under circumstances can only be, or under the provisions of this Sublease may be or are required to be, performed after the termination of this Sublease, the Term

and estate granted hereby shall end at 11:59 PM on the date of termination of this Sublease as if such date were the Expiration Date, and, except as provided herein, neither party shall have any further obligation or liability to the other under this Sublease. Notwithstanding the foregoing, any liability of Lessor or Lessee to make any payment under this Sublease, which shall have accrued prior to the termination of this Sublease, shall survive the termination of this Sublease. Notwithstanding anything in this Sublease to the contrary, Lessee shall not be responsible for (i) any default under the Prime Lease unless attributable to a default under this Sublease by Lessee or anyone claiming by through or under Lessee, (ii) conditions at the Subleased Premises, for which the obligation to maintain and repair resides with Prime Landlord under the Prime Lease and/or which existed as of the Commencement Date, (iii) the payment of any charges, fees and other costs imposed by Prime Landlord on Lessor as a result of Lessor's default under the Prime Lease except if caused by the act or omission of Lessee or anyone claiming by, through or under Lessee, (iv) the removal and/or restoration of any of the Tenant Improvements or any Alterations or Installations existing in the Subleased Premises as of the Commencement Date (except to the extent of any further alterations of the same by Lessee), or (v) making payment of any sums either to Prime Landlord or Lessor in satisfaction of any charges accruing under the Prime Lease (whether denominated as rent, rental, additional rent or otherwise) for any period prior to the Term of this Sublease. In the event that Lessee desires to terminate this Sublease due to a condemnation or casualty, Lessee shall deliver notice of such termination to Lessor within five (5) days after delivery by Lessor of a copy of the notice delivered by Prime Landlord pursuant to the first sentence of Section 18(b) of the Prime Lease. In the event of condemnation or casualty, Lessee shall be entitled to abatement of rent only to the extent that Lessor actually receives such abatement of rent from Prime Landlord under Section 18 of the Prime Lease. Lessor shall have no obligation to provide or attempt to provide to Lessee any substitute space in the event of condemnation or casualty.

3. Condition of Premises

3.01. Lessee acknowledges and agrees that it is subletting the Subleased Premises in its "as is" condition as of the Commencement Date and that, subject to this Section 3.01, Lessor is not required to perform any work in the Subleased Premises or provide any allowance or other concession to Lessee. Lessee acknowledges that Lessor will continue to occupy the Subleased Premises from the date of this Sublease until shortly before the Commencement Date and accordingly, there will be some changes to the condition of the Subleased Premises arising out of ordinary use and wear and tear. Lessor covenants and agrees that, during the period between the date of this Sublease and the Commencement Date, Lessor will maintain and repair the Subleased Premises in a manner consistent with its past practice and in compliance with the terms of the Prime Lease. Lessor and Lessee shall conduct a walk through immediately prior to the date of this Sublease and immediately prior to the Commencement Date. In the event of any material change in the condition of the Subleased Premises (excluding ordinary wear and tear) between the date of this Sublease and the Commencement Date arising from the breach by Lessor of its covenant contained in the immediately preceding sentence, Lessee's sole remedy shall be that Lessor shall either cure such material changes at Lessor's sole expense or permit Lessee cure such material changes at Lessor's expense, in which event Lessor shall reimburse Lessee for such costs within thirty (30) days after delivery by Lessee to Lessor of all applicable

invoices and other reasonable documentation of the costs of cure. All understandings and agreements heretofore made between the parties hereto are merged in this Sublease which alone fully and completely expresses their agreement, and neither party is relying upon any statement, representation or warranty made by the other not embodied in this Sublease. Lessor makes no representation concerning, and shall have no liability in connection with, the quantity, quality or condition of any and all services, equipment and supplies given to Lessee; provided, however, Lessor agrees that Lessee shall be entitled to receive all services, utilities, repairs and restorations to be provided by Prime Landlord under the Prime Lease with respect to the Subleased Premises. Subject to obtaining the approval of Prime Landlord in accordance with Section 2.02 hereof, the parties intend that the Commencement Date shall be July 1, 2021 ("**Intended Commencement Date**") and that Lessor shall deliver the Subleased Premises to Lessee on such Intended Commencement Date in accordance with this Section 3.01, provided, however, that Lessor shall have the right, to be exercised upon not less than nine (9) months' prior written notice to Lessee, to extend the Intended Commencement Date one or more times by up to six (6) months in the aggregate (i.e., to an outside Intended Commencement Date of January 1, 2022). On the Intended Commencement Date (as extended, if applicable and subject to the approval of Prime Landlord in accordance with Section 2.02 hereof), Lessor shall deliver the Subleased Premises to Lessee in vacant and "broom clean" condition. In addition, Lessor shall remove all interior signage displaying the name of Lessor or its affiliates.

3.02 Promptly following the Commencement Date, Lessor and Lessee shall enter into an agreement in form and substance reasonably satisfactory to Lessor and Lessee confirming the Commencement Date, but the failure to enter into such agreement shall not delay the Commencement Date.

3.03 Not later than one hundred twenty (120) days prior to the expiration of the Term of this Sublease, Lessee shall deliver to Lessor for Lessor's approval a detailed plan for Lessee's surrender of the Subleased Premises at the end of the term, including detailed plans relating to the removal of any signage, rooftop equipment and similar long lead items. Lessor shall have the right to require modifications to such plan to the extent Lessor determines in its sole discretion that such modifications are required in order to effect the timely surrender and vacation of the premises leased under the Prime Lease. Lessee shall cause all work required to be performed by Lessee in connection with the surrender of the Demised Premises to be performed not later than thirty (30) days prior to the expiration of the Term of this Sublease. During the one hundred twenty (120) day period prior to the expiration of the Term of this Sublease, Lessor shall have the right to access the Subleased Premises from time to time to perform and inspect work and otherwise to ensure that the premises leased to Lessor under the Prime Lease will be surrendered and vacated in accordance with the terms of the Prime Lease. Notwithstanding the foregoing, in the event that, prior to the expiration of the Term of this Sublease, Prime Landlord and Lessee enter into a direct lease having a term commencing immediately following the Term of this Sublease and Prime Landlord releases Lessor from all surrender, restoration and similar obligations contained in the Prime Lease relating to the physical condition of the Premises and the compliance of the Premises with applicable laws, then in such event this Section 3.03 shall not be applicable, and Lessee shall be relieved of its surrender and restoration obligations as between Lessor and Lessee under this Sublease.

4. Rental

4.01. Lessee shall pay to Lessor rent ("**Base Rent**") at the rate of Twenty-Six Million Seven Hundred Fourteen Thousand Four Hundred Thirty-Six and 10/100 Dollars ($26,714,436.10) per annum (i.e., at a rate of Ninety-Nine and 95/100 Dollars ($99.95) per rentable square foot), in equal monthly installments in accordance with the Base Rent schedule attached as Schedule 1 hereto, on the first day of each calendar month, commencing on the Commencement Date, subject to Section 4.03 below.

4.02 Base Rent, Additional Rent (as hereinafter defined) and all other costs, charges and sums payable by Lessee hereunder are sometimes herein collectively defined as "**Rental**". If the Rent Commencement Date (as hereinafter defined) falls on any day other than the first of a month, then the Base Rent for such month shall be prorated on a per diem basis, and Lessee agrees to pay the amount thereof for such partial month on the Rent Commencement Date along with any other amounts due Lessor under this Sublease. The obligation of Lessee to pay Rental and other sums to Lessor and the obligations of Lessor hereunder are independent obligations. Except as expressly provided in Section 4.03 or Section 4.06, Lessee shall have no right at any time to abate, withhold, reduce or set off any Rental due hereunder.

4.03. Subject to the provisions of this Section 4, Lessee shall (i) not be required to pay the Base Rent for the period commencing on the Commencement Date and ending on the Rent Commencement Date, and (ii) shall not be required to pay the Operating Expense Payment for the period commencing on the Commencement Date and ending on the day that is forty-five (45) days following the Commencement Date (the "**Operating Expense Payment Commencement Date**"). Subject to the provisions of this Sublease, the term "**Rent Commencement Date**" shall mean the date which is the earlier to occur of (i) the date which is ninety (90) days following the Commencement Date and (ii) the date Lessee takes occupancy of all or any portion of the Subleased Premises for the purpose of operating its business. So long as Lessee is not in default beyond any applicable notice and cure periods, Lessor hereby excuses (y) Lessee's obligation to pay Base Rent (but not Additional Rent) for the period commencing on the Commencement Date and ending on the Rent Commencement Date, and (z) Lessee's obligation to pay the Operating Expense Payment for the period commencing on the Commencement Date and ending on the Operating Expense Payment Commencement Date. Except as expressly set forth in the preceding sentence, there shall be no abatement or excusal of Lessee's obligation to pay Additional Rent in accordance with this Sublease and Lessee shall pay all Additional Rent, other than the Operating Expense Payment, due hereunder from and after the Commencement Date.

4.04. In addition to the Base Rent, Lessee covenants and agrees to pay Lessor an amount equal to the Operating Expense Payment (as hereinafter defined). The term "**Operating Expense Payment**" shall mean one hundred percent (100%) of Lessor's obligations to make payments to Prime Landlord in accordance with Section 5 of the Prime Lease, it being understood and agreed that such payments contemplated under Section 5 of the Prime Lease include, among other things, (i) Operating Expenses, (ii) Taxes, (iii) Landlord's Property Management Fee, and (iv) Tenant's share of Operating Expenses for the Garage, the Project, the Campus and the Premises (each such term, as defined in the Prime Lease).

4.05 Upon receipt by Lessor of statements of Operating Expenses from Prime Lessor under the Prime Lease, Lessor shall deliver copies of the same to Lessee, along with and any other supporting documentation received from Prime Landlord, which statements shall set forth the Additional Rent payable by Lessee. The Additional Rent shall be payable by Lessee to Lessor in the same manner as the same is payable by Lessor to Prime Landlord, except that, subject to Section 5.02(11) hereof, Lessee shall pay all installments of Additional Rent directly to Lessor at least five (5) business days prior to the respective due dates under the Prime Lease. As used herein the term "**Additional Rent**" shall mean the Operating Expense Payment and all other costs, charges and sums payable under this Sublease. Additionally, Lessee shall be required to pay for any additional charges incurred by Lessee on account of Services (as hereinafter defined) offered at the Building utilized by Lessee or provided at the request of Lessee or supplies requested or utilized by Lessee.

4.06 Lessee shall pay all utility charges as Operating Expenses or otherwise in accordance with the Prime Lease. For the avoidance of doubt, as of the Effective Date of this Sublease, all utilities are separately metered for the Subleased Premises. Lessee shall not use or install any fixtures, equipment or machines the use of which in conjunction with other fixtures, equipment and machines in the Subleased Premises would result in an overload of the electrical equipment supplying electric current to the Subleased Premises or would otherwise violate the terms of the Prime Lease. Lessee shall not permit its use of electric current to exceed the capacity of the then existing feeders, risers, wiring or bus ducts to the Subleased Premises. In no event shall Lessor be liable or responsible to Lessee for any loss, damage or expense that Lessee sustains or incurs if either the quantity or character of electric service is changed or interrupted or is no longer available or suitable for Lessee's requirements except to the extent due to the negligence or willful misconduct of Lessor. To the extent that, for any period during the Term of this Sublease, Lessor actually receives an abatement or set-off of rent under the Prime Lease (and such abatement or set-off of rent is not disputed by Prime Landlord after expiration of all notice and cure periods set forth in the Prime Lease), Lessor shall provide to Lessee an abatement or set-off, as applicable, against the Rental due hereunder in a like amount. Lessor agrees that, if under the Prime Lease any right or remedy of Lessor related to an abatement or set-off is subject to or conditioned upon Lessor making any demand upon Prime Landlord or giving any notice or request to Prime Landlord then, if Lessee shall so request, Lessor, at Lessee's expense, shall promptly make such demand or give such notice or request on Lessee's behalf.

4.07 Lessee shall pay all Rental in lawful money of the United States, when due and payable, without setoff, offset or deduction of any kind whatsoever, except as expressly provided for in this Sublease (including Prime Lease provisions which may be incorporated by reference), and in the event Lessee fails to pay the same when due, Lessor shall have the rights and remedies provided for herein or at law or in equity, in the case of non-payment of Rental.

4.08. Except as otherwise specifically provided for herein, Rental shall be paid by Lessee to Lessor at the address of Lessor set forth above, or such other place as Lessor may designate in writing, without prior notice or demand therefor and without any abatement, deduction or setoff.

4.09 If any Rental due from Lessee is not received by Lessor when due, Lessee shall pay to Lessor on demand a late payment charge of four percent (4%) of the past-due amount; provided, however, Lessor agrees to waive such late charge one time in any twelve (12) month period, provided that the late payment is made within five (5) days of Lessor's written notice demanding payment. Acceptance of any late charge shall not constitute a waiver of Lessee's default with respect to the overdue amount, or prevent Lessor from exercising any of the other rights and remedies available to Lessor under this Sublease or under applicable law. In addition to the late charge, Rental not paid when due shall bear interest at the Default Rate from the date due until paid.

4.10 At the request of Lessee and at Lessee's sole cost (except to the extent Prime Landlord is obligated to pay for the same in accordance with Section 5 of the Prime Lease, and Lessor receives such amount from Prime Landlord, which Lessor shall then provide to Lessee for the cost of its Independent Review, as such term is defined in the Prime Lease), Lessor shall exercise the audit rights granted to the Tenant under Section 5 of the Prime Lease. In the event that Lessee elects to exercise such audit rights, such audit rights shall relate solely to Prime Landlord's determination of Operating Expenses. Lessee shall reimburse Lessor within thirty (30) days of Lessor's written demand for any and all third party out of pocket costs incurred by Lessor in connection with exercising such audit rights and Lessee shall defend, indemnify and hold Lessee harmless from and against any and all claims, damages and liabilities incurred by Lessor in connection with Lessee's exercise of such audit rights. Lessor shall have no liability whatsoever in connection with any errors or omissions relating to Prime Landlord's determination of Operating Expenses or other charges under the Prime Lease.

5. Subordination to and Incorporation of Prime Lease; Certain Rights of Lessee

5.01. This Sublease is subordinate to, and Lessee accepts this Sublease subject to (except as modified herein), all of the terms, covenants, provisions, conditions and agreements contained in the Prime Lease and the matters to which the Prime Lease is subject and subordinate. Lessee acknowledges that a redacted copy of the Prime Lease has been delivered to and examined by Lessee.

5.02. Except as otherwise provided in this Sublease, all of the terms, covenants, conditions, provisions and agreements of the Prime Lease (including, without limitation, definitions and constructions therein contained), except such as by their nature or purport do not relate to the Subleased Premises pursuant to this Sublease or are inconsistent with any of the provisions of this Sublease, are hereby incorporated in and made part of this Sublease with the same force and effect as though set forth at length herein, it being understood and agreed that, for purposes of this Sublease:

(1) references in the Prime Lease to "Landlord" and to "Tenant" shall be deemed to refer to "Lessor" and "Lessee" hereunder (except as otherwise expressly provided in this Sublease);

(2) references in the Prime Lease to "Rent" shall be deemed to refer to the "Rental" as defined herein;

(3) references in the Prime Lease to "Base Rent" shall be deemed to refer to the "Base Rent" as defined herein;

(4) references in the Prime Lease to "Additional Rent" shall be deemed to refer to the "Additional Rent" as defined herein;

(5) references in the Prime Lease to "this Lease" shall be deemed to refer to this Sublease;

(6) references in the Prime Lease to "Premises" shall be deemed to refer to the "Subleased Premises" as defined herein;

(7) references in the Prime Lease to the "Term" shall be deemed to refer to the "Term" as defined herein;

(8) to the extent that the Prime Landlord reserves the right to enter the Subleased Premises, for purposes of incorporation herein, such right shall inure to the Lessor and to the Prime Landlord;

(9) in any case in the Prime Lease where the consent or approval of Prime Landlord is required pursuant to the terms of the Prime Lease, for purposes of incorporation herein such consent or approval shall include the Lessor and the Prime Landlord;

(10) in any case in the Prime Lease where the Prime Landlord's architects or engineers have the right to review any plans or specifications of Tenant with respect to alterations, for purposes of incorporation herein, such right shall inure to Lessor, Lessor's architects and engineers and Prime Landlord and Prime Landlord's architects and engineers; and

(11) the time limits provided in the provisions of the Prime Lease for the giving of notice, for making demands, for the performance of any act, condition or covenant, or for the exercise of any right, remedy or option, by either party, are amended for the purposes of this Sublease, by lengthening or shortening the same in each instance by one (1) business day, as appropriate, so that notices may be given, demands made, or any act, condition or covenant performed, or any right, remedy or option hereunder exercised, by Lessor or Lessee, as the case may be, within the time limits relating thereto contained in the Prime Lease. Notwithstanding, the foregoing, if the Prime Lease allows only (i) ten (10) days or fewer for non-monetary obligations, or (ii) five (5) days or fewer for monetary obligations, for Lessor as tenant to perform any act, or to undertake to perform such act, or to correct a failure relating to the Subleased Premises of this Sublease, then, Lessee shall perform or undertake such act and/or correct such failure prior to the expiration of the applicable time limitations set forth in the Prime Lease.

5.03. The following sections of the Prime Lease shall not be incorporated herein by reference:

1) Basic Lease Provisions -
   a) Base Rent
   b) Security Deposit
   c) Delivery Date/Initial Premises
   d) Delivery Date/Remainder Premises
   e) Rent Commencement Date/Initial Premises
   f) Rent Commencement Date/Remainder Premises
   g) Base Rent Adjustment Percentage
   h) Base Term
2) Exhibit A
3) Exhibit A-1
4) Exhibit A-3
5) Exhibit A-4
6) Exhibit C-1
7) Exhibit C-2
8) Exhibit N
9) Section 1(a), fourth sentence
10) Section 1(c)
11) Sections 2(a), 2(b), 2(c) and 2(d)
12) Section 3
13) Section 4
14) Section 5 - the two grammatical paragraphs prior to the final grammatical paragraph.
15) Section 14 (delete the words “subject to Landlord’s Warranty under the Work Letter”)
16) Section 17(b), third grammatical paragraph is deleted. All insurance must be provided by insurance companies having the qualifications set forth in the second grammatical paragraph of Section 17(b)
17) Section 18(a)
18) Section 21(b)
19) Section 22(c)
20) Section 35
21) Section 36 – as this section shall relate to Lessor and Lessee. Such provision shall still apply to Prime Landlord.
22) Section 38 (other than the first grammatical paragraph, which shall remain incorporated as part of this Sublease)
23) Section 39
24) Section 40
25) Entire Agreement Regarding Early Access, Waiver and Related Matters dated as of June 19, 2017
26) Entire Second Amendment to Lease dated as of June 30, 2018

For the avoidance of doubt, (i) in no event shall Lessee be responsible for any redacted provisions of the Prime Lease and (ii) though the same are incorporated herein by reference, the parties agree that as between Lessor and Lessee, in no event shall Lessor have any obligations or liabilities to Lessee under the final grammatical paragraph of Section 5, Section 10(a), Section 10(b), or Sections 16(b), 27, 30 or 36 and Exhibit H of the Prime Lease.

5.04. Alterations. The provisions of this Section 5.04 are in addition to and not in substitution for the provisions of Section 12 of the Prime Lease. Lessor shall have the right to reasonably approve Lessee's contractors for work having a value of more than $100,000. Lessor and Prime Landlord shall be named as additional insured in each contractor's builder's risk policy (if applicable) and liability policies for each construction project. Any alterations, decorations and installations made by Lessee, or any assignee or subtenant of Lessee shall be removed by Lessee prior to the expiration of the Term if Prime Landlord or Lessor requires such removal or if required under the Prime Lease. Lessee shall indemnify, defend and hold harmless Lessor against any and all loss, cost, liability, claim, damage and expenses, including, without limiting the generality of the foregoing, reasonable attorneys' fees and expenses, court costs, penalties and fines incurred in connection with or arising from any such changes, alterations and improvements. Lessee shall not be obligated to remove or restore any alterations or improvements existing in the Subleased Premises on the Commencement Date unless Prime Landlord and Lessee enter into a direct lease having a term commencing immediately following the Term of this Sublease and Prime Landlord releases Lessor from all surrender, restoration and similar obligations under the Prime Lease.

6. Services; Disputes with Prime Landlord. Notwithstanding anything to the contrary contained herein, the only services, utilities, repairs, access, and equipment (collectively, together with similar rights, "**Services**") to which Lessee is entitled are only those to which Lessor is entitled under the Prime Lease. Lessee acknowledges and understands that the Services provided by Prime Landlord are not comprehensive and do not include all repair, maintenance or management services necessary or customary for the operation of the Subleased Premises and that Lessee will be responsible at its sole cost for contracting with Prime Landlord or its affiliate to provide such services, provided that, if Prime Landlord or its affiliate is not willing to provide such services (or is not willing to provide them on commercially reasonable market terms) then Lessee shall contract with a reputable third party property management company to provide such services, which third party management company is in the business of providing property management services to tenants in buildings comparable to the Building in Cambridge, Massachusetts. Lessee acknowledges and agrees that all Services shall be provided solely by Prime Landlord, and Lessor shall not have any obligation during the term of this Sublease to provide any Services (but Lessee shall be permitted to use such services in accordance with and subject to the terms hereof). Lessor shall in no event be liable to Lessee nor shall the obligations of Lessee hereunder be impaired or the performance thereof excused because of any failure or delay on Prime Landlord's part in furnishing such Services unless such failure or delay is caused by Lessor's negligent acts or misconduct or its default under the Prime Lease or this Sublease and such default is not caused by Lessee. If, at any time during the Term, Prime Landlord shall default in any of its obligations to furnish Services to the Subleased Premises, then, if Lessee is not in then in breach of any of its obligations under this Sublease beyond applicable notice and cure periods, upon Lessor's receipt of a written notice from Lessee specifying such default, Lessor shall, at Lessee's sole cost and expense, promptly use its reasonable efforts to cause Prime Landlord to cure such default. Lessor agrees, upon Lessee's request, to use reasonable efforts (excluding litigation), at Lessee's expense to cause Prime Landlord to provide the services and utilities described in Section 11 of the Prime Lease or to make the repairs or restorations described in Sections 13 or 18 of the Prime Lease, as applicable. Lessor agrees that, if under the Prime Lease any right or remedy of Lessor or any duty or obligation of Prime Landlord is subject to or conditioned upon Lessor making any demand upon Prime Landlord or giving any notice or request to Prime Landlord then, if Lessee shall so request, Lessor, at Lessee's expense, shall make such demand or give such notice or request on Lessee's behalf.

7. Insurance. Lessee, at Lessee's sole expense, shall maintain such policies of insurance as required of Lessor under the Prime Lease with respect to the Subleased Premises, in the manner set forth therein, listing Prime Landlord and Lessor as additional insureds and Lessee shall cause its insurance carrier to include any clauses or endorsements in favor of both Lessor and the Prime Landlord which Lessor is required to provide pursuant to the provisions of the Prime Lease.

8. Breach of Prime Lease. Lessee shall not do or permit to be done anything which would constitute a violation or breach of any of the terms, conditions or provisions of the Prime Lease or which would cause the Prime Lease to be terminated or forfeited by virtue of any rights of termination or forfeiture reserved by or vested in Prime Landlord. Lessee shall comply with all Rules and Regulations of the Building now or hereafter in effect. In addition, Lessee agrees to indemnify and hold harmless Lessor from and against any and all liability, loss, damage, claim or expense (including reasonable attorneys' fees) of any kind whatsoever in any way arising out of or connected with any breach, default or failure to perform on the part of the Lessee, as the case may be, under this or any other section of this Sublease. Lessor shall indemnify and hold harmless Lessee from and against any and all liability, loss, damage, claim or expense (including reasonable attorneys' fees) of any kind whatsoever in any way arising out of or in connection with any breach, default or failure to perform on the part of Lessor, as the case may be, under this or any other section of this Sublease. The indemnity obligations under this section shall survive the expiration or sooner termination of this Sublease. Lessee acknowledges and agrees that, in the event that Lessor becomes liable for any failure by Lessee to manage or maintain the Subleased Premises in accordance with the requirements of the Prime Lease, Lessee shall be solely responsible at its sole expense for all costs, claims, damages and liabilities associated with such failure.

9. Assignment and Subletting

9.01. Lessor shall have all of the rights of the Prime Landlord under Section 22 of the Prime Lease as though Lessor were the Prime Landlord and Lessee were the Tenant. The provisions of this Section 9.01 are in addition to and not in substitution for the provisions of Section 22 of the Prime Lease.

9.02 Lessee shall not have the right to sublease, assign, transfer, pledge, mortgage (or otherwise encumber) or allow the Subleased Premises to be occupied by anyone other than Lessee without the consent of (a) Prime Landlord, to the extent required under the Prime Lease and subject to any other rights of Landlord set forth therein with respect to subleases or assignments and (b) Lessor, to the same extent that Prime Landlord's consent is required under the Prime Lease. No assignment or subletting or any Permitted Assignment (as defined in the Prime Lease) shall release Lessee from its obligations hereunder and Lessee shall provide all such notices and other deliveries to Lessor in connection with any of the foregoing as and when required under the Prime Lease. Subject to the consent of the Prime Landlord and/or Lessor pursuant to the terms hereof and the terms of the Prime Lease, in the event of an assignment of this Sublease or a further sublet of all or a portion of the Subleased Premises, or other transfer or transaction involving this Sublease pursuant to which Lessee is entitled to receive consideration in excess of the Rental payable by Lessee hereunder to Lessor, after first deducting such actual and reasonable third party expenses such as tenant improvement costs, brokerage fees, legal costs and any design or construction fees directly related to and required pursuant to the terms of any such sublease or assignment ("**Excess Sublease Rent**"), then Lessee shall pay Sixty-Six and Two-Thirds Percent (66 2/3%) of such Excess Sublease Rent to Lessor in accordance with Section 22 of the Prime Lease as incorporated herein.

9.03 In addition to Lessee's rights to a permitted transfer pursuant to Section 22(b) of the Prime Lease, Lessee shall have the right to assign this Lease, upon not less than 30 days' advance notice to Lessor but without obtaining Lessor's consent, to a corporation or other entity which is a successor in interest to Tenant by way of merger, consolidation or corporate reorganization, or by the purchase of all or substantially all of the ownership interests or assets of Lessee, provided that (i) the proposed assignee's Net Worth (as such term is defined in Section 43(b) of the Prime Lease with references to Tenant being references to the proposed assignee) is no less than an amount equal to the Net Worth of the Lessee immediately prior to the effectiveness of such assignment, merger, consolidation, corporate reorganization or purchase of all or substantially all of the ownership interests or assets of Lessee, as evidenced by a certification from the Chief Financial Officer of such assignee of such assignee's Net Worth in the form of the Required Net Worth Certification a balance sheet attached as **Exhibit C** hereof and (ii) such assignee shall agree in writing to assume all of the terms, covenants and conditions of this Lease arising after the effective date of the assignment. For purposes hereof, "**Net Worth**" shall mean the excess of the Lessee's total assets (less intangible assets) over Lessee's liabilities.

9.04 In the event of termination, re-entry or dispossession of Lessor by Prime Landlord under the Prime Lease, Prime Landlord may, at its option, take over all of the right, title and interest of Lessor, as sublessor under this Sublease, and Lessee, at Prime Landlord's option, shall attorn to Prime Landlord pursuant to the then executory provisions of this Sublease, except that Prime Landlord shall not be: (i) liable for any act or omission of Lessor under this Sublease, (ii) subject to any defense or offsets which Lessee may have against Lessor, except for offset rights to which Lessee is entitled pursuant to this Sublease; (iii) bound by any previous payment which Lessee may have made to Lessor more than one (1) month in advance of the date upon which such payment was due, unless previously approved by Prime Landlord; (iv) bound by any obligation to make any payment to or on behalf of Lessee; (v) bound by any obligation to perform any work or to make improvements to the Premises (as such term is defined in the Prime Lease) or the Subleased Premises, provided the foregoing shall not relieve the Prime Landlord from the continuing obligations required of the Landlord under the Prime Lease; (vi) bound by any amendment or modification of this Sublease made without Prime Landlord's consent; or (vii) bound to return Lessee's security deposit, if any, until such deposit has come into its actual possession and Lessee would be entitled to such security deposit pursuant to the terms of this Sublease. Notwithstanding anything to the contrary contained herein, nothing contained shall limit Lessee's rights, defenses or remedies for any default by a prior sublandlord (including Lessor) under this Sublease which remains uncured following the time Prime Landlord succeeds to the interest of Lessor under the Sublease, nor relieve Prime Landlord of the obligation to cure ongoing defaults that are continuing following the date that Prime Landlord succeeds in the interest of Lessor under this Sublease, provided that Prime Landlord is given written notice of such default and thereafter fails to cure the same within the cure period provided for in this Sublease.

9.05 Notwithstanding anything to the contrary contained in the Prime Lease, excluding any such Permitted Assignment pursuant to Section 22(b) or (c) of the Prime Lease, if at any time or from time to time during the period excluding the final thirty-six (36) months of the Term, Lessee desires to (i) assign this Sublease or its entire interest under this Sublease, or (ii) sublet (y) greater than one-hundred eighty thousand (180,000) rentable square feet of the Subleased Premises (in one or more transactions, whether or not related), or (z) any portion of the Subleased Premises for substantially the remainder of the Term (such proposed transfer in (i) and (ii) being considered a "**Recapture Event**"), then at least fifteen (15) days prior to the date when Lessee desires the assignment or subletting to be effective (the "**Transfer Date**"), Lessee shall deliver a notice to Lessor (the "**Notice**") which shall set forth the name, address and business of the proposed assignee or sublessee, information (including financial statements) concerning the character of the proposed assignee or sublessee, a detailed description of the space proposed to be assigned or sublet, which must be a single, self-contained unit or have the ability to be demised into a single, self-contained unit (the "**Space**"), any rights of the proposed assignee or sublessee to use Lessee's improvements and the like, the Transfer Date, and the fixed rent and/or other consideration and all other material terms and conditions of the proposed assignment or subletting, all in such detail as Lessor may reasonably require. If Lessor requests additional detail, the Notice shall not be deemed to have been received until Lessor receives such additional detail. In the event of a Recapture Event, Lessor shall have the option, exercisable by giving notice to Lessee at any time within fifteen (15) days after Lessor's receipt of the Notice ("**Recapture Notice**"), to terminate this Sublease as to the Space as of the Transfer Date, in which event Lessee shall be relieved of all further obligations hereunder as to the Space. If Lessor exercises its option to recapture the Space, then Lessor shall install a demising wall separating the Space from the balance of the Subleased Premises and shall separate utility lines to the extent required, at Lessor's sole cost and expense. No failure of Lessor to exercise its recapture right with respect to the Space shall be deemed to be Lessor's consent to the assignment or subletting of all/or any portion of the Space. Provided Lessor has consented to such assignment or subletting, Lessee may assign or sublet the Space to the transferee named in the Notice in accordance with the terms and conditions of the Prime Lease. For the avoidance of doubt, during the final thirty-six (36) months of the Term, the recapture conditions of this Section 9.05 shall no longer apply.

9.06 If (a) Lessee desires to enter into a transaction to sublease a portion of the Subleased Premises and (b) the number of rentable square feet then contemplated to be subleased by Lessee, when aggregated with the number of rentable square feet of the Subleased Premises previously subleased by Lessee, exceeds one hundred eighty thousand (180,000) rentable square feet of space, a Recapture Event shall be deemed to have occurred with respect to the current proposed subleased space as well as all previously subleased space and Lessee shall deliver a Notice to Lessor identifying all of the space that is the subject of the Recapture Event, together with true and correct copies of all applicable subleases. In such event, Lessor shall have (i) the rights set forth in Section 9.05 with respect to the space that Lessee then currently proposes to sublease and (ii) as to the remainder of the space that is the subject of earlier subleases, Lessor shall have the right (which shall be contained in all subleases entered into by Lessee) to terminate the sublease between Lessee and the subtenant in which event Lessor shall recognize the sublease as a direct lease between Lessor and the subtenant until the end of the applicable sublease term.

10. Indemnification; Damage.

10.01 Subject to any applicable waiver of subrogation and/or release provisions applicable to the parties, and except to the extent resulting from the negligence or willful misconduct of Lessor or any of Lessor's employees, agents, contractors or invitees, Lessee shall indemnify, defend and hold harmless Lessor and its employees and agents from and against any and all loss, cost, liability, claim, damage and expense, including, without limiting the generality of the foregoing, reasonable attorneys' fees and expenses and court costs, penalties and fines incurred in connection with or arising from any injury, damage or loss (by theft or otherwise) occurring in or about the Subleased Premises or the Building and arising from any acts, omissions or negligence of Lessee, its employees, licenses or agents. Subject to any applicable waiver of subrogation and/or release provisions applicable to the parties, and except to the extent resulting from the negligence or willful misconduct of Lessee or any of Lessee's employees, agents, contractors or invitees, Lessor shall indemnify, defend and hold harmless Lessee and its employees and agents, from and against any and all loss, cost, liability, claim, damage and expense, including, without limiting the generality of the foregoing, reasonable attorneys' fees and expenses and court costs, penalties and files incurred in connection with or arising from any negligence or willful misconduct of Lessor or Lessor's employees, agents, contractors or invitees.

10.02 Notwithstanding any other provision of this Sublease or the Prime Lease to the contrary, except to the extent resulting from Lessor's negligence or willful misconduct, Lessor shall not be liable to Lessee, or to Lessee's employees, agents, subtenants, licensees, invitees, or visitors, or to any other person whomever, for any loss, or any damage to or loss of any property or death or injury to any person occasioned by or arising out of (a) the condition or design of or any defect in or failure to repair the Subleased Premises or the Building or any part or component thereof (including without limitation any mechanical, electrical, plumbing, heating, air conditioning or other systems or equipment); or (b) acts or omissions of Prime Landlord, other tenants or occupants in the Building or of any other persons whomever; or (c) burglary, theft, vandalism, malicious mischief, fire, act of God, public enemy, criminal conduct, court order or injunction, riot, strike, insurrection, war, requisition or order of governmental authority, or any other matter beyond the reasonable control of Lessor; (d) repair or alteration of any part of the Subleased Premises or Building; or (e) violation or default by Prime Landlord under the Prime Lease (including without limitation slowdown, interruption, failure or cessation of any service to be provided by Prime Landlord).

11. Consents and Approvals. In any instance when Lessor's consent or approval is required under this Sublease, Lessor's refusal to consent to or approve any matter or thing shall be deemed reasonable if, inter alia, such consent or approval has not been obtained from Prime Landlord (if required under the Prime Lease). In the event that Lessee shall seek the approval by or consent of Lessor and Lessor shall fail or refuse to give such consent or approval, Lessee shall not be entitled to any damages for any withholding or delay of such approval or consent by Lessor, it being intended that Lessee's sole remedy shall be an action for injunction or specific performance and that said remedy of any action for injunction or specific performance shall be available only in those cases where Lessor shall have expressly agreed not unreasonably to withhold or delay its consent. Notwithstanding anything to the contrary contained herein, in the event Prime Landlord agrees to provide its consent where necessary pursuant to the Prime Lease, Lessor agrees it shall not unreasonably withhold, condition or delay its consent hereunder.

12. Brokerage. Lessee represents that it dealt with no broker in connection with this Sublease other than Jones Lang LaSalle. Lessee shall indemnify, defend and hold Lessor harmless against liability arising out of any inaccuracy or alleged inaccuracy of the foregoing representation of Lessee. Lessor represents that it dealt with no broker in connection with this Sublease other than Zell Partnership, Inc. Lessor shall indemnify, defend and hold Lessee harmless against liability arising out of any inaccuracy or alleged inaccuracy of the foregoing representation of Lessor. Lessor shall be responsible for paying any commissions due to Jones Lang LaSalle and Zell Partnership, Inc. arising out of the execution of this Sublease pursuant to separate agreements. Lessor shall have no liability for brokerage commissions arising out of a sublease or assignment by Lessee and Lessee shall and does hereby indemnify Lessor against all liability for brokerage commissions arising out of any such sublease or assignment. The provisions of this Section 12 shall survive the expiration or earlier termination of this Sublease.

13. Notices

13.01. All rent and other payments required to be made by Lessee shall be payable to Lessor at Lessor's address set forth on the first page hereof or at such other address as Lessor may specify from time to time by Notice (as hereinafter defined) to Lessee. Whenever this Sublease requires or permits any consent, approval, notice, request or demand from one party to the other (collectively, "**Notice**"), such Notice must be in writing to be effective and shall be effective on the date of actual receipt of such Notice by the addressee or when the attempted initial delivery is refused or when it cannot be made because of a change of address of which the sending party has not been notified. The following shall, without limitation, be prima facia evidence of actual receipt of Notice by the addressee: (a) if mailed, by a United States certified mail return receipt, signed by the addressee or the addressee's agent or representative, (b) if sent by overnight courier with receipt signed by the addressee or the addressee's agent or representative; or (c) if hand delivered, by a delivery receipt signed by the addressee or the addressee's agent or representative. All notices or other communications required or desired to be given hereunder to Lessor shall be delivered to the address set forth in the preamble, Attn: Head of Real Estate, with a copy to: Aventis Inc., North American Legal Department, U.S. Corporate, 55 Corporate Drive, Bridgewater , New Jersey 08807-0977, Attn: General Counsel, North America and with a copy to; and with a copy to Arnold & Porter, 601 Massachusetts Avenue NW, Washington, DC 20001, Attn: Kenneth Schwartz. All such notices or other communications to Lessee shall be delivered to BLUEBIRD BIO, INC., a Delaware corporation, 60 Binney Street, Cambridge, Massachusetts 02142, Attn: General Counsel.

13.02 Any notices, approvals, consents or other communications under this Sublease shall be in writing and sent by either (a) certified mail, return receipt requested, postage prepaid, (b) personal delivery or (c) nationally recognized overnight courier service to the parties at their respective addresses set forth in this Sublease. Any notice, approval, consent or other communication shall be deemed given if sent by certified mail, return receipt requested on the third business day following the date mailed, if sent by personal delivery on the date delivered or if sent by nationally recognized overnight courier service on the next business day after the date delivered to such courier service.

14. Confidentiality. Except as otherwise required by law, neither Lessor nor Lessee shall disclose the terms of this Sublease to any other person. Notwithstanding the foregoing, Lessor and Lessee shall have the right to disclose the terms of this Sublease to their respective (i) members, partners, shareholders, directors, officers, employees and agents of each of their constituent entities and (ii) their respective legal counsel and advisors. All persons described in the foregoing clauses (i) and (ii) shall be informed by Lessor or Lessee, as applicable, of the confidential nature of such information and shall be directed to keep such information confidential. Notwithstanding the foregoing, each of Lessor and Lessee acknowledges that the rules and regulations promulgated by the United States Securities and Exchange Commission (the "**SEC**") may require the other party to disclose certain basic information concerning this Sublease and the transactions contemplated herein in documents to be filed with the SEC. The parties agree that Lessor and Lessee shall be permitted to make such disclosures and that such disclosures shall not constitute a breach or a violation of this Section 14 or any other confidentiality or non-disclosure agreement executed by the parties (or any of their respective affiliates).

15. Representations

15.01. Lessor's Representations. To induce Lessee to enter into this Sublease, Lessor hereby represents, warrants and covenants to Lessee that:

(a) Lessor holds the entire tenant's interest under the Prime Lease;

(b) Lessor has not sublet the Subleased Premises or any portion of the Subleased Premises; and

(c) Lessor is a duly formed and validly existing Delaware corporation. This Sublease has been duly authorized, executed and delivered by Lessor.

15.02. Lessee's Representations. To induce Lessor to enter into this Sublease, Lessee hereby represents, warrants and covenants to Lessor that:

(a) Lessee is a duly formed and validly existing Delaware corporation; and

(b) This Sublease has been duly authorized, executed and delivered by Lessee.

16. Lessor's Liability. Lessor, its partners, officers, directors, shareholders and principals, disclosed or undisclosed, shall have no personal liability under this Sublease. If Lessor shall fail to perform any covenant, term or condition of this Sublease upon Lessor's part required to be performed, or if Lessee shall make any claim arising out of Lessee's occupancy or use of the Subleased Premises, Lessor's liability from and after the date of this Sublease shall not exceed the Rental payable hereunder, and in no event shall Lessor's partners, officers, directors, shareholders or principals, disclosed or undisclosed, be subject to lien, levy, execution or other enforcement procedure for the satisfaction of Lessee's remedies under or with respect to this Sublease, the relationship of Lessor and Lessee hereunder or Lessee's use or occupancy of the Subleased Premises. If Lessee shall acquire a lien on such other property or assets by judgment or otherwise, Lessee shall promptly release such lien by executing and delivering to Lessor any instrument, prepared by Lessor, required for such lien to be released. This paragraph shall inure to the benefit of Lessor and its successors and assigns and shall survive the expiration or sooner termination of this Sublease.

17. No Renewals. Lessee shall have no renewal or extension rights hereunder and, notwithstanding anything herein to the contrary, no rights of Lessor to renewals under the Prime Lease shall be incorporated herein, provided, however, that if requested by Lessee, Lessor shall work in good faith with Lessee to obtain renewal rights for Lessee directly from Prime Landlord.

18. Parking; Signage.

18.01 Lessee and its employees and invitees shall have the right to use Two Hundred Sixteen (216) parking spaces in the Garage at market monthly rates, subject to the terms and conditions for the use thereof set forth in the Prime Lease. Lessee shall be solely responsible for paying directly to Prime Landlord or the Garage operator for all of such parking spaces at the monthly market rate designated by Prime Landlord pursuant to and in accordance with the terms of Section 10(b) of the Prime Lease. In addition, Lessee shall be obligated to pay Lessee's Share of Operating Expenses for the Garage as additional rent hereunder. Notwithstanding anything to the contrary contained in Sections 10(a) and 10(b) of the Prime Lease, as between Lessor and Lessee, Lessor shall have no obligations or liabilities to Lessee relating in any way to Lessee's rights to park in the Garage.

18.02 On or prior to the Commencement Date, Lessor shall request that Prime Landlord replace Lessor's name with that of Lessee on the monument sign located on the exterior of the Building, all of which shall be at the sole cost of Lessee. Lessee shall have no other exterior signage rights granted under the Prime Lease to Lessor or otherwise.

19. Cleaning. Notwithstanding anything herein or in the Prime Lease to the contrary, Lessee shall be responsible, at its sole cost and expense, for performing all services for the Premises in accordance with first class standards and otherwise as required under the Prime Lease.

20. Security. Lessor shall have no responsibility or liability for the security of the Building, the Subleased Premises or the safety of any of Lessee's employees, agents or contractors and Lessee hereby waives any right to make any claims against Lessor with regard to any such security matters. Lessee shall have the right to provide security in accordance with Section 33 of the Prime Lease.

21. Security Deposit.

21.01 Not later than five (5) business days following delivery by Prime Landlord of its written consent to this Sublease, Lessee shall deliver to Lessor the sum of Forty Million Seventy One Thousand Six Hundred Fifty Four and 15/100 Dollars ($40,071,654.15) (the "**Security Deposit**") in the form of a letter of credit ("**Letter of Credit**") in accordance with the requirements set forth below. Such Security Deposit shall be security for the payment and performance by Lessee of all obligations, covenants, conditions and agreements under this Sublease, and Lessor shall have the right, but shall not be obligated, to apply all or any portion of the Security Deposit to cure any monetary Default or material non-monetary Default under this Sublease by Lessee, in which event Lessee shall be obligated to promptly deposit with Lessor the amount necessary (or deliver an amendment to the Letter of Credit) to restore the Security

Deposit to its original amount within fifteen (15) days. In the event a monetary Default or material non-monetary Default occurs and is continuing, said Security Deposit shall not be deemed liquidated damages and Lessor may apply that portion of the Security Deposit to cure the monetary Default or material non-monetary Default on Lessee's behalf, and such application shall not preclude Lessor from recovering from Lessee all additional damages incurred by Lessor. In the event Lessee fully and faithfully complies with all terms, covenants, and conditions of this Sublease, the Letter of Credit shall be returned to Lessee within forty-five (45) days following the expiration or earlier termination hereof and Lessee's surrender of the Subleased Premises in accordance with the terms of this Sublease. Lessor shall transfer at its sole cost and expense the Letter of Credit to any purchaser or other successor or assignee of its interest hereunder and upon such transfer, Lessor shall be discharged and released from all further liability with respect to the Security Deposit and Lessee agrees to look solely to the successor or assignee for the return thereof. The Letter of Credit shall be an unconditional, irrevocable Letter of Credit in a form and from a financial institution reasonably acceptable to Lessor and shall have a term equal to the period expiring on the sixtieth (60th) day following the expiration of the Term or, at Lessee's option, shall have a term equal to the period expiring on an earlier date, which shall be no less than the first anniversary of the date of issuance thereof, in which event Lessee covenants that a renewal or replacement shall be delivered to Lessor by that date which is thirty (30) days prior to the expiration date of such Letter of Credit. If Lessee fails to so timely renew (or so replace) and deliver said Letter of Credit, Lessor may draw upon the Letter of Credit then in effect without the necessity of any other notice, in which event the proceeds thereof shall be held by Lessor until Lessee delivers a renewal or replacement. Said Letter of Credit shall provide that Lessor shall be permitted to draw on same following its declaration that it is permitted to so draw pursuant to the terms of this Sublease without requiring any additional certifications or evidence of Default. In the event said Letter of Credit would expire during the pendency of any litigation and Lessee does not renew or replace the same at least thirty (30) days prior to the expiration date of such Letter of Credit, Lessor may draw upon said Letter of Credit after a Default by Lessee and hold the proceeds thereof as a Security Deposit hereunder. Said Letter of Credit shall provide that Lessor be permitted to draw on same either by presentation (i) in person at a location in the United States of America or (ii) by overnight courier service, or (iii) by facsimile. The use, application or retention of the proceeds of the Letter of Credit, or any portion thereof, by Lessor shall not prevent Lessor from exercising any other right or remedy provided by this Sublease or by law, and shall not limit any recovery to which Lessor may otherwise be entitled. Notwithstanding anything to the contrary contained in this Sublease, Lessee acknowledges and agrees that if Lessee fails to timely make any payment required to be made by Lessee under that certain Purchase Agreement by and between Lessor and Lessee dated as of the date hereof relating to certain FF&E, and Lessee fails thereafter to make such payment within three (3) business days after written notice from Lessor, then failure to make such payment shall constitute an immediate Default under this Sublease without any further cure right on the part of Lessee.

21.02 If, on each of the anniversaries of the Commencement Date (each, an "**Anniversary Date**"), Lessee meets or exceeds the requirements that (i) Lessee's working capital shall be at least $1,000,000,000, with such "working capital" defined as total current assets plus any other marketable securities that are readily convertible into cash minus the total current liabilities of Lessee as reported in Lessee's SEC filings, and (ii) no Default by Lessee under this Sublease shall have occurred and be continuing (collectively, the "**Reduction Requirements**", and each a **Reduction Requirement**"), then as provided below in this Section, the Security Deposit shall be reduced by the amounts set forth in the table below.

Anniversary Date:	**Amount of Reduction to Security Deposit ("Reduction Amount"):**	**Resulting Reduced Security Deposit:**
Fourth (4th) anniversary of the Commencement Date	$13,357,218.03	$26,714,436.12
Seventh (7th) anniversary of the Commencement Date	$13,357,218.03	$13,357.218.06

The "**Reduced Security Deposit**" shall mean the amount of the Security Deposit required to be held by Lessor under this Sublease as of the Reduction Date, less the Reduction Amount. If Lessee provides Lessor with written evidence reasonably satisfactory to Lessor that Lessee has met all of the Reduction Requirements, then Lessor shall return the unapplied portion of the Security Deposit then held by Lessor, less the Reduced Security Deposit, to Lessee within fifteen (15) days of Lessee's delivery of such written evidence. If Lessor returns to Lessee any portion of the Security Deposit in accordance with this Section, then from and after the date such monies are returned to Lessee, the "**Security Deposit**" shall be deemed the Reduced Security Deposit for all purposes of this Sublease.

22. Miscellaneous.

22.01 In the event of any action or proceeding brought by either party under this Sublease against the other party hereto, the prevailing party shall be entitled to recover from the other party all costs and expenses, including reasonable attorneys' fees, in such action or proceeding.

22.02 Submission of this Sublease to Lessee for signature does not constitute a reservation of space or an option to Sublease. This Sublease is not effective until execution by and delivery to both Lessor and Lessee.

22.03 If any provision of this Sublease or the application thereof to any person or circumstances shall be invalid or unenforceable to any extent, the remainder of this Sublease and the application of such provisions to other persons or circumstances shall not be affected thereby and shall be enforced to the greatest extent permitted by law.

22.04 This Sublease shall be binding upon and inure to the benefit of Lessor and Lessee and their respective heirs, personal representatives, successors and assigns (subject to any other express provisions addressing subleasing and assignment).

22.05 The captions appearing in this Sublease are for convenience only and in no way define, limit, construe or describe the scope or intent of any Section. The laws of the Commonwealth of Massachusetts and applicable United States federal law shall govern the validity, performance and enforcement of this Sublease. This Sublease shall not be construed more or less favorably with respect to either party as a consequence of the Sublease or various provisions hereof having been drafted by one of the parties hereto.

22.06 This Sublease may not be altered, waived, amended or extended except by an instrument in writing signed by Lessor and Lessee.

22.07 LESSOR AND LESSEE EXPRESSLY AGREE THAT THERE ARE AND SHALL BE NO IMPLIED WARRANTIES OF MERCHANTABILITY, SUITABILITY, HABITABILITY, FITNESS FOR A PARTICULAR PURPOSE OR OF ANY OTHER KIND ARISING OUT OF THIS SUBLEASE, AND THERE ARE NO WARRANTIES WHICH EXTEND BEYOND THOSE EXPRESSLY SET FORTH IN THIS SUBLEASE.

22.08 Lessee represents and warrants that the financial statements that it provided to Lessor prior to the execution of this Sublease truly, accurately and fairly represent the financial results, cash flows and financial condition of Lessee as of the date of such statements and do not misstate any material fact or omit any material information or contingent liability.

22.09 This Sublease may be executed in counterparts.

(Remainder of page intentionally left blank; signature page follows.)

IN WITNESS WHEREOF, Lessor and Lessee have executed this Sublease as of the day and year first above written.

AVENTIS INC.
a Pennsylvania corporation

By: /s/ Doug McLeester
Name: Doug McLeester
Title: Head of Sanofi Business Services

BLUEBIRD BIO, INC.
a Delaware corporation

By: /s/ Jason Cole
Name: Jason Cole
Title: Chief Operating and Legal Officer

SCHEDULE 1

[***]

23

[***] INDICATES MATERIAL THAT HAS BEEN OMITTED BECAUSE IT IS BOTH (I) NOT MATERIAL, AND (II) WOULD LIKELY CAUSE COMPETITIVE HARM TO THE COMPANY IF PUBLICLY DISCLOSED.

EXHIBIT A

[***]

24

[***] INDICATES MATERIAL THAT HAS BEEN OMITTED BECAUSE IT IS BOTH (I) NOT MATERIAL, AND (II) WOULD LIKELY CAUSE COMPETITIVE HARM TO THE COMPANY IF PUBLICLY DISCLOSED.

EXHIBIT B

[***]

25

[***] INDICATES MATERIAL THAT HAS BEEN OMITTED BECAUSE IT IS BOTH (I) NOT MATERIAL, AND (II) WOULD LIKELY CAUSE COMPETITIVE HARM TO THE COMPANY IF PUBLICLY DISCLOSED.

EXHIBIT C

[***]

[***] INDICATES MATERIAL THAT HAS BEEN OMITTED BECAUSE IT IS BOTH (I) NOT MATERIAL, AND (II) WOULD LIKELY CAUSE COMPETITIVE HARM TO THE COMPANY IF PUBLICLY DISCLOSED.

Exhibit 10.43

Amendment to Sublease

Reference is made to that certain Sublease (the "Agreement"), dated April 16, 2019, between **bluebird bio, Inc.** ("bluebird bio") and **Aventis Inc.** ("Seller").

This is an amendment ("Amendment") to the Agreement**.** To the extent any provision of this Amendment conflicts with any of the provisions of the Agreement, the provisions of this Amendment shall govern. Capitalized terms but not otherwise defined herein shall have the respective meanings ascribed to such terms in the Agreement, as applicable. Except for the amendments made hereby, the above referenced Agreement remains in full force and effect. This Amendment is effective as of **April 19, 2019** (the "Amendment Effective Date").

1) Section 4.02. Base Rent, Additional Rent is hereby amended to include the following sentence: "All Rental and other sums due and payable to Lessor by Lessee shall be paid by Lessee to Lessor's wholly-owned subsidiary, Genzyme Corporation."

2) This Amendment, together with the Agreement, constitutes the final, complete and exclusive statement of the agreement between the parties pertaining to its subject matter and supersedes any and all prior and contemporaneous understandings or agreements of the parties with respect thereto.

3) This Amendment may be executed in counterparts, each of which shall constitute an original, but all of which when taken together shall constitute a single instrument. Delivery of an executed counterpart of a signature page to this Amendment by telecopier or other electronic means (e.g., via PDF) shall be effective delivery of a manually executed counterpart of this Amendment.

[signature page follows]

The parties, acting through their duly authorized representatives, have executed this Amendment as of the Amendment Effective Date.

"Seller" AVENTIS INC.		"bluebird bio" BLUEBIRD BIO, INC.	
By:	/s/ Ashley K. Gross	By:	/s/ Jason F. Cole
Name:	Ashley K. Gross	Name:	Jason F. Cole
Title:	Head Real Estate Facilities and Records Mgmt NA	Title:	Chief Operating and Legal Officer

Exhibit 31.1

CERTIFICATIONS

I, Nick Leschly, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of bluebird bio, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15(d)-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: August 1, 2019

By: /s/ Nick Leschly
Nick Leschly
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, Chip Baird, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of bluebird bio, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15(d)-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: August 1, 2019

By: /s/ Chip Baird
Chip Baird
Chief Financial Officer
(Principal Financial Officer)

Exhibit 32.1

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

In connection with the Quarterly Report on Form 10-Q of bluebird bio, Inc. (the "Company") for the period ended June 30, 2019 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers of the Company hereby certifies, pursuant to 18 U.S.C. Section 1350, that to his or her knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: August 1, 2019

By: /s/ Nick Leschly
Nick Leschly
President, Chief Executive Officer and Director (Principal Executive Officer and Duly Authorized Officer)

Date: August 1, 2019

By: /s/ Chip Baird
Chip Baird
Chief Financial Officer (Principal Financial Officer and Duly Authorized Officer)