# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION

**Washington, DC 20549**

# FORM 10-Q

**(Mark One)**

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

**For the quarterly period ended March 31, 2021**

**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 Stock 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.

| | | | |
|---|---|---|---|
| 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 April 30, 2021, there were 67,447,548 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, and to ensure adequate supply of our viral vectors and drug products;
- the timing or likelihood of regulatory filings and approvals for our product candidates;
- the timing or success of commercialization of our approved product, and any future approved products;
- our ability to obtain adequate pricing and reimbursement of our approved product, and any future approved products;
- 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 approved product, 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;
- the impact of the COVID-19 pandemic;
- the timing and results of our investigation into the cause of recent safety events in our HGB-206 clinical study, and whether there is a relationship with the use of our lentiviral vector in the manufacture of LentiGlobin for SCD;
- the timing, effects, costs, and benefits, including the tax treatment of the planned separation of our portfolio of products and programs into two independent, publicly-traded companies; 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.

**Summary of the Material and Other Risks Associated with Our Business**

*Below is a summary of the material risks to our business, operations and the investment in our common stock. This summary does not address all of the risks that we face. Risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Additional discussion of the risks summarized in this risk factor summary, and other risks that we face, can be found below under the heading "Risk Factors" and should be carefully considered, together with other information in this Quarterly Report on Form 10-Q in its entirety before making investment decisions regarding our common stock.*

- The EMA has paused the renewal procedure for the conditional marketing authorization of ZYNTEGLO™ while the EMA's pharmacovigilance risk assessment committee reviews the risk-benefit assessment for ZYNTEGLO and determines whether any additional pharmacovigilance measures are necessary, and we have no assurance as to what the EMA may require, or the timing, if ever, of when ZYNTEGLO may return to the market in Europe.
- The FDA has placed our HGB-206 and HGB-210 clinical studies of LentiGlobin for SCD on clinical hold, and we have no assurance as to what the FDA may require, or the timing, if ever, of when the clinical hold may be lifted.
- 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.
- The commercial success of ZYNTEGLO, and of any future products, will depend upon the degree of market acceptance by physicians, patients, third-party payers and others in the medical community. If we fail to obtain sufficient pricing or reimbursement approval for ZYNTEGLO or any future products, our revenues may be adversely affected and our business may suffer.
- 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 rely on a complex supply chain for ZYNTEGLO and our product candidates. The manufacture and delivery of our lentiviral vector and drug products present significant challenges for us, and we may not be able to produce our vector and drug products at the quality, quantities, locations or timing needed to support commercialization and clinical programs. In addition, we may encounter challenges with engaging or coordinating with qualified treatment centers needed to support commercialization.
- 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.
- 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 may not be successful in our efforts to identify or discover additional product candidates.
- We are dependent on BMS for the successful development and commercialization of ABECMA® (idecabtagene vicleucel; ide-cel) and bb21217. If BMS does not devote sufficient resources to the development of ABECMA and bb21217, is unsuccessful in its efforts, or chooses to terminate its agreements with us, our business will be materially harmed.
- We have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future.
- 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.
- Our business may be materially and adversely affected by the ongoing COVID-19 pandemic. The COVID-19 pandemic has had, and will likely continue to have, an impact on various aspects of our business and that of third parties on which we rely. The extent to which the COVID-19 pandemic impacts our business will depend in part on future developments, which are uncertain and unpredictable in nature.

- The proposed separation of our business into two independent, publicly traded companies is subject to various risks and uncertainties and may not be completed on the terms or timeline currently contemplated, if at all, and will involve significant time, effort and expense, which could harm our business, results of operations and financial condition.

**bluebird bio, Inc.**

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## PART I. FINANCIAL INFORMATION

### Item 1. Financial Statements

**bluebird bio, Inc.**

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

| | As of March 31, 2021 | As of December 31, 2020 |
|---|---|---|
| **Assets** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 439,714 | $ 317,705 |
| Marketable securities | 572,722 | 833,546 |
| Prepaid expenses | 42,258 | 37,472 |
| Receivables and other current assets | 24,762 | 16,116 |
| Inventory | 18,079 | 10,698 |
| Total current assets | 1,097,535 | 1,215,537 |
| Marketable securities | 81,115 | 122,891 |
| Property, plant and equipment, net | 165,198 | 162,831 |
| Intangible assets, net | 11,469 | 10,041 |
| Goodwill | 13,128 | 13,128 |
| Operating lease right-of-use assets | 197,970 | 184,019 |
| Restricted cash and other non-current assets | 70,864 | 72,805 |
| Total assets | $ 1,637,279 | $ 1,781,252 |
| **Liabilities and Stockholders' Equity** | | |
| Current liabilities: | | |
| Accounts payable | $ 20,232 | $ 21,602 |
| Accrued expenses and other current liabilities | 146,791 | 145,406 |
| Operating lease liability, current portion | 28,063 | 25,024 |
| Deferred revenue, current portion | 1,330 | 2,320 |
| Collaboration research advancement, current portion | 9,899 | 9,236 |
| Total current liabilities | 206,315 | 203,588 |
| Deferred revenue, net of current portion | 25,762 | 25,762 |
| Collaboration research advancement, net of current portion | 19,399 | 21,581 |
| Operating lease liability, net of current portion | 177,702 | 167,997 |
| Other non-current liabilities | 7,768 | 7,268 |
| Total liabilities | 436,946 | 426,196 |
| Commitments and contingencies *(Note 9)* | | |
| Stockholders' equity: | | |
| Preferred stock, $0.01 par value, 5,000 shares authorized; 0 shares issued and outstanding at March 31, 2021 and December 31, 2020 | — | — |
| Common stock, $0.01 par value, 125,000 shares authorized; 67,422 and 66,432 shares issued and outstanding at March 31, 2021 and December 31, 2020, respectively | 675 | 665 |
| Additional paid-in capital | 4,311,462 | 4,260,443 |
| Accumulated other comprehensive loss | (5,449) | (5,505) |
| Accumulated deficit | (3,106,355) | (2,900,547) |
| Total stockholders' equity | 1,200,333 | 1,355,056 |
| Total liabilities and stockholders' equity | $ 1,637,279 | $ 1,781,252 |

*See accompanying notes to unaudited condensed consolidated financial statements.*

**bluebird bio, Inc.**

**Condensed Consolidated Statements of Operations and Comprehensive Loss**
**(unaudited)**
**(in thousands, except per share data)**

| | For the three months ended March 31, | |
|---|---|---|
| | 2021 | 2020 |
| Revenue: | | |
| Service revenue | $ 5,918 | $ 16,833 |
| Collaborative arrangement revenue | 1,519 | 2,302 |
| Royalty and other revenue | 5,357 | 2,728 |
| Total revenues | 12,794 | 21,863 |
| Operating expenses: | | |
| Research and development | 154,478 | 154,123 |
| Selling, general and administrative | 86,874 | 73,248 |
| Cost of royalty and other revenue | 2,281 | 1,025 |
| Change in fair value of contingent consideration | 369 | (3,108) |
| Total operating expenses | 244,002 | 225,288 |
| Loss from operations | (231,208) | (203,425) |
| Interest income, net | 710 | 5,355 |
| Other income (expense), net | 24,756 | (4,447) |
| Loss before income taxes | (205,742) | (202,517) |
| Income tax expense | (66) | (94) |
| Net loss | $ (205,808) | $ (202,611) |
| Net loss per share - basic and diluted: | $ (3.07) | $ (3.64) |
| Weighted-average number of common shares used in computing net loss per share - basic and diluted: | 66,976 | 55,590 |
| Other comprehensive income (loss): | | |
| Other comprehensive income (loss), net of tax benefit (expense) of $0.0 million for the three months ended March 31, 2021 and 2020 | 56 | (906) |
| Total other comprehensive income (loss) | 56 | (906) |
| Comprehensive loss | $ (205,752) | $ (203,517) |

*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, 2020** | 66,432 | $ 665 | $ 4,260,443 | $ (5,505) | $ (2,900,547) | $ 1,355,056 |
| Vesting of restricted stock units | 294 | 3 | (3) | — | — | — |
| Exercise of stock options | 207 | 2 | 1,217 | — | — | 1,219 |
| Purchase of common stock under ESPP | 67 | 1 | 1,706 | — | — | 1,707 |
| Stock-based compensation | — | — | 36,090 | — | — | 36,090 |
| Issuance of unrestricted stock awards to settle accrued employee compensation | 422 | 4 | 12,009 | — | — | 12,013 |
| Other comprehensive income | — | — | — | 56 | — | 56 |
| Net loss | — | — | — | — | (205,808) | (205,808) |
| **Balances at March 31, 2021** | 67,422 | $ 675 | $ 4,311,462 | $ (5,449) | $ (3,106,355) | $ 1,200,333 |

| | Common stock | | Additional paid-in capital | Accumulated other comprehensive loss | Accumulated deficit | Total stockholders' equity |
|---|---|---|---|---|---|---|
| | Shares | Amount | | | | |
| **Balances at December 31, 2019** | 55,368 | $ 554 | $ 3,568,184 | $ (1,893) | $ (2,281,852) | $ 1,284,993 |
| Vesting of restricted stock units | 204 | 2 | (2) | — | — | — |
| Exercise of stock options | 20 | — | 750 | — | — | 750 |
| Purchase of common stock under ESPP | 28 | — | 1,872 | — | — | 1,872 |
| Stock-based compensation | — | — | 36,335 | — | — | 36,335 |
| Other comprehensive loss | — | — | — | (906) | — | (906) |
| Net loss | — | — | — | — | (202,611) | (202,611) |
| **Balances at March 31, 2020** | 55,620 | $ 556 | $ 3,607,139 | $ (2,799) | $ (2,484,463) | $ 1,120,433 |

*See accompanying notes to unaudited condensed consolidated financial statements.*

**bluebird bio, Inc.**

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

| | For the three months ended March 31, | |
|---|---|---|
| | **2021** | **2020** |
| **Cash flows from operating activities:** | | |
| Net loss | $ (205,808) | $ (202,611) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | |
| Change in fair value of contingent consideration | 369 | (3,108) |
| Depreciation and amortization | 5,360 | 4,880 |
| Stock-based compensation expense | 42,527 | 36,293 |
| (Gain) loss on equity securities | (28,372) | 4,520 |
| Other non-cash items | 2,513 | (1,387) |
| Changes in operating assets and liabilities: | | |
| Prepaid expenses and other assets | (8,979) | (9,285) |
| Inventory | (7,103) | (1,699) |
| Operating lease right-of-use assets | 8,098 | 5,842 |
| Accounts payable | 67 | (9,519) |
| Accrued expenses and other liabilities | (184) | (20,557) |
| Operating lease liabilities | (9,306) | (5,070) |
| Deferred revenue | (990) | (2,118) |
| Collaboration research advancement | (1,519) | (2,302) |
| Net cash used in operating activities | (203,327) | (206,121) |
| **Cash flows from investing activities:** | | |
| Purchase of property, plant and equipment | (7,626) | (10,676) |
| Purchases of marketable securities | (53,200) | (101,421) |
| Proceeds from maturities of marketable securities | 350,860 | 336,675 |
| Proceeds from sales of marketable securities | 31,318 | — |
| Net cash provided by investing activities | 321,352 | 224,578 |
| **Cash flows from financing activities:** | | |
| Proceeds from exercise of stock options and ESPP contributions | 3,796 | 963 |
| Net cash provided by financing activities | 3,796 | 963 |
| Increase in cash, cash equivalents and restricted cash | 121,821 | 19,420 |
| Cash, cash equivalents and restricted cash at beginning of period | 373,728 | 381,709 |
| Cash, cash equivalents and restricted cash at end of period | $ 495,549 | $ 401,129 |
| **Reconciliation of cash, cash equivalents and restricted cash:** | | |
| Cash and cash equivalents | $ 439,714 | $ 346,629 |
| Restricted cash included in receivables and other current assets | $ 1,330 | $ — |
| Restricted cash included in restricted cash and other non-current assets | $ 54,505 | $ 54,500 |
| Total cash, cash equivalents and restricted cash | $ 495,549 | $ 401,129 |
| **Supplemental cash flow disclosures from investing and financing activities:** | | |
| Purchases of property, plant and equipment included in accounts payable and accrued expenses | $ 2,238 | $ 1,125 |
| Right-of-use assets obtained in exchange for operating lease liabilities | $ 22,049 | $ 14,425 |
| Issuance of unrestricted stock awards to settle accrued employee compensation | $ 12,013 | $ — |

*See accompanying notes to unaudited condensed consolidated financial statements.*

**bluebird bio, Inc.**

**Notes to Condensed Consolidated Financial Statements**
**(unaudited)**

## 1. Description of the business

bluebird bio, Inc. (the “Company” or “bluebird”) was incorporated in Delaware on April 16, 1992, and is headquartered in Cambridge, Massachusetts. The Company 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 selling, general and administrative support for these operations, including commercial-readiness activities.

The Company’s programs in severe genetic diseases include programs for transfusion-dependent β-thalassemia, or TDT, sickle cell disease, or SCD, and cerebral adrenoleukodystrophy, or CALD. The Company’s programs in oncology are focused on developing novel engineered cell and gene therapies for cancer, including the anti-BCMA CAR T programs for multiple myeloma under the Company’s collaboration arrangement with Bristol-Myers Squibb ("BMS"). Please refer to Note 10, *Collaborative arrangements*, for further discussion of the Company’s collaboration with BMS.

In March 2021, BMS received marketing approval from the U.S. Food and Drug Administration for ABECMA® (idecabtagene vicleucel; ide-cel) as a treatment of adult patients with relapsed or refractory multiple myeloma after four or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody. In October 2020, the Company's marketing authorization application was accepted by the European Medicines Agency, or EMA, for elivaldogene autotemcel (eli-cel; formerly Lenti-D gene therapy) as a treatment for cerebral adrenoleukodystrophy. In June 2019, the Company received conditional marketing authorization from the European Commission for betibeglogene autotemcel (beti-cel; formerly LentiGlobin for β-thalassemia gene therapy) as a treatment of patients 12 years and older with TDT who do not have a $\beta^0/\beta^0$ genotype, for whom hematopoietic stem cell (HSC) transplantation is appropriate but a human leukocyte-matched related HSC donor is not available. beti-cel is being marketed as ZYNTEGLO™ in the European Union. The Company began recognizing product revenue from product sales of ZYNTEGLO during the first quarter of 2021. In February 2021, the Company temporarily suspended marketing of ZYNTEGLO in light of safety events in the HGB-206 study of LentiGlobin gene therapy for SCD, which is manufactured using the same vector as ZYNTEGLO. Additionally, the EMA has paused the renewal procedure for ZYNTEGLO's conditional marketing authorization while the EMA's pharmacovigilance risk assessment committee reviews the risk-benefit assessment for ZYNTEGLO and determines whether any additional pharmacovigilance measures are necessary.

In January 2021, the Company announced its intent to separate its severe genetic disease and oncology programs into two separate, independent publicly traded companies, bluebird bio, Inc. and 2seventy bio, Inc., a newly-formed Delaware corporation and wholly-owned subsidiary of the Company prior to the separation. bluebird bio, Inc. intends to retain focus on its severe genetic disease programs and 2seventy bio, Inc. is expected to focus on the Company's oncology programs. The transaction is expected to be completed in late 2021 and is anticipated to be tax-free, subject to receipt of a favorable Internal Revenue Service (“IRS”) ruling.

In accordance with Accounting Standards Codification (“ASC”) 205-40, *Going Concern*, the Company evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about its ability to continue as a going concern within one year after the date that the consolidated financial statements are issued. The Company has incurred losses since inception and to date has financed its operations primarily through the sale of equity securities and, to a lesser extent, through collaboration agreements and grants from governmental agencies and charitable foundations. As of March 31, 2021, the Company had an accumulated deficit of $3.11 billion. During the three months ended March 31, 2021, the Company incurred a loss of $205.8 million and used $203.3 million of cash in operations. The Company expects to continue to generate operating losses and negative operating cash flows for the next few years and will need additional funding to support its planned operating activities through profitability. The transition to profitability is dependent upon the successful development, approval, and commercialization of the Company’s product and product candidates and the achievement of a level of revenues adequate to support its cost structure.

As of March 31, 2021, the Company had cash, cash equivalents and marketable securities of $1.09 billion. The Company expects its cash, cash equivalents and marketable securities will be sufficient to fund current planned operations for at least the next twelve months from the date of issuance of these financial statements, though it may pursue additional cash resources

through public or private equity or debt financings or by establishing additional collaborations with other companies. Management's expectations with respect to its ability to fund current planned operations is based on estimates that are subject to risks and uncertainties. If actual results are different from management's estimates, the Company may need to seek additional strategic or financing opportunities sooner than would otherwise be expected. However, there is no guarantee that any of these strategic or financing opportunities will be executed or executed on favorable terms, and some could be dilutive to existing stockholders. If the Company is unable to obtain additional funding on a timely basis, it may be forced to significantly curtail, delay, or discontinue one or more of its planned research or development programs or be unable to expand its operations or otherwise capitalize on its commercialization of its product and product candidates.

**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 Updates (“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 condensed consolidated financial statements, in the opinion of management, reflect all normal recurring adjustments necessary for a fair presentation of the Company’s financial position and results of operations for the interim periods ended March 31, 2021 and 2020.

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 condensed consolidated financial statements should be read in conjunction with the audited consolidated financial statements as of and for the year ended December 31, 2020, 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 23, 2021.

Inventory in the prior year’s condensed consolidated financial statements have been reclassified to conform to the current presentation on the condensed consolidated balance sheets and condensed consolidated statements of cash flows. However, no subtotals in the prior year condensed consolidated financial statements were impacted as a result.

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 months ended March 31, 2021 are consistent with those discussed in Note 2 to the consolidated financial statements included in the Company’s 2020 Annual Report on Form 10-K, except as noted immediately below and as noted within the *"Recent accounting pronouncements - Recently adopted"* section.

*Royalty and other revenue*

During the first quarter of 2021, the Company recognized an immaterial amount of product revenue related to the sale of ZYNTEGLO in the European Union and the related cost of goods sold, which is included within royalty and other revenue and cost of royalty and other revenue, respectively.

*Inventory*

Inventories are stated at the lower of cost or net realizable value under the first-expired, first-out (FEFO) methodology. Given human gene therapy products are a new and novel category of therapeutics and future economic benefit is not probable until regulatory approval for the product has been obtained, the Company has only considered inventory for capitalization upon regulatory approval. Manufacturing costs incurred prior to regulatory approval for pre-launch inventory that did not qualify for capitalization and clinical manufacturing costs are charged to research and development expense in the Company’s condensed consolidated statements of operations and comprehensive loss as costs are incurred. Additionally, inventory that initially

qualifies for capitalization but that may ultimately be used for the production of clinical drug product is expensed as research and development expense when it has been designated for the manufacture of clinical drug product.

Inventory consists of cell banks, plasmids, vectors, other materials and compounds sourced from third party suppliers and utilized in the manufacturing process, and drug product, which has been produced for the treatment of specific patients, that are owned by the Company.

Management periodically reviews inventories for excess or obsolescence, considering factors such as sales forecasts compared to quantities on hand and firm purchase commitments as well as remaining shelf life of on hand inventories. The Company writes-down its inventory that is obsolete or otherwise unmarketable to its estimated net realizable value in the period in which the impairment is first identified. Any such adjustments are included as a component of cost of goods sold.

***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 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 recognition, income taxes, inventory capitalization, and the assessment of the Company's ability to fund its operations for at least the next twelve months from the date of issuance of these financial statements.

***Recent accounting pronouncements***

*Recently adopted*

*ASU No. 2019-12, Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes*

In December 2019, the FASB issued ASU 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes* (“ASU 2019-12”), which is intended to simplify the accounting for income taxes. ASU 2019-12 removes certain exceptions to the general principles in Topic 740 and also clarifies and amends existing guidance to improve consistent application. The new standard was effective beginning January 1, 2021. The adoption of ASU 2019-12 did not have a material impact on the Company's financial position or results of operations upon adoption.

*ASU No. 2020-06, Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity’s Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity’s Own Equity*

In August 2020, the FASB issued ASU 2020-06, *Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity’s Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity’s Own Equity* (“ASU 2020-06”). ASU 2020-06 simplifies the complexity associated with applying U.S. GAAP for certain financial instruments with characteristics of liabilities and equity. More specifically, the amendments focus on the guidance for convertible instruments and derivative scope exception for contracts in an entity's own equity. The Company early adopted the new standard, effective January 1, 2021. The adoption of ASU 2020-06 did not have an impact on the Company's financial position or results of operations upon adoption.

*ASU No. 2020-08, Codification Improvements to Subtopic 310-20, Receivables - Nonrefundable Fees and Other Costs*

In October 2020, the FASB issued ASU 2020-08, *Codification Improvements to Subtopic 310-20, Receivables - Nonrefundable Fees and Other Costs* (“ASU 2020-08”) to provide further clarification and update the previously issued guidance in ASU 2017-08, *Receivables - Nonrefundable Fees and Other Costs (Subtopic 310-20: Premium Amortization on*

*Purchased Callable Debt Securities)* (“ASU 2017-08”). ASU 2017-08 shortened the amortization period for certain callable debt securities purchased at a premium by requiring that the premium be amortized to the earliest call date. ASU 2020-08 requires that at each reporting period, to the extent that the amortized cost of an individual callable debt security exceeds the amount repayable by the issuer at the next call date, the excess premium shall be amortized to the next call date. The new standard was effective beginning January 1, 2021. The adoption of ASU 2020-08 did not have a material impact on the Company's financial position or results of operations upon adoption.

*ASU No. 2020-10, Codification Improvements*

In October 2020, the FASB issued ASU 2020-10, *Codification Improvements* ("ASU 2020-10"). The amendments in this ASU represent changes to clarify the ASC, correct unintended application of the guidance, or make minor improvements to the ASC that are not expected to have a significant effect on current accounting practice or create a significant administrative cost to most entities. This new standard was effective beginning January 1, 2021. The adoption of ASU 2020-10 did not 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 March 31, 2021 and December 31, 2020 (in thousands):

| Description | Amortized cost / Cost | Unrealized gains | Unrealized losses | Fair value |
|---|---|---|---|---|
| **March 31, 2021** | | | | |
| U.S. government agency securities and treasuries | $ 429,039 | $ 256 | $ (16) | $ 429,279 |
| Corporate bonds | 142,773 | 163 | (40) | 142,896 |
| Commercial paper | 78,955 | — | — | 78,955 |
| Equity securities | 4,305 | — | (1,598) | 2,707 |
| Total | $ 655,072 | $ 419 | $ (1,654) | $ 653,837 |
| **December 31, 2020** | | | | |
| U.S. government agency securities and treasuries | $ 675,043 | $ 302 | $ (74) | $ 675,271 |
| Corporate bonds | 197,171 | 432 | (40) | 197,563 |
| Commercial paper | 77,949 | 1 | — | 77,950 |
| Equity securities | 20,017 | — | (14,364) | 5,653 |
| Total | $ 970,180 | $ 735 | $ (14,478) | $ 956,437 |

No available-for-sale debt securities held as of March 31, 2021 or December 31, 2020 had remaining maturities greater than five years.

**4. Fair value measurements**

The following table sets forth the Company's assets and liabilities that are measured at fair value on a recurring basis as of March 31, 2021 and December 31, 2020 (in thousands):

| Description | Total | Quoted prices in active markets (Level 1) | Significant other observable inputs (Level 2) | Significant unobservable inputs (Level 3) |
|---|---|---|---|---|
| **March 31, 2021** | | | | |
| Assets: | | | | |
| Cash and cash equivalents | $ 439,714 | $ 410,715 | $ 28,999 | $ — |
| Marketable securities: | | | | |
| U.S. government agency securities and treasuries | 429,279 | — | 429,279 | — |
| Corporate bonds | 142,896 | — | 142,896 | — |
| Commercial paper | 78,955 | — | 78,955 | — |
| Equity securities | 2,707 | 2,707 | — | — |
| Total | $ 1,093,551 | $ 413,422 | $ 680,129 | $ — |
| Liabilities: | | | | |
| Contingent consideration | $ 1,878 | $ — | $ — | $ 1,878 |
| Total | $ 1,878 | $ — | $ — | $ 1,878 |
| **December 31, 2020** | | | | |
| Assets: | | | | |
| Cash and cash equivalents | $ 317,705 | $ 317,705 | $ — | $ — |
| Marketable securities: | | | | |
| U.S. government agency securities and treasuries | 675,271 | — | 675,271 | — |
| Corporate bonds | 197,563 | — | 197,563 | — |
| Commercial paper | 77,950 | — | 77,950 | — |
| Equity securities | 5,653 | 5,653 | — | — |
| Total | $ 1,274,142 | $ 323,358 | $ 950,784 | $ — |
| Liabilities: | | | | |
| Contingent consideration | $ 1,509 | $ — | $ — | $ 1,509 |
| Total | $ 1,509 | $ — | $ — | $ 1,509 |

***Cash and cash equivalents***

The Company considers all highly liquid securities with original final maturities of 90 days or less from the date of purchase to be cash equivalents. As of March 31, 2021, cash and cash equivalents comprise funds in cash, money market accounts, and commercial paper. As of December 31, 2020, cash and cash equivalents comprise funds in cash and money market accounts.

***Marketable securities***

Marketable securities classified as Level 2 within the valuation hierarchy generally consist of U.S. government agency securities and treasuries, 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 next call date for premiums or to maturity for discounts. At March 31, 2021 and December 31, 2020, the balance in the Company's accumulated other comprehensive loss includes 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 debt securities during the three months ended March 31, 2021 or 2020.

Accrued interest receivable on the Company's available-for-sale debt securities totaled $2.2 million and $3.1 million as of March 31, 2021 and December 31, 2020, respectively. No accrued interest receivable was written off during the three months ended March 31, 2021 or 2020.

The following table summarizes available-for-sale debt securities in a continuous unrealized loss position for less than and greater than twelve months, and for which an allowance for credit losses has not been recorded at March 31, 2021 and December 31, 2020 (in thousands):

| | Less than 12 months | | 12 months or greater | | Total | |
|---|---|---|---|---|---|---|
| **Description** | **Fair value** | **Unrealized losses** | **Fair value** | **Unrealized losses** | **Fair value** | **Unrealized losses** |
| **March 31, 2021** | | | | | | |
| U.S. government agency securities and treasuries | $ 48,802 | $ (16) | $ — | $ — | $ 48,802 | $ (16) |
| Corporate bonds | 92,855 | (40) | — | — | 92,855 | (40) |
| Total | $ 141,657 | $ (56) | $ — | $ — | $ 141,657 | $ (56) |
| **December 31, 2020** | | | | | | |
| U.S. government agency securities and treasuries | $ 211,384 | $ (74) | $ — | $ — | $ 211,384 | $ (74) |
| Corporate bonds | 76,598 | (40) | 1,205 | — | 77,803 | (40) |
| Total | $ 287,982 | $ (114) | $ 1,205 | $ — | $ 289,187 | $ (114) |

The Company determined that there was no material change in the credit risk of the above investments during the three months ended March 31, 2021. As such, an allowance for credit losses was not recognized. As of March 31, 2021, the Company does not intend to sell such securities and it is not more likely than not that the Company will be required to sell the securities before recovery of their amortized cost bases.

The Company held equity securities with an aggregate fair value of $2.7 million and $5.7 million as of March 31, 2021 and December 31, 2020, respectively, within short-term marketable securities on its condensed consolidated balance sheets. In January 2021, the Company sold a portion of its equity securities for proceeds of $31.3 million. During the three months ended March 31, 2021 and 2020, the Company recorded gains of $28.4 million and losses of $4.5 million, respectively, related to its equity securities, which are included in other income (expense), 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. Contingent consideration is included in accrued expenses and other current liabilities and other non-current liabilities on the condensed consolidated balance sheets.

Please refer to Note 9, *Commitments and contingencies*, for further information.

**5. Inventory**

Inventory consists of the following (in thousands):

| | As of March 31, 2021 | As of December 31, 2020 |
|---|---|---|
| Raw materials | $ 16,892 | $ 8,967 |
| Finished goods | 1,187 | 1,731 |
| Inventory | $ 18,079 | $ 10,698 |

**6. Property, plant and equipment, net**

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

| | As of March 31, 2021 | As of December 31, 2020 |
|---|---|---|
| Land | $ 1,210 | $ 1,210 |
| Building | 88,591 | 15,745 |
| Computer equipment and software | 6,919 | 6,950 |
| Office equipment | 7,633 | 7,665 |
| Laboratory equipment | 66,600 | 55,521 |
| Leasehold improvements | 34,104 | 34,286 |
| Construction-in-progress | 14,939 | 92,514 |
| Total property, plant and equipment | 219,996 | 213,891 |
| Less accumulated depreciation and amortization | (54,798) | (51,060) |
| Property, plant and equipment, net | $ 165,198 | $ 162,831 |

***North Carolina manufacturing facility***

In November 2017, the Company acquired a manufacturing facility in Durham, North Carolina for the future manufacture of lentiviral vector for the Company's gene therapies. As of March 31, 2021, the majority of the facility has been placed into service. The remainder of the facility is still in process of qualification, which is required for the facility to be ready for its intended use. Construction-in-progress as of March 31, 2021 and December 31, 2020 includes $14.2 million and $91.1 million, respectively, related to the North Carolina manufacturing facility.

**7. Accrued expenses and other current liabilities**

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

| | As of March 31, 2021 | As of December 31, 2020 |
|---|---|---|
| Employee compensation | $ 45,916 | $ 55,802 |
| Manufacturing costs | 24,726 | 22,571 |
| Clinical and contract research organization costs | 23,377 | 23,766 |
| Collaboration research costs | 23,679 | 20,004 |
| Property, plant and equipment | 1,543 | 789 |
| License and milestone fees | 303 | 278 |
| Professional fees | 1,993 | 1,541 |
| Other | 25,254 | 20,655 |
| Accrued expenses and other current liabilities | $ 146,791 | $ 145,406 |

**8. Leases**

The Company leases certain office and laboratory space, primarily located in Cambridge, Massachusetts and Seattle, Washington. Additionally, the Company has embedded leases at various contract manufacturing organizations in both the United States and internationally. Except as described below, there have been no material changes in lease obligations from those disclosed in Note 8 to the consolidated financial statements included in the Company's 2020 Annual Report on Form 10-K.

***Embedded operating leases***

In July 2020, the Company entered into an agreement reserving manufacturing capacity with a contract manufacturing organization. The Company concluded that this agreement contains an embedded operating lease as a controlled environment room at the facility is designated for the Company's exclusive use during the term of the agreement, with the option to sublease the space if the Company provides notice that it will not utilize it for a specified duration of time. Under the terms of the agreement, the Company will be required to pay up to $5.4 million per year in maintenance fees in addition to the cost of any services provided and may terminate this agreement with eighteen months' notice. The term of the agreement is five years, with the option to extend. The Company recorded a right-of-use asset and lease liability for this operating lease upon lease commencement in March 2021 and is recognizing rent expense on a straight-line basis throughout the remaining term of the embedded lease.

**9. Commitments and contingencies**

***Contingent consideration related to business combinations***

In June 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 equity holders 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 condensed consolidated balance sheets at fair value. Estimating the fair value of contingent consideration requires the use of significant assumptions primarily relating to probabilities of successful achievement of certain 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.

***Other funding commitments***

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. Please refer to Note 10, *Collaborative arrangements*, for further information on the Company's collaboration agreements and to Note 11, *Royalty and other revenue*, for further information on the Company's license agreements.

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. There have been no material changes in future minimum purchase commitments from those disclosed in Note 9 to the consolidated financial statements included in the Company's 2020 Annual Report on Form 10-K.

While there are no material legal proceedings the Company is aware of, the Company may become party to various claims and complaints arising in the ordinary course of business. 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. Management does not believe that any ultimate liability resulting from any of these claims will have a material adverse effect on its results of operations, financial position, or liquidity. However, management cannot give any assurance regarding the ultimate outcome of any claims, and their resolution could be material to operating results for any particular period.

The Company also indemnifies each of its directors and officers for certain events or occurrences, subject to certain limits, while the officer or director is or was serving at the Company's request in such capacity, as permitted under Delaware law and in accordance with its certificate of incorporation and by-laws. The term of the indemnification period lasts as long as a director may be subject to any proceeding arising out of acts or omissions of such director or officer in such capacity. The maximum amount of potential future indemnification is unlimited; however, the Company currently holds director and officer liability insurance. This insurance allows the transfer of risk associated with the Company's exposure and may enable it to recover a portion of any future amounts paid. The Company believes that the fair value of these indemnification obligations is minimal. Accordingly, it has not recognized any liabilities relating to these obligations.

**10. Collaborative arrangements**

To date, the Company's revenue has been primarily generated from its collaboration arrangements with BMS and Regeneron Pharmaceuticals, Inc. ("Regeneron"), each as further described below.

**Bristol-Myers Squibb**

***BMS Original Collaboration Agreement***

In March 2013, the Company entered into a Master Collaboration Agreement (the "BMS Collaboration Agreement") with Celgene (now BMS following its acquisition of Celgene in November 2019) 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, in March 2013, the Company entered into a Platform Technology Sublicense Agreement (the "Sublicense Agreement") with BMS pursuant to which the Company obtained a sublicense to certain intellectual property from BMS, originating under BMS's license from Baylor College of Medicine, for use in the collaboration.

Under the terms of the BMS Collaboration Agreement, the Company received an up-front, non-refundable, non-creditable payment of $75.0 million. 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 BMS Collaboration Agreement, or three years.

***BMS Amended Collaboration Agreement***

In June 2015, the Company and BMS amended and restated the BMS Collaboration Agreement (the "Amended BMS Collaboration Agreement"). Under the Amended BMS 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. In connection with the Amended BMS Collaboration Agreement, the Company received an up-front, non-refundable, non-creditable payment of $25.0 million to fund research and development under the collaboration. Under the terms of the Amended BMS 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 candidate.

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 Company had granted BMS an option to obtain an exclusive worldwide license to develop and commercialize such product. Following BMS'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.

***BMS Ide-cel License Agreement***

In February 2016, BMS exercised its option to obtain an exclusive worldwide license to develop and commercialize ide-cel, the first product candidate under the Amended BMS Collaboration Agreement, pursuant to an executed license agreement ("Ide-cel License Agreement") entered into by the parties in February 2016 and paid to the Company the associated $10.0 million option fee. Pursuant to the Ide-cel License Agreement, BMS 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 BMS's request, throughout commercialization, the costs of which were reimbursable by BMS in accordance with the terms of the Amended and Restated Co-Development, Co-Promote and Profit Share Agreement, as further described below. BMS was responsible for the manufacture of drug product throughout development and commercialization. Under the Ide-cel License Agreement, the Company was eligible to receive U.S. milestones of up to $85.0 million for the first indication to be addressed by ide-cel and royalties for U.S. sales of ide-cel.

Additionally, the Company was eligible to receive ex-U.S. milestones of up to $55.0 million and royalties for ex-U.S. sales of ide-cel.

***BMS Ide-cel Co-Development, Co-Promote and Profit Share Agreement***

In March 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. As a result of executing the Ide-cel CCPS, the responsibilities of the parties remained 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. BMS is responsible for the costs incurred to manufacture vector and associated payload for use outside of the U.S., plus a mark-up. As a result of electing to co-develop and co-promote ide-cel within the U.S., the milestones and royalties payable under the Ide-cel License Agreement were adjusted. Under the Ide-cel CCPS, the Company was eligible to receive a $10.0 million milestone related to the development of ide-cel in the U.S. and, for the first indication to be addressed by ide-cel, ex-U.S. regulatory and commercial milestones of up to $60.0 million. Additionally, the Company was eligible to receive royalties for ex-U.S. sales of ide-cel, but not for U.S. sales of ide-cel. Under the Ide-cel CCPS, the $10.0 million development milestone was achieved in the second quarter of 2019 and subsequently paid by BMS.

In May 2020, the First Amendment to the Amended and Restated Co-Development, Co-Promote and Profit Share Agreement (as amended, the "Amended Ide-cel CCPS") was executed, which amended the Ide-cel CCPS. Under the Amended Ide-cel CCPS, the parties will continue to share equally in all profits and losses relating to developing, commercializing and manufacturing ide-cel within the U.S. Under the Amended Ide-cel CCPS and the Amended bb21217 License Agreement, described further below, BMS was relieved of its obligations to pay the Company for future ex-U.S. milestones and royalties on ex-U.S. sales for each of ide-cel and bb21217 in exchange for an up-front, non-refundable, non-creditable payment of $200.0 million, which represents the aggregate of the probability-weighted, net present value of the future ex-U.S. milestones and royalties on ex-U.S. sales for each of ide-cel and bb21217. In connection with these amendments, BMS assumed the contract manufacturing agreements relating to ide-cel adherent lentiviral vector. Over time, BMS is assuming responsibility for manufacturing ide-cel suspension lentiviral vector outside of the U.S., with bluebird responsible for manufacturing ide-cel suspension lentiviral vector in the U.S. In addition, under the Amended Ide-cel CCPS and the Amended bb21217 License Agreement, described further below, the parties are released from future exclusivity related to BCMA-directed T cell therapies. There are no remaining milestones or royalties under the Amended Ide-cel CCPS.

Ide-cel is marketed as ABECMA in the U.S. following its approval by the FDA in March 2021 for the treatment of adult patients with relapsed or refractory multiple myeloma after four or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody. Under the Amended Ide-cel CCPS, BMS is primarily responsible for the commercialization of ABECMA and the Company has concluded BMS is the principal for purposes of recognition of product sales. Accordingly, the Company will continue to account for its share of the profits and losses relating to developing, commercializing, and manufacturing ABECMA in the U.S. as collaborative arrangement revenue (expense). There were no product sales of ABECMA during the first quarter of 2021.

***BMS bb21217 License Agreement***

In September 2017, BMS exercised its option to obtain an exclusive worldwide license to develop and commercialize bb21217, the second product candidate under the Amended BMS Collaboration Agreement, pursuant to an executed license agreement (“bb21217 License Agreement”) entered into by the parties in September 2017 and paid the Company an option fee of $15.0 million. Pursuant to the bb21217 License Agreement, BMS is responsible for development and related funding of bb21217 after the substantial completion of the ongoing phase 1 clinical trial. In 2019, the parties amended the protocol for the ongoing phase 1 clinical trial to enroll additional patients for which the Company will be reimbursed based upon an agreed-upon amount per patient. Under the bb21217 License Agreement, the Company is eligible to receive U.S. milestones of up to $85.0 million for the first indication to be addressed by bb21217 and royalties for U.S. sales of bb21217. Additionally, the Company was eligible to receive ex-U.S. milestones of up to $55.0 million and royalties for ex-U.S. sales of bb21217.

In May 2020, the Second Amended and Restated License Agreement ("Amended bb21217 License Agreement") was executed, which replaced the bb21217 License Agreement. Under the Amended bb21217 License Agreement, over time, BMS is assuming responsibility for manufacturing suspension lentiviral vector outside of the U.S., with bluebird responsible for manufacturing suspension lentiviral vector in the U.S. Under the Amended bb21217 License Agreement, expenses incurred by the Company associated with these activities are fully reimbursable by BMS at cost plus a mark-up. Throughout both development and commercialization, BMS is responsible for the manufacture of drug product. There are no remaining

milestones and royalties related to the ex-U.S. development or commercialization of bb21217 following execution of the Amended bb21217 License Agreement.

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. Under this scenario, the U.S. milestones and royalties payable under the Amended bb21217 License Agreement would be adjusted and the Company would be eligible to receive a $10.0 million development milestone payment related to the development of bb21217 within the U.S. The Company would not be eligible for royalties on U.S. sales of bb21217 under this scenario.

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, there would be no change to the U.S. milestones and royalties for U.S. sales of bb21217, as previously described above, for which the Company would be eligible to receive.

***Accounting Analysis – Amended Ide-cel CCPS and Amended bb21217 License Agreement***

In accordance with the Company's accounting policies related to variable consideration, as further described in the Company's Annual Report on Form 10-K filed with the SEC on February 23, 2021, if an arrangement includes variable consideration, including milestone payments, the Company evaluates whether the milestones are considered probable of being achieved and estimates the amount to be included in the transaction price of an arrangement. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the Company's control, such as regulatory approvals, are generally not considered probable of being achieved until those approvals are received. The Company recognizes royalty revenue and sales-based milestones at the later of (i) when the related sales occur, or (ii) when the performance obligation to which the royalty has been allocated has been satisfied.

Prior to the May 2020 amendments, the Company had constrained all variable consideration related to the remaining ex-U.S. milestones and royalties for ex-U.S. sales under the Ide-cel CCPS and bb21217 License Agreement. As a result of the May 2020 amendments, the uncertainty associated with the previously constrained variable consideration for future ex-U.S. milestones and royalties on ex-U.S. sales for each of ide-cel and bb21217 was resolved in exchange for an up-front, non-refundable, non-creditable payment of $200.0 million.

While the Ide-cel CCPS and bb21217 License Agreement were historically accounted for as separate contracts, the May 2020 amendments to each agreement were negotiated as a package with a single commercial objective and, as such, the Amended Ide-cel CCPS and Amended bb21217 License Agreement were combined for accounting purposes and treated as a single arrangement.

At the time of the May 2020 amendments, there was one remaining performance obligation under each of the Ide-cel CCPS and bb21217 License Agreement, neither of which were fully satisfied: a combined performance obligation of the ide-cel license and ide-cel vector manufacturing through development; and a combined performance obligation of the bb21217 license and bb21217 vector manufacturing through development. Subsequent to the May 2020 amendments, the Company concluded the two performance obligations are distinct from each other as BMS can benefit from each license and associated manufacturing services separately and the respective licenses and manufacturing services do not modify one another and are not interdependent. Accordingly, the Company will continue to account for each performance obligation separately.

The Company allocated the $200.0 million up-front payment received in connection with the May 2020 amendments to the remaining performance obligations described above based on the general allocation principles of Topic 606. In applying these principles, the Company considered the $200.0 million up-front payment is representative of previously constrained variable consideration that has been changed and the related uncertainties resolved by the May 2020 amendments. Moreover, the Company considered that a portion of the $200.0 million was specifically attributable to each remaining performance obligation as the amount represents the aggregate of the probability-weighted, net present value of the future ex-U.S. milestones and royalties on ex-U.S. sales for each of ide-cel and bb21217 and that each respective portion therefore (i) relates specifically to the Company's satisfaction of each of its remaining performance obligations and (ii) is representative of the amount of consideration the Company expects to be entitled to in exchange for satisfying the respective performance obligations. As such, the Company concluded that the portion of the $200.0 million up-front payment specifically attributable to each of ide-cel and

bb21217 should be allocated to each respective performance obligation pursuant to the variable consideration allocation exception.

The Amended Ide-cel CCPS and Amended bb21217 License Agreement represent a contract modification to an existing contract under Topic 606 given the May 2020 amendments resulted in a reduction in scope of the Company's responsibilities under each performance obligation described above. Specifically, the May 2020 amendments reduced the scope of the Company's obligation to provide ex-U.S. vector manufacturing services through development for both ide-cel and bb21217 as those activities will transition to BMS over time. In addition, the May 2020 amendments resulted in a change in the overall transaction price under the arrangement. The May 2020 amendments did not include any additional promised goods and services.

The remaining goods and services to be provided in order to fully satisfy each performance obligation described above are not distinct from those previously provided with respect to each performance obligation. Therefore, for each performance obligation, the remaining goods and services are part of a single performance obligation that is partially satisfied at the date of the contract modification. Accordingly, the effect that the contract modification had on the transaction price and the measure of progress toward complete satisfaction of each respective performance obligation has been recognized on a cumulative catch-up basis. The accounting for any previously satisfied performance obligations as of the contract modification date are not affected by the modification.

*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 (including those performance obligations that were completed as of the May 2020 contract modification date), and the amount of the transaction price unsatisfied as of March 31, 2021 (in thousands):

| | Ide-cel transaction price as of March 31, 2021 |
|---|---|
| Up-front non-refundable payments, option fee and milestone payments received prior to May 2020 contract modification (1) | $ 120,000 |
| Allocated portion of the up-front non-refundable payment received in connection with the Amended Ide-cel CCPS and bb21217 License Agreement (2) | 184,029 |
| Estimated variable consideration (3) | 83,900 |
| | $ 387,929 |

(1) Composed of all up-front payments and option fee and milestone payments received under the BMS Collaboration Agreement, Amended BMS Collaboration Agreement, Ide-cel License Agreement, and Ide-cel CCPS. This consideration was allocated to the performance obligations under the Ide-cel CCPS based on a relative standalone selling price (“SSP”) basis. The Company estimated the SSP of the ide-cel 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 ide-cel research and development services and ide-cel 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.

(2) This represents the portion of the $200.0 million up-front payment received under the Amended Ide-cel CCPS and Amended bb21217 License Agreement which was allocated to ide-cel.

(3) Estimated variable consideration represents the estimated reimbursement from BMS for the manufacture of vectors and associated payload through development.

| | Allocation of transaction price to performance obligations | Transaction price unsatisfied as of March 31, 2021 |
|---|---|---|
| Ide-cel research and development services | $ 40,912 | $ — |
| Ide-cel license and manufacturing services | 347,017 | — |
| | $ 387,929 | $ — |

*Ide-cel 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 research and development performance obligation was satisfied prior to the May 2020 amendments and, as a result, the accounting for this previously satisfied performance obligation was not affected by the modification. The Company recognized no revenue related to ide-cel research and development services for the three months ended March 31, 2021 and 2020.

*Ide-cel license and manufacturing services*

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

The Company recognizes revenue associated with the combined performance obligation 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 BMS, 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 collaborative arrangement revenue recognized or expense incurred for the joint ide-cel development efforts in the U.S. under ASC 808 related to the combined performance obligation for the license and vector manufacturing of ide-cel in the U.S. for the three months ended March 31, 2021, and 2020 (in thousands):

| | For the three months ended March 31, | |
|---|---|---|
| | 2021 | 2020 |
| ASC 808 ide-cel research and development expense - U.S. (1) | $ (16,825) | $ (5,080) |

(1) As noted above, the calculation of collaborative arrangement 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 ex-U.S. 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 ex-U.S. license and vector manufacturing services for the three months ended March 31, 2021, and 2020 (in thousands):

| | For the three months ended March 31, | |
|---|---|---|
| | 2021 | 2020 |
| ASC 606 ide-cel license and manufacturing revenue - ex-U.S. | $ 5,104 | $ 13,970 |

As of March 31, 2021, the Company has satisfied its performance obligation related to ide-cel license and manufacturing services and thus, the aggregate amount of the transaction price allocated to the combined performance obligation that is unsatisfied, or partially unsatisfied, is $0.0 million. As of March 31, 2021 and December 31, 2020, the Company had $0.0 million and $0.8 million, respectively, of deferred revenue associated with the combined performance obligation consisting of the ide-cel license and manufacturing services.

*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 (including those performance obligations that were completed as of the May 2020 contract modification date), and the amount of the transaction price unsatisfied as of March 31, 2021 (in thousands):

| | bb21217 transaction price as of March 31, 2021 |
|---|---|
| Up-front non-refundable payment received prior to May 2020 contract modification (1) | $ 15,000 |
| Allocated portion of the up-front non-refundable payment received in connection with the Amended Ide-cel CCPS and bb21217 License Agreement (2) | 15,971 |
| Estimated variable consideration (3) | 1,803 |
| | $ 32,774 |

(1) Composed of the up-front non-refundable payment received under the bb21217 License Agreement. This consideration was allocated to the performance obligations under the bb21217 License Agreement based on a relative SSP basis. The Company estimated the SSP of the bb21217 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 bb21217 research and development services and bb21217 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.

(2) This represents the portion of the $200.0 million up-front payment received under the Amended Ide-cel CCPS and Amended bb21217 License Agreement which was allocated to bb21217.

(3) Estimated variable consideration represents the estimated reimbursement from BMS for the manufacture of vectors and associated payload through development.

| | Allocation of transaction price to performance obligations | Transaction price unsatisfied as of March 31, 2021 |
|---|---|---|
| bb21217 research and development services | $ 5,444 | $ — |
| bb21217 license and manufacturing services | 27,330 | 27,330 |
| | $ 32,774 | $ 27,330 |

All of the remaining development, regulatory, and commercial milestones under the Amended bb21217 License Agreement are related to U.S. development, regulatory and commercialization activities and are fully constrained and are therefore 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 U.S. 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 BMS 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 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 two years through projected substantial completion of the initial phase 1 clinical study, or through September 2019. The research and development performance obligation was satisfied prior to the May 2020 amendments, and as a result, the accounting for this previously satisfied performance obligation was not affected by the modification.

The agreement to expand the bb21217 phase 1 trial that occurred in 2019 was previously treated as a separate contract for accounting purposes, because the trial expansion was for the addition of a promised good or service that is distinct and the associated consideration reflected the standalone selling price of the additional promised good or service. This contract was not affected by the May 2020 amendments and, accordingly, the accounting for this agreement was not impacted by the May 2020 amendments. The transaction price associated with these additional patients consists of variable consideration and is based upon an agreed-upon amount per patient which will be recognized as revenue as the patients are treated. The Company began fulfilling the performance obligation in the fourth quarter of 2019 and it was satisfied in the fourth quarter of 2020. In connection with treating additional patients in the phase 1 trial, the Company recognized revenue of $0.0 million and $2.4 million for the three months ended March 31, 2021 and 2020, respectively.

*bb21217 license and manufacturing services*

The Company will satisfy its performance obligation related to the manufacture of vectors and associated payload for incorporation into bb21217 through development as the bb21217 manufacturing services are performed. As of March 31, 2021, the manufacturing services for bb21217 had not yet commenced. Therefore, no amounts have been recognized for the combined performance obligation in the condensed consolidated statements of operations and comprehensive loss for the three months ended March 31, 2021 and 2020.

The aggregate amount of the transaction price allocated to the combined performance obligation, which consists of the bb21217 license and manufacturing services, is $27.3 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 condensed consolidated balance sheets. The Company had $25.8 million of remaining deferred revenue as of March 31, 2021 and as of December 31, 2020, 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 BMS receivables and contract liabilities during the three months ended March 31, 2021 (in thousands):

| | Balance at December 31, 2020 | Additions | Deductions | Balance at March 31, 2021 |
|---|---|---|---|---|
| Receivables | $ 400 | $ — | $ (400) | $ — |
| Contract liabilities: | | | | |
| Deferred revenue | $ 26,582 | $ — | $ (820) | $ 25,762 |

The decrease in the receivables balance for the three months ended March 31, 2021 is driven by amounts collected from BMS in the period.

The decrease in deferred revenue during the three months ended March 31, 2021 is driven by the release of the remaining $0.8 million of deferred revenue associated with the combined performance obligation consisting of the ide-cel license and manufacturing services.

**Regeneron**

***Regeneron Collaboration Agreement***

In August 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. In August 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 to add to or replace any of the initial targets 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 in August 2018. In August 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 collaborative arrangement 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 collaborative arrangement 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 March 31, 2021 and December 31, 2020, the Company has $29.3 million and $30.8 million, respectively, of the amount attributed to the joint research activities remaining to be recognized, which is classified as collaboration research advancement, current portion and collaboration research advancement, net of current portion on the condensed consolidated balance sheets.

The Company recognized $1.5 million and $2.3 million of collaborative arrangement revenue from the Regeneron Collaboration Agreement during the three months ended March 31, 2021 and 2020, respectively.

**11. Royalty and other revenue**

The Company has out-licensed intellectual property to various third parties. Under the terms of these agreements, the Company may be entitled to royalties and milestone payments.

In April 2017, the Company entered into a worldwide license agreement with Novartis, which is further described in the Company's Annual Report on Form 10-K filed with the SEC on February 23, 2021. Beginning in the fourth quarter of 2017, the Company began recognizing royalty revenue from sales of tisagenlecleucel under the agreement. This license agreement was terminated effective March 2021, at which point in time Novartis was no longer required to pay the Company royalty or other payments on net sales of tisagenlecleucel or any future products. Royalty revenue recognized from sales of tisagenlecleucel is included within royalty and other revenue on the condensed consolidated statement of operations and comprehensive loss.

In May 2020, the Company entered into a non-exclusive license agreement with Juno Therapeutics, Inc. ("Juno"), a wholly-owned subsidiary of BMS, related to lentiviral vector technology to develop and commercialize CD-19-directed CAR T cell therapies. Upon regulatory approval of lisocabtagene maraleucel during the first quarter of 2021, the Company received a $2.5 million milestone payment from Juno, which is included within royalty and other revenue.

The Company may also be obligated to pay third-party licensors as a result of revenue recognized under out-license agreements, which is included within cost of royalty and other revenue on the condensed consolidated statement of operations and comprehensive loss.

During the first quarter of 2021, the Company recognized an immaterial amount of product revenue related to the sale of ZYNTEGLO in the European Union and the related cost of goods sold, which is included within royalty and other revenue and cost of royalty and other revenue, respectively.

**12. Stock-based compensation**

In January 2021 and 2020, the number of shares of common stock available for issuance under the 2013 Stock Option and Incentive Plan ("2013 Plan") was increased by approximately 2.7 million and 2.2 million shares, respectively, as a result of the automatic increase provision of the 2013 Plan. As of March 31, 2021, the total number of shares of common stock available for issuance under the 2013 Plan was approximately 3.5 million.

***Stock-based compensation expense***

The Company recognized stock-based compensation expense totaling $42.5 million and $36.3 million for the three months ended March 31, 2021 and 2020, respectively. Stock-based compensation expense by award type included within the condensed consolidated statements of operations and comprehensive loss was as follows (in thousands):

| | For the three months ended March 31, | |
|---|---|---|
| | 2021 | 2020 |
| Stock options | $ 20,659 | $ 24,440 |
| Restricted stock units | 14,733 | 11,853 |
| Employee stock purchase plan and other | 7,082 | — |
| | $ 42,474 | $ 36,293 |

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

| | For the three months ended March 31, | |
|---|---|---|
| | 2021 | 2020 |
| Research and development | $ 19,868 | $ 16,269 |
| Selling, general and administrative | 22,606 | 20,024 |
| | $ 42,474 | $ 36,293 |

Stock-based compensation of $0.3 million and less than $0.1 million was capitalized into inventory for the three months ended March 31, 2021 and 2020, respectively. During the three months ended March 31, 2021, capitalized stock-based compensation of less than $0.1 million was recognized within cost of royalty and other revenue when the related product was sold. As of March 31, 2021, the Company had approximately $252.4 million of unrecognized stock-based compensation expense, which is expected to be recognized over a weighted-average period of approximately 2.2 years.

***Unrestricted stock awards***

During the first quarter of 2021, the Company granted 0.4 million unrestricted stock awards to employees as part of its 2020 annual incentive program. In addition, the Company implemented a retention program designed to incentivize and retain employees through the separation of its severe genetic disease and oncology programs, which is intended to occur by the end of 2021. Under the retention program, employees are entitled to a one-time bonus payment, consisting of both a cash payment and unrestricted stock awards, with the condition that the employee remains employed at the end of 2021. For the three months ended March 31, 2021, the Company recognized $13.3 million in expense related to this program, which includes $6.7 million in stock compensation expense related to the anticipated grants of stock.

***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, 2020 | 6,262 | $ 105.02 |
| Granted | 671 | $ 29.17 |
| Exercised | (207) | $ 5.88 |
| Canceled, forfeited, or expired | (268) | $ 110.62 |
| Outstanding at March 31, 2021 | 6,458 | $ 100.08 |
| Exercisable at March 31, 2021 | 3,829 | $ 111.17 |
| Vested and expected to vest at March 31, 2021 | 6,458 | $ 100.08 |

During the three months ended March 31, 2021, 0.2 million stock options were exercised, resulting in total proceeds to the Company of $1.2 million.

***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, 2020 | 1,495 | $ 102.34 |
| Granted | 990 | $ 29.17 |
| Vested | (294) | $ 108.85 |
| Forfeited | (118) | $ 84.63 |
| Unvested balance at March 31, 2021 | 2,073 | $ 67.48 |

***Employee stock purchase plan***

In June 2013, the Company adopted its 2013 Employee Stock Purchase Plan ("2013 ESPP"), which authorized the initial issuance of up to a total of 0.2 million shares of the Company's common stock to participating employees. During each of the three months ended March 31, 2021 and 2020, less than 0.1 million shares of common stock were issued under the 2013 ESPP.

**13. 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 expense recognized during the three months ended March 31, 2021 is due to income taxes on foreign earnings.

In March 2020, the Coronavirus Aid, Relief and Economic Security Act ("CARES Act") was enacted. This law temporarily suspends and adjusts certain law changes enacted in the Tax Cuts and Jobs Act in 2017. In December 2020, the Consolidated Appropriations Act was enacted. This law modified the employee retention credit under the CARES Act and created credit extenders for certain credits. In March 2021, the American Rescue Plan Act ("ARPA") was enacted and contained extenders to the refundable employee retention credit and provided further limitations to executive compensation effective for tax years beginning after 2026. The Company has concluded that the provisions in the CARES Act, Consolidated Appropriations Act, and ARPA have an immaterial impact on the Company's income tax expense due to its cumulative losses and full valuation allowance position.

**14. Net loss per share**

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

| | For the three months ended March 31, | |
|---|---|---|
| | 2021 | 2020 |
| Outstanding stock options | 6,458 | 6,478 |
| Restricted stock units | 2,073 | 1,585 |
| ESPP shares and other | 884 | — |
| | 9,415 | 8,063 |

**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 23, 2021.*

*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. We have built an integrated product platform with broad therapeutic potential in a variety of indications based on our lentiviral gene addition platform, gene editing and cancer immunotherapy capabilities. We believe that gene therapy for severe genetic diseases has the potential to change the way patients living with these diseases are treated by addressing the underlying genetic defect that is the cause of their disease, rather than offering treatments that only address their symptoms. Our gene therapy programs in severe genetic diseases include programs for transfusion-dependent β-thalassemia (TDT), sickle cell disease (SCD), and cerebral adrenoleukodystrophy (CALD). The Company's programs in oncology are focused on developing novel engineered cell and gene therapies for cancer, including the anti-BCMA CAR T programs for multiple myeloma under the Company's collaboration arrangement with Bristol-Myers Squibb (BMS).

We are commercializing betibeglogene autotemcel (beti-cel; formerly LentiGlobin for β-thalassemia gene therapy) as ZYNTEGLO in the European Union and began to treat patients in the commercial context in the first quarter of 2021. However, in February 2021, we temporarily suspended marketing of ZYNTEGLO in light of safety events reported in the HGB-206 clinical study of LentiGlobin for SCD, which is manufactured using the same vector as ZYNTEGLO. Additionally, the European Medicines Agency (EMA) has paused the renewal procedure for ZYNTEGLO's conditional marketing authorization while the EMA's pharmacovigilance risk assessment committee reviews the risk-benefit assessment for ZYNTEGLO and determines whether any additional pharmacovigilance measures are necessary. We are engaged with the EMA in discussions regarding our proposed development plans for beti-cel as a treatment for patients with TDT who are less than 12 years of age and for patients who have a $\beta^0/\beta^0$ genotype. We are engaged with the FDA in discussions regarding our proposed development plans for beti-cel as a treatment for patients with TDT. We currently expect to complete our BLA submission for beti-cel in mid-2021 for the treatment of all patients with TDT across all genotypes, including non-$\beta^0/\beta^0$ and $\beta^0/\beta^0$ genotypes.

Based on our discussions with the FDA, we believe that we may be able to seek accelerated approval for LentiGlobin for SCD in the United States on the basis of clinical data from Group C of our ongoing HGB-206 clinical study, and with our ongoing HGB-210 clinical study providing confirmatory data for full approval. However, in light of safety events reported in

our HGB-206 clinical study, the FDA has placed our clinical studies of LentiGlobin for SCD on clinical hold in the first quarter of 2021. We are investigating these events and plan to continue to work closely with the FDA in their review of these events. In addition, we are also engaged with the EMA in discussions regarding our proposed development plans for LentiGlobin for SCD in Europe.

In October 2020, the EMA accepted our Marketing Authorization Application in the EU for eli-cel for the treatment of patients with CALD. Based on our discussions with the FDA, we believe that we may be able to seek approval for eli-cel for the treatment of patients with CALD on the basis of our clinical data from our ongoing Starbeam study, safety data from our ongoing ALD-104 study, and the completed ALD-103 observational study. We currently expect to submit the BLA for eli-cel for the treatment of patients with CALD in mid-2021.

In collaboration with BMS, we are developing the ide-cel and bb21217 product candidates 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 as ABECMA in the United States with BMS and we have exclusively licensed to BMS the development and commercialization rights for ide-cel outside of the United States. We have exclusively licensed the development and commercialization rights for the bb21217 product candidate to BMS, with an option for us to elect to co-develop and co-promote bb21217 within the United States. In May 2020, we and BMS entered into an amendment and restatement of the ide-cel co-promotion/co-development agreement, an amendment and restatement of the bb21217 license agreement, and a non-exclusive license agreement to certain patent rights controlled by us and related to lentiviral vector technology for BMS to develop and commercialize CD19-directed CAR T cell therapies. Under the amended agreements, BMS was relieved of its obligations to pay us for future ex-U.S. milestones and royalties on ex-U.S. sales for each of ide-cel and bb21217 in exchange for an up-front, non-refundable, non-creditable payment of $200.0 million, which represents the aggregate of the probability-weighted, net present value of the future ex-U.S. milestones and royalties on ex-U.S. sales for each of ide-cel and bb21217. BMS also assumed the contract manufacturing agreements relating to ide-cel adherent lentiviral vector and over time, BMS is assuming responsibility for manufacturing ide-cel suspension lentiviral vector outside of the U.S., with bluebird responsible for manufacturing ide-cel suspension lentiviral vector in the U.S. In addition, the parties are released from future exclusivity related to BCMA-directed T cell therapies. In March 2021, BMS received marketing approval from the FDA for ide-cel, marketed as ABECMA, as a treatment of adult patients with relapsed or refractory multiple myeloma after four or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody. There were no product sales of ABECMA during the first quarter of 2021.

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 selling, general and administrative support for these operations and to protect our intellectual property. We have generated immaterial revenues from product sales. We have funded our operations primarily through the sale of common stock in our public offerings, private placements of preferred stock and warrants, and through collaborations.

As of March 31, 2021, we had cash, cash equivalents and marketable securities of approximately $1.09 billion. We have never been profitable and have incurred net losses in each year since inception. Our net loss was $205.8 million for the three months ended March 31, 2021, and our accumulated deficit was $3.11 billion as of March 31, 2021. Substantially all of our net losses resulted from costs incurred in connection with our research and development programs and from selling, 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 our clinical programs in β-thalassemia, SCD, and ALD, fund our share of the costs of clinical studies for our program in multiple myeloma in collaboration with BMS, and advance our preclinical programs into clinical development;
- increase research and development-related activities for the discovery and development of product candidates in severe genetic diseases and oncology;
- 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;

- fund activities related to the commercialization of ZYNTEGLO in multiple markets in Europe, the potential commercial launch of beti-cel in the United States, and the potential commercial launches of additional late-stage product candidates in the United States and Europe;
- fund our share of the costs of commercialization of ABECMA in collaboration with BMS; and
- incur costs related to the separation of our portfolio of programs and product in severe genetic disease and oncology into two separate, independent publicly traded companies.

In March 2021, we placed a portion our internal lentiviral vector manufacturing facility into service, while still completing qualification of the remaining portion. 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 and begin product sales, marketing, commercial 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 product, 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.

***Business update***

Beginning in late 2019, the outbreak of a novel strain of coronavirus (COVID-19) has evolved into a global pandemic. As a result, we continue to experience disruptions and increased risk in our operations and those of third parties upon whom we rely, which may materially and adversely affect our business. These include disruptions and risks related to the conduct of our clinical trials, manufacturing, and commercialization efforts, as policies at various clinical sites and federal, state, local and foreign laws, rules and regulations continue to evolve, including quarantines, travel restrictions, and direction of healthcare resources toward pandemic response efforts. The COVID-19 pandemic has impacted the timing of our ongoing clinical studies, with the result of slower patient enrollment and treatment in our clinical studies and delays in post-treatment follow up visits, the impact of which has varied by clinical study and by program. It has also affected our activities with and operations at our third party manufacturers. It is unknown how long these disruptions could continue. The COVID-19 pandemic has also impacted the timing of our regulatory interactions for marketing approval across our programs, as well as our discussions with payers for market access and reimbursement for ZYNTEGLO in Europe, due to shifting priorities of the local authorities and healthcare system. As a result of the demands upon healthcare regulatory authorities, review, inspection, and other activities related to review of regulatory submissions in drug development may be impacted, and may result in delays for an unknown period of time.

We continue to evaluate the impact of the COVID-19 global pandemic on patients, healthcare providers and our employees, as well as our operations and the operations of our business partners and healthcare communities. In response to the COVID-19 pandemic, we have implemented policies at our locations to mitigate the risk of exposure to COVID-19 by our personnel, including restrictions on the number of staff in any given research and development laboratory or manufacturing facility, a work-from-home policy applicable to the majority of our personnel, and a phased approach to bringing personnel back to our locations over time. Given the importance of supporting our patients, we are diligently working with our suppliers, healthcare providers and partners to provide patients with access to ZYNTEGLO, while taking into account regulatory, institutional, and government guidance, policies and protocols. Further, we are working with our clinical study sites to understand the duration and scope of the impact on enrollment, develop protocols to help mitigate the impact of the COVID-19 pandemic, and other activities for our ongoing clinical studies. However the ultimate impact of the COVID-19 pandemic on our business operations is highly uncertain and subject to change and will depend on future developments which are difficult to predict. In April 2021, we announced plans to reduce and reshape our workforce, primarily in Europe. This reduction and reallocation of resources is intended to enable us to focus on priority European markets and streamline global operations going forward based on our current business plans.

We expect our cash, cash equivalents and marketable securities of $1.09 billion as of March 31, 2021 will be sufficient to fund planned operations for at least the next twelve months from the date of issuance of these financial statements, though we

may pursue additional cash resources through public or private equity or debt financings or by establishing additional collaborations with other companies.

In January 2021, we announced our intent to separate our severe genetic disease and oncology programs into two separate, independent publicly traded companies, bluebird bio, Inc. and 2seventy bio, Inc., a newly-formed Delaware corporation and wholly-owned subsidiary prior to the separation. bluebird bio, Inc. intends to retain focus on our severe genetic disease programs and 2seventy bio, Inc. is expected to focus on our oncology programs. The transaction is expected to be completed in late 2021 and is anticipated to be tax-free, subject to receipt of a favorable IRS ruling.

**Financial operations overview**

***Revenues***

To date, we have generated immaterial revenues from the sale of products. Our revenues have primarily been derived from collaboration arrangements, out-licensing arrangements, research fees, and grant revenues.

To date, revenue recognized under our collaborative arrangements has been primarily generated from our collaboration arrangement with BMS. 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. These performance obligations were fully satisfied during the first quarter of 2021. 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. We entered into an agreement with BMS to co-develop and co-promote ide-cel in March 2018, which was subsequently amended in May 2020, in which both parties will share equally in U.S. costs and profits. Revenue from our collaborative arrangements is recognized as the underlying 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 ASC 606, *Revenue from Contracts with Customers* (“Topic 606” or "ASC 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 collaborative arrangement revenues as such amounts are incurred by the collaboration partner. Where amounts owed to a collaboration partner exceed our collaborative arrangement 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.

Non-refundable 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 out-license agreements, under which 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 inventory;

- 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 up-front 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;
- new manufacturing processes or protocols that we may choose to or be required to implement in the manufacture of our lentiviral vector or drug product;
- regulatory feedback on requirements for regulatory approval, as well as changing standards for regulatory approval; and
- the timing and receipt of any regulatory approvals.

We plan to continue to invest in research and development for the foreseeable future as we continue to advance the development of beti-cel, eli-cel, LentiGlobin for SCD, 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 BMS, 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 beti-cel in the treatment of patients with TDT and a non-$\beta^0/\beta^0$ genotype.
- Northstar-3 Study (HGB-212) – a multi-site, international phase 3 study to examine the safety and efficacy of beti-cel in the treatment of patients with TDT and a $\beta^0/\beta^0$ 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 – a multi-site, international phase 3 study of LentiGlobin in patients with SCD and a history of vaso-occlusive events.
- Starbeam Study (ALD-102) – a multi-site, international phase 2/3 study to examine the safety and efficacy of eli-cel in the treatment of patients with CALD.
- ALD-104 study – our multi-site, international phase 3 study to examine the safety and efficacy of eli-cel after myeloablative conditioning using busulfan and fludarabine in the treatment of patients with CALD.
- 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 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.
- KarMMa-2 – 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 – 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.
- KarMMa-4 – a multi-cohort, open-label, multicenter phase 1 study intended to determine the optimal target dose and safety of ide-cel in subjects with newly-diagnosed 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.
- We will continue to incur costs related to the manufacture of clinical study materials in support of our clinical studies.

We expect that the timing of investment in our ongoing clinical studies will reflect COVID-19 related delays in our ongoing clinical studies.

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

| | For the three months ended March 31, | |
|---|---|---|
| | 2021 | 2020 |
| | (in thousands) | |
| beti-cel | $ 13,706 | $ 20,588 |
| LentiGlobin for SCD | 13,162 | 16,293 |
| eli-cel | 13,311 | 7,813 |
| ide-cel | 29,369 | 31,162 |
| bb21217 | 2,706 | 6,071 |
| Preclinical programs | 13,690 | 17,450 |
| Total direct research and development expense | 85,944 | 99,377 |
| Employee-and contractor-related expenses | 22,583 | 15,904 |
| Stock-based compensation expense | 19,868 | 16,269 |
| Laboratory and related expenses[(1)] | 3,389 | 3,795 |
| License and other collaboration expenses[(1)] | 1,042 | 1,222 |
| Facility expenses | 20,787 | 16,752 |
| Other expenses | 865 | 804 |
| Total other research and development expenses | 68,534 | 54,746 |
| Total research and development expense | $ 154,478 | $ 154,123 |

(1) Prior to the fourth quarter of 2020, costs within these categories were disclosed in the aggregate as "platform-related expenses."

***Selling, general and administrative expenses***

Selling, 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 selling, 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.

***Cost of royalty and other revenue***

Cost of royalty and other revenue consists of expense associated with amounts owed to third party licensors as a result of revenue recognized under our out-license arrangements as well as an immaterial amount of cost of goods sold related to product revenue.

***Change in fair value of contingent consideration***

In June 2014, we acquired Precision Genome Engineering, Inc., or Pregenen. The agreement provided for up to $135.0 million in future contingent cash payments by us upon the achievement of certain preclinical, clinical and commercial milestones related to the Pregenen technology.

As of March 31, 2021, 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 $1.9 million as of March 31, 2021, which are classified within accrued expenses and other current liabilities and other non-current liabilities on our condensed consolidated balance sheets.

***Interest income, net***

For the three months ended March 31, 2021 and 2020, interest income, net consists primarily of interest income earned on investments.

***Other income (expense), net***

Other income (expense), net consists primarily of gains and losses on equity securities held by us, gains and losses on disposal of assets, and gains and losses on foreign currency.

***Critical accounting policies and estimates***

Our management's discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in accordance with generally accepted accounting principles. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, and expenses and the disclosure of contingent assets and liabilities in our financial statements. On an ongoing basis, we evaluate our estimates and judgments, including expected business and operational changes, sensitivity and volatility associated with the assumptions used in developing estimates, and whether historical trends are expected to be representative of future trends. We base our estimates on historical experience, known trends and events and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. In making estimates and judgments, management employs critical accounting policies. During the three months ended March 31, 2021, 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, 2020, which was filed with the SEC on February 23, 2021, 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 March 31, 2021 and 2020:***

| | For the three months ended March 31, | | |
|---|---|---|---|
| | 2021 | 2020 | Change |
| | (in thousands) | | |
| Revenue: | | | |
| Service revenue | $ 5,918 | $ 16,833 | $ (10,915) |
| Collaborative arrangement revenue | 1,519 | 2,302 | (783) |
| Royalty and other revenue | 5,357 | 2,728 | 2,629 |
| Total revenues | 12,794 | 21,863 | (9,069) |
| Operating expenses: | | | |
| Research and development | 154,478 | 154,123 | 355 |
| Selling, general and administrative | 86,874 | 73,248 | 13,626 |
| Cost of royalty and other revenue | 2,281 | 1,025 | 1,256 |
| Change in fair value of contingent consideration | 369 | (3,108) | 3,477 |
| Total operating expenses | 244,002 | 225,288 | 18,714 |
| Loss from operations | (231,208) | (203,425) | (27,783) |
| Interest income, net | 710 | 5,355 | (4,645) |
| Other income (expense), net | 24,756 | (4,447) | 29,203 |
| Loss before income taxes | (205,742) | (202,517) | (3,225) |
| Income tax expense | (66) | (94) | 28 |
| Net loss | $ (205,808) | $ (202,611) | $ (3,197) |

***Revenues.*** Total revenue was $12.8 million for the three months ended March 31, 2021, compared to $21.9 million for the three months ended March 31, 2020. The decrease of $9.1 million was primarily attributable to a decrease in ide-cel license and manufacturing services revenue and a decrease in revenue recognized in connection with treating patients in the bb21217 phase 1 trial under our agreements with BMS.

***Research and development expenses.*** Research and development expenses were $154.5 million for the three months ended March 31, 2021, compared to $154.1 million for the three months ended March 31, 2020. The overall increase of $0.4 million was primarily attributable to the following:

- $15.3 million of increased collaboration research funding costs, primarily due to an increase in collaboration costs incurred by BMS as a result of BMS assuming the contract manufacturing agreements relating to ide-cel adherent lentiviral vector under the May 2020 contract modification;
- $7.8 million of increased employee compensation, benefit, and other headcount related expenses, which is primarily driven by our employee retention program which commenced during the first quarter of 2021. This increase includes a $3.6 million increase in stock-based compensation expense; and
- $5.1 million of increased information technology and facility-related costs.

These increased costs were partially offset by:

- $21.3 million of decreased material production costs, primarily in clinical manufacturing due to the timing of clinical trials and in light of the clinical hold due to safety events in the HGB-206 study of LentiGlobin gene therapy for SCD;
- $3.7 million of decreased laboratory expenses and other platform costs; and
- $1.7 million of decreased clinical trials and medical research costs.

***Selling, general and administrative expenses.*** Selling, general and administrative expenses were $86.9 million for the three months ended March 31, 2021, compared to $73.2 million for the three months ended March 31, 2020. The overall increase of $13.6 million was primarily attributable to the following:

- $9.4 million of increased employee compensation, benefit, and other headcount related expenses, which is primarily driven by our employee retention program which commenced during the first quarter of 2021. This increase includes a $2.6 million increase in stock-based compensation expense; and
- $6.5 million of increased consulting fees associated with the on-going project to separate our severe genetic disease and oncology programs into two separate, independent publicly traded companies.

The increased cost was partially offset by:

- $2.3 million of decreased commercial readiness and digital marketing costs due to delays in commercialization as a result of the COVID-19 pandemic and in light of safety events in the HGB-206 study of LentiGlobin gene therapy for SCD.

***Cost of royalty and other revenue.*** Cost of royalty and other revenue was $2.3 million for the three months ended March 31, 2021, compared to $1.0 million for the three months ended March 31, 2020. The increase is attributable to increased royalty and other revenue in the same periods.

***Change in fair value of contingent consideration.*** The change in fair value of contingent consideration was primarily due to the change in significant unobservable inputs used in the fair value measurement of contingent consideration, including the probabilities of successful achievement of clinical and commercial milestones and discount rates.

***Interest income, net.*** The decrease in interest income, net was primarily related to decreased interest income earned on investments due to an overall decrease in interest rates.

***Other income (expense), net.*** The increase in other income (expense), net was primarily related to the gain recognized on equity securities.

**Liquidity and Capital Resources**

As of March 31, 2021, we had cash, cash equivalents and marketable securities of approximately $1.09 billion. We expect our cash, cash equivalents, and marketable securities will be sufficient to fund planned operations for at least the next twelve months from the date of issuance of these financial statements, though we may pursue additional cash resources through public or private equity or debt financings or by establishing additional collaborations with other companies. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to liquidity and capital preservation. As of March 31, 2021, our funds are primarily held in U.S. Treasury securities, U.S. government agency securities, equity securities, corporate bonds, commercial paper and money market accounts.

We have incurred losses and cumulative negative cash flows from operations since our inception in April 1992, and as of March 31, 2021 we had an accumulated deficit of $3.11 billion. We expect that our research and development and selling, 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. The likelihood of our long-term success must be considered in light of the expenses, difficulties, and potential delays to be encountered in the development and commercialization of new pharmaceutical products, competitive factors in the marketplace and the complex regulatory environment in which we operate. We may never achieve significant revenue or profitable operations.

***Sources of Liquidity***

*Cash Flows*

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

| | For the three months ended March 31, | |
|---|---|---|
| | 2021 | 2020 |
| | (in thousands) | |
| Net cash used in operating activities | $ (203,327) | $ (206,121) |
| Net cash provided by investing activities | 321,352 | 224,578 |
| Net cash provided by financing activities | 3,796 | 963 |
| Net increase in cash, cash equivalents and restricted cash | $ 121,821 | $ 19,420 |

*Cash Flows from Operating Activities.* The $2.8 million decrease in cash used in operating activities for the three months ended March 31, 2021 compared to the three months ended March 31, 2020 was primarily due to changes in operating assets and liabilities, partially offset by the increase in net loss for the period of $3.2 million.

*Cash Flows from Investing Activities.* The $96.8 million increase in cash provided by investing activities for the three months ended March 31, 2021 was due to a decrease in cash used to purchase marketable securities of $48.2 million, an increase in cash provided from the sales of marketable securities of $31.3 million, an increase in proceeds for maturities of marketable securities of $14.2 million, and a decrease in cash used to purchase property, plant and equipment of $3.1 million, compared to the three months ended March 31, 2020.

*Cash Flows from Financing Activities.* The $2.8 million increase in cash provided by financing activities was driven by an increase in proceeds from exercise of stock options and ESPP contributions in the three months ended March 31, 2021 compared to the three months ended March 31, 2020.

***Contractual Obligations and Commitments***

Except as discussed in Note 8, *Leases*, and Note 9, *Commitments and contingencies*, in the Notes to Condensed Consolidated Financial Statements, 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 23, 2021.

**Off-Balance Sheet Arrangements**

As of March 31, 2021, we did not have any off-balance sheet arrangements as defined in the rules and regulations of the SEC.

**Item 3. Quantitative and Qualitative Disclosures About Market Risks**

We are exposed to market risk related to changes in interest rates. As of March 31, 2021 and December 31, 2020, we had cash, cash equivalents and marketable securities of $1.09 billion and $1.27 billion, respectively, primarily invested in U.S. government agency securities and Treasuries, equity securities, corporate bonds, commercial paper and money market accounts invested in U.S. government agency securities. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are in short-term securities. Our available for sale securities are subject to interest rate risk and will fall in value if market interest rates increase. If market interest rates were to increase immediately and uniformly by 100 basis points, or one percentage point, from levels at March 31, 2021, the net fair value of our interest-sensitive marketable securities would have resulted in a hypothetical decline of approximately $2.6 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 Exchange Act of 1934 is (1) recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms and (2) accumulated and communicated to our management, including our principal executive officer and principal financial officer, to allow timely decisions regarding required disclosure.

As of March 31, 2021, 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 Exchange Act of 1934). Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our principal executive officer and principal financial officer have concluded based upon the evaluation described above that, as of March 31, 2021, our disclosure controls and procedures were effective at the reasonable assurance level.

***Changes in Internal Control over Financial Reporting***

During the quarter ended March 31, 2021 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 March 31, 2021, 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 Annual Report on Form 10-K, 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 23, 2021.*

***Our business may be materially and adversely affected by the ongoing COVID-19 pandemic. The COVID-19 pandemic has had, and will likely continue to have, an impact on various aspects of our business and that of third parties on which we rely. The extent to which the COVID-19 pandemic impacts our business will depend in part on future developments, which are uncertain and unpredictable in nature.***

In December 2019, a novel strain of coronavirus (COVID-19) was reported and in March 2020, the World Health Organization characterized COVID-19 as a pandemic. The COVID-19 pandemic, which has continued to spread, and the related adverse public health developments, including orders to shelter-in-place, travel restrictions, and the imposition of additional requirements on businesses, have adversely affected workforces, organizations, healthcare communities, economies, and financial markets globally, leading to an economic downturn and increased market volatility. It has also disrupted the normal operations of businesses across industries, including ours. As a result of the COVID-19 pandemic, we are experiencing disruptions in our operations and business, and those of third parties upon whom we rely. For instance, we have experienced disruptions in the conduct of our clinical trials, manufacturing and commercialization efforts, including the treatment of patients in the commercial context. We cannot reasonably assess or predict at this time the full extent of the negative impact that the COVID-19 pandemic and related effects may have on our business, financial condition, results of operations and cash flows. We expect to continue experiencing these disruptions in our operations and those of our third parties for an unknown period of time, as the trajectory of the COVID-19 pandemic remains uncertain and continues to evolve in the United States and globally. These impacts, which may materially and adversely affect our business, include the following:

- We are conducting a number of clinical studies across our programs in geographies which are affected by the COVID-19 pandemic. The COVID-19 pandemic has had, and will likely continue to have, an impact on various aspects of our clinical studies. Policies at various clinical sites and federal, state, local and foreign laws, rules and regulations are continuing to evolve, including through the implementation of quarantines and travel restrictions, and direction of healthcare resources toward pandemic response efforts. For instance, the availability of intensive care unit beds and related healthcare resources available to support activities unrelated to COVID-19 response have fluctuated with the incidence of severe cases of COVID-19 in the surrounding communities, and we anticipate that the availability of healthcare resources will continue to fluctuate and may become significantly constrained, with variability across geographies. The COVID-19 pandemic has disrupted the conduct of our ongoing clinical studies, with the result of slower patient enrollment and treatment as well as delays in post-treatment patient follow-up visits, the impact of which has varied by clinical study, with the most significant impacts being on our ongoing HGB-210 study for LentiGlobin for SCD. It is possible that these delays may impact the timing of our regulatory submissions. It is unknown how long these disruptions could continue. Moreover, the COVID-19 pandemic affected our commercialization activities for ZYNTEGLO in Europe, and impacted our ability to treat patients in the commercial context. In addition to the constraints on healthcare systems and resources described above, which are also applicable in the commercial treatment context, we may experience decreased patient demand for our approved product during this period of disruption and increased uncertainty because potential patients may choose not to undergo treatment, or to delay treatment, with ZYNTEGLO.

- We currently rely on third parties to manufacture, perform quality testing, and ship our lentiviral vectors and drug products for our clinical studies and support commercialization efforts. The third parties in our supply chain are subject to restrictions in operations arising from the COVID-19 pandemic, and in addition, a number of these third parties have experienced operational disruptions, which have affected activities necessary for our research, development, and commercialization efforts. These restrictions and disruptions in operations have also given rise to staffing shortages from time to time, which may result in production slowdowns and/or disruptions in delivery systems, potentially interrupting our supply chain and limiting our ability to manufacture our lentiviral vectors and drug products for our clinical studies and for commercial use. At this time, it is unknown how long these disruptions may continue, or the full extent of their impacts.
- The operations of health regulatory agencies globally have been impacted as a result of the COVID-19 pandemic. They have communicated slower response times to regulatory interactions and submissions and, in the future, may lack resources to continue to monitor our clinical studies or to engage in other activities related to review of regulatory submissions in drug development. As a result, timelines for the review of regulatory submissions for our programs have been impacted, and we may experience other delays of unknown duration in the review, inspection, and other regulatory interactions. Any de-prioritization of our clinical studies or delay in regulatory review or interaction resulting from such disruptions could materially affect the development of our product candidates. In addition, we have been engaging in reimbursement discussions with governmental health programs as part of our commercial preparation activities. It is not clear to what extent shifting priorities of the local health authorities and healthcare systems due to the COVID-19 pandemic will impact our ability to achieve market access and reimbursement for ZYNTEGLO across Europe.
- We have implemented policies at our locations to mitigate the risk of exposure to COVID-19 by our personnel, including restrictions on the number of staff in any given research and development laboratory or manufacturing facility, a work-from-home policy applicable to the majority of our personnel, and a phased approach to bringing personnel back to our locations over time. Our increased reliance on personnel working from home may negatively impact productivity, or disrupt, delay, or otherwise adversely impact our business. In addition, this could increase our cyber security risk, create data accessibility concerns, and make us more susceptible to communication disruptions, any of which could adversely impact our business operations or delay necessary interactions with local and federal regulators, ethics committees, manufacturing sites, research or clinical study sites and other important agencies and contractors. Furthermore, since the onset of the COVID-19 pandemic, our employees and contractors conducting research and development activities have been limited in the activities that they may conduct, and will continue to be subject to policies restricting access to our laboratories for an extended period of time. As a result, this could delay timely completion of preclinical activities, including completing Investigational New Drug-enabling studies or our ability to select future development candidates, and initiation of additional clinical trials for our development programs.
- The trading prices for our shares of common stock and other biopharmaceutical companies have been highly volatile as a result of the economic volatility and uncertainty caused by the COVID-19 pandemic. As a result, we may face difficulties raising capital through sales of shares of our common stock or such sales may be on unfavorable terms. In addition, a recession, depression or other sustained adverse market event resulting from the spread of the COVID-19 pandemic will materially and adversely affect our business, the value of our common stock, and our ability to operate under our operating plan and execute our strategy. Our business and operating plan have already been impacted by the COVID-19 pandemic, the associated governmental restrictions, and the resulting economic conditions, leading us to reduce and defer costs, adjust our priorities, timelines and expectations, and implement a revised operating plan in the first half of 2020 with the intention that it would enable us to advance our corporate strategy and pipeline during this period of uncertainty. Additionally, in the first half of 2021, we have announced plans to reduce and reshape our workforce, primarily in Europe.

The extent of the impacts described above will depend on numerous evolving factors that we may not be able to accurately predict, including:

- the duration, severity, and scope of the pandemic in the United States and globally;
- the effectiveness of governmental, business and individuals' protocols and actions that have been and continue to be taken in response to the pandemic;
- the impact of the pandemic on economic activity and actions taken in response;
- the effect on patients, healthcare providers and business partners;
- demand for our products, including as a result of reduced patient visits to healthcare providers, travel restrictions, social distancing, quarantines and other containment measures;

- uncertainty as to when we will be able to resume normal clinical study enrollment and patient treatment activities, particularly at clinical study sites and qualified treatment centers located in highly impacted geographies as a result of disruptions at these sites;
- the ability to obtain or deliver sufficient and timely supplies, given the disruptions to the production capabilities of our manufacturers and suppliers, particularly with respect to the priority given to the development, regulatory approval, and manufacture of COVID-19 vaccines;
- our access to the debt and equity markets on satisfactory terms, or at all;
- disruptions in regulatory oversight and actions, as a result of significant and unexpected resources expended to address the COVID-19 by regulators and industry professionals; and
- any closures of our and our partners' offices, operations and facilities.

The ultimate impact of the COVID-19 pandemic on our business operations is highly uncertain and subject to change and will depend on future developments which are difficult to predict, including the duration of the pandemic, the ultimate geographic spread of the disease, additional or modified government actions, new information that will emerge concerning the severity and impact of COVID-19 and other actions taken to contain or address its impact in the short and long term, among others. We do not yet know the full extent of potential delays or impacts on our business, our commercialization efforts, our clinical studies, our research programs, healthcare systems or the global economy, and if the ultimate impact of the COVID-19 pandemic and the resulting uncertain economic and healthcare environment is more severe than we anticipated, we may not be able to execute on our current operating plan or on our strategy. If the duration of the COVID-19 pandemic and the associated period of business and social restrictions and economic uncertainty is longer than we anticipated, our cash, cash equivalents, and marketable securities may not be sufficient to fund the activities under our operating plan for the time period that we anticipated, and we may be required to revise our operating plan further. To the extent the COVID-19 pandemic adversely affects our business and financial results, it may also have the effect of heightening many of the other risks described in this "Risk Factors" section.

**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 have limited experience as a commercial company. Consequently, 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 and any future products, we will need to successfully:

- gain regulatory acceptance for the development and commercialization of the product candidates in our pipeline;
- obtain adequate pricing and reimbursement for ZYNTEGLO and any future products in each of the jurisdictions in which we plan to commercialize approved products;
- establish and maintain, in the geographies where we hope to treat patients, relationships with qualified treatment centers who will be treating the patients who receive ZYNTEGLO and any future products;
- manage our spending as costs and expenses increase due to clinical trials, marketing approvals, and commercialization, including for any extension of marketing approval of ZYNTEGLO, and for any future products; and
- develop and maintain successful strategic alliances.

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 payers 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 payers 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 payers 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 of 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 payers 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. 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, in our HGB-206 clinical study of LentiGlobin for SCD, we have received notice of safety events of acute myeloid leukemia. If these safety events are shown to be related to the use of our lentiviral vector in the manufacture of the gene therapy or the use of myeloablative regimens prior to treatment, or if we are not able to rule out our drug product as a potential cause, the market opportunity for our gene therapies may be negatively impacted even if our gene therapies ultimately receive marketing approval.

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, we received conditional marketing approval in Europe of ZYNTEGLO for the treatment of adult and adolescent patients with TDT who do not have a $\beta^0/\beta^0$ genotype. We do not have any assurance of whether or when ZYNTEGLO may be commercially available to pediatric patients less than 12 years of age, or to patients with all genotypes of TDT, or in markets outside of Europe. 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. For example, BMS has received approval from the FDA for ABECMA as a treatment for relapsed and refractory multiple myeloma following four or more prior lines of therapy. BMS is conducting additional studies with the intention to generate data to support marketing approvals for earlier lines of therapy in multiple myeloma, but there is no assurance that such studies will be successful or be sufficient.

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 lentiviral vector and drug products present significant challenges for us, and we may not be able to produce our vector and drug products at the quality, quantities, locations or timing needed to support commercialization and our clinical programs. 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 in the commercial setting and for any clinical trials that we initiate. Currently, SAFC is the sole manufacturer of the lentiviral vector and Minaris Regenerative Medicine is the sole manufacturer of the drug product to support commercialization of ZYNTEGLO in Europe. 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 our late-stage product candidates, if they receive marketing approval. 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 with third-party manufacturers at commercially reasonable terms. If we fail to secure adequate capacity to manufacture our drug products or lentiviral vectors used in the manufacture of our drug products, we may be unable to execute on our development and commercialization plans on the timing that we expect.

The manufacture of our lentiviral vector and drug product is complex and requires significant expertise. Even with the relevant experience and expertise, manufacturers of cell therapy products often encounter difficulties in production, particularly in scaling out and validating initial production, managing the transition from clinical manufacturing to manufacturing in the commercial setting, 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 in a timely manner or with available funds problems that occur. Because of the complexity of manufacturing our product and product candidates, transitioning production of either lentiviral vector or drug products to backup or second source manufacturing, or to internal manufacturing capacity, requires a lengthy technology transfer process and may require additional significant financial expenditures. 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 commercialization of our product and any future products may be materially harmed. Furthermore, if we or our third-party manufacturers are unable to produce our lentiviral vectors or our drug product in quantities, in accordance with regulatory requirements, including 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 used as starting material for our drug product have a limited window of stability following procurement from a patient, 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 strategy is to engage apheresis and transplant 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 train and conduct quality assessments of each center as part of engagement. These qualified treatment centers are the first and last points on our complex supply chain to reach patients in the commercial setting. We may not be able to 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 third-party 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 are required 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 limited sales and 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.***

We have limited 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 further develop these capabilities. We may need to 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 has required, and will continue to require, substantial investment in commercial capabilities. We are competing with companies that currently have extensive and well-funded marketing and sales operations. Without significant commercial experience as a company 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 lifetime 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 payers is essential for most patients to be able to afford expensive treatments, such as gene therapy products. 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 payers. In addition, because our therapies represent new treatment approaches, the estimation of potential revenues will be complex.

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 payers 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, the 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 or recognize from the sale of the product in that particular country. For instance, although we have received conditional marketing approval for ZYNTEGLO in the European Union and the United Kingdom, we were not able to reach an agreement on an acceptable price for ZYNTEGLO in Germany and are still in the process of negotiating pricing and reimbursement approval in other jurisdictions where we are commercializing ZYNTEGLO. There is no assurance that the approved prices or reimbursement levels that payers will be willing to pay will be acceptable to us.

Moreover, increasing efforts by governmental and third-party payers, 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. Net prices for drugs may be reduced by mandatory discounts or rebates required by government or private payers and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. 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. 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.

In addition, the administration of autologous drug products requires procedures for the collection of HSCs or T cells 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.

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 payers, there is no assurance that there will be widespread adoption of these payment models by payers. These payment models may not be sufficient for payers 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, or our ability to recognize revenue from product sales may be delayed. 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. We plan on commercializing our product candidates in the United States once approved, and will be subject to price reporting obligations set forth by CMS. To the extent reimbursement for our product or any future products by U.S. governmental payers is subject to outcomes-based arrangements, the increased complexity increases the risk that CMS may disagree with the assumptions and judgments that we use in our price reporting calculations, which may result in significant fines and liability.

Collectively, these factors could affect our ability to successfully commercialize our product and any future products and generate or recognize 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. If our product candidates are not approved in a timely manner or at all for any reason, our business prospects, results of operations, and financial condition would be adversely affected.***

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, and 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.

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. 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. 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 ZYNTEGLO suggested that patients with TDT who do not have a $\beta^0/\beta^0$ genotype experienced better outcomes from treatment than patients with TDT who have a $\beta^0/\beta^0$ genotype. Consequently, we received conditional approval in the European Union initially for the treatment of patients with TDT who do not have a $\beta^0/\beta^0$ genotype. In order to support an application for marketing approval of ZYNTEGLO in patients with TDT who have a $\beta^0/\beta^0$ genotype, we are conducting the HGB-212 study, but we do not know if or when ZYNTEGLO may be commercially available to all genotypes of TDT or types of β-thalassemia in Europe.

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, changes in regulatory agency policy, or additional regulatory feedback or guidance during the period of product development, clinical studies and the review process. The field of cell and gene therapy is evolving, and as more products are reviewed by regulatory authorities, regulatory authorities may impose additional requirements that were not previously anticipated. 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. Because beti-cel has been granted the FDA's Fast Track and Breakthrough Therapy designations, we are engaged in discussions with the FDA regarding the development plans for beti-cel to enable a submission of a BLA prior to the completion of our ongoing studies. Based on these discussions, we believe the results from our ongoing Northstar-2 and Northstar-3 clinical studies, together with data from our Northstar study, the LTF-303 long-term follow up protocol, and completed HGB-205 study, could be sufficient to form the basis for a BLA submission for beti-cel to treat patients with TDT. 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 of a BLA for beti-cel for the treatment of patients with TDT. Furthermore, we are required to submit data relating to certain release assays designed to confirm the quality, purity and strength (including potency) of beti-cel as a condition for completing the BLA submission, which has the potential for further delaying the completion of our BLA submission, with the potential consequence of delaying any approval and commercial launch of beti-cel in the United States. In addition, in February 2021 we temporarily suspended marketing of ZYNTEGLO and the EMA has paused the renewal procedure for ZYNTEGLO's conditional marketing authorization while the EMA's pharmacovigilance risk assessment committee reviews the risk-benefit assessment for ZYNTEGLO and determines whether any additional pharmacovigilance measures are necessary, in light of safety events arising from our HGB-206 clinical study of LentiGlobin gene therapy for SCD. We cannot make any assurances as to what the EMA may require for ZYNTEGLO to return to the market in Europe, or what the FDA may require for approval of beti-cel in the United States.

In September 2020, we submitted a MAA to the EMA to seek approval in Europe for eli-cel for the treatment of patients with CALD. Based on our discussions with the FDA, we believe that we may be able to seek approval for eli-cel for the treatment of patients with CALD in the United States on the basis of safety and efficacy data from our ongoing Starbeam study, safety data from our ongoing ALD-104 study, and the completed ALD-103 observational study. Whether eli-cel 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 eli-cel is eligible for approval.

Based on our discussions with the FDA, we believe that we may be able to seek accelerated approval for our LentiGlobin for SCD product candidate in the United States on the basis of clinical data from Group C of our ongoing HGB-206 clinical study, with our ongoing HGB-210 clinical study providing confirmatory data for full approval. We cannot be certain that data from our HGB-206 or HGB-210 clinical studies will be sufficiently robust from a safety and/or efficacy perspective to support either accelerated approval or full approval. We are also engaged with the EMA in discussions regarding our proposed development plans for LentiGlobin for SCD in Europe. Our development plan in the United States is contingent upon LentiGlobin for SCD demonstrating complete resolution of severe vaso-occlusive events, with globin response as a key secondary endpoint, and an acceptable safety profile in the study participants. 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 our discussions with FDA regarding the transition of manufacturing to the commercial setting from the clinical context, we are finalizing our plans for validating our commercial manufacturing processes and for providing the FDA with the comparability data that it requires. The FDA may not agree with these plans, or may require additional validation or comparability data as a condition for completing the BLA submission and filing. Any of these may result in delays in our ability to submit a BLA for regulatory approval of LentiGlobin for SCD. Furthermore, in light of reported safety events in our HGB-206 clinical study, the FDA has placed our clinical studies of LentiGlobin for SCD on clinical hold. We are investigating these events and plan to continue to work closely with the FDA in their review of these events, and we cannot make any assurances as to what the FDA may require to lift the clinical hold, if

ever. Taken together, these factors are likely to result in delays in our ability to submit a BLA for regulatory approval of LentiGlobin for 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 HGB-210 study will be sufficient to form the basis for an initial MAA submission in Europe for the treatment of patients with SCD.

If our product candidates are ultimately not approved for any reason, our business, prospects, results of operations and financial condition would be adversely affected.

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

The manufacturing processes for our lentiviral vectors and our drug products are complex. We explore improvements to our manufacturing processes on a continual basis, as we evaluate clinical and manufacturing data and based on discussions with regulatory authorities. In some circumstances, changes in the manufacturing process may require us to perform additional comparability studies, collect additional data from patients, submit additional regulatory filings, or comply with additional requirements, which may lead to delays in our clinical development and commercialization plans. For instance, following the conditional approval of ZYNTEGLO by the European Commission, we continued to refine our commercial drug product manufacturing process to narrow some of the manufacturing process parameters and to tighten the range of commercial drug product release specifications, based on an ongoing discussion with the EMA and evolving clinical data. Implementing these changes to the ZYNTEGLO commercial manufacturing process had the effect of delaying our ability to treat the first patient in the commercial context in Europe. In LentiGlobin for SCD, we plan to seek regulatory approval for drug product utilizing lentiviral vector manufactured using the scalable suspension manufacturing process, rather than the adherent manufacturing process. The FDA and EMA may not agree with our proposed plans for demonstrating the comparability of the two processes, and may require us to conduct additional studies, collect additional data, develop additional assays, or modify release specifications, which may delay our ability to submit a BLA or MAA for regulatory approval of LentiGlobin for SCD. Over time, we also intend to transition the lentiviral vector manufacturing process for ZYNTEGLO in the European Union, and beti-cel in the United States, to the suspension manufacturing process, and the timing in which we are able to make the transition will be dependent upon reaching agreement with regulatory authorities, which may require us to conduct additional studies, collect additional data, develop additional assays, or modify release specifications.

***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 the development of gene therapies for severe genetic diseases and cancer, and both fields are competitive and rapidly changing. 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, more experienced manufacturing capabilities, or more established commercial infrastructure. 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 of 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 platform technologies, including our gene editing technology and cancer immunotherapy capabilities. 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.

***Insertional oncogenesis is a potential risk of gene therapies using viral vectors. If the vectors for our product or product candidates are shown to lead to insertional oncogenesis, or if there are other safety events that require us to halt or delay further clinical development of our product candidates, or to suspend or cease the commercialization of our approved product, the commercial potential of our product and any future products may be materially and negatively impacted.***

A potentially significant risk in any gene therapy product using 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, known as insertional oncogenesis. In published studies, lentiviral vectors have demonstrated an improved safety profile over gamma-retroviral vectors used in early gene therapy studies, which we believe is due to a number of factors including the tendency of the lentiviral vectors to integrate within genes rather than in areas that control gene expression, as well as their lack of strong viral enhancers. Notwithstanding the historical data regarding the potential safety improvements of lentiviral vectors, insertional oncogenesis leading to leukemia or lymphoma remains a risk. For instance, vector insertion into or near genes previously associated with cancer in the general population and clonal predominance without malignancy has been detected in some patients treated with eli-cel. We cannot make any assurances that insertional oncogenesis leading to leukemia or lymphoma will not occur in any of our 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. Furthermore, treatment with our gene therapy product and product candidates involve chemotherapy or myeloablative treatments which can cause side effects or adverse events that may impact the perception of the potential benefits of our product and any future products. For instance, myelodysplastic syndrome leading to acute myeloid leukemia is a known risk of certain myeloablative regimens. Additionally, our product and any future products, or procedures associated with the administration of our product or with the collection of patients' cells, could potentially cause other adverse events that have not yet been predicted. The inclusion of patients with significant underlying medical problems 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. Any of these events could impair our ability to develop or commercialize our product and any future products, and the commercial potential of our products may be materially and negatively impacted.

In February 2021, safety events reported in our HGB-206 clinical study resulted in the FDA placing our clinical studies of LentiGlobin for SCD and beti-cel on clinical hold, and caused us to temporarily suspend marketing of ZYNTEGLO in Europe. Investigation into the causes of any safety events, including these safety events, may not be conclusive or may not be definitive in eliminating the lentiviral vector or the drug product as a cause. For instance, it is possible that myelodysplastic syndrome and acute myeloid leukemia was caused by the LentiGlobin for SCD drug product, in combination with underlying sickle cell disease, transplant procedure, and stress on the bone marrow following drug product infusion. Even if a product such as LentiGlobin for SCD or beti-cel is ultimately approved, such safety events may result in the product being removed from the market or its market opportunity being significantly reduced. Other patients receiving our product or product candidates may develop leukemia, lymphoma, or myelodysplastic syndrome in the future, which may negatively impact the commercial prospects of our product or product candidates.

***Patients receiving T cell-based immunotherapies, such as ABECMA 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.***

ABECMA 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 ABECMA 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 ABECMA 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 BMS for the successful commercialization and further development of ABECMA. If BMS does not devote sufficient resources to the commercialization or further development of ABECMA, 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, marketed as ABECMA, in the United States with BMS under our amended and restated co-development and co-promotion agreement with BMS, or the Ide-cel CCPS. Under the Ide-cel CCPS, we and BMS share the obligation to develop and commercialize ABECMA in the United States. In addition, we have exclusively licensed to BMS 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 BMS. With respect to bb21217, we are responsible for completing the ongoing CRB-402 study, but BMS 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 BMS will share the obligation to develop and commercialize bb21217 in the United States.

In our partnership with BMS, BMS is obligated to use commercially reasonable efforts to develop and commercialize ABECMA and bb21217. BMS may determine however, that it is commercially reasonable to de-prioritize or discontinue the development of ABECMA and bb21217. These decisions may occur for many reasons, including internal business reasons (including due to the existence of other BMS programs that are potentially competitive with ABECMA 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 BMS, BMS has certain decision-making rights in determining the development and commercialization plans and activities for the programs. We may disagree with BMS about the development strategy it employs, but we will have limited rights to impose our development strategy on BMS. Similarly, BMS may decide to seek marketing approval for, and limit commercialization of, ABECMA or bb21217 to narrower indications than we would pursue. More broadly, if BMS elects to discontinue the development of ABECMA or bb21217, we may be unable to advance the product candidate ourselves.

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

- BMS 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 that we may receive under such partnership will depend on, among other things, BMS’s efforts, allocation of resources and successful development and commercialization of ABECMA.
- BMS may develop and commercialize, either alone or with others, products that are similar to or competitive with ABECMA. For example, BMS is currently commercializing a number of its existing products, including lenalidomide and pomalidomide, for certain patients with relapsed and refractory multiple myeloma and is also developing another CAR-T product candidate targeting BCMA that it obtained through its acquisition of Juno Therapeutics, Inc.
- BMS 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.
- BMS 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.
- BMS may not comply with all applicable regulatory requirements, or may fail to report safety data in accordance with all applicable regulatory requirements.
- If BMS 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 BMS due to BMS's breach or BMS terminated the agreement without cause, the development and commercialization of ABECMA 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.

BMS 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 BMS'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 re-prioritize BMS's development programs such that BMS ceases to diligently pursue the development of our programs and/or cause the respective collaboration with us to terminate.

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

We do not independently conduct all aspects of our lentiviral vector production, drug product manufacturing, and testing. We currently rely, and expect to continue to rely, on third parties with respect to these items, including manufacturing and testing in the commercial context.

Our reliance on these third parties for manufacturing, testing, research and development activities 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, whether due to the impacts of COVID-19 or otherwise, 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 products, 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 $205.8 million for the three months ended March 31, 2021. As of March 31, 2021, we had an accumulated deficit of $3.11 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 have not generated material revenues from the sale of ZYNTEGLO in the European Union, and we do not expect to generate meaningful product revenues until our conditional marketing approval for ZYNTEGLO is renewed. 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 payers and adequate market share for our product and any future products in those markets. We are dependent upon the commercialization efforts of BMS for any collaboration revenue from sales of ABECMA through our profit-loss sharing arrangement.

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 BMS;
- 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 not generated material 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 payers;
- 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 material 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 our programs in β-thalassemia, SCD, CALD, and 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 and progress our commercialization efforts.

As of March 31, 2021, our cash, cash equivalents and marketable securities were $1.09 billion. In response to the ongoing COVID-19 pandemic and the associated economic conditions, we revised our operating plan to execute on our strategy during this period of uncertainty. Based on our current business plan, we expect our cash, cash equivalents and marketable securities will be sufficient to fund planned operations for at least the next twelve months from the date of issuance of these financial statements. Our current business plan assumes continued rigorous prioritization and focus on our expenses, real estate optimization, and exploration of additional sources of funding to further strengthen our financial position. However, our operating plan may change further as a result of the COVID-19 pandemic and the surrounding economic conditions, as well as many other factors currently unknown to us. In addition, we may seek additional funds through public or private equity or debt financings, government or other third-party funding, marketing and distribution arrangements or other collaborations, strategic alliances and licensing arrangements or a combination of these approaches, during this period. 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 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, or if revenues from collaboration arrangements or product sales are less than we have projected, 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, 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. 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 revenue 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 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. As we begin to generate product sales of ZYNTEGLO in Europe, we expect that our product sales will be difficult to predict from period to period, given the absence of historical sales data. This uncertainty is heightened by the unpredictable scope of the impact of the COVID-19 pandemic, which has adversely affected the operations of third parties upon which we rely in our commercialization efforts, patient access to hospitals, physicians' offices, clinics and other administration sites, and global economic conditions, as well as caused a re-prioritization of healthcare services.

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, the achievement of milestones under our existing collaboration and license agreements, and profit-sharing arrangements for any approved products, including, in particular, our collaborations with BMS 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, further exacerbated by the impacts of the ongoing COVID-19 pandemic on healthcare systems and economic conditions, will likely 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 ZYNTEGLO 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, including as a result of the COVID-19 pandemic;
- 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, including as a result of the United Kingdom's exit from the European Union, or Brexit.

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, preclinical research and clinical development into a company that develops and commercializes multiple drugs with an international presence, we may 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 have launched ZYNTEGLO in Europe, 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 may expand our operations in the United States and Europe. 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, regulatory authorities 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. In February 2021, we temporarily suspended marketing of ZYNTEGLO and the EMA has paused the renewal procedure for ZYNTEGLO's conditional marketing authorization while the EMA's pharmacovigilance risk assessment committee reviews the risk-benefit assessment for ZYNTEGLO and determines whether any additional pharmacovigilance measures are necessary. 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 described in more detail under *"Item 1. Business--Government regulation"* in our Annual Report. These include the federal Anti-Kickback Statute, federal civil and criminal false claims laws and civil monetary penalty laws (including False Claims Laws), HIPAA, transparency requirements created under the Affordable Care Act, as well as analogous state and foreign laws.

These laws apply to, among other things, our sales, marketing and educational programs. 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 addition, we may be subject to patient privacy laws by both the federal government and the states in which we conduct our business. For example, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, imposes requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions In addition to HIPAA, as amended by HITECH, and their respective implementing regulations, California recently enacted the California Consumer Privacy Act, or CCPA, which creates new individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA will require covered companies to provide certain disclosures to consumers about its data collection, use and sharing practices, and to provide affected California residents with ways to opt-out of certain sales or transfers of personal information. The CCPA went into effect on January 1, 2020, and the California Attorney General will commence enforcement actions against violators beginning July 1, 2020. While there is currently an exception for protected health information that is subject to HIPAA, as currently written, the CCPA may impact our business activities. The California Attorney General has proposed draft regulations, which have not been finalized to date, that may further impact our business activities if they are adopted. The uncertainty surrounding the implementation of CCPA exemplifies the vulnerability of our business to the evolving regulatory environment related to personal data and protected health information.

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. Further, Brexit has created uncertainty with regard to data protection regulation in the United Kingdom. In particular, it is unclear how data transfers to and from the United Kingdom will be regulated.

***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, expanded the types of entities eligible for the 340B drug discount program, and a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% (increased pursuant to the Bipartisan Budget Act of 2018, effective as of 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer’s outpatient drugs to be covered under Medicare Part D.

Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the Affordable Care Act, and we expect there will be additional challenges and amendments to the Affordable Care Act in the future. Various portions of the Affordable Care Act are currently undergoing legal and constitutional challenges in the Fifth Circuit Court and the United States Supreme Court. It is unclear whether the Affordable Care Act will be overturned, repealed, replaced, or further amended. We cannot predict what effect further changes to the Affordable Care Act would have on 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 2029 through subsequent legislative amendments. 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 years 2019 and 2020 contain further drug price control measures that could be enacted during the 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. 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 payers.

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.

***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. In addition, we rely on third-party service providers for management of the manufacture and delivery of drug product to patients in the commercial context, including for chain of identity and chain of custody. 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. These events 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 the proposed separation of our business**

***The proposed separation of our business into two independent, publicly traded companies is subject to various risks and uncertainties and may not be completed on the terms or timeline currently contemplated, if at all, and will involve significant time, effort and expense, which could harm our business, results of operations and financial condition.***

In January 2021, we announced our intent to separate our oncology programs from our severe genetic disease programs, resulting in two independent, publicly traded companies, bluebird bio and 2seventy bio. Following the separation, bluebird bio is expected to focus on the development and commercialization of therapies in β-thalassemia, cerebral adrenoleukodystrophy and sickle cell disease in the United States and Europe. 2seventy bio is expected to focus on the research and development efforts in our oncology pipeline, as well as supporting the commercialization of ABECMA and development of the bb21217 product candidate through the BMS collaboration.

The separation is expected to be completed by the end of 2021, subject to receipt of a favorable IRS ruling and the satisfaction of certain conditions. Unexpected developments, including adverse market conditions or tax consequences or delays or difficulties effecting the proposed separation, could delay, prevent or otherwise adversely impact the anticipated benefits from the proposed separation. Consummation of the separation also will require final approval from our board of directors. We may not complete the separation on the terms or on the timeline that we announced, or may, for any or no reason and at any time until the proposed separation is complete, abandon the separation or modify or change its terms. Any of the foregoing may result in our not achieving the operational, financial, strategic and other benefits we anticipate realizing as a result of the separation, and in each case, our business, results of operations and financial condition could be adversely affected.

We will incur significant expenses in connection with the proposed separation, and such costs and expenses may be greater than we anticipate. In addition, completion of the separation will require a significant amount of management time and effort, which may disrupt our business or otherwise divert management’s attention from other aspects of our business, including strategic initiatives, discovery, development and commercialization efforts and relationships with our partners and other third parties. Any of the foregoing could adversely affect our business, results of operations and financial condition.

***We may fail to realize some or all of the anticipated benefits of the proposed separation.***

Even if the separation is completed, the anticipated operational, financial, strategic and other benefits of the separation may not be achieved. The combined value of the common stock of the two publicly-traded companies may not be equal to or greater than what the value of our common stock would have been had the separation not occurred. The combined value of the common stock of the two companies could be lower than anticipated for a variety of reasons, including the failure of either company to operate and compete effectively as an independent company. The common stock price of each company may experience periods of extreme volatility. In addition, the two independent companies will be smaller and less diversified, with a narrower business focus, and may be more vulnerable to changing market conditions. The separation also presents a number of significant risks to our internal processes, including the failure to maintain an adequate control environment due to changes to our infrastructure technology systems and financial reporting processes.

***If the distribution of shares of 2seventy bio, together with certain related transactions, does not qualify as a transaction that is generally tax-free for U.S. federal income tax purposes, our stockholders and we could be subject to significant tax liabilities.***

In connection with the distribution of shares in of 2seventy bio, we may seek a private letter ruling from the IRS (the "IRS Ruling") and an opinion from our tax advisor (the "Tax Opinion") to the effect that, among other things, the distribution of shares in 2seventy bio, together with certain related transactions, will generally qualify as tax-free for U.S. federal income tax purposes under Sections 368(a)(1)(D) and 355 of the U.S. Internal Revenue Code of 1986, as amended (the “Code”). The IRS Ruling and the Tax Opinion will rely on certain facts, assumptions, representations, and undertakings from us and 2seventy bio, including those regarding the past and future conduct of the companies' respective businesses and other matters. Notwithstanding the IRS Ruling and the Tax Opinion, the IRS could determine that the distribution or any such related transaction is taxable if it determines that any of these facts, assumptions, representations or undertakings are not correct or have been violated, or that the distribution should be taxable for other reasons, including if the IRS were to disagree with the

conclusions in the Tax Opinion. The Tax Opinion will not be binding on the IRS or the courts. Accordingly, the IRS or the courts may challenge the conclusions stated in the Tax Opinion and such challenge could prevail.

If the distribution were determined to be taxable for U.S. federal income tax purposes, our stockholders that receive shares of 2seventy bio in the distribution would be treated as having received a distribution of property in an amount equal to the fair value of such 2seventy bio shares on the distribution date and could incur significant income tax liabilities. Such distribution would be taxable to our stockholders as a dividend to the extent of our current and accumulated earnings and profits. Any amount that exceeded our current and accumulated earnings and profits would be treated first as a non-taxable return of capital to the extent of the relevant stockholder's tax basis in its shares of stock, with any remaining amount being taxed as capital gain. We would recognize a taxable gain in an amount equal to the excess, if any, of the fair market value of the shares of 2seventy bio common stock held by us on the distribution date over our tax basis in such shares.

**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, and 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 part*e 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 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 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 has been volatile in the past, and may continue to be volatile for the foreseeable future. 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 regulatory authority'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 payers;
- failure to obtain market acceptance and adoption of ZYNTEGLO or any other potential product following marketing approval;
- developments concerning the proposed separation of our programs into two independent, publicly-traded companies;
- 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 are subject to securities class action litigation, which may result in substantial costs and a diversion of management's attention and resources, which could harm our business.***

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities, and on February 12, 2021, a class action complaint was filed in the United States District Court for the Eastern District of New York, *Leung v. bluebird bio, Inc., et. al.*, Case No. 1:21-cv-00777, by a purported stockholder against us and certain of our officers, and we may face additional securities class action litigation in the future. This risk is especially relevant for us because biotechnology and pharmaceutical companies have experienced significant stock price volatility in recent years, and we expect to experience continued stock price volatility. Defending against the current litigation and any future litigation 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 and prior to our initial public offering in 2013, which we believe have resulted in a change in control as defined by IRC Section 382. We completed a study through September 2019 confirming no ownership changes have occurred since our initial public offering in 2013. 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 cash 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.

***Changes in tax law could adversely affect our business and financial condition.***

The rules dealing with U.S. federal, state, and local income taxation are constantly under review by persons involved in the legislative process and by the IRS and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. For example, on March 27, 2020, President Trump signed into law the "Coronavirus Aid, Relief, and Economic Security Act" or the CARES Act, which included certain changes in tax law intended to stimulate the U.S. economy in light of the COVID-19 pandemic, including temporary beneficial changes to the treatment of net operating losses, interest deductibility limitations and payroll tax matters. On December 27, 2020, President Trump signed into law the "Consolidated Appropriations Act", which included additional stimulus relief for the COVID-19 pandemic in the form of modifications to the refundable employee retention credit under the CARES Act and credit extenders, and spending bill for the 2021 fiscal year. On March 11, 2021, President Biden signed into law the "American Rescue Plan Act" ("ARPA"), which included extenders to the refundable employee retention credit under the CARES Act and limitations to executive compensation effective for tax years beginning after 2026. Future changes in tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations. We urge investors to consult with their legal and tax advisers regarding the implications of potential changes in tax laws on an investment in 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 none of our officers 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 | 10-K | 001-35966 | 3.2 | February 23, 2021 |
| 4.1 | Specimen Common Stock Certificate | S-1/A | 333-188605 | 4.1 | June 4, 2013 |
| 10.1# | Second Amended and Restated 2002 Employee, Director and Consultant Stock Plan, as amended, and forms of award agreement thereunder | S-1 | 333-188605 | 10.1 | May 14, 2013 |
| 10.2# | 2010 Stock Option and Grant Plan, as amended, and forms of award agreement thereunder | S-1 | 333-188605 | 10.2 | May 14, 2013 |
| 10.3# | 2013 Stock Option and Incentive Plan and forms of award agreement thereunder | S-1/A | 333-188605 | 10.3 | June 4, 2013 |
| 10.4 | Form of Indemnification Agreement between the Registrant and each of its Executive Officers and Directors | S-1 | 333-188605 | 10.4 | May 14, 2013 |
| 10.5† | Patent License Agreement, dated December 11, 1996, by and between the Registrant (formerly known as Genetix Pharmaceuticals Inc., successor-in-interest to Innogene Pharmaceuticals, Inc.) and Massachusetts Institute of Technology, as amended | S-1 | 333-188605 | 10.6 | May 14, 2013 |
| 10.6† | Fourth Amendment to Patent License Agreement, dated October 28, 2016, by and between the Registrant and Massachusetts Institute of Technology | 10-K | 001-35966 | 10.7 | February 22, 2017 |
| 10.7† | Patent and Know-How License Agreement No. 07554F30, dated May 14, 2009, by and between the Registrant (formerly known as Genetix Pharmaceuticals Inc.) and INSERM-TRANSFERT, as amended | S-1 | 333-188605 | 10.7 | May 14, 2013 |
| 10.8† | License Agreement, dated September 13, 2011, by and between the Registrant and Institut Pasteur, as amended | S-1 | 333-188605 | 10.8 | May 14, 2013 |
| 10.9† | Amendment No. 3 to License Agreement, dated September 10, 2013, by and between the Registrant and Institut Pasteur | 10-Q | 001-35966 | 10.2 | November 14, 2013 |
| 10.10† | Amendment No. 4 to License Agreement, dated April 1, 2015, by and between the Registrant and Institut Pasteur | 10-Q | 001-35966 | 10.10 | May 6, 2015 |
| 10.11† | License Agreement, dated December 7, 2011, by and between the Registrant and Research Development Foundation | S-1 | 333-188605 | 10.9 | May 14, 2013 |
| 10.12† | Novation Agreement, dated April 2, 2012, by and between the Registrant and The Board of Trustees of the Leland Stanford Junior University | S-1 | 333-188605 | 10.10 | May 14, 2013 |
| 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 |

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| 10.18†† | Second Amended and Restated License Agreement by and between the Registrant and Celgene Corporation and Celgene European Investment Company LLC, dated May 8, 2020 | 10-Q | 001-35966 | 10.18 | August 5, 2020 |
| 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†† | First Amendment to 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 May 8, 2020 | 10-Q | 001-35966 | 10.20 | August 5, 2020 |
| 10.21† | License Agreement by and between the Registrant and Biogen Idec MA Inc., dated August 13, 2014 | 10-Q/A | 001-35966 | 10.17 | November 2, 2016 |
| 10.22† | Letter Agreement by and between the Registrant and Biogen MA Inc., dated September 29, 2017 | 10-Q | 001-35966 | 10.21 | November 1, 2017 |
| 10.23† | Exclusive Patent License Agreement by and between the Registrant and the National Institutes of Health, dated August 31, 2015 | 10-Q/A | 001-35966 | 10.18 | November 2, 2016 |
| 10.24† | License Agreement, dated December 23, 2015, by and between the Registrant and SIRION Biotech GmbH | 10-K | 001-35966 | 10.23 | February 21, 2019 |
| 10.25†† | Toll Manufacturing and Service Agreement, dated November 18, 2016 by and between the Registrant and Minaris Regenerative Medicine GmbH (formerly APCETH Biopharma GmbH), as amended | 10-Q | 001-35966 | 10.24 | August 1, 2019 |
| 10.26†† | Amendment Agreement No. 3 to the Toll Manufacturing and Service Agreement by and between bluebird bio (Switzerland) GmbH and Minaris Regenerative Medicine GmbH (formerly Apceth Biopharma GmbH) | 8-K | 001-35966 | 10.1 | March 12, 2020 |
| 10.27†† | Clinical and Commercial Supply Agreement – Viral Vector Product, dated November 27, 2017, by and between the Registrant and SAFC Carlsbad, Inc., as amended | 10-Q | 001-35966 | 10.25 | August 1, 2019 |
| 10.28†† | Amendment No. 2 to Clinical and Commercial Supply Agreement Viral Vector Product by and between bluebird bio (Switzerland) GmbH and SAFC Carlsbad, Inc. | 8-K | 001-35966 | 10.1 | January 21, 2020 |
| 10.29 | Amendment No. 3 to Clinical and Commercial Supply Agreement Viral Vector Product by and between bluebird bio (Switzerland) GmbH and SAFC Carlsbad, Inc. | 10-K | 001-35966 | 10.28 | February 23, 2021 |
| 10.30# | Amended and Restated Employment Agreement by and between the Registrant and Nick Leschly | S-1/A | 333-188605 | 10.12 | June 4, 2013 |
| 10.31# | Amended and Restated Employment Agreement by and between the Registrant and Jeffrey T. Walsh | S-1/A | 333-188605 | 10.13 | June 4, 2013 |
| 10.32# | 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 |
| 10.33# | Employment Agreement, dated February 3, 2014, by and between the Registrant and Jason F. Cole | 10-Q | 001-35966 | 10.18 | May 13, 2014 |
| 10.34# | 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 |
| 10.35# | 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 |
| 10.36# | Employment Agreement, dated May 30, 2015, by and between the Registrant and Philip D. Gregory | 10-Q | 001-35966 | 10.21 | August 7, 2015 |
| 10.37# | 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 |
| 10.38# | 2013 Employee Stock Purchase Plan | S-1/A | 333-188605 | 10.17 | June 4, 2013 |
| 10.39# | First Amendment of the Bluebird Bio, Inc. 2013 Employee Stock Purchase Plan | 10-K | 001-35966 | 10.38 | February 21, 2018 |

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| 10.40# | Offer Letter, dated November 16, 2017, by and between the Registrant and Kory Wentworth | 10-K | 001-35966 | 10.39 | February 21, 2018 |
| 10.41# | Executive Cash Incentive Bonus Plan | S-1 | 333-188605 | 10.18 | May 14, 2013 |
| 10.42# | Employment Agreement, dated December 18, 2018, by and between the Registrant and William ("Chip") Baird | 8-K | 001-35966 | 10.1 | February 11, 2019 |
| 10.43† | 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 |
| 10.44 | 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 |
| 10.45 | 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 |
| 10.46†† | Sublease, dated April 16, 2019, by and between the Registrant and Aventis Inc. | 10-Q | 001-35966 | 10.42 | August 1, 2019 |
| 10.47 | Amendment to Sublease, dated April 19, 2019, by and between the Registrant and Aventis Inc. | 10-Q | 001-35966 | 10.43 | August 1, 2019 |
| 31.1 | Certification of Principal Executive Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. | — | — | — | Filed herewith |
| 31.2 | Certification of Principal Financial Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. | — | — | — | Filed herewith |
| 32.1 | Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002. | — | — | — | Furnished herewith |
| 101.INS | Inline 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 | Inline XBRL Taxonomy Extension Schema Document. | — | — | — | Filed herewith |
| 101.CAL | Inline XBRL Taxonomy Extension Calculation Linkbase Document. | — | — | — | Filed herewith |
| 101.DEF | Inline XBRL Taxonomy Extension Definition Linkbase Document. | — | — | — | Filed herewith |
| 101.LAB | Inline XBRL Taxonomy Extension Label Linkbase Document. | — | — | — | Filed herewith |
| 101.PRE | Inline 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: May 5, 2021

By: /s/ Nick Leschly

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

Date: May 5, 2021

By: /s/ Chip Baird

Chip Baird
*Chief Financial Officer (Principal Financial Officer, Principal Accounting Officer and Duly Authorized 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: May 5, 2021

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: May 5, 2021

By: /s/ Chip Baird

Chip Baird
Chief Financial Officer
(Principal Financial Officer, Principal Accounting Officer and Duly Authorized 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 March 31, 2021 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: May 5, 2021

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

Date: May 5, 2021

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