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: 001-40030

Decibel Therapeutics, Inc.

(Exact name of Registrant as specified in its Charter)

Delaware	**46-4198709**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
1325 Boylston Street, Suite 500	
Boston, Massachusetts	**02215**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (617) 370-8701

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, par value $0.001 per share	DBTX	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, 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 May 10th, 2021, the registrant had 24,901,931 shares of common stock, $0.001 par value per share, outstanding.

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Cautionary Note Regarding Forward-Looking Statements and Industry Data

This Quarterly Report on Form 10-Q contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical fact, contained in this Quarterly Report on Form 10-Q, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “might,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “would,” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this Quarterly Report on Form 10-Q include, among other things, statements about:

- the initiation, timing, progress and results of our current research and development programs, preclinical studies and clinical trials;
- our estimates regarding expenses, future revenue, capital requirements and need for additional financing;
- our plans to develop our product candidates and programs;
- the timing of and our ability to submit applications for, obtain and maintain regulatory approvals for our product candidates;
- our estimates regarding the potential patient populations for our programs;
- our expectations regarding our ability to fund our operating expenses and capital expenditure requirements with our cash, cash equivalents and available-for-sale securities;
- the potential advantages of our product candidates and programs;
- the potential advantages of our platform;
- the rate and degree of market acceptance and clinical utility of our product candidates and programs;
- our estimates regarding the potential market opportunity for our product candidates and programs;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates;
- the impact of government laws and regulations;
- our competitive position;
- developments relating to our competitors and our industry;
- our ability to maintain and establish collaborations or obtain additional funding;
- the potential direct or indirect impact of the COVID-19 pandemic on our business; and
- our expectations regarding the time during which we will be an emerging growth company under the Jumpstart our Business Startup Acts of 2012.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Quarterly Report on Form 10-Q, particularly in the “Risk Factor Summary” below and in Part II, Item 1A. “Risk Factors,” that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this Quarterly Report on Form 10-Q and the documents that we reference herein and have filed or incorporated by reference hereto completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements contained in this Quarterly Report on Form 10-Q are made as of the date of this Quarterly Report on Form 10-Q, and we do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by applicable law.

This Quarterly Report on Form 10-Q includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties as well as our own estimates of potential market opportunities. The market data used in this Quarterly Report on Form 10-Q involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. Although we are responsible for the disclosure contained in this Quarterly Report on Form 10-Q and we believe the information from industry publications and other third-party sources included in this Quarterly Report on Form 10-Q is reliable, such information is inherently imprecise. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our estimates of the potential market opportunities for our product candidates include several key assumptions based on our industry knowledge, industry publications, third-party research and other surveys, which may be based on a small sample size and may fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions.

Risk Factor Summary

Our business is subject to a number of risks of which you should be aware before making an investment decision. Below we summarize what we believe to be the principal risks facing our business, in addition to the risks described more fully in Item 1A, “Risk Factors” of Part II of this Quarterly Report on Form 10-Q and other information included in this report. The risks and uncertainties described below are not the only risks and uncertainties we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations.

If any of the following risks occurs, our business, financial condition and results of operations and future growth prospects could be materially and adversely affected, and the actual outcomes of matters as to which forward-looking statements are made in this report could be materially different from those anticipated in such forward-looking statements.

- We have incurred significant losses since our inception, have no products approved for sale and we expect to incur substantial losses for the foreseeable future and may never achieve or maintain profitability;

- We will need substantial additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our research and development programs or commercialization efforts;

- The COVID-19 pandemic has disrupted our ongoing Phase 1b clinical trial of DB-020 and may affect our ability to initiate and complete preclinical studies, delay the initiation of our planned clinical trials or future clinical trials, disrupt regulatory activities, disrupt our manufacturing and supply chain or have other adverse effects on our business and operations. In addition, this pandemic has caused substantial disruption in the financial markets and may adversely impact economies worldwide, both of which could result in adverse effects on our business, operations and ability to raise capital;

- Our limited operating history may make it difficult for stockholders to evaluate the success of our business to date and to assess our future viability;

- We are very early in our development efforts. Our business is dependent on our ability to advance our lead gene therapy product candidate, DB-OTO, and our other current and future product candidates through preclinical studies and clinical trials, obtain marketing approval and ultimately commercialize them. If we are unable to complete clinical development, obtain regulatory approval for or commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed;

- Clinical development involves a lengthy and expensive process with uncertain outcomes, and results of earlier studies and trials may not be predictive of future clinical trial results. If our preclinical studies and clinical trials are not sufficient to support regulatory approval of any of our product candidates, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development of such product candidate;

- Gene therapy is an emerging field of drug development that poses many risks. We have only limited prior experience in gene therapy research and no prior experience in gene therapy clinical development. Our lack of experience and the limited patient populations for our gene therapy programs may limit our ability to be successful or may delay our development efforts;

- If we experience delays or difficulties in participant enrollment for clinical trials, our research and development efforts and the receipt of necessary regulatory approvals could be significantly delayed or prevented;

- Our product candidates or the process for administering our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit their commercial potential or result in significant negative consequences following any potential marketing approval;

- The manufacture of gene therapy products is complex and difficult and is subject to a number of scientific and technical risks, some of which are common to the manufacture of drugs and biologics and others of which are unique to the manufacture of gene therapies. We could experience manufacturing problems that result in delays in our gene therapy development or commercialization programs;

- We rely, and expect to continue to rely, on third parties to conduct some or all aspects of our product manufacturing, research, preclinical and clinical testing, and these third parties may not perform satisfactorily;

- We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do; and

- Our rights to develop and commercialize any product candidates are subject and may in the future be subject, in part, to the terms and conditions of licenses granted to us by third parties. If we fail to comply with our obligations under our current or future intellectual property license agreements or otherwise experience disruptions to our business relationships with our current or any future licensors, we could lose intellectual property rights that are important to our business.

PART I—FINANCIAL INFORMATION

Item 1. Financial Statements.

DECIBEL THERAPEUTICS, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(Unaudited)
(In thousands, except share and per share data)

	March 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 52,239	$ 27,742
Available-for-sale securities	129,839	26,568
Accounts receivable from related party	4,237	1,237
Prepaid expenses and other current assets	4,419	2,281
Total current assets	190,734	57,828
Available-for-sale securities, long-term	8,999	—
Property and equipment, net	5,975	6,337
Other assets	1,378	3,120
Total assets	$ 207,086	$ 67,285
Liabilities, Convertible Preferred Stock and Stockholders' (Deficit) Equity		
Current liabilities:		
Accounts payable	$ 1,000	$ 2,131
Accrued expenses and other current liabilities	3,835	5,665
Deferred collaboration liability, current	9,725	10,968
Deferred rent and lease incentive obligation, current	631	610
Total current liabilities	15,191	19,374
Long-term liabilities:		
Deferred collaboration liability, long term	6,515	4,177
Deferred rent and lease incentive obligation, long term	4,738	4,901
Other long-term liabilities	376	523
Total liabilities	26,820	28,975
Commitments and contingencies (Note 7)		
Series A convertible preferred stock, $0.001 par value; no shares authorized, issued and outstanding at March 31, 2021; 57,758,734 shares authorized, issued and outstanding at December 31, 2020; aggregate liquidation preference of $40,284 at December 31, 2020	—	16,176
Series B convertible preferred stock, $0.001 par value; no shares authorized, issued and outstanding at March 31, 2021; 12,500,000 shares authorized, issued and outstanding at December 31, 2020; aggregate liquidation preference of $16,334 at December 31, 2020	—	5,700
Series C convertible preferred stock, $0.001 par value; no shares authorized, issued and outstanding at March 31, 2021; 37,528,581 shares authorized, issued and outstanding at December 31, 2020; aggregate liquidation preference of $45,457 at December 31, 2020	—	16,759
Series D convertible preferred stock, $0.001 par value; no shares authorized, issued and outstanding at March 31, 2021; 47,610,763 shares authorized, 31,740,554 shares issued and outstanding at December 31, 2020; aggregate liquidation preference of $55,509 at December 31, 2020	—	54,456
Stockholders' (deficit) equity:		
Preferred stock, $0.001 par value; 5,000,000 shares authorized, no shares issued and outstanding at March 31, 2021; no shares authorized, issued and outstanding at December 31, 2020	—	—
Common stock, $0.001 par value; 200,000,000 shares authorized, 24,901,577 shares issued and 24,859,038 outstanding at March 31, 2021; 115,000,000 shares authorized, 573,793 shares issued and 521,052 shares outstanding at December 31, 2020	25	1
Additional paid-in capital	353,821	107,908
Accumulated other comprehensive loss	(21)	(1)
Accumulated deficit	(173,559)	(162,689)
Total stockholders' equity (deficit)	180,266	(54,781)
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	$ 207,086	$ 67,285

The accompanying notes are an integral part of these condensed consolidated financial statements.

DECIBEL THERAPEUTICS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(Unaudited)
(In thousands, except share and per share data)

	Three Months Ended March 31,	
	2021	2020
Operating expenses:		
Research and development	$ 6,020	$ 7,436
General and administrative	4,883	4,178
Total operating expenses	10,903	11,614
Loss from operations	(10,903)	(11,614)
Other income:		
Interest income	33	79
Total other income, net	33	79
Net loss	$ (10,870)	$ (11,535)
Cumulative dividends on convertible preferred stock	(2,309)	(2,749)
Net loss attributable to common stockholders	$ (13,179)	$ (14,284)
Net loss per share attributable to common stockholders, basic and diluted	$ (1.09)	$ (31.84)
Weighted average shares of common stock outstanding, basic and diluted	12,105,464	448,616
Comprehensive loss:		
Net loss	$ (10,870)	$ (11,535)
Other comprehensive loss:		
Unrealized loss on available-for-sale securities, net of tax of $0	(20)	(9)
Total other comprehensive loss	(20)	(9)
Comprehensive loss	$ (10,890)	$ (11,544)

The accompanying notes are an integral part of these condensed consolidated financial statements.

DECIBEL THERAPEUTICS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' (DEFICIT) EQUITY
(Unaudited)
(In thousands, except share data)

	Series A Convertible Preferred Stock		Series B Convertible Preferred Stock		Series C Convertible Preferred Stock		Series D Convertible Preferred Stock		Common Stock		Additional Paid-In	Accumulated Other Comprehensive	Accumulated	Total Stockholders' (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Capital	(Loss) Income	Deficit	Equity
Balance at December 31, 2019	57,758,734	$ 57,682	12,500,000	$ 24,957	27,528,581	$ 55,005	—	$ —	434,942	$ —	1,546	$ 10	$ (123,352)	$ (121,796)
Vesting of restricted common stock	—	—	—	—	—	—	—	—	21,872	—	11	—	—	11
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	225	—	—	225
Unrealized loss on available-for-sale securities	—	—	—	—	—	—	—	—	—	—	—	(9)	—	(9)
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	(11,535)	(11,535)
Balance at March 31, 2020	57,758,734	$ 57,682	12,500,000	$ 24,957	27,528,581	$ 55,005	—	$ —	456,814	$ —	$ 1,782	$ 1	$ (134,887)	$ (133,104)
Balance at December 31, 2020	57,758,734	$ 16,176	12,500,000	$ 5,700	37,528,581	$ 16,759	31,740,554	$ 54,456	521,052	$ 1	$ 107,908	$ (1)	$ (162,689)	$ (54,781)
Issuance of common stock upon exercise of stock options	—	—	—	—	—	—	—	—	3,773	—	17	—	—	17
Vesting of restricted common stock	—	—	—	—	—	—	—	—	10,202	—	4	—	—	4
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	646	—	—	646
Issuance of Series D convertible preferred stock	—	—	—	—	—	—	15,870,209	27,400	—	—	—	—	—	—
Conversion of convertible preferred stock into common stock upon completion of initial public offering	(57,758,734)	(16,176)	(12,500,000)	(5,700)	(37,528,581)	(16,759)	(47,610,763)	(81,856)	16,662,011	17	120,474	—	—	120,491
Issuance of common stock upon completion of initial public offering, net of commissions, underwriting discounts and offering costs of $13,137	—	—	—	—	—	—	—	—	7,662,000	7	124,772	—	—	124,779
Unrealized loss on available-for-sale securities	—	—	—	—	—	—	—	—	—	—	—	(20)	—	(20)
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	(10,870)	(10,870)
Balance at March 31, 2021	—	$ —	—	$ —	—	$ —	—	$ —	24,859,038	$ 25	$ 353,821	$ (21)	$ (173,559)	$ 180,266

The accompanying notes are an integral part of these condensed consolidated financial statements.

DECIBEL THERAPEUTICS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
(Unaudited)
(In thousands)

	Three Months Ended March 31,	
	2021	2020
Operating activities		
Net loss	$ (10,870)	$ (11,535)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	646	225
Depreciation	427	487
Amortization (accretion) of available-for-sale securities	88	(44)
Changes in operating assets and liabilities:		
Accounts receivable from related party	(3,000)	—
Prepaid expenses and other current assets	(2,138)	(273)
Accounts payable	(1,131)	(57)
Accrued expenses and other current liabilities	(1,180)	(186)
Deferred rent and lease incentive	(142)	(119)
Deferred collaboration liability	1,095	(589)
Other long-term liabilities	(101)	185
Net cash used in operating activities	(16,306)	(11,906)
Investing activities		
Purchases of available-for-sale securities	(116,156)	—
Proceeds from maturities of available-for-sale securities	3,778	11,750
Purchases of property and equipment	(65)	(56)
Net cash (used in) provided by investing activities	(112,443)	11,694
Financing activities		
Proceeds from the issuance of Series D convertible preferred stock	27,400	—
Proceeds from issuance of common stock upon completion of initial public offering net of commissions and underwriting discounts	128,240	—
Payment of initial public offering costs	(2,463)	—
Proceeds from the exercise of stock options	17	—
Principal payments on equipment financing	(46)	—
Net cash provided by financing activities	153,148	—
Net increase (decrease) in cash, cash equivalents and restricted cash	24,399	(212)
Cash, cash equivalents and restricted cash at beginning of period	29,218	20,039
Cash, cash equivalents and restricted cash at end of period	$ 53,617	$ 19,827
Supplemental disclosure of non-cash activities:		
Vesting of early exercised restricted stock	$ 4	$ 11
Initial public offering costs included in accrued expenses	$ 792	$ —

The accompanying notes are an integral part of these condensed consolidated financial statements.

1. Nature of the Business

Decibel Therapeutics, Inc. (the "Company") was formed on November 26, 2013. The Company is a clinical-stage biotechnology company dedicated to discovering and developing transformative treatments for hearing and balance disorders, one of the largest areas of unmet need in medicine. The Company aims to restore and improve hearing and balance through the restoration and regeneration of functional hair cells and non-sensory support cells within the inner ear.

On October 30, 2020, the Company's board of directors approved a 1-for-10 reverse stock split of the Company's common stock, par value $0.001 per share. On February 5, 2021, the Company's board of directors approved a 1-for-5.3 reverse stock split of the Company's common stock. All share and per share amounts in the condensed consolidated financial statements and notes thereto have been retroactively adjusted for all periods presented to give effect to both reverse stock splits.

Initial Public Offering

On February 17, 2021, the Company completed an initial public offering (the "IPO"), issuing and selling 7,062,000 shares of common stock at a public offering price of $18.00 per share, and on February 24, 2021, the Company issued and sold an additional 600,000 shares pursuant to the underwriters' partial exercise of their option to purchase additional shares. The aggregate net proceeds received by the Company from the offering were approximately $124.8 million. Upon closing of the IPO, all outstanding shares of convertible preferred stock automatically converted into shares of common stock.

Liquidity

Since its inception, the Company's operations have been focused on organizing and staffing, business planning, raising capital, establishing the Company's intellectual property portfolio and performing research and development of its product candidates, programs and platform.

The Company is subject to risks and uncertainties common to early-stage companies in the biotechnology industry, including but not limited to, risks associated with completing preclinical studies and clinical trials, obtaining regulatory approvals for product candidates, development by competitors of new biopharmaceutical products, dependence on key personnel, protection of proprietary technology, compliance with government regulations and the ability to secure additional capital to fund operations. Programs currently under development will require significant additional research and development efforts, including preclinical and clinical testing and will need to obtain regulatory approval prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel and infrastructure and extensive compliance-reporting capabilities. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will realize revenue from product sales.

As of March 31, 2021, the Company had cash, cash equivalents and available-for-sale securities of $191.1 million. The Company has determined that its existing capital resources will be sufficient to meet its projected operating expenses and capital expenditure requirements for at least twelve months from the date of issuance of these condensed consolidated financial statements. The Company expects to experience negative cash flows from operations and net losses for the foreseeable future as it continues to invest significantly in research and development of its product candidates, preclinical and clinical development and platform. Management's conclusion with respect to its ability to fund its operations is based on estimates that are subject to risks and uncertainties that may prove to be incorrect. If actual results differ from management's estimates, the Company may be required to seek additional funding or curtail planned activities to reduce operating expenses, which may have an adverse impact on the Company's ability to achieve its business objectives.

Impact of the COVID-19 Pandemic

The worldwide COVID-19 pandemic has affected and may affect in the future the Company's ability to initiate and complete preclinical studies, delay the initiation and completion of the Company's current and planned clinical trials, disrupt regulatory activities or have other adverse effects on the Company's business, results of operations, financial condition and prospects. In addition, the pandemic has caused substantial disruption in the financial markets and may adversely impact economies worldwide, both of which could adversely affect the Company's business, operations and ability to raise funds to support its operations.

The Company is following, and plans to continue to follow, recommendations from federal, state and local governments regarding workplace policies, practices and procedures. In response to the direction from state and local governmental authorities, the

Company has restricted access to its facility to those individuals who must perform critical research, translational medicine and laboratory support activities that must be completed on site, limited the number of such people that can be present at its facility at any one time and required that most of its employees work remotely. In addition, screening and enrollment in the Company's ongoing Phase 1b clinical trial of DB-020 in Australia and the United States have been adversely impacted by the COVID-19 pandemic. Patient screening and enrollment were paused in the second quarter of 2020 in both Australia and the United States, and screening for enrollment did not resume until early in the third quarter of 2020 in Australia and early in the fourth quarter of 2020 in the United States. The Company has also experienced delays in site start-up and the withdrawal of some sites in the United States. In addition, the Company and the third-party manufacturers, contract research organizations and academic collaborators that the Company engages have faced in the past and may face in the future disruptions that could affect its ability to initiate and complete preclinical studies or clinical trials, including disruptions in procuring items that are essential for its research and development activities, such as, for example, raw materials used in the manufacture of its product candidates, laboratory supplies for its preclinical studies and clinical trials, or animals that are used for preclinical testing, in each case, for which there may be shortages because of ongoing efforts to address the COVID-19 pandemic.

The Company cannot be certain what the overall impact of the COVID-19 pandemic will be on its business, and the pandemic has the potential to adversely affect the Company's business, financial condition, results of operations and prospects.

2. Summary of Significant Accounting Policies

Basis of Presentation

These condensed consolidated financial statements have been prepared in conformity with the rules and regulations of the Securities and Exchange Commission ("SEC") for interim consolidated financial statements. Certain information and footnote disclosures normally included in the financial statements prepared in accordance with accounting principles generally accepted in the United States of America ("GAAP") have been condensed or omitted pursuant to such rules and regulations. These condensed consolidated financial statements should be read in conjunction with the Company's audited consolidated financial statements and the notes thereto included in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2020. Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASUs") of the Financial Accounting Standards Board ("FASB").

Unaudited Interim Condensed Consolidated Financial Information

The accompanying condensed consolidated balance sheet as of March 31, 2021, the condensed consolidated statements of operations and comprehensive loss and statements of cash flows for the three months ended March 31, 2021 and 2020 and the condensed consolidated statements of convertible preferred stock and stockholders' (deficit) equity for the three months ended March 31, 2021 and 2020 are unaudited. The financial data and other information contained in the notes thereto as of and for the three months ended March 31, 2021 and 2020 are also unaudited. The condensed consolidated balance sheet data as of December 31, 2020 was derived from the Company's audited consolidated financial statements for the year ended December 31, 2020.

The unaudited interim condensed consolidated financial statements have been prepared on the same basis as the audited annual consolidated financial statements, and in the opinion of management, reflect all adjustments, which include only normal recurring adjustments necessary for the fair presentation of the Company's financial position as of March 31, 2021 and the results of its operations and cash flows for the three months ended March 31, 2021 and 2020. These unaudited 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.

The results for the three months ended March 31, 2021 are not necessarily indicative of results to be expected for the year ending December 31, 2021, or any other interim periods, or any future year or period.

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 condensed consolidated 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. Significant estimates and assumptions reflected in these condensed consolidated financial statements include, but are not limited to, the valuation

of common stock awards, the estimated cost to perform research which is an input into the measurement of research and development expenses recognized under the Company's collaboration agreement with Regeneron Pharmaceuticals, Inc. ("Regeneron"), as described below, and the accrual of research and development expenses. Estimates are periodically reviewed considering changes in circumstances, facts and historical experience. Actual results may differ from the Company's estimates.

Cash, Cash Equivalents and Restricted Cash

Cash equivalents are short-term, highly liquid investments that are readily convertible into cash, with original maturities of three months or less. Cash equivalents are mainly comprised of corporate debt securities and money market accounts invested in U.S. Treasury securities.

Restricted cash is comprised of deposits with a financial institution used to collateralize letters of credit related to the Company's lease arrangements. Restricted cash is presented as a component of other assets on the condensed consolidated balance sheets.

Cash, cash equivalents and restricted cash consisted of the following (in thousands):

	March 31,	
	2021	2020
Cash and cash equivalents	$ 52,239	$ 18,388
Restricted cash	1,378	1,439
Total cash, cash equivalents and restricted cash as shown on the statement of cash flows	$ 53,617	$ 19,827

Restricted cash decreased by $0.1 million during the three months ended March 31, 2021 due to a reduction in deposits with a financial institution used to collateralize letters of credit related to the Company's lease arrangements.

Fair Value Measurements

Certain assets and liabilities of the Company are carried at fair value under GAAP. The fair values of the Company's financial assets and liabilities reflect the Company's estimate of the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- Level 1—Quoted prices in active markets for identical assets or liabilities.
- Level 2—Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.
- Level 3—Unobservable inputs that are supported by little or no market activity that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

To the extent the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

The carrying amounts reflected in the consolidated balance sheets for cash, accounts receivable, prepaid expenses and other current assets, accounts payable and accrued expenses approximate their fair values due to the short-term nature of these assets and liabilities. Items measured at fair value on a recurring basis include cash equivalents and available-for-sales securities as of March 31, 2021 and December 31, 2020.

Deferred Offering Costs

The Company capitalizes certain legal, professional, accounting and other third-party fees that are directly associated with in-process equity financings as deferred offering costs until the related financings are consummated. After consummation of the equity

financing, such costs are reclassified as a reduction to additional paid-in capital generated as a result of the related financing. Should an in-process equity financing be abandoned, the deferred offering costs would be expensed immediately as a charge to operating expenses in the condensed consolidated statements of operations and comprehensive loss. Deferred offering costs are presented as a component of other assets on the condensed consolidated balance sheets. The Company had no deferred offering costs as of March 31, 2021. As of December 31, 2020, the Company capitalized $1.6 million of deferred offering costs related to the IPO.

Recently Issued Accounting Pronouncements

Refer to Note 2 of the audited consolidated financial statements included in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2020 for the Company's summary of recently issued accounting pronouncements that have not yet been adopted.

3. Fair Value Measurements

The Company measures the following financial assets at fair value on a recurring basis. The fair value of these assets was determined as follows (in thousands):

	Balance at March 31, 2021	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash equivalents:				
Corporate debt securities	$ 27,360	$ —	$ 27,360	$ —
Money market mutual funds	12,587	12,587	—	—
Commercial paper	7,248	—	7,248	—
Total cash equivalents	$ 47,195	$ 12,587	$ 34,608	$ —
Available-for-sale securities:				
Commercial paper	$ 84,231	$ —	$ 84,231	$ —
Corporate debt securities	39,838	—	39,838	—
US Treasury securities	3,015	—	3,015	—
Certificates of deposit	2,755	—	2,755	—
Total available-for-sale securities	$ 129,839	$ —	$ 129,839	$ —
Available-for-sale securities, long-term:				
US Treasury securities	$ 5,001	$ —	$ 5,001	$ —
Agency bonds	3,998	—	3,998	—
Total available-for-sale securities, long-term	$ 8,999	$ —	$ 8,999	$ —

	Balance at December 31, 2020	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash equivalents:				
Corporate debt securities	$ 4,001	$ —	$ 4,001	$ —
Money market mutual funds	7,962	7,962	—	—
Commercial paper	12,499	—	12,499	—
Total cash equivalents	$ 24,462	$ 7,962	$ 16,500	$ —
Available-for-sale securities:				
Commercial paper	$ 19,481	$ —	$ 19,481	$ —
Corporate debt securities	1,286	—	1,286	—
US Treasury securities	3,027	—	3,027	—
Certificates of deposit	2,774	—	2,774	—
Total available-for-sale securities	$ 26,568	$ —	$ 26,568	$ —

Money market funds were valued by the Company using quoted prices in active markets for identical securities, which represent a Level 1 measurement within the fair value hierarchy. During the three months ended March 31, 2021 and the year ended December 31, 2020 there were no transfers between Level 1, Level 2 and Level 3.

4. Available-For-Sale Securities

The following table summarizes the Company's available-for-sale securities (in thousands):

	March 31, 2021			
	Amortized Cost	Gross Unrealized Gain	Gross Unrealized Loss	Fair Value
Available-for-sale securities:				
Commercial paper	$ 84,231	$ 3	$ (3)	$ 84,231
Corporate debt securities	39,857	—	(19)	39,838
US Treasury securities	3,015	—	—	3,015
Certificates of deposit	2,756	—	(1)	2,755
Total available-for-sale securities	$ 129,859	$ 3	$ (23)	$ 129,839
Available-for-sale securities, long-term:				
US Treasury securities	$ 5,001	$ —	$ —	$ 5,001
Agency bonds	3,999	—	(1)	3,998
Total available-for-sale securities, long-term	$ 9,000	$ —	$ (1)	$ 8,999

	December 31, 2020			
	Amortized Cost	Gross Unrealized Gain	Gross Unrealized Loss	Fair Value
Available-for-sale securities:				
Commercial paper	$ 19,481	$ 1	$ (1)	$ 19,481
Corporate debt securities	1,286	—	—	1,286
US Treasury securities	3,027	—	—	3,027
Certificates of deposit	2,775	—	(1)	2,774
Total available-for-sale securities	$ 26,569	$ 1	$ (2)	$ 26,568

The Company had 30 investments in available-for-sale securities in an unrealized loss position as of March 31, 2021 with a fair value of $115.8 million. The Company had eight investments in available-for-sale securities in an unrealized loss position as of December 31, 2020 with a fair value of $17.1 million. These investments were in a loss position for less than 12 months and the Company considered the loss to be temporary in nature. The Company considered the decline in market value for these securities to be primarily attributable to economic and market conditions. As of March 31, 2021 and December 31, 2020, the Company did not intend to sell, and it was not more likely than not that the Company would be required to sell the investments that were in an unrealized loss position before recovery of their amortized cost basis. Accordingly, the Company did not recognize any other-than-temporary impairments related to its available-for-sale securities in an unrealized loss position. As of March 31, 2021, the Company did not hold any investments that matured beyond five years. During the three months ended March 31, 2021 and the year ended December 31, 2020, the Company did not sell any available-for-sale securities and therefore did not recognize any realized gains or losses.

5. Accrued Expenses and Other Current Liabilities:

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

	March 31, 2021	December 31, 2020
Accrued professional fees	$ 1,524	$ 1,854
Accrued research and development expense	741	680
Accrued payroll and related expenses	702	2,381
Equipment financing, current	197	193
Accrued other and other current liabilities	671	557
	$ 3,835	$ 5,665

6. Commitments and Contingencies

License Agreements

The Company is a party to a number of license agreements related to certain patent rights used in developing its product candidates. Under such license agreements, the Company paid nominal upfront fees and is obligated to pay certain nominal annual license maintenance fees. The Company is also obligated to make certain payments based on specified clinical and regulatory milestones and royalty payments based on sales volume and milestones. The Company may terminate these agreements by providing prior written notice to the respective counterparty. All payments made have been expensed as research and development expenses in the condensed consolidated statements of operations and comprehensive loss. The condensed consolidated balance sheets as of March 31, 2021 and December 31, 2020 do not include liabilities with respect to these license agreements as the Company has not yet generated revenue and the achievement of the milestones is not probable.

Indemnification Agreements

The Company enters into standard indemnification agreements and/or indemnification sections in other 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 and/or sections is unlimited. The Company has never incurred costs to defend lawsuits or settle claims related to these indemnification agreements and/or sections. The Company does not believe that the outcome of any claims under indemnification arrangements will have a material effect on its financial position, results of operations or cash flows, and it had not accrued any liabilities related to such obligations in its condensed consolidated financial statements as of March 31, 2021 or December 31, 2020.

Research & Development Tax Incentive

The Company benefits from research and development tax incentive programs in certain jurisdictions that provide a cash refund to companies conducting eligible research and development activities. The Company obtained aggregate cash refunds of $1.2 million related to research and development activities as of March 31, 2021. Although management has determined it has a reasonable basis to claim its research and development activities are eligible core or supporting activities under the research and development tax incentive requirements, should the Company be subject to a tax audit resulting in an unfavorable outcome, it is reasonably possible it may have to repay some or all of these incentives.

7. Restructuring

In January and May 2020, the Company conducted a reduction in force that resulted in the termination of 45 full-time employees. Accordingly, during the three months ended March 31, 2020, the Company recorded a restructuring charge of $2.9 million, which was comprised of termination benefits including severance, benefits and other payroll-related charges. These accrued restructuring costs are included as a component of accrued expenses and other current liabilities on the condensed consolidated balance sheets at December 31, 2020.

The following table summarizes the restructuring activity during the three months ended March 31, 2020 and 2021 (in thousands):

	Accrued Restructuring Costs
Balance at December 31, 2019	$ —
Restructuring costs incurred	2,919
Termination benefits paid	(1,496)
Balance at March 31, 2020	$ 1,423
Balance at December 31, 2020	$ 8
Restructuring costs incurred	—
Termination benefits paid	(8)
Balance at March 31, 2021	$ —

The following table summarizes the classification of restructuring expense in the condensed consolidated statements of operations and comprehensive loss (in thousands):

	Three Months Ended March 31,	
	2021	2020
Research and development	$ —	$ 2,219
General and administrative	—	700
Total restructuring expense	$ —	$ 2,919

During the first quarter of 2020, the Company entered into retention agreements with certain key employees. Under the terms of these agreements, the Company agreed to make three retention payments to each key employee totaling $1.6 million in the aggregate if they remained employed at the Company through specified milestones. The first payments of $0.7 million in the aggregate were paid upon execution of the retention agreements. The second payments of $0.4 million in the aggregate were paid to the key employees upon the closing of the Series D financing in November 2020. The third payments of $0.5 million in the aggregate have been paid as of March 31, 2021, including payments to certain employees who are required to remain employed through January 1, 2022 in order to retain the first and third payments. These prepayments are being amortized over the remaining employee service terms under the retention agreements.

8. Stockholders' Equity

On February 17, 2021, the Company amended the Certificate of Incorporation (the "Certificate of Incorporation") concurrent with the IPO of the Company's common stock, which authorized 200,000,000 shares of common stock, $0.001 par value per share and 5,000,000 shares of undesignated preferred stock, $0.001 par value per share. As of December 31, 2020, the Company's Fourth Amended and Restated Certificate of Incorporation authorized the Company to issue 115,000,000 shares of $0.001 par value common stock.

Common Stock Reserved

The Company had the following shares of common stock reserved for future issuance:

	March 31, 2021	December 31, 2020
Series A convertible preferred stock	—	3,719,410
Series B convertible preferred stock	—	989,299
Series C convertible preferred stock	—	2,970,149
Series D convertible preferred stock	—	5,988,773
Shares reserved for exercise of outstanding stock options under the 2015 Stock Incentive Plan	2,682,347	2,686,120
Shares reserved for exercise of outstanding stock options under the 2021 Stock Incentive Plan	80,000	—
Shares reserved for future awards under the 2015 Stock Incentive Plan	—	790,596
Shares reserved for future awards under the 2021 Stock Incentive Plan	1,561,102	—
Shares reserved for future awards under the 2021 Employee Stock Purchase Plan	566,037	—
Total common stock reserved	4,889,486	17,144,347

9. Convertible Preferred Stock

Immediately prior to the closing of the IPO, the Company had an aggregate of 155,398,078 shares of convertible preferred stock issued and outstanding which automatically converted into 16,662,011 shares of common stock upon the closing of the IPO. Subsequent to the closing of the IPO, no shares of preferred stock were issued or outstanding.

As of December 31, 2020, the Company's Series A convertible preferred stock ("Series A Preferred Stock"), Series B convertible preferred stock ("Series B Preferred Stock"), Series C convertible preferred stock ("Series C Preferred Stock") and Series

D convertible preferred stock ("Series D Preferred Stock," and collectively with the Series A Preferred Stock, Series B Preferred Stock and Series C Preferred Stock, the "Convertible Preferred Stock") consisted of the following (in thousands, except share data):

	December 31, 2020				
	Preferred Stock Authorized	Preferred Stock Issued and Outstanding	Carrying Value	Liquidation Preference	Common Stock Issuable Upon Conversion
Series A Preferred Stock	57,758,734	57,758,734	$ 16,176	$ 40,284	3,719,410
Series B Preferred Stock	12,500,000	12,500,000	5,700	16,334	989,299
Series C Preferred Stock	37,528,581	37,528,581	16,759	45,457	2,970,149
Series D Preferred Stock	47,610,763	31,740,554	54,456	55,509	5,988,773
	155,398,078	139,527,869	$ 93,091	$ 157,584	13,667,631

Cumulative accrued dividends on the Company's Convertible Preferred Stock consisted of the following (in thousands):

	December 31, 2020
Series A Preferred Stock	$ 10,399
Series B Preferred Stock	3,398
Series C Preferred Stock	6,623
Series D Preferred Stock	709
	$ 21,129

During the three months ended March 31, 2021, $2.3 million of cumulative dividends accrued prior to completion of the IPO. Subsequent to the completion of the IPO, no shares of convertible preferred stock were issued or outstanding and therefore no dividends accrued.

10. Stock-Based Compensation

2015 Stock Incentive Plan

As of December 31, 2020, there were 3,930,701 shares of common stock authorized for issuance under the 2015 Stock Incentive Plan (the "2015 Plan") under which the Company could grant equity awards to eligible employees, officers, directors, consultants and advisors. Subsequent to the pricing of the Company's IPO on February 11, 2021, no further awards will be made under the 2015 Plan; however, awards outstanding under the 2015 Plan will continue to be governed by the 2015 Plan.

2021 Stock Incentive Plan

In connection with the IPO, the Company adopted the 2021 Stock Incentive Plan (the "2021 Plan"). The 2021 Plan has 1,639,652 shares initially reserved for future issuance, subject to annual increases, and provides for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock units and other stock-based awards. As of March 31, 2021, 80,000 shares were subject to outstanding awards granted under the 2021 Plan and 1,561,102 shares remained available for issuance.

2021 Employee Stock Purchase Plan

In connection with the IPO, the Company adopted the 2021 Employee Stock Purchase Plan (the "2021 ESPP"). The 2021 ESPP has reserved for future issuance 566,037 shares of our common stock, subject to annual increases, and will enable eligible employees to purchase shares of common stock at a specified discount. As of March 31, 2021, no shares have been issued under the 2021 ESPP and as such, 566,037 shares remained available for issuance.

Restricted Stock

A summary of the Company's restricted stock activity and related information is as follows:

	Number of Shares of Restricted Stock	Weighted Average Grant Date Fair Value
Unvested as of December 31, 2020	52,741	$ 19.10
Vested	(10,202)	15.06
Repurchased	—	—
Canceled/Forfeited	—	—
Unvested as of March 31, 2021	42,539	$ 20.06

The aggregate fair value of restricted stock awards that vested during the three months ended March 31, 2021 and 2020 was $0.1 million and $0.5 million, respectively. As of March 31, 2021, total unrecognized compensation cost related to unvested restricted stock awards was approximately $0.8 million, which is expected to be recognized over a weighted-average period of 1.3 years.

Stock Options

A summary of the Company's stock option activity and related information is as follows:

	Number of Stock Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value
			(In years)	(In thousands)
Outstanding as of December 31, 2020	2,686,120	$ 4.53	9.9	$ 3,781
Granted	80,000	18.00		
Exercised	(3,773)	4.40		
Cancelled/forfeited	(1,450)	5.83		
Outstanding as of March 31, 2021	2,760,897	$ 4.92	9.7	$ 18,519
Exercisable as of March 31, 2021	742,603	$ 4.62	9.7	$ 5,105
Vested and expected to vest as of March 31, 2021	2,760,897	$ 4.92	9.7	$ 18,519

As of March 31, 2021, total unrecognized compensation cost related to unvested stock options was approximately $7.4 million, which is expected to be recognized over a weighted-average period of 3.6 years. The weighted-average grant-date fair value per share of stock options granted during the three months ended March 31, 2021 was $14.60.

Stock-Based Compensation Expense

The following table presents the components and classification of stock-based compensation expense (in thousands):

	Three Months Ended March 31,	
	2021	2020
Research and development	$ 271	$ 128
General and administrative	375	97
Total stock-based compensation expense	$ 646	$ 225

11. Net Loss per Share

The following table sets forth the outstanding shares of common stock equivalents, presented based on amounts outstanding at each period end, that were excluded from the calculation of diluted net loss per share attributable to common stockholders for the periods indicated because including them would have been anti-dilutive:

	Three Months Ended March 31,	
	2021	2020
Series A Preferred Stock	—	1,089,785
Series B Preferred Stock	—	235,849
Series C Preferred Stock	—	519,396
Outstanding stock options	2,760,897	36,911
Unvested restricted stock	42,539	108,655
	2,803,436	1,990,596

12. License and Collaboration Agreement with Regeneron

Agreement Overview

In November 2017, the Company entered into a license and collaboration agreement with Regeneron (the "Regeneron Agreement") under which Regeneron made an upfront, nonrefundable $25.0 million payment to the Company. The parties were to undertake specified activities with respect to the discovery or development of new potential therapies directed to a set of defined collaboration targets. Each party was responsible for its own respective costs and agreed to use commercially reasonable efforts to complete the activities as designated in the agreed-upon research plan. The Company was primarily responsible for the direction and conduct of the research program whereas Regeneron was primarily responsible for the contribution of various technologies and expertise of its own as well as contribution of employees and research services.

In October 2020, the parties amended the Regeneron Agreement (the "Amended Agreement") pursuant to which, among other things, ATOH1, the target of the DB-ATO program, was removed as a collaboration target and the terms and plans for the DB-OTO and AAV.103 programs were modified. The primarily responsibilities of each party remain consistent with those under the Regeneron Agreement. In connection with the amendment, the Company issued 10,000,000 shares of Series C Preferred Stock to Regeneron in consideration for its entry into the amendment. Pursuant to the Amended Agreement, Regeneron agreed to pay the Company $0.3 million to fund the Company's ongoing research plan and $0.5 million to help secure the services of a contract development and manufacturing organization (the "CDMO Initiation Fee"). The $0.5 million payment was creditable against the milestone associated with the initiation of manufacturing to support GLP toxicology studies of DB-OTO. Additionally, Regeneron agreed to reimburse the Company for up to $10.5 million of third-party costs related to investigational new drug ("IND") enabling studies for DB-OTO as such costs are incurred.

In November 2020, the Company achieved its first pre-IND milestone in connection with the initiation of manufacturing to support GLP toxicology studies of DB-OTO.

Accounting Analysis

The Company accounted for the Regeneron Agreement in accordance with FASB ASC Topic ASC 808, *Collaborative Arrangements* ("ASC 808"), and applied ASC 606, *Revenue from Contracts with Customers* ("ASC 606"), by analogy. All research activities under the Regeneron Agreement were considered a single performance obligation and the transaction price consisted of the $25.0 million upfront payment. Future milestones were considered variable consideration and fully constrained until such time as the achievement of such milestone was considered probable. The Company satisfied its promises under the agreement over time as Regeneron received the benefit of the research services as the services were performed and measured progress towards completion of the performance obligation using an input method that was based on costs incurred.

The Amended Agreement increased the transaction price to $35.8 million consisting of (i) $25.0 million received pursuant to the Regeneron Agreement, (ii) $0.3 million received to fund the ongoing research plan, (iii) $4.4 million for the first pre-IND milestone achieved in November 2020, $0.5 million of which was received as the CDMO Initiation Fee in October 2020, and (iv) $10.5 million in reimbursements for third-party costs related to IND-enabling studies for DB-OTO, partially offset by the fair value of the Series C Preferred Stock issued to Regeneron of approximately $4.4 million. Future milestones continue to be fully constrained. The Company continues to satisfy its single performance obligation over time and measures progress towards completion using an input method based on costs incurred.

The Company concluded the consideration received under the Regeneron Agreement and the Amended Agreement represented reimbursements of the Company's cost incurred and should therefore be accounted for as contra-research and development in the

Company's condensed consolidated statements of operations and comprehensive income (loss). Deferred collaboration liability is classified in the condensed consolidated balance sheets based on the expected timing of when the costs will be recognized in the future.

The Company recognized $1.9 million and $0.6 million as contra-research and development expenses for the three months ended March 31, 2021 and 2020, respectively. As of March 31, 2021 and December 31, 2020, there was deferred collaboration liability classified in current liabilities of $9.7 million and $11.0 million, respectively, and classified in long term liabilities of $6.5 million and $4.2 million, respectively. As of March 31, 2021, the Company had $4.2 million of accounts receivable due from Regeneron of which $3.0 million was unbilled. As of December 31, 2020, the Company had $1.2 million of unbilled accounts receivable due from Regeneron. Unbilled and billed accounts receivable are classified in accounts receivable, net from related party on the condensed consolidated balance sheets and relate to reimbursements of third-party costs incurred related to the Company's IND enabling study for DB-OTO.

13. Related Party Transactions

As of March 31, 2021, Regeneron held 2,097,314 shares of common stock. As of December 31, 2020, Regeneron held 12,500,000 shares of Series B Preferred Stock and 14,000,000 shares of Series C Preferred Stock. During the three months ended March 31, 2021 and 2020, the Company recognized $1.9 million and $0.6 million as contra-research and development expense during the three months ended March 31, 2021 and 2020, respectively, in its condensed consolidated statements of operations and comprehensive loss based on its progress towards completion of its research activities under the research plan for the collaboration. As of March 31, 2021, the Company had $4.2 million of accounts receivable due from Regeneron, of which $3.0 million was unbilled. As of December 31, 2020, the Company had $1.2 million of unbilled accounts receivable due from Regeneron. As of March 31, 2021 and December 31, 2020, the Company did not have any amounts due to Regeneron (see Note 13).

Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations.

You should read the following discussion and analysis of our financial condition and results of operations together with our condensed consolidated financial statements and related notes thereto appearing elsewhere in this Quarterly Report on Form 10-Q, or Quarterly Report, and our audited financial statements and related notes for the year ended December 31, 2020 included in our Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 29, 2021, which we refer to as the 2020 Annual Report on Form 10-K. Some of the information contained in this discussion and analysis includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the section entitled "Risk Factors," our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis. Please also see the section entitled "Cautionary Note Regarding Forward-Looking Statements and Industry Data" of this Quarterly Report.

Overview

We are a clinical-stage biotechnology company dedicated to discovering and developing transformative treatments for hearing and balance disorders, one of the largest areas of unmet need in medicine. We aim to restore and improve hearing and balance through the restoration and regeneration of functional hair cells and non-sensory support cells within the inner ear. We have built a proprietary platform that integrates single-cell genomics and bioinformatics analyses, precision gene therapy technologies and our expertise in inner ear biology. We are leveraging our platform to advance our pipeline of preclinical gene therapy programs that are designed to selectively replace genes for the treatment of congenital, monogenic hearing loss and to regenerate inner ear hair cells for the treatment of acquired hearing and balance disorders. We are developing our lead gene therapy product candidate, DB-OTO, to provide hearing to individuals born with profound hearing loss due to mutation of the otoferlin, or OTOF, gene. We are also advancing our gene therapy programs designed to restore balance in patients with bilateral vestibulopathy, or BVP, by regenerating lost hair cells within the inner ear. In addition to our gene therapy programs, we are developing DB-020 for the prevention of cisplatin-induced hearing loss, which we are currently evaluating in patients in a Phase 1b clinical trial.

We are developing our lead gene therapy product candidate, DB-OTO, to provide hearing to individuals born with profound hearing loss due to an OTOF deficiency. OTOF is a protein expressed in the inner hair cells of the cochlea that enables communication between sensory cells of the inner ear and the auditory nerve by regulating synaptic transmission. We have designed DB-OTO utilizing a proprietary, cell-selective promoter to provide expression of OTOF that is limited to hair cells. In our preclinical studies, the hair cell-selective expression of OTOF provided by DB-OTO enabled restoration of hearing in mice that was more durable than when OTOF was expressed under the control of a ubiquitous promoter, which is designed to drive expression in all cells. In addition to the loss of durability, we observed that use of a ubiquitous promoter in mice resulted in the loss of inner hair cells throughout the cochlea. DB-OTO is an AAV-based gene therapy intended to be delivered to patients using the surgical approach employed by otologists and pediatric otolaryngologists during a standard cochlear implantation procedure. We believe the cell-selective expression of DB-OTO and its delivery by this established surgical procedure will provide a core competitive advantage important to the success of DB-OTO. Based on feedback from the U.S. Food and Drug Administration, or FDA, we are currently conducting preclinical studies of DB-OTO to support our planned submission of an investigational new drug application, or IND, to the FDA. We have solicited feedback from European regulatory authorities to support our planned submission of a CTA within the European Union. We plan to submit an IND or CTA in 2022. Subject to the acceptance of our IND or CTA, we expect to initiate a Phase 1/2 clinical trial in 2022. In addition to DB-OTO, we are advancing AAV.103 and AAV.104, additional gene therapy programs targeting hearing loss resulting from other single gene mutations, or monogenic forms of hearing loss. AAV.103 aims to restore hearing in individuals with mutations in the gap junction beta-2, or GJB2, gene. We anticipate that we will identify a product candidate for our AAV.103 program in 2022. We anticipate that we will announce the target for our AAV.104 program in 2021.

We are also using our platform to design and develop a pipeline of gene therapies for hair cell regeneration within the inner ear. We are engineering gene therapies to convert supporting cells, the cells adjacent to hair cells, into both cochlear and vestibular hair cells in order to restore hearing and balance function. These gene therapies are designed to express the developmental or reprogramming factors that control cell fate and use our proprietary, cell-selective promoters to control expression spatially and temporally. We are developing AAV.201 and DB-ATO under our gene therapy programs to regenerate hair cells for the treatment of BVP, a debilitating, acquired condition that significantly impairs balance, mobility and stability of vision. AAV.201 is an AAV-based gene therapy that combines ATOH1, a transcription factor required for hair cell differentiation with another reprogramming factor. DB-ATO is an AAV-based gene therapy that utilizes a proprietary supporting cell-selective promoter to express ATOH1. These programs aim to restore balance by promoting regeneration of hair cells in the vestibular system, the sensory system responsible for balance. In preclinical studies, selective expression of ATOH1 in vestibular supporting cells following treatment with DB-ATO led to conversion of supporting cells into vestibular hair cell-like cells, as characterized at both the morphological and transcriptional level. In recently completed in vivo behavioral studies of DB-ATO, we did not see sufficient functional recovery to continue to move DB-ATO to development candidate in 2021. We plan to continue to evaluate the potential of ATOH1 gene therapy to restore lost vestibular function. We intend to announce the program target for AAV.201 in 2022. In addition, we are advancing our cochlear hair

cell regeneration program to treat acquired hearing loss by regenerating cochlear outer hair cells. We plan to announce the targets for our cochlear hair cell regeneration program in 2022.

In addition to our gene therapy product candidate and programs, we are developing a clinical-stage product candidate, DB-020, for the prevention of cisplatin-induced hearing loss. DB-020 is a novel formulation of sodium thiosulfate, or STS, that we have optimized for local delivery to the ear. STS inactivates cisplatin, a widely used chemotherapy that often leads to hearing loss and related complications in patients being treated for cancer. We are developing DB-020 to prevent cisplatin-induced hearing loss without impacting the beneficial, anti-tumor effect of cisplatin. In 2019, we completed a randomized, double-blind, placebo-controlled Phase 1 clinical trial of DB-020 in healthy volunteers, in which DB-020 was well tolerated. Following the Phase 1 clinical trial, we initiated a randomized, double-blind, placebo-controlled, multicenter Phase 1b clinical trial in 2020 to evaluate the safety and efficacy of DB-020 for the prevention of cisplatin-induced hearing loss. Due to continued impact of the COVID-19 pandemic on the pace of patient screening and enrollment, including delays in site start-up and withdrawal of some sites in the United States, we now expect to report results from an interim analysis of the ongoing Phase 1b clinical trial of DB-020 in the first half of 2022. All remaining sites in the United States are now open, along with all sites in Australia, which have been open and actively recruiting since the fourth quarter of 2020. The FDA has granted fast track designation for DB-020 for the prevention of cisplatin-related ototoxicity.

Since inception, we have devoted substantially all of our resources on organizing and staffing, business planning, raising capital, establishing our intellectual property portfolio and performing research and development of our product candidates, programs and platform. On February 5, 2021, we issued and sold 15,870,209 shares of our Series D convertible preferred stock for $27.4 million of aggregate cash proceeds, net of issuance costs. On February 17, 2021, we completed an initial public offering, or IPO, of our common stock in which we issued and sold 7,062,000 shares of our common stock at a public offering price of $18.00 per share, and on February 24, 2021, we issued and sold an additional 600,000 shares of common stock pursuant to the underwriters' partial exercise of their option to purchase additional shares of common stock, for aggregate net proceeds of $124.8 million. Upon the closing of our IPO, all of our outstanding shares of convertible preferred stock automatically converted into 16,662,011 shares of common stock. Subsequent to the closing of our IPO, there were no shares of preferred stock outstanding. To date, we have financed our operations primarily with proceeds from sales of our convertible preferred stock (including borrowings under convertible promissory notes, which converted into convertible preferred stock in 2015), payments under our license and collaboration agreement with Regeneron Pharmaceuticals, Inc., or Regeneron, and, most recently, from the sale of common stock in our IPO.

We have not generated any revenue from product sales, and do not expect to generate any revenue from product sales for at least the next several years. All of our programs are still in preclinical and early-stage clinical development. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our product candidates, if approved. Since inception, we have incurred significant operating losses, including net losses of $10.9 million for the three months ended March 31, 2021 and $39.3 million and $42.7 million for the years ended December 31, 2020 and 2019, respectively. As of March 31, 2021, we had an accumulated deficit of $173.6 million. We expect to incur significant expenses and operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if and as we:

- submit an investigational new drug application, or IND, or clinical trial application, or CTA, and initiate a planned Phase 1/2 clinical trial of our lead gene therapy product candidate, DB-OTO, for the treatment of profound hearing loss due to mutation of the OTOF gene;
- continue our current research programs and our preclinical development of DB-OTO, AAV.103, AAV.104, AAV.201 and DB-ATO and any product candidates that may arise from our current or future research programs;
- continue our clinical development of DB-020, including our ongoing Phase 1b clinical trial;
- advance additional product candidates into preclinical and clinical development;
- expand the capabilities of and invest in our platform;
- seek marketing approvals for any product candidates that successfully complete clinical trials;
- ultimately establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- expand, maintain and protect our intellectual property portfolio;
- hire additional clinical, regulatory, quality control and scientific personnel;
- establish and maintain agreements with manufacturers for our product candidates; and
- add operational, legal, compliance, financial and management information systems and personnel, including personnel to support our research, product development and future commercialization efforts and support our operations as a public company.

In addition, as we progress toward marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution.

As a result, we will need substantial additional funding to support our continuing operations and pursue our strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of equity offerings, debt financings and other sources of capital, which may include collaborations with other companies or other strategic transactions. We may be unable to raise additional funds or enter into other collaborations, strategic alliances or licensing arrangements with third parties when needed or on favorable terms, or at all. If we are unable to raise additional funds through equity or debt financings or enter into such other agreements when needed, we may have to significantly delay, reduce or eliminate some or all of our product development or future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

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 profitability. Even if we are able to generate revenue from product sales, 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 or terminate our operations.

As of March 31, 2021, we had cash, cash equivalents and available-for-sale securities of $191.1 million. We believe that our cash, cash equivalents and available-for-sale securities as of March 31, 2021 will enable us to fund our operating expenses and capital expenditure requirements into 2024. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we anticipate.

Impact of COVID-19 on Our Business

The worldwide COVID-19 pandemic has affected and may affect in the future our ability to initiate and complete preclinical studies, delay the initiation and completion of our current and planned clinical trials, disrupt regulatory activities or have other adverse effects on our business, results of operations, financial condition and prospects. In addition, the pandemic has caused substantial disruption in the financial markets and may adversely impact economies worldwide, both of which could adversely affect our business, operations and ability to raise funds to support our operations.

We are following, and plan to continue to follow, recommendations from federal, state and local governments regarding workplace policies, practices and procedures. In response to the direction from state and local governmental authorities, we have restricted access to our facility to those individuals who must perform critical research, translational medicine and laboratory support activities that must be completed on site, limited the number of such people that can be present at our facility at any one time and required that most of our employees work remotely. In addition, screening and enrollment in our ongoing Phase 1b clinical trial of DB-020 in Australia and the United States have been adversely impacted by the COVID-19 pandemic. Patient screening and enrollment were paused in the second quarter of 2020 in both Australia and the United States, and screening for enrollment did not resume until early in the third quarter of 2020 in Australia and early in the fourth quarter of 2020 in the United States. We have also experienced delays in site start-up and the withdrawal of some sites in the United States. In addition, we and the third-party manufacturers, contract research organizations, or CROs, and academic collaborators that we engage have faced in the past and may face in the future disruptions that could affect our ability to initiate and complete preclinical studies or clinical trials. This includes disruptions in procuring items that are essential for our research and development activities, such as, for example, raw materials used in the manufacture of our product candidates, laboratory supplies for our preclinical studies and clinical trials, or animals that are used for preclinical testing, in each case, for which there may be shortages because of ongoing efforts to address the COVID-19 pandemic.

We cannot be certain what the overall impact of the COVID-19 pandemic will be on our business, and it has the potential to adversely affect our business, financial condition, results of operations and prospects.

License and Collaboration Agreement with Regeneron

In November 2017, we entered into a license and collaboration agreement with Regeneron, or the Regeneron Agreement. The Regeneron Agreement has a research term of five years, and Regeneron has the right to extend the research term for up to two years in one-year intervals. The Regeneron Agreement is focused on the discovery and development of new potential therapies directed to a set of defined collaboration targets. We are currently developing DB-OTO, AAV.103 and AAV.104 in collaboration with Regeneron under the Regeneron Agreement. In October 2020, we entered into an amendment to the Regeneron Agreement pursuant to which, among other things, ATOH1, the target of our DB-ATO program, was removed as a collaboration target and the terms and plans for the DB-OTO and AAV.103 programs were modified. We issued 10,000,000 shares of our Series C convertible preferred stock to Regeneron in consideration for its entry into the amendment.

Pursuant to the Regeneron Agreement, Regeneron paid us an upfront fee of $25.0 million and purchased 12,500,000 shares of our Series B convertible preferred stock at a price per share of $2.00. If Regeneron elects to extend the term of the research program, it will be obligated to pay us $10.0 million for each of up to two one-year extensions. On a collaboration-product-by-collaboration-product basis, upon achievement of pre-defined milestones which begin at initiation of manufacturing to support GLP toxicology studies and conclude at initiation of a Phase 2 clinical trial, Regeneron is obligated to pay us milestone payments of up to $35.5 million in aggregate if the collaboration product is a biologic or up to $33.5 million in aggregate if the collaboration product is a small molecule, which is intended to reflect approximately half of the total cost needed to achieve the next milestone. From and after the initiation of a registration-enabling trial, unless Regeneron decides to opt-out, we have agreed to split development and regulatory costs with Regeneron on an equal basis through the registration-enabling trials.

Under the Regeneron Agreement, we are required to pay Regeneron tiered royalties on the worldwide net sales of collaboration products at percentages which range from mid-single digit to mid-thirties, with the exact royalty rate depending on the extent to which Regeneron shared in the funding of the collaboration product, the level of net sales of the collaboration product, the nature of any intellectual property contributed by Regeneron included in the collaboration product and whether the product is sold inside or outside the field. In the case of collaboration products for which Regeneron does not opt-out, our obligation to pay tiered royalties on the worldwide net sales ranges from percentages in the mid-twenties to mid-thirties. In the case of collaboration products for which Regeneron opts-out, our obligation to pay tiered royalties on the worldwide net sales ranges from percentages in the mid-single digits to mid-twenties. Our obligation to make royalty payments to Regeneron on account of worldwide net sales of collaboration products continues so long as we, our affiliates, licensees or sublicensees sell collaboration products. To date, we have not made any royalty or other payments to Regeneron under the Regeneron Agreement.

Pursuant to the amendment to the Regeneron Agreement, Regeneron agreed to pay us $0.3 million to fund our ongoing research program and $0.5 million to help secure the services of a contract development and manufacturing organization. The $0.5 million payment is creditable against the milestone associated with the initiation of manufacturing to support GLP toxicology studies of DB-OTO. Additionally, Regeneron agreed to reimburse us for up to $10.5 million of third-party costs related to the GLP toxicology studies of DB-OTO as such costs are incurred, and we agreed that the aggregate potential milestone payments for DB-OTO would be reduced by $15.0 million. In addition, notwithstanding its removal from the collaboration, for DB-ATO, we agreed to pay to Regeneron a royalty calculated as a low-to mid-single digit percentage of net sales of DB-ATO, on a country-by-country basis, until the latest of the expiration of the last patent covering DB-ATO in such country, the expiration of all applicable regulatory exclusivities for DB-ATO in such country and the tenth anniversary of the first commercial sale of DB-ATO in such country.

In November 2020, we achieved our first milestone in connection with the initiation of manufacturing to support GLP toxicology studies of DB-OTO, and, in December 2020, we received a milestone payment of $4.4 million, less the $0.5 million creditable payment previously paid to us by Regeneron. For a more detailed description of the Regeneron Agreement and the amendment, see “Business – License and Collaboration Agreements – License and Collaboration Agreement with Regeneron Pharmaceuticals, Inc.” in our Annual Report on Form 10-K as filed with the SEC on March 20, 2021.

Because we consider Regeneron a collaborative partner that is subject to the significant risks and rewards under the Regeneron Agreement, we have accounted for the Regeneron Agreement under FASB ASC Topic 808, *Collaborative Arrangements*, or ASC 808. Under ASC 808, we view the $25.0 million upfront payment and any milestone payments as reimbursement of our costs under the Regeneron Agreement. These costs are accounted for as research and development expenses in our condensed consolidated statements of operations and comprehensive loss. As such, we are recognizing the upfront payment, the additional payment of $0.3 million received from Regeneron pursuant to the amendment, the expected reimbursement of $10.5 million of third-party costs related to the GLP toxicology studies of DB-OTO, and the $4.4 million milestone payment received, net of the $4.4 million in fair value of the Series C convertible preferred stock issued to Regeneron, over the research term as a reduction to research and development expenses (contra-research and development expense) in our condensed consolidated statements of operations and comprehensive loss based on our progress toward completion of our research activities under the research plan. Any future milestone payments will be included in the measurement of contra-research and development expense if and when achieved. We recognized $1.9 million as contra-research and development expenses during the three months ended March 31, 2021 and $0.6 million as contra-research and development expenses during the three months ended March 31, 2020. As of March 31, 2021, we had $4.2 million of accounts receivable due from Regeneron, of which $3.0 million was unbilled. As of December 31, 2020, we had $1.2 million of unbilled accounts receivable due from Regeneron, all of which was unbilled. As of March 31, 2021, we had deferred collaboration liabilities of $16.2 million on our condensed consolidated balance sheet, which consisted of $9.7 million classified as current deferred collaboration liabilities and $6.5 million classified as long-term collaboration liabilities. See Note 13 to our condensed consolidated financial statements appearing elsewhere in this Quarterly Report on Form 10-Q.

Financial Operations Overview

Revenue

We have not generated any revenue since inception and do not expect to generate any revenue from the sale of products for at least the next several years. If our development efforts for our current or future product candidates are successful and result in marketing approval or if we enter into collaboration or license agreements with third parties, we may generate revenue in the future from product sales or payments from third-party collaborators or licensors.

Operating Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities and development of our programs and product candidates. These expenses include:

- personnel-related expenses, including salaries, benefits and stock-based compensation expense for employees engaged in research and development functions;
- expenses incurred under agreements with third parties, such as consultants and investigative sites that conduct our preclinical studies and clinical trials and in-licensing arrangements;
- costs incurred to maintain compliance with regulatory requirements;
- costs incurred with third-party contract development and manufacturing organizations, or CDMOs, to acquire, develop and manufacture materials for preclinical and clinical studies;
- costs associated with our technology and our intellectual property portfolio;
- expenses incurred for the procurement of materials, laboratory supplies and non-capital equipment used in the research and development process; and
- depreciation, amortization and other direct and allocated expenses, including rent, insurance and other operating costs, incurred as a result of our research and development activities.

We use our employee and infrastructure resources for the advancement of our platform and for discovering and developing programs and product candidates. We track direct research and development costs, consisting primarily of external costs, such as fees paid to CDMOs, CROs and consultants in connection with our preclinical studies, clinical trials and experiments by program after a development candidate has been identified. Due to the number of ongoing programs and our ability to use resources across several projects, personnel-related expenses and indirect or shared operating costs incurred for our research and development programs are not recorded or maintained on a program-by-program basis, nor are our external program costs incurred for our programs prior to the identification of a development candidate for such program.

Additionally, consideration we receive under our license and collaboration agreement with Regeneron is being recognized as a reduction to research and development expense (contra-research and development expense) in our condensed consolidated statements of operations and comprehensive income (loss) based on our progress towards completion of our research activities under the research plan for the collaboration. The following table reflects our research and development expense, including direct program-specific expense summarized by program, personnel-related expenses and indirect or shared operating costs recognized during each period presented (in thousands):

	Three Months Ended March 31,	
	2021	2020
DB-020	$ 295	$ 1,079
Personnel-related (including stock-based compensation)	2,103	3,918
Other indirect research and development expenses	3,622	2,439
Total research and development expenses	$ 6,020	$ 7,436

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that our research and development expenses will continue to increase for the foreseeable future as we advance our programs and product candidates into and through the development phase, and as we continue to develop additional product candidates. We also expect our discovery research efforts and our related personnel costs will increase and, as a result, we expect our research and development expenses, including costs associated with stock-based compensation, will increase above historical levels. In addition, we may incur additional expenses related to milestone and royalty

payments payable to third parties with whom we may enter into license, acquisition and option agreements to acquire the rights to future product candidates.

At this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the development of, and obtain regulatory approval for, any of our product candidates or programs. This is due to the numerous risks and uncertainties associated with drug development, including the uncertainty of:

- the timing and progress of preclinical and clinical development activities;
- the number and scope of preclinical and clinical programs we decide to pursue;
- our ability to successfully complete clinical trials with safety, potency and purity profiles that are satisfactory to the FDA or any comparable foreign regulatory authority;
- our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize, our product candidates;
- our ability to hire and retain key research and development personnel;
- our successful enrollment in and completion of clinical trials;
- the costs associated with the development of any additional product candidates we develop or acquire through collaborations;
- our ability to establish and maintain agreements with third-party manufacturers for clinical supply for our clinical trials and commercial manufacturing, if our product candidates are approved;
- the terms and timing of any collaboration, license or other arrangement, including the terms and timing of any milestone payments thereunder;
- our ability to obtain and maintain patent, trade secret and other intellectual property protection and regulatory exclusivity for our product candidates if and when approved;
- our receipt of marketing approvals from applicable regulatory authorities;
- our ability to commercialize products, if and when approved, whether alone or in collaboration with others;
- the continued acceptable safety profiles of the product candidates following approval; and
- the effects of COVID-19 to our research and development employees, contractors and those who may participate in our studies.

A change in any of these variables with respect to the development of any of our product candidates would significantly change the costs, timing and viability associated with the development of that product candidate. We may never succeed in obtaining regulatory approval for any product candidate we may develop.

General and Administrative Expense

General and administrative expenses consist primarily of personnel-related costs, including salaries, benefits and stock-based compensation, for personnel in our executive, finance, legal, business development, human resources and administrative functions. General and administrative expenses also include legal fees relating to corporate matters and costs to secure and defend our intellectual property; professional fees for accounting, auditing, tax, human resources and administrative consulting services; insurance costs; administrative travel expenses and facility-related expenses, which include direct depreciation costs and allocated expenses for office rent and other operating costs. These costs relate to the operation of the business, unrelated to the research and development function, or any individual program.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support the expected growth in our research and development activities and the potential commercialization of our product candidates. We also expect to incur increased expenses associated with being a public company, including increased costs of accounting, audit, legal, regulatory and tax-related services associated with maintaining compliance with exchange listing and SEC requirements, director and officer insurance costs and investor and public relations costs. We also expect to incur additional intellectual property-related expenses as we file patent applications to protect innovations arising from our research and development activities.

Interest Income

Interest income consists of interest income earned from our cash, cash equivalents and available-for-sale securities.

Income Taxes

Since our inception, we have not recorded any U.S. federal or state income tax benefits for the net losses we have incurred in each year or for our earned research and development tax credits, due to our uncertainty of realizing a benefit from those items. We have also not recognized any reserves related to uncertain tax positions. We have U.S. federal and state net operating loss carryforwards and research and development tax credit carryforwards to offset future federal and state taxable income.

Income taxes are determined at the applicable tax rates adjusted for non-deductible expenses, research and development tax credits and other permanent differences. Our income tax provision may be significantly affected by changes to our estimates.

Restructuring

In January and May 2020, we had a reduction in force that included 45 full-time employees, which represented approximately 52% of our full-time employee workforce. The reduction in force was primarily comprised of positions related to research and general and administrative services and was implemented in connection with our determination to focus and reprioritize our resources on gene therapy programs for hearing and balance disorders and to eliminate our research efforts on other discovery programs for hearing loss. As a result of the reduction, we incurred expenses of approximately $2.9 million during the first quarter of 2020 and $0.6 million during the second quarter of 2020, comprised of termination benefits including severance, benefits and other payroll-related charges. During the first quarter of 2020, we established retention agreements with certain key employees, including one of our executive officers. Under the terms of these agreements, we agreed to make three retention payments to each key employee totaling $1.6 million in the aggregate if they remained employed at the Company through specified milestones. The first payments of $0.7 million in the aggregate were paid upon execution of the retention agreements. The second payments of $0.4 million in the aggregate became due to the key employees upon the closing of the Series D financing in November 2020. The third payments of $0.5 million in the aggregate have been paid as of March 31, 2021, including payments to certain employees who are required to remain employed through January 1, 2022 in order to retain the first and third payments. These prepayments are being amortized over the remaining employee service terms under the retention agreements.

Restructuring expenses are classified as research and development expenses or general and administrative expenses in the condensed consolidated statements of operations and comprehensive loss in the manner in which the respective employee's salary and related costs were classified.

Results of Operations

Comparison of the Three Months Ended March 31, 2021 and 2020

The following tables summarizes our results of operations for each period presented (in thousands):

	Three Months Ended March 31,		
	2021	2020	Change
Operating expenses:			
Research and development	$ 6,020	$ 7,436	$ (1,416)
General and administrative	4,883	4,178	705
Total operating expenses	10,903	11,614	(711)
Loss from operations	(10,903)	(11,614)	711
Other income:			
Interest income	33	79	(46)
Total other income, net	33	79	(46)
Net loss	$ (10,870)	$ (11,535)	$ 665

Research and Development Expenses

The following tables summarizes our research and development expenses for each period presented (in thousands):

	Three Months Ended March 31,		
	2021	2020	Change
DB-020	$ 295	$ 1,079	$ (784)
Personnel-related (including stock-based compensation)	2,103	3,918	(1,815)
Other indirect research and development expenses	3,622	2,439	1,183
Total research and development expenses	$ 6,020	$ 7,436	$ (1,416)

Research and development expenses for the three months ended March 31, 2021 were $6.0 million, compared to $7.4 million for the three months ended March 31, 2020. The decrease of $1.4 million was primarily attributable to the following:

- $0.8 million decrease in expenses incurred to advance our DB-020 program, driven primarily by a decrease in clinical activity primarily driven by reduced enrollment in our clinical program as a result of delays due to the COVID-19 pandemic;
- $1.8 million decrease in personnel-related costs due to reduced headcount, driven primarily by the reduction in force conducted in January 2020 and May 2020; and
- $1.2 million net increase in other indirect research and development expenses, driven primarily by an increase in manufacturing costs related to toxicology studies. Included as reductions to other indirect research and development expenses are $1.9 million and $0.6 million of contra-research and development expenses for the three months ended March 31, 2021 and 2020, respectively, recognized pursuant to our collaboration agreement with Regeneron.

General and Administrative Expense

General and administrative expenses for the three months ended March 31, 2021 were $4.9 million, compared to $4.2 million for the three months ended March 31, 2020. The increase of $0.7 million was primarily attributable to the following:

- $1.0 million increase in professional fees, driven primarily by expenses related to consulting, accounting advisory and audit services incurred as a result of becoming a public company;
- $0.4 million increase in other general expenses, driven primarily by our director’s and officer’s insurance policy effective upon our initial public offering; and
- $0.7 million decrease in personnel-related costs due to reduced headcount, driven primarily by the reduction in force conducted in January 2020 and May 2020.

Interest Income

The decrease in interest income was primarily due to a reduction in interest rates, partially offset by the increase in our holdings following receipt of the proceeds from the issuance and sale of our Series D convertible preferred stock and from our IPO.

Liquidity and Capital Resources

Sources of Liquidity and Capital

Since our inception, we have incurred significant operating losses and negative cash flows from operations. We have not yet commercialized any of our product candidates, which are in various phases of preclinical and clinical development, and we do not expect to generate revenue from sales of any products for several years, if at all. Through March 31, 2021, we funded our operations primarily from net proceeds of $219.5 million from the issuance and sale of our convertible preferred stock, $29.7 million from our collaboration agreement with Regeneron and $124.8 million from the issuance and sale of our common stock in our IPO.

Cash Flows

The following table provides information regarding our cash flows for each period presented (in thousands):

	Three Months Ended March 31,	
	2021	2020
Net cash provided by (used in):		
Operating activities	$ (16,306)	$ (11,906)
Investing activities	(112,443)	11,694
Financing activities	153,148	—
Net increase (decrease) in cash, cash equivalents and restricted cash	$ 24,399	$ (212)

Operating Activities

Our cash flows from operating activities are greatly influenced by our use of cash for operating expenses and working capital requirements to support the business. We have historically experienced negative cash flows from operating activities as we invested in developing our pipeline, platform, drug discovery efforts and related infrastructure. The cash used in operating activities resulted primarily from our net losses adjusted for non-cash charges, which are generally attributable to stock-based compensation, depreciation and amortization and accretion of discounts on available-for-sale securities, as well as changes in components of operating assets and liabilities, which are generally attributable to increased expenses, timing of vendor payments and performance under our collaboration agreement.

During the three months ended March 31, 2021, net cash used in operating activities of $16.3 million was primarily due to our net loss of $10.9 million and changes in operating assets and liabilities of $6.6 million, partially offset by net non-cash expenses of $1.2 million.

During the three months ended March 31, 2020, net cash used in operating activities of $11.9 million was primarily due to our net loss of $11.5 million and changes in operating assets and liabilities of $1.1 million, partially offset by net non-cash expenses of $0.7 million.

Investing Activities

During the three months ended March 31, 2021, net cash used in investing activities of $112.4 million was primarily due to purchases of available-for-sale securities of $116.2 million and purchases of property and equipment of $0.1 million, partially offset by maturities of available-for-sale securities of $3.8 million.

During the three months ended March 31, 2020, net cash provided by investing activities of $11.7 million was primarily due to maturities of available-for-sale securities of $11.8 million, partially offset by purchases of property and equipment of $0.1 million.

Financing Activities

During the three months ended March 31, 2021, net cash provided by financing activities of $153.1 million consisted primarily of proceeds from the issuance and sale of common stock, net of cash paid for offering costs, in connection with our IPO of $125.8 million and proceeds from the issuance and sale of our Series D convertible preferred stock of $27.4 million, net of cash paid for offering costs.

Funding Requirements

We expect our expenses to increase substantially in connection with our ongoing research and development activities, particularly as we advance the preclinical activities and clinical trials of our product candidates. In addition, we expect to incur additional costs associated with operating as a public company. As a result, we expect to incur substantial operating losses and negative operating cash flows for the foreseeable future.

As of March 31, 2021, our cash, cash equivalents and available-for-sale securities of $191.1 million. We believe that our cash, cash equivalents and available-for-sale securities as of March 31, 2021 will enable us to fund our operating expenses and capital expenditure requirements into 2024. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we anticipate.

Because of the numerous risks and uncertainties associated with product development, and because the extent to which we may enter into collaborations with third parties for the development of our product candidates is unknown, we may incorrectly estimate the timing and amounts of increased capital outlays and operating expenses associated with completing the research and development of our product candidates. Our funding requirements and timing and amount of our operating expenditures will depend on many factors, including, but not limited to:

- the progress, costs and results of our ongoing preclinical development, our planned Phase 1/2 clinical trial of DB-OTO and any future clinical development of DB-OTO;
- the progress, costs and results of clinical development of DB-020, including our ongoing Phase 1b clinical trial;
- the scope, progress, costs and results of preclinical and clinical development for our other product candidates and programs, including AAV.103, AAV.104, AAV.201 and DB-ATO;
- the number of, and development requirements for, other product candidates that we may identify and develop;
- the scope, costs, timing and outcome of regulatory review of our product candidates;
- the cost and timing of completion of commercial-scale manufacturing activities;
- the success of our collaboration with Regeneron;
- the payment or receipt of milestones and of other collaboration-based revenues, if any;
- our ability to establish and maintain additional strategic collaborations, licensing or other arrangements and the financial terms of such arrangements;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;
- the amount and timing of revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property and proprietary rights and defending any intellectual property-related claims;
- the extent to which we may acquire or in-license other products, product candidates and technologies;
- the impacts of the COVID-19 pandemic;
- the ability to receive additional non-dilutive funding, including grants from organizations and foundations; and
- the costs of operating as a public company.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for several years, if ever. Accordingly, we will need to obtain substantial additional funds to achieve our business objectives.

Our expectation with respect to our ability to fund current planned operations is based on estimates that are subject to risks and uncertainties. Our operating plan may change as a result of many factors currently unknown to management and there can be no assurance that the current operating plan will be achieved in the time frame anticipated by us, and we may need to seek additional funds sooner than planned.

Adequate additional funds may not be available to us on acceptable terms, or at all. We do not currently have any committed external source of funds, other than the reimbursements to which we are entitled under the Regeneron Agreement for up to $10.5 million of third-party costs related to the GLP toxicology studies of DB-OTO. Market volatility resulting from the COVID-19 pandemic or other factors could also adversely impact our ability to access capital as and when needed. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of holders of our common stock. Additional debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends and may require the issuance of warrants, which could potentially dilute the ownership interests of holders of our common stock.

We may be unable to raise additional funds or enter into other collaborations, strategic alliances or licensing arrangements with third parties when needed on favorable terms, or at all. If we are unable to raise additional funds through equity or debt financings or enter into such agreements when needed, we may have to significantly delay, reduce or eliminate some or all of our product development or future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves or on terms that may not be favorable to us.

Off-Balance Sheet Arrangements.

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined in the rules and regulations of the U.S. Securities and Exchange Commission.

Critical Accounting Policies and Significant Judgement and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our condensed consolidated financial statements, which have been prepared in accordance with GAAP. The preparation of these condensed consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the reported expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

We define our critical accounting policies as those accounting principles generally accepted in the United States of America that are most critical to the judgments and estimates used in the preparation of our condensed consolidated financial statements. While our significant accounting policies are described in more detail in Note 2 to our consolidated financial statements in our 2020 Annual Report on Form 10-K, we believe that our most critical accounting policies are those relating to Collaboration Agreements, Research and Development Expenses and Related Accruals and Stock-Based Compensation, which are described under the heading "Management's Discussion and Analysis of Financial Condition and Results of Operations – Critical Accounting Policies and Significant Judgement and Estimates" in our 2020 Annual Report on Form 10-K.

There have been no material changes to our critical accounting policies from those described in our 2020 Annual Report on Form 10-K.

Emerging Growth Company and Smaller Reporting Company Status

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act, or the JOBS Act, enacted in April 2012. As a result, we may take advantage of reduced reporting requirements that are otherwise applicable to public companies. In particular, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. We have elected not to "opt out" of such extended transition period, which means that when a standard is issued or revised and it has different application dates for public or private companies, we can adopt the new or revised standard at the time private companies adopt the new or revised standard and may do so until such time that we either (1) irrevocably elect to "opt out" of such extended transition period or (2) no longer qualify as an emerging growth company.

We are also a "smaller reporting company" as defined in Rule 12b-2 under the Exchange Act. We may continue to be a smaller reporting company if either (i) the market value of our shares held by non-affiliates is less than $250 million or (ii) our annual revenue was less than $100 million during the most recently completed fiscal year and the market value of our shares held by non-affiliates is less than $700 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies.

Recently Issued Accounting Pronouncements

We have reviewed all recently issued accounting pronouncements and have determined that, other than as disclosed in Note 2 to our consolidated financial statements included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2020 as filed with the SEC on March 29, 2021, such standards will not have a material impact on our financial statements or do not otherwise apply to our current operations.

Item 3. Quantitative and Qualitative Disclosures About Market Risk.

Interest Rate Fluctuation Risk

We are exposed to market risk related to changes in interest rates. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our cash equivalents are invested in short-term U.S. Treasury obligations and our available-for-sale securities are invested in corporate obligations. However, because of the short-term nature of the instruments in our portfolio, an immediate change in market interest rates of 100 basis points would not have a material impact on the fair market value of our investment portfolio or on our financial position or results of operations.

Foreign Currency Fluctuation Risk

We are not currently exposed to significant market risk related to changes in foreign currency exchange rates; however, we have contracted with and may continue to contract with foreign vendors. Our operations may be subject to fluctuations in foreign currency exchange rates in the future.

Inflation Fluctuation Risk

Inflation generally affects us by increasing our cost of labor. We do not believe that inflation had a material effect on our business, financial condition or results of operations during the three months ended March 31, 2021 and 2020.

Item 4. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

We maintain "disclosure controls and procedures" as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, that are designed to ensure that information required to be disclosed in the reports we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports we file or submit under the Exchange Act is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosure. In designing and evaluating our disclosure controls and procedures, 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 benefits of possible controls and procedures relative to their costs.

Our management, with the participation of our chief executive officer and chief financial officer, who serve as our principal executive officer and principal financial officer, respectively, has evaluated the effectiveness of our disclosure controls and procedures as of March 31, 2021. Based on such evaluation, our chief executive officer and chief financial officer have concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of March 31, 2021.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the fiscal quarter ended March 31, 2021 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.

From time to time, we may become involved in legal proceedings arising in the ordinary course of our business. We are not currently subject to any material legal proceedings.

Item 1A. Risk Factors.

Our business is subject to a number of risks. You should carefully consider the risks and uncertainties described below together with all of the other information contained in this Quarterly Report on Form 10-Q, including the Management's Discussion and Analysis of Financial Condition and Results of Operations section and the condensed consolidated financial statements and the related notes thereto in evaluating our company. The risks described below are not the only risks facing us. The occurrence of any of the following risks, or of additional risks and uncertainties not presently known to us or that we currently believe to be immaterial, could cause our business, prospects, results of operations and financial condition to suffer materially.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses since our inception, have no products approved for sale and we expect to incur substantial losses for the foreseeable future and may never achieve or maintain profitability.

Since inception, we have incurred significant operating losses. Our net losses were $10.9 million for the three months ended March 31, 2021 and $39.3 million and $42.7 million for the years ended December 31, 2020 and 2019, respectively. As of March 31, 2021, we had an accumulated deficit of $173.6 million. To date, we have financed our operations primarily with proceeds from sales of preferred stock (including borrowings under convertible promissory notes, which converted into preferred stock in 2015), payments under the license and collaboration agreement, or the Regeneron Agreement, to which we are a party with Regeneron Pharmaceuticals, Inc., or Regeneron, and, most recently, from the sale of common stock in our initial public offering, or IPO. Since inception, we have devoted substantially all of our resources on organizing and staffing, business planning, raising capital, establishing our intellectual property portfolio and performing research and development of our product candidates, programs and platform. We are still in the early stages of development of our product candidates, and we have not completed development of any product candidates. We expect to continue to incur significant expenses and operating losses over the next several years. Our operating expenses and net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses and capital expenditures will increase substantially if and as we:

- submit an investigational new drug application, or IND, or clinical trial application, or CTA, and initiate a planned Phase 1/2 clinical trial of our lead gene therapy product candidate, DB-OTO, for the treatment of profound hearing loss due to mutation of the otoferlin, or OTOF, gene;
- continue our current research programs and our preclinical development of DB-OTO, AAV.103, AAV.104, AAV.201 and DB-ATO and any product candidates that may arise from our current or future research programs;
- continue our clinical development of DB-020, including our ongoing Phase 1b clinical trial;
- advance additional product candidates into preclinical and clinical development;
- expand the capabilities of and invest in our platform;
- seek marketing approvals for any product candidates that successfully complete clinical trials;
- ultimately establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- expand, maintain and protect our intellectual property portfolio;
- hire additional clinical, regulatory, quality control and scientific personnel;
- establish and maintain agreements with manufacturers for our product candidates; and
- add operational, legal, compliance, financial and management information systems and personnel, including personnel to support our research, product development and future commercialization efforts and support our operations as a public company.

In addition, our expenses will increase if, among other things:

- we are required by the U.S. Food and Drug Administration, or the FDA, the European Medicines Agency, or the EMA, or other regulatory authorities to perform trials or studies in addition to, or different than, those expected;

- there are any delays in completing our clinical trials or the development of any of our product candidates; or
- there are any third-party challenges to our intellectual property or we need to defend against any intellectual property-related claim.

We have no products for which we have obtained marketing approval and have not generated any revenue from product sales. Even if we obtain marketing approval of and are successful in commercializing one or more of our product candidates, we expect to incur substantial research and development and other expenditures to develop and market additional product candidates. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue.

We have never generated revenue from product sales and may never achieve or maintain profitability.

We have never generated revenue from product sales and our most advanced product candidate is in early clinical trials. We expect that it will be many years, if ever, before we have a product candidate ready for commercialization. To become and remain profitable, we must succeed in developing, and eventually commercializing, a product or products that generate significant revenue. The ability to achieve this success will require us to be effective in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, discovering additional product candidates, obtaining marketing approval for these product candidates and manufacturing, marketing and selling any products for which we may obtain marketing approval. We are only in the preliminary stages of these activities. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability. Because of the numerous risks and uncertainties associated with biopharmaceutical product development, we are unable to accurately estimate or know the nature, timing or costs of the efforts that will be necessary to complete the preclinical and clinical development and commercialization of our product candidates or when, or if, we will be able to generate revenues or achieve profitability.

Our ability to generate revenue from product sales and achieve profitability depends on our ability to successfully develop and obtain the marketing approvals necessary to commercialize our product candidates. We do not have any products approved for sale and do not anticipate generating revenue from product sales for the next several years, if ever. Our ability to generate future revenue from product sales depends heavily on our success in:

- completing preclinical and clinical development of our product candidates in a timely manner and identifying and developing new product candidates;
- seeking and obtaining marketing approvals for any of our product candidates;
- commercializing product candidates for which we obtain marketing approval by establishing a sales force, marketing, medical affairs and distribution infrastructure or, alternatively, collaborating with a commercialization partner;
- achieving formulary status in hospitals and adequate coverage and reimbursement by government and third-party payors for our product candidates, if approved;
- establishing and maintaining supply and manufacturing relationships with third parties that can provide adequate products and services, in both amount and quality, to support clinical development and the market demand for our product candidates, if approved;
- obtaining market acceptance of our product candidates, if approved, as viable treatment options;
- addressing any competing technological and market developments;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter and performing our obligations in such collaborations;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how;
- defending against third-party interference or infringement claims, if any; and
- attracting, hiring and retaining qualified personnel.

Even if one or more of our product candidates is approved for commercial sale, we anticipate incurring significant costs in commercializing any approved product candidate. Our expenses could increase beyond expectations if we are required by the FDA, EMA or other regulatory agencies to perform clinical trials or studies in addition to those that we currently anticipate. Even if we are able to generate revenue from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis as we expect to continue to engage in substantial research and development activities and to incur substantial expenses to develop and commercialize product candidates.

Our failure to become and remain profitable would depress our market value and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our pipeline of product candidates or even continue our operations. A decline in the value of our company could also cause our stockholders to lose all or part of their investment.

We will need substantial additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our research and development programs or commercialization efforts.

Since inception, we have used substantial amounts of cash. The development of biopharmaceutical product candidates is capital intensive and we expect that we will continue to expend substantial resources for the foreseeable future in connection with our ongoing activities. In particular, substantial resources will be required as we continue to conduct additional preclinical studies and prepare for and initiate our planned Phase 1/2 clinical trial of DB-OTO, continue research and development, initiate preclinical testing and clinical trials of AAV.103, AAV.104, AAV.201, DB-ATO and any product candidates that may arise from our current or future research programs, continue our clinical development of DB-020, including our ongoing Phase 1b clinical trial, and advance our platform. Identifying potential product candidates, conducting preclinical testing and clinical trials and potentially submitting approvals of our product candidates is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. Furthermore, we have incurred and expect to continue to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital or obtain adequate funds when needed or on acceptable terms, we may be required to delay, limit, reduce or terminate our research and development programs or any future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

We believe that our existing cash, cash equivalents and available-for-sale securities will enable us to fund our operating expenses and capital expenditure requirements into 2024. However, we have based this estimate on assumptions that may prove to be wrong, and our operating plan may change as a result of many factors currently unknown to us. As a result, we could deplete our capital resources sooner than we currently expect.

Our future capital requirements will depend on many factors, including:

- the progress, costs and results of our ongoing preclinical development, our planned Phase 1/2 clinical trial of DB-OTO and any future clinical development of DB-OTO;
- the progress, costs and results of clinical development of DB-020, including our ongoing Phase 1b clinical trial;
- the scope, progress, costs and results of preclinical and clinical development for our other product candidates and programs, including AAV.103, AAV.104, AAV.201 and DB-ATO;
- the number of, and development requirements for, other product candidates that we may identify and develop;
- the scope, costs, timing and outcome of regulatory review of our product candidates;
- the cost and timing of completion of commercial-scale manufacturing activities;
- the success of our collaboration with Regeneron;
- the payment or receipt of milestones and of other collaboration-based revenues, if any;
- our ability to establish and maintain additional strategic collaborations, licensing or other arrangements and the financial terms of such arrangements;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;
- the amount and timing of revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property and proprietary rights and defending any intellectual property-related claims;
- the extent to which we may acquire or in-license other products, product candidates and technologies;
- the impacts of the COVID-19 pandemic;

- the ability to receive additional non-dilutive funding, including grants from organizations and foundations; and
- the costs of operating as a public company.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial revenues from product sales, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. We do not have any committed external source of funds, other than the reimbursements we are entitled to under the Regeneron Agreement for up to $10.5 million of third-party costs for preclinical studies of DB-OTO. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect their rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, selling or licensing our assets, making capital expenditures or declaring dividends. Such restrictions could adversely impact our ability to conduct our operations and execute our business plan. In addition, securing financing could require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of our product candidates.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed or on terms acceptable to us, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our limited operating history may make it difficult for stockholders to evaluate the success of our business to date and to assess our future viability.

We commenced operations in 2013, and our operations to date have been limited to organizing and staffing our company, business planning, raising capital, conducting research and development activities, identifying potential product candidates, soliciting input from regulators regarding development of these product candidates, securing intellectual property rights and undertaking preclinical studies and clinical trials. All of our gene therapy product candidates are still in the research or preclinical stage of development. We have not yet demonstrated our ability to successfully develop any product candidate, obtain marketing approvals, manufacture a commercial scale product, arrange for a third party to do so on our behalf, or conduct sales, marketing and distribution activities necessary for successful product commercialization. Consequently, any predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing products.

In addition, as our business grows, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition at some point from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We expect our financial condition and operating results to fluctuate significantly from quarter-to-quarter and year-to-year due to a variety of factors, many of which are beyond our control. Accordingly, stockholders should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

Our ability to use our NOLs and research and development tax credit carryforwards to offset future taxable income may be subject to certain limitations.

As of December 31, 2020, we had U.S. federal net operating loss carryforwards of approximately $148.7 million to offset future federal taxable income. Federal net operating losses, or NOLs, of $41.7 million will expire beginning in 2033. As of December 31, 2020, we had NOLs of $107.0 million which had an indefinite life. As of December 31, 2020, we had state net operating loss carryforwards of $146.0 million to offset future state taxable income, which will begin to expire in 2035. As of December 31, 2020, we had foreign net operating loss carryforwards of approximately $3.0 million to offset future foreign taxable income, which do not expire. As of December 31, 2020, we had federal research and development tax credit carryforwards of $0.8 million, which expire beginning in 2033, and state research and development tax credit carryforwards of $0.5 million, which expire beginning in 2032. These net operating loss and tax credit carryforwards could expire unused and be unavailable to offset future income tax liabilities.

We have a history of cumulative losses and anticipate that we will continue to incur significant losses in the foreseeable future; thus, we do not know whether or when we will generate taxable income necessary to utilize our NOLs or research and development tax credit carryforwards.

In general, under Section 382 of the Code and corresponding provisions of state law, a corporation that undergoes an "ownership change," generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders over a three-year period, is subject to limitations on its ability to utilize its pre-change NOLs and research and development tax credit carryforwards to offset future taxable income. We have not conducted a study to assess whether any such ownership changes have occurred. We may have experienced such ownership changes in the past and may experience such ownership changes in the future as a result of subsequent changes in our stock ownership (which may be outside our control). As a result, if, and to the extent that, we earn net taxable income, our ability to use our pre-change NOLs and research and development tax credit carryforwards to offset such taxable income may be subject to limitations. Our NOLs or credits may also be impaired under state law.

There is also a risk that due to regulatory changes, such as suspensions on the use of NOLs, or other unforeseen reasons, our existing NOLs could expire or otherwise become unavailable to offset future income tax liabilities. As described above in "Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition," the TCJA includes changes to U.S. federal tax rates and the rules governing NOL carryforwards that may significantly impact our ability to utilize our NOLs to offset taxable income in the future. For these reasons, even if we attain profitability, we may be unable to use a material portion of our NOLs and other tax attributes.

Risks Related to Discovery and Development

We are very early in our development efforts. Our business is dependent on our ability to advance our lead gene therapy product candidate, DB-OTO, and our other current and future product candidates through preclinical studies and clinical trials, obtain marketing approval and ultimately commercialize them. If we are unable to complete clinical development, obtain regulatory approval for or commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.

We are very early in our development efforts. We have advanced only one product candidate, DB-020, into clinical trials, and it is still in early clinical trials. In addition, we have identified only one gene therapy product candidate, DB-OTO, which is in preclinical development. We expect to submit an IND to the FDA or a CTA within the European Union with respect to DB-OTO in 2022. Additionally, we have a portfolio of programs that are in earlier stages of preclinical development and may never identify another gene therapy product candidate or advance a gene therapy product candidate to clinical-stage development. Our ability to generate product revenue, which we do not expect will occur for many years, if ever, will depend heavily on the successful development, marketing approval and eventual commercialization of our product candidates, which may never occur. We have not sought regulatory approval for DB-OTO or any other product candidate and do not expect to be in a position to do so for the foreseeable future. We currently generate no revenue from sales of any product, and we may never be able to develop or commercialize a marketable product.

The clinical and commercial success of our product candidates will depend on several factors, including the following:

- timely and successful completion of preclinical studies, including IND-enabling studies;
- effective INDs or comparable foreign applications that allow commencement of our planned clinical trials or future clinical trials for our product candidates;
- successful enrollment and completion of clinical trials, including under the FDA's Good Clinical Practices, or GCPs, Good Laboratory Practices, or GLPs, and any additional regulatory requirements from foreign regulatory authorities;
- positive results from our future clinical programs that support a finding of safety and effectiveness and an acceptable risk-benefit profile of our product candidates in the intended populations;
- receipt of marketing approvals from the FDA and other applicable regulatory authorities;
- establishment of arrangements for clinical supply and, where applicable, commercial manufacturing capabilities, including with third-party manufacturers;
- commercial launch of our product candidates, if approved, whether alone or in collaboration with others;
- acceptance of the benefits and use of our product candidates, including method of administration, if and when approved, by patients, the medical community and third-party payors;
- effective competition with other therapies;

- establishment and maintenance of healthcare coverage and adequate reimbursement and patients' willingness to pay out-of-pocket in the absence of such coverage and adequate reimbursement;
- procurement of intellectual property protection and regulatory exclusivity for our product candidates, and enforcement and defense of intellectual property rights and claims; and
- maintenance of a continued acceptable safety, tolerability and efficacy profile of our product candidates following approval.

Many of these factors are beyond our control, including preclinical and clinical outcomes, the regulatory review process, potential threats to our intellectual property rights and the manufacturing, marketing, distribution and sales efforts of any collaborator. If we do not succeed in one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully develop and commercialize our product candidates, which would materially harm our business. If we are unable to advance our gene therapy product candidates to clinical development, obtain regulatory approval and ultimately commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed. Our limited experience in conducting clinical development activities, including with respect to gene therapies, may adversely impact the likelihood that we will be successful in advancing our product candidates or programs.

We are heavily dependent on the success of our lead gene therapy product candidate, DB-OTO.

We currently have no products that are approved for commercial sale and may never be able to develop marketable products. We expect that a substantial portion of our efforts and expenditures for the foreseeable future will be devoted to DB-OTO. Accordingly, our business currently depends heavily on the successful development, regulatory approval and commercialization of DB-OTO. We cannot be certain that DB-OTO will receive regulatory approval or be successfully commercialized even if we receive regulatory approval. If we were required to discontinue development of DB-OTO, or if DB-OTO does not receive regulatory approval, fails to achieve significant market acceptance or fails to receive reimbursement, we would be delayed by many years in our ability to achieve profitability, if ever, and may not be able to generate sufficient revenue to continue our business.

Clinical development involves a lengthy and expensive process with uncertain outcomes, and results of earlier studies and trials may not be predictive of future clinical trial results. If our preclinical studies and clinical trials are not sufficient to support regulatory approval of any of our product candidates, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development of such product candidate.

All of our product candidates are in preclinical development or early clinical trials and their risk of failure is high. Clinical testing is expensive, is difficult to design and implement, can take many years to complete and is uncertain as to outcome. We cannot guarantee that any of our clinical trials will be conducted as planned or completed on schedule, or at all. A failure of one or more clinical trials can occur at any stage of testing, which may result from a multitude of factors, including, but not limited to, flaws in trial design, dose selection issues, participant enrollment criteria and failure to demonstrate favorable safety or efficacy traits.

Before we can commence clinical trials for a product candidate, we must complete extensive preclinical testing and studies that support our planned INDs and other regulatory filings in the United States and abroad. We cannot be certain of the timely completion or outcome of our preclinical testing and studies and cannot predict if regulatory authorities will accept our proposed clinical programs or if the outcome of our preclinical testing and studies will ultimately support the further development of any product candidates. Our preclinical studies, particularly in our regeneration programs, are in the early stage, and we may not identify development candidates for IND-enabling studies or product candidates for clinical development when anticipated or at all. As a result, we cannot be sure that we will be able to submit INDs or corresponding regulatory filings for our preclinical programs on the timelines we expect, if at all, and we cannot be sure that submission of INDs or these regulatory filings will result in regulatory authorities allowing clinical trials to begin.

The time required to obtain approval from the FDA, EMA or other comparable foreign regulatory authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of regulatory authorities. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. We have not yet completed a clinical trial of any of our product candidates other than the Phase 1 clinical trial of DB-020 in healthy volunteers. Clinical trials may fail to demonstrate that our product candidates are safe for humans and effective for indicated uses. Even if the clinical trials are successful, changes in marketing approval policies during the development period, changes in or the enactment or promulgation of additional statutes, regulations or guidance or changes in regulatory review for each submitted product application may cause delays in the approval or rejection of an application.

Furthermore, product candidates are subject to continued preclinical safety studies, which may be conducted concurrently with our clinical testing. The outcomes of these safety studies may delay the launch of or enrollment in future clinical trials and could impact our ability to continue to conduct our clinical trials.

Other events that may prevent successful or timely completion of clinical development include:

- inability to generate sufficient preclinical, toxicology or other in vivo or in vitro data to support the initiation of clinical trials;
- delays in reaching a consensus with regulatory authorities on trial design;
- delays in reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites;
- delays related to COVID-19 disruptions at CROs, contract development and manufacturing organizations, or CDMOs, and/or clinical trial sites;
- delays in opening clinical trial sites or obtaining required institutional review board, or IRB, or institutional biosafety committee, or IBC, approval, or the equivalent review groups for sites outside the United States, at each clinical trial site;
- imposition of a clinical hold by regulatory authorities, including as a result of a serious adverse event or after an inspection of our clinical trial operations or trial sites;
- failure by us, any CROs we engage or any other third parties to adhere to clinical trial requirements;
- failure to perform in accordance with GCPs;
- failure by investigators and clinical sites to adhere to protocols leading to variable results;
- failure of our delivery approach in humans;
- delays in the testing, validation, manufacturing and delivery of our product candidates to the clinical sites, including delays by third parties with whom we have contracted to perform certain of those functions;
- failure of our third-party contractors to comply with regulatory requirements or to meet their contractual obligations to us in a timely manner, or at all;
- inability to enroll participants or delays in having enrolled participants complete their participation in a trial or return for post-administration follow-up;
- clinical trial sites or participants dropping out of a trial;
- selection of clinical endpoints that require prolonged periods of clinical observation or analysis of the resulting data;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon development programs;
- occurrence of serious adverse events associated with the product candidate or administration of the product candidate that are viewed to outweigh its potential benefits;
- occurrence of serious adverse events or other unexpected events in trials of the same class of agents conducted by other sponsors;
- changes in regulatory requirements and guidance that require amending or submitting new clinical trial protocols;
- changes in the legal or regulatory regimes domestically or internationally related to patient rights and privacy; or
- lack of adequate funding to continue the clinical trial.

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

Gene therapy is an emerging field of drug development that poses many risks. We have only limited prior experience in gene therapy research and no prior experience in gene therapy clinical development. Our lack of experience and the limited patient populations for our gene therapy programs may limit our ability to be successful or may delay our development efforts.

Gene therapy is an emerging field of drug development with a limited number of gene therapies having received regulatory approval to date. Our gene therapy research and development programs are at an early stage and there remain several areas of drug development risk, which pose particular uncertainty for our programs given the relatively limited development history of, and our limited prior experience with, gene therapies. Translational science, manufacturing materials and processes, safety concerns, regulatory pathway and clinical trial design and execution all pose particular risk to our drug development activities. Furthermore, the medical community's understanding of the genetic causes of many diseases continues to evolve and further research may change the medical community's views on what therapies and approaches are most effective for addressing certain diseases.

As an organization, we have not previously conducted any clinical trials of gene therapies. We have begun to establish our own gene therapy technical capabilities, but we will need to continue to expand those capabilities by either hiring internally or seeking assistance from outside service providers. Gene therapy is an area of significant investment by biotechnology and pharmaceutical companies and there may be a scarcity of talent available to us in these areas. If we are not able to expand our gene therapy capabilities, we may not be able to develop in the way we intend or desire any promising product candidates that emerge from our program or our other collaborative gene therapy sponsored research programs, which would limit our prospects for future growth. We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approvals of gene therapy product candidates that we develop. Failure to commence or complete, or delays in, our planned clinical trial or future clinical trials of gene therapy product candidates could prevent us from or delay us in commercializing our gene therapy product candidates.

As we prepare for the potential initiation of our first gene therapy clinical trial, we will need to build our internal and external capabilities in designing and executing a gene therapy clinical trial. There are many known and unknown risks involved in translating preclinical development of gene therapies to clinical development, including selecting appropriate endpoints and dosage levels for dosing humans based on preclinical data. If we are unable to initiate and conduct our gene therapy clinical trials in a manner that satisfies our expectations or regulatory requirements, the value of our gene therapy programs may be diminished.

Our gene therapy product candidates and programs are based on a relatively novel technology, which makes it difficult to predict the time and cost of development and of subsequently obtaining regulatory approval, if at all.

We are concentrating our therapeutic product research and development efforts primarily on our gene therapy programs. Our future success is almost entirely dependent on this therapeutic approach. Because our gene therapy product candidates are based on relatively novel technology, development problems we experience in the future related to our gene therapy platform may be difficult to solve and may cause delays and unanticipated costs. We may also experience delays in developing a sustainable, reproducible and scalable manufacturing process or transferring that process to commercial partners, which may prevent us from initiating or conducting clinical trials or commercializing our products on a timely or profitable basis, if at all.

Our gene therapy product candidates will need to meet purity, potency and safety standards applicable to any new biologic under the regulatory framework administered by the FDA. In addition to FDA oversight and oversight by IRBs, under guidelines promulgated by the National Institutes of Health, or NIH, gene therapy clinical trials may also be subject to review and oversight by an IBC, a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. Although the FDA decides whether individual gene therapy protocols may proceed, the review process and determinations of other reviewing bodies can impede or delay the initiation of a clinical trial, even if the FDA has reviewed the trial and approved its initiation.

In the European Union, the EMA's Committee for Advanced Therapies, or CAT, is responsible for assessing the quality, safety and efficacy of advanced-therapy medicinal products. Advanced-therapy medicinal products include gene therapy medicines, somatic-cell therapy medicines and tissue-engineered medicines. The role of the CAT is to prepare a draft opinion on an application for marketing authorization for a gene therapy medicinal candidate that is submitted to the EMA. In the European Union, the development and evaluation of a gene therapy product must be considered in the context of the relevant European Union guidelines. The EMA may issue new guidelines concerning the development and marketing authorization for gene therapy products and require that we comply with these new guidelines. As a result, the procedures and standards applied to gene therapy products and cell therapy products may be applied to any gene therapy product candidate we may develop, but that remains uncertain at this point.

Adverse developments in preclinical studies or clinical trials of gene therapies conducted by others may cause the FDA, the EMA and other regulatory bodies to revise the requirements for approval of any gene therapy product candidates we may develop or limit the use of products utilizing gene regulation technologies, either of which could harm our business. The regulatory approval process for gene therapy product candidates such as ours can be more expensive and take longer than for other, better known, or more extensively studied pharmaceutical or other product candidates. Further, as we are developing novel potential treatments for diseases

in which, in some cases, there is little clinical experience with potential new endpoints and methodologies, there is heightened risk that the FDA, the EMA or other regulatory bodies may not consider the clinical trial endpoints to provide clinically meaningful results, and the resulting clinical data and results may be more difficult to analyze. Any natural history studies that we may conduct or rely upon in our clinical development may not be accepted by the FDA, EMA or other regulatory authorities. Regulatory agencies administering existing or future regulations or legislation may not allow production and marketing of gene therapy products in a timely manner or under technically or commercially feasible conditions. In addition, regulatory action or private litigation could result in expenses, delays, or other impediments to our research programs or the commercialization of resulting products. Further, approvals by one regulatory agency may not be indicative of what other regulatory agencies may require for approval.

The regulatory review committees and advisory groups described above and the new guidelines they promulgate may lengthen the regulatory review process, require us to perform additional preclinical studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates, or lead to significant post-approval limitations or restrictions. As we advance our research programs and develop future product candidates, we will be required to consult with these regulatory and advisory groups and to comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of any product candidates we identify and develop. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delays as a result of an increased or lengthier regulatory approval process or further restrictions on the development of our product candidates can be costly and could negatively impact our ability to complete clinical trials and commercialize our current and future product candidates in a timely manner, if at all. The first approvals of gene therapy products by the FDA only occurred in 2017. As a result, it is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in either the United States or the European Union, or how long it will take to commercialize any product candidate that receives marketing approval.

The outcome of preclinical studies and earlier-stage clinical trials may not be predictive of future results or the success of later-stage clinical trials.

The results of preclinical studies may not be predictive of the results of clinical trials, and the results of any early-stage clinical trials may not be predictive of the results of the later-stage clinical trials or from clinical trials of the same product candidates in other indications. In addition, initial success in clinical trials may not be indicative of results obtained when such trials are completed. For example, the results of the Phase 1 clinical trial of DB-020 in healthy volunteers may not be indicative of the results of the ongoing Phase 1b clinical trial. In addition, if successful, the results of our planned Phase 1/2 clinical trial of DB-OTO may not be predictive of the results of further clinical trials of this product candidate or any other gene therapy product candidates. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. Our future clinical trials may not ultimately be successful or support further clinical development of any of our product candidates. There is a high failure rate for product candidates proceeding through clinical trials, and because our gene therapy product candidates are based on a relatively novel technology, the likelihood of success is harder to determine. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving encouraging results in earlier studies. Any such setbacks in our clinical development could materially harm our business, financial condition, results of operations and prospects.

Interim and preliminary results from our clinical trials that we announce or publish from time to time may change as more participant data become available and are subject to audit and verification procedures, which could result in material changes in the final data.

From time to time, we may publish interim or preliminary results from our clinical trials. Interim results from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as participant enrollment continues and more participant data become available. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully evaluate all data. Preliminary or top-line results also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. Additionally, preliminary data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. As a result, interim and preliminary data should be viewed with caution until the final data are available. Differences between preliminary or interim data and final data could be material and could significantly harm our reputation and business prospects and may cause the trading price of our common stock to fluctuate significantly.

If we experience delays or difficulties in participant enrollment for clinical trials, our research and development efforts and the receipt of necessary regulatory approvals could be significantly delayed or prevented.

Identifying and qualifying individuals to participate in clinical trials of is critical to our success. We may not be able to identify, recruit and enroll a sufficient number of participants, or those with required or desired characteristics, to complete our clinical trials in a timely manner. Any delay or difficulty in participant enrollment could significantly delay or otherwise hinder our research and development efforts and delay or prevent receipt of necessary regulatory approvals.

Participant enrollment and trial completion is affected by factors including:

- perceived risks and benefits in the case of our gene therapy product candidates, of a small virus commonly used in gene therapy, known as adeno-associated virus, or AAV, for the potential treatment of hearing loss and balance disorders;
- size of the patient population, including for rare diseases such as the rare diseases on which our gene therapy programs are currently focused, and process for identifying potential trial participants;
- the potential direct or indirect impact of the COVID-19 pandemic;
- design of the trial;
- inclusion and exclusion criteria;
- perceived risks and benefits of the product candidate;
- availability of competing therapies and clinical trials;
- severity of the disorder under investigation;
- availability of genetic testing for potential participants;
- proximity and availability of clinical trial sites for potential participants;
- ability to obtain and maintain informed consent;
- risk that enrolled participants will drop out before completion of the trial;
- the commitment of our clinical investigators to identify potential participants;
- patient referral practices of physicians;
- ability to monitor participants adequately during and after product candidate administration; and
- ability to recruit and retain trial participants due to other unforeseen circumstances.

For example, due to the continued impact of the COVID-19 pandemic on the pace of patient screening and enrollment and the closure of trial sites in the United States that we had expected to re-open, we have experienced a delay in when we expect to report results from an interim analysis of our ongoing Phase 1b clinical trial of DB-020.

Our gene therapy programs are initially targeting orphan diseases with relatively small populations, which limits the pool of potential participants for our gene therapy clinical trials. Because gene therapy trials generally require participants who have not previously received any other gene therapy or potentially other pharmacological therapeutics for the same indication or treatment with medical devices (for example, cochlear implants), we will also need to compete with others who are also developing gene therapies or pharmacologic therapeutics for these same indications for the same group of potential clinical trial participants. This competition could reduce the number and types of potential participants available to us, as some potential participants who might have opted to enroll in our clinical trials may instead opt to enroll in one being conducted by one of our competitors. In addition, individuals may also be unwilling to participate in our clinical trials because of negative publicity from adverse events in the biotechnology or biopharmaceutical industries, particularly to the extent that such negative publicity is related to gene therapy. Challenges in recruiting and enrolling sufficient numbers of suitable participants in clinical trials could increase costs, affect the timing and outcome of our planned clinical trial or future clinical trials and result in delays to our current development plan for our product candidates. If we have difficulty enrolling a sufficient number of individuals to conduct our clinical trials as planned, we may need to delay, limit or terminate ongoing or planned clinical trials, any of which would harm our business, financial condition, results of operations and prospects.

Our product candidates or the process for administering our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit their commercial potential or result in significant negative consequences following any potential marketing approval.

We have only conducted a clinical trial of DB-020 and have not conducted clinical trials in any of our gene therapy programs.

In past clinical trials that were conducted by others with non-AAV vectors, several significant side effects were caused by gene therapy product candidates, including reported cases of leukemia and death. Other potential side effects associated with both AAV and non-AAV vectors could include immunologic reactions or insertional oncogenesis, which is the process whereby the insertion of a functional gene near a gene that is important in cell growth or division results in uncontrolled cell division, which could potentially enhance the risk of malignant transformation. If our gene therapy product candidates demonstrate a similar adverse effect, or other adverse events, we may be required to halt or delay further clinical development of our gene therapy product candidates.

In addition to side effects caused by the product candidate itself, the administration process also can cause side effects. Although the procedure we have developed to deliver our gene therapy product candidate is based on the surgical approach employed by otologists and pediatric otolaryngologists during a standard cochlear implantation procedure, any surgical procedure runs risks related to infection and damage to parts of the body adjacent to the treated area. In addition, until we are able to test the procedure on humans, we cannot be certain that our delivery mechanism will be successful. If side effects were to occur in connection with the surgical procedure during our planned clinical trials or if we fail to successfully apply our delivery approach in humans, our clinical trials could be suspended or terminated.

If, in the future, we are unable to demonstrate that trial side effects were not caused by our product candidates or the related procedures, the FDA, the EMA or other regulatory authorities could order us to cease further development of, or deny approval of, our product candidates for any or all targeted indications. Even if we are able to demonstrate that any future serious adverse events are not product-related, and regulatory authorities do not order us to cease further development of our product candidates, such occurrences could cause our reputation to suffer and affect patient recruitment or the ability of enrolled participants to complete the trial. Moreover, if we elect, or are required, to delay, suspend or terminate any clinical trial of any of our product candidates, the commercial prospects of such product candidates may be harmed and our ability to generate product revenues from any of these product candidates may be delayed or eliminated. Any of these occurrences may harm our ability to develop other product candidates, and may harm our business, financial condition, results of operations and prospects significantly.

Regulatory approval of and/or demand for our potential products will depend in part on public acceptance of the use of gene therapies for the prevention or treatment of human diseases. Public attitudes may be influenced by claims that gene therapies are unsafe, unethical or immoral and, consequently, our products may not gain the acceptance of the public or the medical community. Adverse public attitudes may adversely impact our ability to enroll clinical trials. Moreover, our success will depend upon physicians prescribing, and their patients being willing to receive, treatments that involve the use of product candidates we may develop. In 1999, there was public backlash against the field of gene therapy following the death of a participant in a clinical trial, which utilized a different type of gene therapy product candidate vector, from an extreme type of immune response that can be life-threatening. Any of these events could prevent us from achieving or maintaining market acceptance of our product candidates and could significantly harm our business, financial condition, results of operations and prospects.

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

A key element of our strategy is to apply our proprietary platform to expand our pipeline of gene therapies for the treatment of acquired hearing and balance disorders. The discovery activities that we are conducting may not be successful in identifying product candidates that are useful in restoring or improving hearing or balance. The process by which we identify product candidates may fail to yield product candidates for clinical development for a number of reasons, including those discussed in these risk factors and also:

- we may not be able to assemble sufficient resources to acquire or discover additional product candidates;
- competitors may develop alternatives that render our potential product candidates obsolete or less attractive;
- potential product candidates we develop may nevertheless be covered by third parties' patents or other exclusive rights;
- potential product candidates may, on further study, be shown to have harmful side effects, toxicities or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance;
- potential product candidates may not be effective in treating their targeted disorders;
- the market for a potential product candidate may change so that the continued development of that product candidate is no longer reasonable;
- a potential product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; or
- the regulatory pathway for a potential product candidate may be too complex and difficult to navigate successfully or economically.

We may expend our limited resources to pursue a particular program, product candidate or indication and fail to capitalize on programs, product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on research programs and expect to focus on product candidates that we identify for specific indications among many potential options. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential, or we may choose to focus our efforts and resources on a potential product candidate that ultimately proves to be unsuccessful. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable medicines. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. Any such event could have a material adverse effect on our business, financial condition, results of operations and prospects.

Clinical trial and product liability lawsuits against us could divert our resources, cause us to incur substantial liabilities and limit commercialization of our product candidates.

We face an inherent risk of clinical trial and product liability exposure related to the testing of product candidates in clinical trials, and we will face an even greater risk if we commercially sell any products that we may develop. While we currently have no products that have been approved for commercial sale, the current and future use of product candidates by us in clinical trials, and the sale of any approved products in the future, may expose us to liability claims. These claims might be made by patients that use the product, healthcare providers, pharmaceutical companies or others selling such products. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for our product candidates;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend any related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize our product candidates.

We will need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of any product candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. If a successful clinical trial or product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be impaired.

Risks Related to Manufacturing

The manufacture of gene therapy products is complex and difficult and is subject to a number of scientific and technical risks, some of which are common to the manufacture of drugs and biologics and others of which are unique to the manufacture of gene therapies. We could experience manufacturing problems that result in delays in our gene therapy development or commercialization programs.

Gene therapy drug products are complex and difficult to manufacture. For our IND-enabling studies of DB-OTO and our planned Phase 1/2 clinical trial of DB-OTO, we intend to rely on the manufacturing facility of Catalent Maryland, Inc., or Catalent, for supply of the product candidate. In addition to Catalent, we also rely upon other CROs and CDMOs for providing certain materials for the manufacturing process.

We believe that the high demand for clinical gene therapy material and a scarcity of potential contract manufacturers may cause long lead times for establishing manufacturing capabilities for gene therapy drug development activities. Even after a manufacturer is engaged, any problems that arise during manufacturing process development may result in unanticipated delays to our timelines, including delays attributable to securing additional manufacturing slots. There may also be long lead times to manufacture or procure starting materials such as plasmids and cell lines, especially for high-quality starting materials that are current good manufacturing

process, or cGMP, compliant. In particular, plasmids, cell lines and other starting materials for gene therapy manufacture are usually sole sourced, as there are a limited number of qualified suppliers. The progress of our gene therapy programs is highly dependent on these suppliers providing us or our contract manufacturers with the necessary starting materials that meet our requirements in a timely manner. A failure to procure or a shortage of necessary starting materials likely would delay our manufacturing and development timelines.

Problems with the manufacturing process, including even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, product recalls, product liability claims and insufficient inventory. If we successfully develop product candidates, we may encounter problems achieving adequate quantities and quality of clinical-grade materials that meet FDA or other applicable standards or specifications with consistent and acceptable production yields and costs.

A number of factors common to the manufacturing of biologics and small molecules could also cause production issues or interruptions for gene therapies, including raw material or starting material variability in terms of quality, cell line viability, productivity or stability issues, shortages of any kind, shipping, distribution, storage and supply chain failures, growth media contamination, equipment malfunctions, operator errors, facility contamination, labor problems, natural disasters, public health epidemics, disruption in utility services, terrorist activities or acts of god that are beyond our or our contract manufacturers' control. It is often the case that early-stage process development is conducted with materials that are not manufactured using cGMP starting materials, techniques or processes and which are not subject to the same level of analysis that would be required for clinical grade material. We may encounter difficulties in translating the manufacturing processes used to produce research grade materials to cGMP compliant processes, and any changes in the manufacturing process may affect the safety and efficacy profile of our product candidates.

In addition, the FDA and comparable regulatory authorities in other jurisdictions may require us to submit samples of any lot of any approved biological product together with the protocols showing the results of applicable tests at any time. Under some circumstances, the FDA or comparable regulatory authorities in other jurisdictions may prohibit the distribution of a lot until the agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the product that could result in lot failures and product recalls.

Given the nature of biologics manufacturing, there is a risk of contamination during manufacturing. Any contamination could materially harm our ability to produce product candidates on schedule and could harm our results of operations and cause reputational damage. Some of the raw materials that we anticipate will be required in our manufacturing process are derived from biologic sources. Such raw materials are difficult to procure and may be subject to contamination or recall. A material shortage, contamination, recall or restriction on the use of biologically derived substances in the manufacture of any product candidates we may develop could adversely impact or disrupt the commercial manufacturing or the production of clinical material, which could materially harm our development timelines and our business, financial condition, results of operations and prospects.

An important part of manufacturing drug products is performing analytical testing. Analytical testing of gene therapies involves tests that are more numerous, more complex in scope and take a longer time to develop and to conduct as compared to traditional drugs. We and our contract manufacturers need to expend considerable time and resources to develop assays and other analytical tests for our gene therapy product candidates, including assays to assess the titer and potency of our gene therapy product candidates. Some assays need to be outsourced to specialized testing laboratories. Even when assays are developed, they need to be further tested, qualified or validated depending on the nature of the assay and the stage of product candidate development, which may take substantial time and resources. Because of the lagging nature of analytical testing, we may proceed with additional manufacturing and other development activities without having first fully characterized our manufactured materials. If the results of the testing fail to meet our expectations, we may need to delay or repeat certain manufacturing and development activities.

Changes in methods of product candidate manufacturing or formulation may result in additional costs or delay.

As product candidates proceed through preclinical studies to late-stage clinical trials towards potential approval and commercialization, it is common that various aspects of the program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our product candidates to perform differently and affect the results of our planned clinical trial or future clinical trials conducted with the materials manufactured using altered processes. Such changes may also require additional testing, FDA notification or FDA approval. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and jeopardize our ability to commence sales and generate revenue.

We depend on third-party suppliers for materials used in the manufacture of our product candidates, and the loss of these third-party suppliers or their inability to supply us with adequate materials could harm our business.

We rely on third-party suppliers for certain materials and components required for the production of our product candidates. Our dependence on these third-party suppliers and the challenges we may face in obtaining adequate supplies of materials involve several risks, including limited control over pricing, availability and quality and delivery schedules. There is substantial demand and limited supply for certain of the raw materials used to manufacture gene therapy products. As a small company, our negotiation leverage is limited, and we are likely to get lower priority than other companies that are larger than we are. We cannot be certain that our suppliers will continue to provide us with the quantities of these raw materials that we require or satisfy our anticipated specifications and quality requirements. Any supply interruption in limited or sole sourced raw materials could materially harm our ability to manufacture our product candidates until a new source of supply, if any, could be identified and qualified. We may be unable to find a sufficient alternative supply channel in a reasonable time or on commercially reasonable terms. Any performance failure on the part of our suppliers could delay the development and potential commercialization of our product candidates, including limiting supplies necessary for clinical trials and regulatory approvals, which would have a material adverse effect on our business.

Risks Related to Our Dependence on Third Parties

We and our contract manufacturers are subject to significant regulation with respect to manufacturing our products. The manufacturing facilities on which we rely may not continue to meet regulatory requirements and have limited capacity.

All entities involved in the preparation of therapeutics for clinical trials or commercial sale, including our existing contract manufacturers for our product candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical trials must be manufactured in accordance with cGMP. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We or our contract manufacturers must supply all necessary documentation in support of a new drug application, or NDA, or biologics license application, or BLA, on a timely basis and must adhere to the FDA's GLP and cGMP regulations enforced by the FDA through its facilities inspection program. Our facilities and quality systems and the facilities and quality systems of some or all of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our product candidates or any of our other potential products. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidates or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted. If these facilities do not pass a pre-approval plant inspection, FDA approval of the products will not be granted.

The regulatory authorities also may, at any time following approval of a product for sale, audit our manufacturing facilities or those 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 trial 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 can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new drug product or biologic product, or revocation of a pre-existing approval. As a result, our business, financial condition, results of operations and prospects may be materially harmed.

Additionally, if supply from one approved manufacturer is interrupted, there could be a significant disruption in supply. An alternative manufacturer would need to be qualified through an NDA or BLA supplement, which could result in further delay. The regulatory agencies may also require additional studies or trials 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 trials, regulatory submissions, required approvals or commercialization of our product candidates, cause us to incur higher costs and prevent us from commercializing our products successfully. Furthermore, if our suppliers fail to meet contractual requirements, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials may be delayed or we could lose potential revenue.

We rely, and expect to continue to rely, on third parties to conduct, supervise and monitor our clinical trials, and if these third parties perform in an unsatisfactory manner, it may harm our business.

We rely, and expect to continue to rely, on CROs and clinical trial sites to ensure our clinical trials are conducted properly and on time and we expect to have limited influence over their actual performance. We control only certain aspects of our CROs' activities. Nevertheless, we are responsible for ensuring that each of our clinical trials 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 GCPs for conducting, recording and reporting the results of clinical trials to assure that the data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. The FDA enforces these GCPs through periodic inspections of sponsors, principal investigators and clinical sites. If we or our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving any marketing applications. Upon inspection, the FDA may determine that our clinical trials did not comply with GCPs. In addition, our clinical trials will require a sufficient number of participants to evaluate the safety and effectiveness of our product candidates. Accordingly, if our CROs fail to comply with these regulations or fail to recruit a sufficient number of participants, we may be required to repeat such clinical trials, which would delay the regulatory approval process.

Our CROs are not our employees, and we are therefore unable to directly monitor whether or not they devote sufficient time and resources to our clinical programs. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities that could harm our competitive position. If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements, or for any other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize, our product candidates. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

The federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, and their respective implementing regulations, impose obligations on "covered entities," including certain healthcare providers, health plans and healthcare clearinghouses, as well as their respective "business associates" that create, receive, maintain or transmit individually identifiable health information for or on behalf of a covered entity, with respect to safeguarding the privacy, security and transmission of individually identifiable health information. Such obligations may require us to pass certain obligations on to our CROs or other third parties with whom we do business, including transferal of personal information or individually identifiable health information.

We depend on single-source suppliers for some of the components and materials used in our product candidates.

We depend on single-source suppliers for some of the components and materials used in our product candidates. We cannot ensure that these suppliers or service providers will remain in business, have sufficient capacity or supply to meet our needs or that they will not be purchased by one of our competitors or another company that is not interested in continuing to work with us. Our use of single-source suppliers of raw materials, components, key processes and finished goods exposes us to several risks, including disruptions in supply, price increases or late deliveries. There are, in general, relatively few alternative sources of supply for substitute components. These vendors may be unable or unwilling to meet our future demands for our clinical trials or commercial sale. Establishing additional or replacement suppliers for these components, materials and processes could take a substantial amount of time and it may be difficult to establish replacement suppliers who meet regulatory requirements. Any disruption in supply from any single-source supplier or service provider could lead to supply delays or interruptions, which would damage our business, financial condition, results of operations and prospects.

If we have to switch to a replacement supplier, the manufacture and delivery of any product candidates we may develop could be interrupted for an extended period, which could adversely affect our business. Establishing additional or replacement suppliers, if required, may not be accomplished quickly. If we are able to find a replacement supplier, the replacement supplier would need to be qualified and may require additional regulatory authority approval, which could result in further delay. While we seek to maintain adequate inventory of the single source components and materials used in our products, any interruption or delay in the supply of components or materials, or our inability to obtain components or materials from alternate sources at acceptable prices in a timely manner, could impair our ability to meet the demand for our product candidates.

We expect to depend on collaborations with third parties for the research, development, manufacture and commercialization of programs or product candidates. If these collaborations are not successful, our business could be adversely affected.

As part of our strategy, we intend to maximize the value of our pipeline and our platform by exploring strategic collaborations. If we enter into such arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of any product candidates we develop or commercialize with them. Our ability to generate revenue from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. For instance, under the Regeneron Agreement, we are dependent on Regeneron to contribute various technologies, employees and research services.

Collaborations that we enter into may not be successful, and any success will depend heavily on the efforts and activities of our collaborators. For example, in September 2018, we entered into a collaboration and license agreement with Oricula Therapeutics, LLC, but in September 2019, we terminated the agreement. Collaborations pose a number of risks, including the following:

- collaborators have significant discretion in determining the amount and timing of efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development of our product candidates or may elect not to continue or renew programs based on results of clinical trials or other studies, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may not pursue commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew commercialization programs based on results of clinical trials or other studies, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that may divert resources or create competing priorities;
- collaborators may delay programs, preclinical studies or clinical trials, provide insufficient funding for programs, preclinical studies or clinical trial programs, stop a preclinical study or clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- we may not have access to, or may be restricted from disclosing, certain information regarding product candidates being developed or commercialized under a collaboration and, consequently, may have limited ability to inform our stockholders about the status of such product candidates on a discretionary basis;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates and products if the collaborators believe that the competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator may fail to comply with applicable regulatory requirements regarding the development, manufacture, distribution or marketing of a product candidate or product;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over intellectual property or proprietary rights, contract interpretation or the preferred course of development, might cause delays or terminations of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly obtain, maintain, enforce, defend or protect our intellectual property or proprietary rights or may use our proprietary information in such a way as to potentially lead to disputes or legal proceedings that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- disputes may arise with respect to the ownership of intellectual property developed pursuant to our collaborations;
- collaborators may infringe, misappropriate or otherwise violate the intellectual property or proprietary rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated, and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner, or at all. If any collaborations that we enter into do not result in the successful development and commercialization of products or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development of our product candidates could be delayed and we may need additional resources to develop our product candidates. All of the risks relating to product development, regulatory approval and commercialization described in this Quarterly Report on Form 10-Q also apply to the activities of our collaborators.

Additionally, subject to its contractual obligations to us, if a collaborator of ours is involved in a business combination, the collaborator might deemphasize or terminate the development or commercialization of any product candidate licensed to it by us. If one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception in the business and financial communities could be adversely affected.

If conflicts arise between us and our current or future collaborators, these parties may act in a manner adverse to us and could limit our ability to implement our strategies.

If conflicts arise between us and Regeneron or any future collaborators, the other party may act in a manner adverse to us and could limit our ability to implement our strategies. Our collaborators may develop, either alone or with others, products in related fields that are competitive with our product candidates that are the subject of these collaborations with us. Competing products, either developed by the collaborators or to which the collaborators have rights, may result in the withdrawal of support for our product candidates.

Some of our future collaborators could also become our competitors. Our collaborators could develop competing products, preclude us from entering into collaborations with their competitors, fail to obtain timely regulatory approvals, terminate their agreements with us prematurely, fail to devote sufficient resources to the development and commercialization of products, or merge with or be acquired by a third party who may do any of these things. Any of these developments could harm our product development efforts.

If we are not able to establish or maintain collaborations on commercially reasonable terms, we may have to alter our development and commercialization plans and our business could be adversely affected.

We face significant competition in attracting appropriate collaborators, and a number of more established companies may also be pursuing strategies to license or acquire third-party intellectual property rights that we consider attractive. These established companies may have a competitive advantage over us due to their size, financial resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA, EMA or other regulatory authorities, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, the terms of any existing collaboration agreements, and industry and market conditions generally. The collaborator may also have the opportunity to collaborate on other product candidates or technologies for similar indications and will have to evaluate whether such a collaboration could be more attractive than the one with us for our product candidate.

Collaborations are complex and time-consuming to negotiate, document and execute. In addition, consolidation among large pharmaceutical and biotechnology companies has reduced the number of potential future collaborators.

We may not be able to negotiate additional collaborations on a timely basis, on acceptable terms or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its program or one or more of our other programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market or continue to develop our platform.

Risks Related to Commercialization

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The development and commercialization of new drug products is highly competitive. We face competition with respect to our product candidates from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of many of the disorders for which we are developing our product candidates. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

We expect to face competition from existing products and product candidates in development for each of our programs. There are currently no approved drugs for the treatment of hearing loss or balance disorders.

We expect that our product candidates and programs for congenital, monogenic hearing loss and for acquired hearing loss will compete with product candidates and programs being advanced by:

- Akouos, Inc., which is developing AK-OTOF, a gene therapy for profound hearing loss resulting from deficiency in OTOF, which is in preclinical development and has preclinical gene therapy programs targeting GJB2 and Usher Syndrome Type 3A and for treatment of sensorineural hearing loss through hair cell regeneration;
- Frequency Therapeutics, Inc., which is developing in collaboration with Astellas Pharma Inc. FX-322, a small molecule intended to treat sensorineural hearing loss through regeneration of cochlear hair cells through activation of inner ear progenitor cells, which is currently in a Phase 2a clinical trial;
- Otonomy, Inc., or Otonomy, and Applied Genetic Technologies Corporation, which are collaborating on the development of an AAV-based gene therapy to restore hearing in individuals with profound hearing loss caused by mutation of the GJB2 gene, which is in preclinical development; and
- Sensorion SA, which has three gene therapy programs targeting GJB2-mediated hearing loss, Usher Syndrome Type I and OTOF-deficiency in preclinical development.

We are aware of product candidates in development to protect against chemotherapy-induced ototoxicity, including PEDMARK, a formulation of STS delivered via systemic injection, being developed by Fennec Pharmaceuticals, Inc., or Fennec, for the prevention of platinum-induced ototoxicity in pediatric cancer patients with localized, non-metastatic, solid tumors. In August 2020, Fennec received a complete response letter from the FDA for its or NDA for PEDMARK. We are also aware of D-methionine, an amino acid that has been shown to protect against hearing loss in experimental settings, and SPI-3005, an oral agent primarily being developed by Sound Pharmaceuticals for noise and age-related hearing loss that is in Phase 2 clinical trials for chemotherapy-related hearing loss. We are also aware of additional therapeutic approaches in preclinical development that may target prevention of hearing loss in patients receiving cisplatin chemotherapy.

We are aware of other companies developing product candidates for balance disorders, including Otonomy and Sound Pharmaceuticals, which are both independently pursuing treatments for Meniere’s Disease.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than our product candidates, or that would render any product candidates that we may develop obsolete or non-competitive. Our competitors also may obtain FDA or other regulatory approval for their product candidates more rapidly than we may obtain approval for ours, or may obtain regulatory exclusivity, any of which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, technologies developed by our competitors may render our product candidates uneconomical or obsolete, and we may not be successful in marketing any product candidates we may develop against competitors.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Furthermore, mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors.

The market opportunities for our product candidates may be smaller than we anticipated or may be limited to those patients who are ineligible for or have failed prior treatments. If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

Our current and future target patient populations are based on our beliefs and estimates regarding the incidence or prevalence of certain types of the indications that may be addressable by our product candidates, which is derived from a variety of sources, including scientific literature and surveys of clinics. Our projections may prove to be incorrect and the number of potential patients may turn out to be lower than expected. The total addressable market opportunity for our product candidates will ultimately depend upon a number of factors including the diagnosis and treatment criteria included in the final label, if approved for sale in specified indications, acceptance by the medical community, patient access and product pricing and reimbursement. Even if we obtain significant market share for our product candidates, because the potential target populations could be small, we may never achieve profitability without obtaining regulatory approval for additional indications.

Negative public opinion of gene therapy and increased regulatory scrutiny of gene therapy and genetic research may adversely impact the development or commercial success of our current and future product candidates.

Our potential therapeutic products involve introducing genetic material into a patient's cells. The clinical and commercial success of our potential products will depend in part on public acceptance of the use of gene therapy and gene regulation for the prevention or treatment of human diseases. Public attitudes may be influenced by claims that gene therapy and gene regulation are unsafe, unethical or immoral, and consequently, our products may not gain the acceptance of the public or the medical community. Adverse public attitudes may adversely impact our ability to enroll clinical trials. Moreover, our success will depend upon physicians prescribing, and their patients being willing to receive, treatments that involve the use of product candidates we may develop in lieu of, or in addition to, existing treatments with which they are already familiar and for which greater clinical data may be available.

More restrictive government regulations or negative public opinion would have a negative effect on our business or financial condition and may delay or impair the development and commercialization of our product candidates or demand for any products once approved. For example, in 2003, trials using early versions of murine gamma-retroviral vectors, which integrate with, and thereby alter, the host cell's DNA, have led to several well-publicized adverse events, including reported cases of leukemia. Although none of our current product candidates utilizes murine gamma-retroviral vectors, our product candidates use AAV viral vectors. Among the risks in any gene therapy product based on viral vectors are the risks of immunogenicity, elevated liver enzymes and insertional oncogenesis. If any of our vectors demonstrate a similar effect, we may decide or be required to halt or delay further clinical development of any product candidates that utilize that vector. Adverse events in our or others' clinical trials, even if not ultimately attributable to our product candidates, and the resulting publicity could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates. The risk of cancer remains a concern for gene therapy and we cannot assure that it will not occur in any of our planned or future clinical trials or in any clinical trials conducted by other companies. In addition, there is 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.

Even if any product candidate we develop receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, patient advocacy groups, third-party payors and others in the medical community necessary for commercial success.

If any product candidate we develop receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, patient advocacy groups, third-party payors and others in the medical community. Sales of medical products depend in part on the willingness of physicians to prescribe the treatment, which is likely to be based on a determination by these physicians that the products are safe, therapeutically effective and cost-effective. In addition, the inclusion or exclusion of products from treatment guidelines established by various physician groups and the viewpoints of influential physicians can affect the willingness of other physicians to prescribe the treatment. We cannot predict whether physicians, physicians' organizations, hospitals, other healthcare providers, government agencies or private insurers will determine that our product is safe, therapeutically effective and cost-effective as compared with competing treatments. Efforts to educate those in the medical community and third-party payors on the benefits of our product candidates may require significant resources and may not be successful. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and potential advantages compared to alternative treatments;
- the effectiveness of sales and marketing efforts;
- the cost of treatment in relation to alternative treatments;

- the clinical indications for which the product is approved;
- the convenience and ease of administration compared to alternative treatments;
- 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;
- the timing of market introduction of competitive products;
- the availability of third-party coverage and adequate reimbursement, and patients' willingness to pay out of pocket for required co-payments or in the absence of third-party coverage or adequate reimbursement;
- the prevalence and severity of any side effects;
- publication of any post-approval data on the effectiveness and safety of the product; and
- any restrictions on the use of our products, if approved, together with other medications.

If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution agreements with third parties, we may not be successful in commercializing our product candidates if and when they are approved.

We currently have no sales, marketing or commercial product distribution capabilities and have no experience in commercializing products. To achieve commercial success for any product for which we have obtained marketing approval, we will need to establish a sales, marketing and distribution organization, either ourselves or through collaborations or other arrangements with third parties.

In the future, we expect to build a sales and marketing infrastructure to market some of our product candidates. There are costs and risks involved with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. These efforts may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel. We must also compete with other biotechnology and biopharmaceutical companies to recruit, hire, train and retain marketing and sales personnel.

Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales, marketing, coverage or reimbursement, customer service, medical affairs and other support personnel;
- the inability of sales personnel to educate adequate numbers of physicians on the benefits of any future products;
- the inability of reimbursement professionals to negotiate arrangements for formulary access, reimbursement and other acceptance by payors;
- the inability to price our products at a sufficient price point to ensure an adequate and attractive level of profitability;
- restricted or closed distribution channels that make it difficult to distribute our products to segments of the patient population;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines;
- unforeseen costs and expenses associated with creating an independent sales and marketing organization; and
- unforeseen issues impacting supply, distribution, sales and marketing.

If we are unable to establish our own sales, marketing and distribution capabilities and we enter into arrangements with third parties to perform these services, our product revenues and our profitability, if any, are likely to be lower than if we were to market, sell and distribute any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute our product candidates or may be unable to do so on terms that are acceptable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. There can be no assurance that we will be able to develop in-house sales, marketing and distribution capacities or establish or maintain relationships with third parties to perform these services. As a result, we may not successfully commercialize any product in any jurisdiction.

If any of our product candidates receives marketing approval and we, or others, later discover that the drug is less effective than previously believed or causes undesirable side effects that were not previously identified, our ability to market the drug could be compromised.

Clinical trials of our product candidates are conducted in carefully defined subsets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If one or more of our product candidates receives regulatory approval, and we, or others, later discover that they are less effective or less durable than previously believed, or cause undesirable side effects, a number of potentially significant negative consequences could result, including:

- withdrawal or limitation by regulatory authorities of approvals of such product;
- seizure of the product by regulatory authorities;
- recall of the product;
- restrictions on the marketing of the product or the manufacturing process for any component thereof;
- requirement by regulatory authorities of additional warnings on the label, such as a “black box” warning or contraindication;
- requirement that we implement a Risk Evaluation and Mitigation Strategy, or REMS, or create a medication guide outlining the risks of such side effects for distribution to patients;
- commitment to expensive post-marketing studies as a prerequisite of approval by regulatory authorities of such product;
- the product may become less competitive;
- initiation of regulatory investigations and government enforcement actions;
- initiation of legal action against us to hold us liable for harm caused to patients; and
- harm to our reputation and resulting harm to physician or patient acceptance of our products.

Any of these events could prevent us from achieving or maintaining market acceptance of a particular product candidate, if approved, and could significantly harm our business, financial condition, and results of operations.

Our future growth depends, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties that, if they materialize, could harm our business.

Our future profitability will depend, in part, on our ability to commercialize our product candidates in markets outside of the United States. If we commercialize our product candidates in foreign markets, we will be subject to additional risks and uncertainties, including:

- economic weakness, including inflation, or political instability in particular economies and markets;
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements, many of which vary between countries;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- tariffs and trade barriers, as well as other governmental controls and trade restrictions;
- other trade protection measures, import or export licensing requirements or other restrictive actions by U.S. or foreign governments;
- longer accounts receivable collection times;
- longer lead times for shipping;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- workforce uncertainty in countries where labor unrest is common;
- language barriers for technical training;
- reduced protection of intellectual property rights in some foreign countries;
- foreign currency exchange rate fluctuations and currency controls;
- differing foreign reimbursement landscapes;

- uncertain and potentially inadequate reimbursement of our products; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

If risks related to any of these uncertainties materializes, it could have a material adverse effect on our business.

Risks Related to Our Intellectual Property

Our rights to develop and commercialize any product candidates are subject and may in the future be subject, in part, to the terms and conditions of licenses granted to us by third parties. If we fail to comply with our obligations under our current or future intellectual property license agreements or otherwise experience disruptions to our business relationships with our current or any future licensors, we could lose intellectual property rights that are important to our business.

We are and expect to continue to be reliant upon third-party licensors for certain patent and other intellectual property rights that are important or necessary to the development of our technology and product candidates. For example, we rely on licenses from the University of California, San Francisco, the University of Florida and the University of Missouri to certain patent rights. These license agreements impose, and we expect that any future license agreement will impose, specified diligence, milestone payment, royalty, commercialization, development and other obligations on us and require us to meet development timelines, or to exercise diligent or commercially reasonable efforts to develop and commercialize licensed products, in order to maintain the licenses.

Furthermore, our licensors have, or may in the future have, the right to terminate a license if we materially breach the agreement and fail to cure such breach within a specified period or in the event we undergo certain bankruptcy events. In spite of our best efforts, our current or any future licensors might conclude that we have materially breached our license agreements and might therefore terminate the license agreements. If our license agreements are terminated, we may lose our rights to develop and commercialize product candidates and technology, lose patent protection, experience significant delays in the development and commercialization of our product candidates and technology, and incur liability for damages. If these in-licenses are terminated, or if the underlying intellectual property fails to provide the intended exclusivity, our competitors or other third parties could have the freedom to seek regulatory approval of, and to market, products and technologies identical or competitive to ours and we may be required to cease our development and commercialization of certain of our product candidates and technology. In addition, we may seek to obtain additional licenses from our licensors and, in connection with obtaining such licenses, we may agree to amend our existing licenses in a manner that may be more favorable to the licensors, including by agreeing to terms that could enable third parties, including our competitors, to receive licenses to a portion of the intellectual property that is subject to our existing licenses and to compete with any product candidates we may develop and our technology. Any of the foregoing could have a material adverse effect on our competitive position, business, financial condition, results of operations and prospects.

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;
- our or our licensors' ability to obtain, maintain and defend intellectual property and to enforce intellectual property rights against third parties;
- the extent to which our technology, product candidates and processes infringe, misappropriate or otherwise violate the intellectual property of the licensor that is not subject to the license agreement;
- the sublicensing of patent and other intellectual property rights under our license agreements;
- our diligence, development, regulatory, commercialization, financial or other obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our current or future licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, our license agreements are, and future license agreements are likely to be, complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our diligence, development, regulatory, commercialization, financial or other obligations under the relevant agreement. In addition, if disputes over intellectual property that we have licensed or any other dispute related to our license agreements prevent or impair our ability to maintain our current license agreements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates and technology. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

License agreements we may enter into in the future may be non-exclusive. Accordingly, third parties may also obtain non-exclusive licenses from such licensors with respect to the intellectual property licensed to us under such license agreements. Accordingly, these license agreements may not provide us with exclusive rights to use such licensed patent and other intellectual property rights, or may not provide us with exclusive rights to use such patent and other intellectual property rights in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and any product candidates we may develop in the future.

Moreover, some of our in-licensed patent and other intellectual property rights may in the future be subject to third-party interests such as co-ownership. If we are unable to obtain an exclusive license to such third-party co-owners' interest, in such patent and other intellectual property rights, such third-party co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. We or our licensors may need the cooperation of any such co-owners of our licensed patent and other intellectual property rights in order to enforce them against third parties, and such cooperation may not be provided to us or our licensors.

Additionally, we may not have complete control over the preparation, filing, prosecution, maintenance, enforcement and defense of patents and patent applications that we license from third parties. It is possible that our licensors' filing, prosecution and maintenance of the licensed patents and patent applications, enforcement of patents against infringers or defense of such patents against challenges of validity or claims of enforceability may be less vigorous than if we had conducted them ourselves, and accordingly, we cannot be certain that these patents and patent applications will be prepared, filed, prosecuted, maintained, enforced and defended in a manner consistent with the best interests of our business. If our licensors fail to file, prosecute, maintain, enforce and defend such patents and patent applications, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated, our right to develop and commercialize any of our technology and any product candidates we may develop that are the subject of such licensed rights could be adversely affected and we may not be able to prevent competitors or other third parties from making, using and selling competing products.

Furthermore, our owned and in-licensed patent rights may be subject to a reservation of rights by one or more third parties. When new technologies are developed with government funding, in order to secure ownership of patent rights related to the technologies, the recipient of such funding is required to comply with certain government regulations, including timely disclosing the inventions claimed in such patent rights to the U.S. government and timely electing title to such inventions. A failure to meet these obligations may lead to a loss of rights or the unenforceability of relevant patents or patent applications. In addition, the U.S. government may have certain rights in such patent rights, including a non-exclusive license authorizing the U.S. government to use the invention or to have others use the invention on its behalf. If the U.S. government decides to exercise these rights, it is not required to engage us as its contractor in connection with doing so. The U.S. government's rights may also permit it to disclose the funded inventions and technology, which may include our confidential information, to third parties and to exercise march-in rights to use or allow third parties to use the technology that was developed using U.S. government funding. The U.S. government may exercise its march-in rights if it determines that action is necessary because we or our licensors failed to achieve practical application of the U.S. government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to U.S. industry. These march-in rights would be applicable to our in-licensed patent rights relating to DB-OTO and potentially applicable to our in-licensed patent rights relating to AAV.104. In addition, our rights in such U.S. government-funded inventions may be subject to certain requirements to manufacture any product candidates we may develop embodying such inventions in the United States. Any of the foregoing could harm our business, financial condition, results of operations and prospects significantly.

If we are unable to obtain, maintain and defend adequate intellectual property protection and regulatory exclusivity for our products and technology, or if the scope of the intellectual property protection and regulatory exclusivity obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to ultimately successfully commercialize our products and technology may be adversely affected.

Our success depends, in large part, on our and our licensors' ability to obtain and maintain intellectual property protection in the United States and other countries with respect to our proprietary technology and product candidates. We and our licensors have sought, and we intend to continue to seek, to protect our proprietary position by filing patent and trademark applications in the United States and abroad related to many of our novel technologies and product candidates that are important to our business.

The patent prosecution process is expensive, time-consuming and complex, and we and our licensors may not be able to file, prosecute, maintain, defend, enforce or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. For example, in some cases, the work of certain academic researchers has entered the public domain, which may compromise our ability to obtain patent protection for certain inventions related to or building upon such prior work. Consequently, we may not be able to obtain any patents to prevent others from using such technology for, and developing and marketing competing products to treat, certain indications. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have

access to confidential or patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach these agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. Consequently, we would not able to prevent any third party from using any of our technology that is in the public domain to compete with any product candidates we may develop.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has, in recent years, been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future owned and licensed patent applications may not result in patents being issued which protect our technology or product candidates or which effectively prevent others from commercializing competitive technologies and product candidates. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

Third parties have developed technologies that may be related or competitive to our own technologies and product candidates and may have filed or may file patent applications, or may have obtained issued patents, claiming inventions that may overlap or conflict with those claimed in our owned or licensed patent applications or issued patents. We may not be aware of all third-party intellectual property rights potentially relating to our product candidates and technology. Publications of discoveries in the scientific literature often lag the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing or, in some cases, not at all. Therefore, we cannot be certain whether the inventors of our owned or licensed patents and patent applications were the first to make the inventions claimed in any owned or any licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions. If a third party can establish that we or our licensors were not the first to make or the first to file for patent protection of such inventions, our owned or licensed patent applications may not issue as patents and even if issued, may be challenged and invalidated or ruled unenforceable.

Even if the patent applications we license or may own in the future do issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us or otherwise provide us with any competitive advantage. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of patent rights, exclusivity or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and product candidates.

In addition, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Any of the foregoing could have a material adverse effect on our competitive position, business, financial condition, results of operations and prospects.

We also rely on regulatory exclusivity for protection of our products. Implementation and enforcement of regulatory exclusivity, which may consist of regulatory data protection and market protection, varies widely from country to country. Failure to qualify for regulatory exclusivity, or failure to obtain or maintain the extent or duration of such protections that we expect in each of the markets for our products due to challenges, changes or interpretations in the law or otherwise, could ultimately adversely affect our ability to successfully commercialize any products and technology.

We may not be successful in obtaining necessary rights to our product candidates through acquisitions and in-licenses. In addition, if we are unable to obtain licenses from third parties on commercially reasonable terms or fail to comply with our obligations under such agreements, our business could be harmed.

We currently have rights to certain intellectual property, through licenses from third parties, to develop and commercialize our product candidates. Because our programs may require the use of additional intellectual property rights held by third parties, the growth of our business likely will depend, in part, on our ability to acquire, in-license or use these intellectual property rights. However, we may be unable to secure such licenses or otherwise acquire or in-license any compositions, methods of use, processes or other intellectual property rights from third parties that we identify as necessary for our product candidates.

The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more established companies may pursue 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, capital resources and greater clinical development

and commercialization capabilities. 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.

We sometimes collaborate with non-profit and 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 option, we may be unable to negotiate a license within the specified timeframe 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 and develop and commercialize our product candidates.

If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may be required to expend significant time and resources to redesign our product candidates or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. 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.

If we are unable to license such intellectual property, or if we are forced to license such intellectual property on unfavorable terms, our business could be materially harmed. If we are unable to obtain a necessary license, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales or an obligation on our part to pay royalties and/or other forms of compensation. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same intellectual property licensed to us, and the applicable licensors could require us to make substantial licensing and royalty payments.

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

Filing, prosecuting, maintaining, enforcing and defending patents and other intellectual property rights on our technology and any product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could 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 and our licensors may not be able to obtain issued patents or other intellectual property rights covering our product candidates and our technology in all countries outside the United States and, as a result, may not be able to prevent third parties from practicing our and our licensors' 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 and our licensors have not obtained patent or other protection to develop their own products and, further, may export otherwise infringing, misappropriating or violating products to territories where we have patent or other intellectual property protection, but enforcement is not as strong as that in the United States. These products may compete with our products or technology and our or our licensors' patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Additionally, 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, misappropriation or other violation of our patent and other intellectual property rights or marketing of competing products in violation of our proprietary rights generally.

Proceedings to enforce our or our licensors' patent and other intellectual property rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patent and other intellectual property rights 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 or our licensors may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. We may choose not to initiate proceedings in certain cases or we may not have the resources to do so. 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.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our

licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

If we do not obtain patent term extension for our product candidates, our business may be harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. In the United States, a patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. The European Union also provides for patent term extension through Supplementary Protection Certificates, or SPCs. The rules and requirements for obtaining a SPC are similar to those in the United States. An SPC may extend the term of a patent for up to five years after its originally scheduled expiration date but cannot extend the remaining term of a patent beyond a total of fifteen years from the marketing approval. Although SPCs are available throughout the European Union, sponsors must apply on a country-by-country basis. Similar patent term extension rights exist in certain other foreign jurisdictions outside the European Union. However, we may not be granted an extension because of lack of availability of extension or, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements.

Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations and prosects could be materially harmed.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by government 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 government fees on patents and/or patent applications will be due to be paid to the United States Patent and Trademark Office, or USPTO, and various government patent agencies outside of the United States over the lifetime of our owned or licensed patents and/or patent applications and any patent rights we may own in the future. We rely on our outside counsel and other professionals or our licensing partners to pay these fees due to the USPTO and non-U.S. government patent agencies. The USPTO and various non-U.S. government patent agencies also require compliance with several procedural, documentary and other similar provisions during the patent application process. We rely on our outside counsel and other professionals to help us comply and we are also dependent on our licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property. 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. There are situations, however, in which non-compliance can result in abandonment, loss of priority 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, potential competitors might be able to enter the market and this circumstance could harm our competitive positions, business, financial condition, results of operations and prospects.

Issued patents covering our product candidates could be found invalid or unenforceable if challenged. We may not be able to protect our trade secrets in court.

If we or one of our licensors initiates legal proceedings against a third party to enforce a patent covering one of our product candidates or our technology, the defendant could counterclaim that the patent covering our product candidate or technology is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, lack of written description or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld information material to patentability from the USPTO, or made a misleading statement, during prosecution. Third parties also may raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, interference proceedings, post grant review, inter partes review and equivalent proceedings such as opposition, invalidation and revocation proceedings in foreign jurisdictions. Such proceedings could result in the revocation or cancellation of or amendment to our patents in such a way that they no longer cover our product candidates or our technology. 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 the patent examiner and we or our licensing partners were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we could lose at least part, and perhaps all, of the patent protection on one

or more of our product candidates or technology. Such a loss of patent protection could harm our business, financial condition, results of operations and prospects.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our product candidate discovery and development processes that involve proprietary know-how, information, or technology that is not covered by patents. However, trade secrets can be difficult to protect, and some courts inside and outside the United States are less willing or unwilling to protect trade secrets. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors, contractors and other parties who have access to such technology and processes. However, we may not be able to prevent the unauthorized disclosure or use of our technical know-how or other trade secrets by the parties to these agreements. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. If any of the collaborators, scientific advisors, employees and consultants who are parties to these agreements breach or violate the terms of any of these agreements, we may not have adequate remedies for any such breach or violation. As a result, we could lose our trade secrets and third parties could use our trade secrets to compete with any product candidates we may develop and our technology. Additionally, we cannot guarantee that we have entered into such agreements with each party that may have or has had access to our trade secrets or proprietary technology and processes. 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; however, such systems and 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.

Third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could harm our business.

Our commercial success depends upon our ability and the ability of our collaborators to research, develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property rights of third parties. The biotechnology and pharmaceutical industries are characterized by extensive and complex litigation regarding patents and other intellectual property rights.

It is possible that we have failed to identify relevant third-party patents or applications that our product candidates and programs may infringe. Because patent applications can take many years to issue, may be confidential for 18 months or more after filing and can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use, sale or importation of any product candidates we may develop or our technology, and we may not be aware of such patents. Furthermore, applications filed before November 29, 2000 and certain applications filed after that date that will not be filed outside the United States may remain confidential until a patent issues. Moreover, it is difficult for industry participants, including us, to identify all third-party patent rights that may be relevant to any product candidates we may develop and our technologies because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. We may fail to identify relevant patents or patent applications or may identify pending patent applications of potential interest but incorrectly predict the likelihood that such patent applications may issue with claims of relevance to our technology. In addition, we may incorrectly conclude that a third-party patent is invalid, unenforceable or not infringed by our activities. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technologies, any product candidates we may develop or the use of any product candidates we may develop.

Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. There is a risk that third parties may choose to engage in litigation with us to enforce or to otherwise assert their patent rights against us. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, which could adversely affect our ability to commercialize our product candidates or any other of our product candidates or technologies covered by the asserted third-party patents. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. If we are found to infringe, misappropriate or otherwise violate a third party's valid and enforceable intellectual property rights, we could be required to obtain a license from such third party to continue developing, manufacturing and marketing our product candidates and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. We could be forced, including by court order, to cease developing, manufacturing and commercializing the infringing technology or product candidates. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right indemnify our customers or collaborators. A finding of infringement could prevent us from manufacturing

and commercializing our product candidates or force us to cease some of our business operations, which could harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business, financial condition, results of operations and prospects.

Intellectual property litigation or other proceedings relating to intellectual property could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Competitors may challenge the validity and enforceability of our patent rights or those of our licensing partners, infringe, misappropriate or otherwise violate our or our licensors' patent and other intellectual property rights, or we may be required to defend against claims of infringement, misappropriation or other violation. Litigation and other proceedings in connection with any of the foregoing claims can be unpredictable, expensive and time-consuming. Even if resolved in our favor, litigation or other proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of intellectual property litigation or other proceedings could adversely affect our ability to compete in the marketplace and could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may be subject to claims asserting that our employees, consultants or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property.

Many of our employees, consultants or advisors are currently, or 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 advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. 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 be required to obtain licenses to such intellectual property rights, which may not be available on commercially reasonable terms or at all. An inability to incorporate such intellectual property rights would harm our business and may prevent us from successfully commercializing any product candidates we may develop or at all. In addition, we may lose personnel as a result of such claims and any such litigation or the threat thereof may adversely affect our ability to hire employees or contract with independent contractors. A loss of key personnel or their work product could hamper or prevent our ability to commercialize any product candidates we may develop and our technology, which would have a material adverse effect on our business, results of operations, financial condition and prospects. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while it is our policy to require our employees, contractors and advisors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property.

In addition, we or our licensors may in the future be subject to claims by former employees, consultants or other third parties asserting an ownership right in our owned or licensed patent rights. An adverse determination in any such submission or proceeding may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar technology and therapeutics, without payment to us, or could limit the duration of the patent protection covering our technology and any product candidates we may develop. Such challenges may also result in our inability to develop, manufacture or commercialize our technology and product candidates without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our owned or licensed patent rights are threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future technology and product candidates. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

Changes in patent law in the United States or worldwide could diminish the value of patents in general, thereby impairing our ability to protect our products.

Changes in either the patent laws or interpretation of patent laws in the United States and worldwide, including patent reform legislation such as the Leahy-Smith America Invents Act, or the Leahy-Smith Act, could increase the uncertainties and costs surrounding the prosecution of our owned and in-licensed patent applications and the maintenance, enforcement or defense of our owned and in-licensed issued patents. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These changes include provisions that affect the way patent applications are prosecuted, redefine prior art, provide more efficient and cost-effective avenues for competitors to challenge the validity of patents, and enable third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent at USPTO-administered post-grant proceedings, including post-grant review, inter partes review, and derivation proceedings. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith Act, the United States transitioned to a first-to-file system in which, assuming that the other statutory requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. As such, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. 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. This combination of events has created uncertainty with respect to the validity and enforceability of patents once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our patent rights and our ability to protect, defend and enforce our patent rights in the future.

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

We or our licensors may be subject to claims that former employees, collaborators or other third parties have an interest in our owned or in-licensed patents, trade secrets or other intellectual property as an inventor or co-inventor. For example, we or our licensors may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing any product candidates or technology. Litigation may be necessary to defend against these and other claims challenging inventorship or our or our licensors' ownership of our owned or in-licensed patents, trade secrets or other intellectual property. If we or our licensors fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could have a material adverse effect on our competitive business position and prospects. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products, which license may not be available on commercially reasonable terms, or at all, or such license may be non-exclusive. 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. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Any registered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively, and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our business, financial condition, results of operations or prospects.

Intellectual property rights do not necessarily address all potential threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make products that are similar to our product candidates but that are not covered by the claims of the patents that we license or own currently or in the future;
- we, or our license partners or current or future collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent applications that we license or own currently or in the future;
- we, or our license partners or current or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing, misappropriating or otherwise violating our owned or in-licensed intellectual property rights;
- it is possible that our pending patent applications or those that we may own or in-license in the future will not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by third parties;
- third parties might conduct research and development activities in countries where we do not have patent or other intellectual property rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we cannot ensure that any of our patents, or any of our pending patent applications, if issued, will include claims having a scope sufficient to protect our product candidates;
- we cannot ensure that any patents issued to us will provide a basis for an exclusive market for our commercial viable product candidates or will provide us with any competitive advantages;
- we cannot ensure that our commercial activities or product candidates will not infringe upon the patents of others;
- we may not develop additional proprietary technologies that are patentable;
- we cannot ensure that we will be able to successfully commercialize our product candidates on a substantial scale, if approved, before our relevant patents expire;
- the patents or other intellectual property rights of others may have an adverse effect on our business; and
- we may choose not to file a patent for certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations and prospects.

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 currently rely on certain third parties to manufacture all or part of our product candidates and to perform quality testing, and because we collaborate with various organizations and academic institutions for the advancement of our product engine and pipeline, we must, at times, share our proprietary technology and confidential information, including any trade secrets we have, with them. We seek to protect our proprietary technology, in part, by entering into confidentiality agreements and, if applicable, material transfer agreements, sponsored research 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, including our 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 or other third parties, 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 any trade secrets we have, a competitor’s discovery of our proprietary technology and confidential information or other unauthorized use or disclosure would impair our competitive position and may harm our business, financial condition, results of operations and prospects.

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 by third parties. A competitor’s

discovery of our trade secrets would impair our competitive position and have an adverse impact on our business, financial condition, results of operations and prospects.

Risks Related to Regulatory Approval and Other Legal Compliance Matters

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming, and uncertain and may prevent us from obtaining approvals for the commercialization of any product candidates we develop. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize, or will be delayed in commercializing, product candidates we develop, and our ability to generate revenue will be materially impaired.

Any product candidates we develop and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory authorities in the United States, and by comparable authorities in other countries. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate in a given jurisdiction. We have not received approval to market any product candidates from regulatory authorities in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party CROs to assist us in this process. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the biologic product candidate's safety, purity and potency or the drug product candidate's safety and efficacy. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Any product candidates we develop may not be effective, may be only moderately effective, or may prove to have undesirable or unintended side effects, toxicities, or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining marketing approvals, both in the United States and outside the United States, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity, and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical, or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit, or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved medicine not commercially viable.

If we experience delays in obtaining approval or if we fail to obtain approval of any product candidates we develop, the commercial prospects for those product candidates may be harmed, and our ability to generate revenues will be materially impaired.

Failure to obtain marketing approval in foreign jurisdictions would prevent any product candidates we develop from being marketed in such jurisdictions, which, in turn, would materially impair our ability to generate revenue.

In order to market and sell any product candidates we develop in the European Union and many other foreign jurisdictions, we or our collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We or these third parties may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our medicines in any jurisdiction, which would materially impair our ability to generate revenue.

Additionally, we could face heightened risks with respect to seeking marketing approval in the United Kingdom as a result of the recent withdrawal of the United Kingdom from the European Union, commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the United Kingdom and the European Union, the United Kingdom withdrew from the European Union, effective December 31, 2020. On December 24, 2020, the United Kingdom and European Union entered into a Trade and Cooperation Agreement. The agreement sets out certain procedures for approval and recognition of medical products in each jurisdiction. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of the Trade and Cooperation

Agreement or otherwise, could prevent us from commercializing any product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for any product candidates, which could significantly and materially harm our business.

Regulatory requirements governing gene therapy products are periodically updated and may continue to change in the future.

Regulatory requirements governing gene and cell therapy products have changed frequently and may continue to change in the future. For example, the FDA has established the Office of Tissues and Advanced Therapies (formerly the Office of Cellular, Tissue and Gene Therapies) within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. Additionally, gene therapy clinical trials conducted at institutions that receive funding for recombinant DNA research from the U.S. National Institutes of Health, or the NIH, also are potentially subject to oversight by a committee within the NIH's Office of Science Policy called the Novel and Exceptional Technology and Research Advisory Committee; however, as of 2019, the charter of this review group has evolved to focus public review on clinical trials that cannot be evaluated by standard oversight bodies and pose unusual risks.

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

The FDA decides whether individual gene therapy protocols may proceed and it can put an IND on a clinical hold. If we were to engage an NIH-funded institution to conduct a clinical trial, that institution's IRB would need to review the proposed clinical trial to assess the safety of the trial. In addition, adverse developments in clinical trials of gene therapy products conducted by others may cause the FDA or other oversight bodies to change the requirements for approval of our product candidates. Similarly, the EMA may issue new guidelines concerning the development and marketing authorization for gene therapy products and require that we comply with these new guidelines.

In addition, ethical, social and legal concerns about gene therapy, genetic testing and genetic research could result in additional regulations or prohibiting the processes we may use. Federal and state agencies, congressional committees and foreign governments have expressed their intentions to further regulate biotechnology. More restrictive regulations or claims that our product candidates are unsafe or pose a hazard could prevent us from commercializing any products. New government requirements may be established that could delay or prevent regulatory approval of our product candidates under development. It is impossible to predict whether legislative changes will be enacted, regulations, policies or guidance changed, or interpretations by agencies or courts changed, or what the impact of such changes, if any, may be.

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

We may seek fast track, breakthrough therapy, and/or regenerative medicine advanced therapy designations or priority review for one or more of our product candidates, but we might not receive such designation or priority review, and even if we do, such designation or priority review may not lead to a faster development or regulatory review or approval process, and does not assure FDA approval of our product candidates.

The FDA has several designations that have the potential to accelerate the regulatory review and approval process, including the fast track, breakthrough therapy and regenerative medicine advanced therapy designations. Each of these designations has specific requirements and, if granted, has the potential for a non-conventional FDA review process. The FDA has granted fast track designation for DB-020 for the prevention of cisplatin-related ototoxicity. In addition, if the FDA determines that a product candidate offers major advances in treatment or provides a treatment where no adequate therapy exists, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months. Any such designation or priority review status does not ensure that the product candidate will receive marketing approval or that approval will be granted within any particular timeframe. As a result, while we may

seek and receive one or more of these designation for our product candidates, we may not experience a faster development process, review, or approval compared to conventional FDA procedures. The FDA has broad discretion with respect to whether or not to grant such designations or priority review status to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, the FDA may decide not to grant it. In addition, the FDA may withdraw a designation if it believes that the designation is no longer supported by data from our clinical development program. Moreover, fast track, breakthrough therapy, or regenerative medicine advanced therapy designations alone do not guarantee qualification for the FDA's priority review procedures.

We may seek a rare pediatric disease designation for one or more of our product candidates. However, a BLA for one or more of our product candidates may not meet the eligibility criteria for a priority review voucher upon approval.

With enactment of the Food and Drug Administration Safety and Innovation Act in 2012, Congress authorized the FDA to award priority review vouchers to sponsors of certain rare pediatric disease product applications that meet the criteria specified in the law. This provision is designed to encourage development of new drug and biological products for prevention and treatment of certain rare pediatric diseases.

Specifically, under this program, a sponsor who receives an approval for a drug or biologic for a "rare pediatric disease" may qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product. The sponsor of a rare pediatric disease drug product receiving a priority review voucher may transfer (including by sale) the voucher to another sponsor. The voucher may be further transferred any number of times before the voucher is used, as long as the sponsor making the transfer has not yet submitted the application.

For the purposes of this program, a "rare pediatric disease" is a (i) serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years, including age groups often called neonates, infants, children, and adolescents; and (ii) rare disease or conditions within the meaning of the Orphan Drug Act. The FDA may determine that an application for one or more of our product candidates does not meet the eligibility criteria for a priority review voucher upon approval.

Moreover, while the opportunity to receive a priority review voucher was meant to expire for those companies that had not received a designation by September 30, 2020, Congress authorized an extension of the program in late 2020. Specifically, on December 27, 2020, the Rare Pediatric Disease Priority Review Voucher Program was extended. Under the current statutory sunset provisions, after September 30, 2024, the FDA may only award a voucher for an approved rare pediatric disease product application if the sponsor has rare pediatric disease designation for the drug or biologic that is the subject of such application, and that designation was granted by September 30, 2024. After September 30, 2026, the FDA may not award any rare pediatric disease priority review vouchers.

We may not be able to obtain orphan drug exclusivity for one or more of our product candidates, and even if we do, that exclusivity may not prevent the FDA or the EMA from approving other competing products.

Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug or biologic intended to treat a rare disease or condition. A similar regulatory scheme governs approval of orphan products by the EMA in the European Union. Generally, if a product candidate with an orphan drug designation subsequently 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 EMA from approving another marketing application for the same product for the same therapeutic indication for that time period. The applicable period is seven years in the United States and ten years in the European Union. The exclusivity period in the European Union can be reduced to six years if a product no longer meets the criteria for orphan drug designation, in particular if the product is sufficiently profitable so that market exclusivity is no longer justified.

In order for the FDA to grant orphan drug exclusivity to one of our products, the agency must find that the product is indicated for the treatment of a condition or disease with a patient population of fewer than 200,000 individuals annually in the United States. The FDA may conclude that the condition or disease for which we seek orphan drug exclusivity does not meet this standard. Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different products can be approved for the same condition. In particular, the concept of what constitutes the "same drug" for purposes of orphan drug exclusivity remains in flux in the context of gene therapies, and the FDA has issued draft guidance suggesting that it would not consider two gene therapy products to be different drugs solely based on minor differences in the transgenes or vectors within a given vector class.

In addition, even after an orphan drug is approved, the FDA can subsequently approve the same product for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusivity may also be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of the patients

with the rare disease or condition. Further, if our gene therapy product candidate is considered the "same" as another product for the same indication, and the other product is designated as an orphan drug and receives approval first, our product would be blocked from approval by the orphan drug exclusivity afforded to the other product unless it qualifies for an exception to that exclusivity. In 2017, the Congress passed the FDA Reauthorization Act of 2017, or FDARA. FDARA, among other things, codified the FDA's pre-existing regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. Moreover, in the Consolidated Appropriations Act of 2021, Congress did not further change this interpretation when it clarified that the interpretation codified in FDARA would apply in cases where the FDA issued an orphan designation before the enactment of FDARA but where product approval came after the enactment of FDARA. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

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

We cannot commercialize a product until the appropriate regulatory authorities have reviewed and approved the product candidate. Even if our product candidates demonstrate safety and efficacy in clinical trials, the regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee or other regulatory authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical trials and the review process. Regulatory agencies also may approve a treatment candidate for fewer or more limited indications than requested or may grant approval subject to the performance of post-marketing commitments. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our treatment candidates. For example, the development of our product candidates for pediatric use is an important part of our current business strategy, and if we are unable to obtain regulatory approval for the desired age ranges, our business may suffer.

Even if we, or any collaborators we may have, obtain marketing approvals for any product candidates we develop, the terms of approvals and ongoing regulation of our products could require the substantial expenditure of resources and may limit how we, or they, manufacture and market our products, which could materially impair our ability to generate revenue.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising, and promotional activities for such medicine, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to quality control, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping. For example, the holder of an approved application is obligated to monitor and report adverse events and any failure of a product to meet the specifications in the BLA. For gene therapies that use AAV vectors as a delivery system, the FDA typically advises that individuals receiving AAV vectors undergo follow-up observations for potential adverse events for up to a five-year period. The holder of an approved application must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling, or manufacturing process. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the medicine may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the medicine.

Accordingly, assuming we, or any collaborators we may have, receive marketing approval for one or more product candidates we develop, we, and such collaborators, and our and their contract manufacturers will continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance, and quality control. If we and such collaborators are not able to comply with post-approval regulatory requirements, we and such collaborators could have the marketing approvals for our products withdrawn by regulatory authorities and our, or such collaborators', ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our business, results of operations, financial condition and prospects.

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

- issue a warning letter asserting that we are in violation of the law;
- seek an injunction or impose civil or criminal penalties or monetary fines;

- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve a pending BLA or supplements to a BLA submitted by us;
- seize product; or
- refuse to allow us to enter into supply contracts, including government contracts.

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

Any product candidate for which we obtain marketing approval could be subject to restrictions or withdrawal from the market, and we may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our medicines, when and if any of them are approved.

The FDA and other regulatory agencies closely regulate the post-approval marketing and promotion of medicines to ensure that they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and other regulatory agencies impose stringent restrictions on manufacturers' communications regarding off-label use, and if we do not market our medicines for their approved indications, we may be subject to enforcement action for off-label marketing by the FDA and other federal and state enforcement agencies, including the Department of Justice. Violation of the Federal Food, Product, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription products may also lead to investigations or allegations of violations of federal and state healthcare fraud and abuse laws and state consumer protection laws.

In addition, later discovery of previously unknown problems with our medicines, manufacturers, or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such medicines, manufacturers, or manufacturing processes;
- restrictions on the labeling or marketing of a medicine;
- restrictions on the distribution or use of a medicine;
- requirements to conduct post-marketing clinical trials;
- receipt of warning or untitled letters;
- withdrawal of the medicines from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of medicines;
- fines, restitution, or disgorgement of profits or revenue;
- suspension or withdrawal of marketing approvals;
- suspension of any ongoing clinical trials;
- refusal to permit the import or export of our medicines;
- product seizure; and
- injunctions or the imposition of civil or criminal penalties.

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 product candidates we develop and adversely affect our business, financial condition, results of operations, and prospects.

Additionally, if any of our product candidates receives marketing approval, the FDA could require us to adopt a REMS to ensure that the benefits outweigh its risks, which may include, among other things, a medication guide outlining the risks of the

product for distribution to patients and a communication plan to healthcare practitioners. Furthermore, if we or others later identify undesirable side effects caused by our product candidate, several potentially significant negative consequences could result, including:

- regulatory authorities may suspend or withdraw approvals of such product candidate;
- regulatory authorities may require additional warnings on the label;
- we may be required to change the way a product candidate is administered or conduct additional clinical trials;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Our relationships with healthcare providers, physicians, and third-party payors will be subject to applicable anti-kickback, fraud and abuse, and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, and diminished profits and future earnings.

Healthcare providers, physicians, and third-party payors play a primary role in the recommendation and prescription of any product candidates that we develop for which we obtain marketing approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell, and distribute our medicines for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal healthcare anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving, or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order, or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid;
- the federal false claims laws, including the federal False Claims Act which can be enforced through civil whistleblower or qui tam actions, impose criminal and civil penalties against individuals or entities for, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval from Medicare, Medicaid, or other government payors that are false or fraudulent or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, as further amended by the Health Information Technology for Economic and Clinical Health Act, which imposes certain requirements, including mandatory contractual terms, with respect to safeguarding the privacy, security, and transmission of individually identifiable health information without appropriate authorization by entities subject to the rule, such as health plans, healthcare clearinghouses, and certain healthcare providers as well as their respective business associates that perform services for them that involve the use or disclosure of individually identifiable health information;
- the federal false statements statute, which prohibits knowingly and willfully falsifying, concealing, or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items, or services;
- the federal transparency requirements under the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics, and medical supplies to report to the Department of Health and Human Services information related to payments and other transfers of value to physicians, as defined by such law, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members and applicable group purchasing organizations; and
- analogous state laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and certain state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures; and state and local laws that require drug manufacturers to register pharmaceutical sales representatives.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order, or use of medicinal products is prohibited in the European Union. The provision of benefits or advantages to physicians is also governed by the national anti-bribery laws of European Union Member States, such as the United Kingdom Bribery Act 2010. 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.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations, or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal, and administrative penalties, damages, fines, disgorgement, exclusion from government funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, and the curtailment or restructuring of our operations, any of which could adversely affect our business, financial condition, results of operations, and prospects. If any of the physicians or other providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to significant criminal, civil, or administrative sanctions, including exclusions from government funded healthcare programs. Liabilities they incur pursuant to these laws could result in significant costs or an interruption in operations, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Recently enacted and future legislation may increase the difficulty and cost for us and any future collaborators to obtain marketing approval of and commercialize our product candidates and affect the prices we, or they, may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability, or the ability of any future collaborators, to profitably sell any products for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any future collaborators, may receive for any approved products.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or the PPACA, which became law in 2010, contains the following provisions of importance to our business, including, without limitation, our ability to commercialize and the prices we may obtain for any of our product candidates that are approved for sale:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of federal healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must now agree to offer 70% point-of-sale discounts off negotiated prices;
- extension of manufacturers' Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program new requirements to report financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2029 unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in

Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Since enactment of the PPACA, there have been, and continue to be, numerous legal challenges and executive and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Additionally, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the PPACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. Further, the Bipartisan Budget Act of 2018, among other things, amended the PPACA, effective January 1, 2019, to increase from 50% to 70% the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." More recently, the CARES Act, which was signed into law on March 27, 2020 and designed to provide financial support and resources to individuals and businesses affected by the COVID-19 pandemic, suspended the 2% Medicare sequester from May 1, 2020 to December 31, 2020 and extended the sequester by one year, through 2030, in order to offset the added expense of the 2020 cancellation.

In addition, the Trump Administration also took executive actions to undermine or delay implementation of the PPACA. For example, President Trump signed executive orders designed to delay the implementation of certain provisions of the PPACA or otherwise circumvent some of the requirements for health insurance mandated by the PPACA. One executive order directed federal agencies with authorities and responsibilities under the PPACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the PPACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. Another executive order terminated the cost-sharing subsidies that reimburse insurers under the PPACA. It remains to be seen how the Biden Administration will address these issues.

Additionally, on December 14, 2018, a Texas U.S. District Court Judge ruled that the PPACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Cuts and Jobs Act of 2017. On December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the PPACA are invalid as well. On March 2, 2020, the U.S. Supreme Court granted the petitions for writs of certiorari to review this case, and it heard oral argument in the case on November 10, 2020.It is unclear how such litigation and other efforts to repeal and replace the PPACA will impact the PPACA.

The costs of prescription pharmaceuticals have also been the subject of considerable discussion in the United States, and members of Congress and the executive branch have stated that they will address such costs through new legislative and administrative measures. To date, there have been several recent U.S. congressional inquiries and proposed and enacted state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. For example, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. Further, in July 2020, President Trump issued five executive orders that are intended to lower the costs of prescription drug products; one that directs HHS to finalize the Canadian drug importation proposed rule previously issued by HHS, which was subsequently finalized in October 2020, and makes other changes allowing for personal importation of drugs from Canada; one that directs HHS to finalize the rulemaking process on modifying the anti-kickback law safe harbors for discounts for plans, pharmacies, and pharmaceutical benefit managers; and one that reduces costs of insulin and epipens to patients of federally qualified health centers. It remains to be seen whether these orders will remain in effect in the Biden Administration.

At the state level, individual states are increasingly aggressive in passing legislation and implementing 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. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our products or additional pricing pressures.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies

and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our potential products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

The commercial success of our products depends on the availability and sufficiency of third-party payor coverage and reimbursement.

Our ability to commercialize any products successfully will depend in part on the extent to which coverage and adequate reimbursement for such products will be available from third-party payors. Even if we succeed in bringing one or more products to the market, these products may not be considered cost-effective, and the amount reimbursed for any products may be insufficient to allow us to sell our products on a competitive basis. Because our programs are in the early stages of development, we are unable at this time to determine their cost-effectiveness or the likely level or method of coverage and reimbursement.

Further, no uniform policy for coverage and reimbursement exists in the United States, and coverage and reimbursement can differ significantly from payor to payor. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates, but also have their own methods and approval process apart from Medicare determinations. As such, one third-party payor's determination to provide coverage for a product does not assure that other payors will also provide coverage for the product. Additionally, we may develop companion diagnostic tests for use with our product candidates. If we do, we will be required to obtain coverage and reimbursement for these tests separate and apart from the coverage and reimbursement we seek for our product candidates, once approved. While we have not yet developed any companion diagnostic test for our product candidates, if we do, there is significant uncertainty regarding our ability to obtain coverage and adequate reimbursement for the same reasons applicable to our product candidates. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for our products and/or any companion diagnostics could have a material and adverse effect on our business, financial condition, results of operations, and prospects.

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

We are exposed to the risk of fraud or other misconduct by our employees, consultants, and partners, and, if we commence clinical trials, our principal investigators. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in the European Union and other jurisdictions, provide accurate information to the FDA, the European Commission, and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately, or disclose unauthorized activities to us. In particular, sales, marketing, and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing, and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing, and promotion, sales commission, customer incentive programs, and other business arrangements. Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, financial condition, results of operations, and prospects, including the imposition of significant fines or other sanctions.

Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain product candidates outside of the United States and require us to develop and implement costly compliance programs.

We are subject to numerous laws and regulations in each jurisdiction outside the United States in which we operate. The creation, implementation and maintenance of international business practices compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required.

The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party, or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. The anti-

bribery provisions of the FCPA are enforced primarily by the Department of Justice. The Securities and Exchange Commission, or SEC, is involved with enforcement of the books and records provisions of the FCPA.

Compliance with the FCPA and other anti-corruption laws potentially applicable to our business is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the compliance with the FCPA and other anti-corruption laws presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

We are also subject to other laws and regulations governing our international operations, including applicable export control laws, economic sanctions on countries and persons, and customs requirements. In addition, various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. Our expansion outside of the United States has required, and will continue to require, us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain drugs and drug candidates outside of the United States, which could limit our growth potential and increase our development costs.

There is no assurance that we will be completely effective in ensuring our compliance with the FCPA and other applicable anti-corruption, export, sanctions, and customs laws. The failure to comply with laws governing international business practices may result in substantial penalties, including suspension or debarment from government contracting. Violations of these laws, including the FCPA, can result in significant civil and criminal penalties. Indictment alone under the FCPA can lead to suspension of the right to do business with the U.S. government until the pending claims are resolved. Conviction of a violation of the FCPA can result in long-term disqualification as a government contractor. The termination of a government contract or relationship as a result of our failure to satisfy any of our obligations under laws governing international business practices would have a negative impact on our operations and harm our reputation and ability to procure government contracts. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Union, including personal health data, is subject to the EU General Data Protection Regulation, or the GDPR, which took effect across all member states of the European Economic Area, or EEA, in May 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR increases our obligations with respect to clinical trials conducted in the EEA by expanding the definition of personal data to include coded data and requiring changes to informed consent practices and more detailed notices for clinical trial subjects and investigators. In addition, the GDPR also imposes strict rules on the transfer of personal data to countries outside the European Union, including the United States, and, as a result, increases the scrutiny that clinical trial sites located in the EEA should apply to transfers of personal data from such sites to countries that are considered to lack an adequate level of data protection, such as the United States. The GDPR also permits data protection authorities to require destruction of improperly gathered or used personal information and or impose substantial fines for violations of the GDPR, which can be up to four percent of global revenues or 20 million Euros, whichever is greater and it 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. In addition, the GDPR provides that European Union member states may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data.

Similar actions are either in place or under way in the United States. There are a broad variety of data protection laws that are applicable to our activities, and a wide range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns based on general consumer protection laws. The Federal Trade Commission and state Attorneys General all are aggressive in reviewing privacy and data security protections for consumers. New laws also are being considered at both the state and federal levels. For example, the California Consumer Privacy Act—which went into effect on January 1, 2020—is creating similar risks and obligations as those created by GDPR, though the Act does exempt certain information collected as part of a clinical trial subject to the Federal Policy for the Protection of Human Subjects (the Common Rule). Many other states are considering

similar legislation. A broad range of legislative measures also have been introduced at the federal level. Accordingly, failure to comply with federal and state laws (both those currently in effect and future legislation) regarding privacy and security of personal information could expose us to fines and penalties under such laws. There also is the threat of consumer class actions related to these laws and the overall protection of personal data. 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 reputation and our business.

Given the breadth and depth of changes in data protection obligations, preparing for and complying with these requirements is rigorous and time intensive and requires significant resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the European Union. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities and increase our cost of doing business, and could lead to government enforcement actions, private litigation and significant fines and penalties against us and could have a material adverse effect on our business, financial condition or results of operations.

Risks Related to Employee Matters, Managing Growth and General Business Operations

The COVID-19 pandemic, which began in late 2019 and has spread worldwide, has disrupted our ongoing Phase 1b clinical trial of DB-020 and may affect our ability to initiate and complete preclinical studies, delay the initiation of our planned clinical trials or future clinical trials, disrupt regulatory activities, disrupt our manufacturing and supply chain or have other adverse effects on our business and operations. In addition, this pandemic has caused substantial disruption in the financial markets and may adversely impact economies worldwide, both of which could result in adverse effects on our business, operations and ability to raise capital.

The COVID-19 pandemic, which began in December 2019 and has spread worldwide, has caused many governments to implement measures to slow the spread of COVID-19 through quarantines, travel restrictions, heightened border scrutiny and other measures. The COVID-19 pandemic and government measures taken in response have also had a significant impact, both directly and indirectly, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen. The future progression of the COVID-19 pandemic and its effects on our business and operations are uncertain.

The extent to which COVID-19 impacts our operations or those of the third parties on which we rely will depend on many factors, which are highly uncertain and cannot be predicted with confidence, including the duration of the pandemic, additional or modified government actions, new information that will emerge concerning the severity and impact of COVID-19, and the actions to contain the COVID-19 pandemic or address its impact in the short and long term. Additionally, the conduct of our clinical trials, preclinical studies and manufacturing activities is dependent upon the availability of clinical trial sites, CROs CDMOs, researchers and investigators, regulatory agency personnel and logistics providers, all of which may be adversely affected by the COVID-19 pandemic.

Any negative impact that the COVID-19 pandemic has on recruiting or retaining patients in our clinical trials, the ability of our suppliers to provide materials for our product candidates, or the regulatory review process could cause delays with respect to product development activities, which could materially and adversely affect our ability to obtain marketing approval for and to commercialize our product candidates, increase our operating expenses, affect our ability to raise additional capital, and have a material adverse effect on our financial results.

Screening and enrollment in our ongoing Phase 1b clinical trial of DB-020 in Australia and the United States have been adversely impacted by the COVID-19 pandemic. Patient screening and enrollment were paused in the second quarter of 2020 in both Australia and the United States, and screening for enrollment did not resume until early in the third quarter of 2020 in Australia and early in the fourth quarter of 2020 in the United States. We have also experienced delays in site start-up and the withdrawal of some sites in the United States. We cannot provide assurance that some factors from the COVID-19 pandemic will not further delay or otherwise adversely affect our clinical development, research, manufacturing and business operations activities, as well as our business generally, in the future.

We and the third-party manufacturers, CROs and academic collaborators that we engage have faced in the past and may face in the future disruptions that could affect our ability to initiate and complete preclinical studies or clinical trials, including disruptions in procuring items that are essential for our research and development activities, such as, for example, raw materials used in the manufacture of our product candidates, laboratory supplies for our preclinical studies and clinical trials, or animals that are used for

preclinical testing, in each case, for which there may be shortages because of ongoing efforts to address the COVID-19 pandemic. Three vaccines for COVID-19 were granted Emergency Use Authorization by the FDA in late 2020 and early 2021, and more are likely to be authorized in the coming months. The resultant demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, may make it more difficult to obtain materials or manufacturing slots for the products needed for our clinical trials, which could lead to delays in these trials. The response to the COVID-19 pandemic may redirect resources with respect to regulatory and intellectual property matters in a way that would adversely impact our ability to pursue marketing approvals and protect our intellectual property. In addition, we may face impediments to regulatory meetings and potential approvals due to measures intended to limit in-person interactions.

In response to the COVID-19 pandemic and in accordance with direction from state and local governmental authorities, we have restricted access to our facility to those individuals who must perform critical research, translational medicine and laboratory support activities that must be completed on site, limited the number of such people that can be present at our facility at any one time, and required that most of our employees work remotely. In the event that governmental authorities were to keep these restrictions in place for an extended period or impose further restrictions, our employees conducting research and development activities may not be able to access our laboratory space, and our core research activities may be significantly limited or curtailed, possibly for an extended period of time.

The COVID-19 pandemic continues to rapidly evolve, and its ultimate scope, duration and effects are unknown. The extent of the impact of the disruptions to our business, preclinical studies and clinical trials as a result of the COVID-19 pandemic will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the COVID-19 pandemic, travel restrictions and actions to contain the COVID-19 pandemic, such as social distancing and quarantines or lock-downs in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease.

The pandemic has already caused significant disruptions in the financial markets, and may continue to cause such disruptions, which could adversely impact our ability to raise additional funds through public offerings or private placements and may also impact the volatility of our stock price and trading in our stock. Moreover, it is possible the pandemic will significantly impact economies worldwide, which could result in adverse effects on our business and operations. We cannot be certain what the overall impact of the COVID-19 pandemic will be on our business and it has the potential to adversely affect our business, financial condition, results of operations, and prospects.

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

We are highly dependent on the research and development, clinical, financial, operational and other business expertise of our executive officers, as well as the other principal members of our management, scientific and clinical teams. Although we have entered into employment agreements with our executive officers, each of them may terminate their employment with us at any time. We do not maintain “key person” insurance for any of our executives or other employees. Recruiting and retaining qualified scientific, clinical, manufacturing, accounting, legal and sales and marketing personnel will also be critical to our success.

The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain marketing approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. Our success as a public company also depends on implementing and maintaining internal controls and the accuracy and timeliness of our financial reporting. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

We expect to expand our development and regulatory capabilities and potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

As we seek to advance our product candidates through clinical trials and commercialization, we will need to expand our development, regulatory, manufacturing, marketing and sales capabilities or contract with third parties to provide these capabilities. We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, clinical, regulatory affairs and, if any product candidate receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial

resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

If we fail to achieve the expected financial and operational benefits of our corporate restructuring, our business and financial results may be harmed.

In January and May 2020, we conducted a reduction in force that included 45 full-time employees, which represented approximately 52% of our full-time employee workforce. The reduction in force was primarily comprised of positions related to research and general and administrative services and was implemented in connection with our determination to focus and reprioritize our resources on gene therapy programs for hearing and balance disorders and eliminate our research efforts on other discovery programs for hearing loss. As a result of the reduction in force, we incurred expenses of approximately $3.5 million, comprised of termination benefits including severance, benefits and other payroll-related charges. The expected cost savings and operational efficiencies from the restructuring activities were based on assumptions and expectations, which were reasonable in our judgment but may not be achieved due to unforeseen difficulties and challenges that are beyond our control. If these assumptions and expectations are incorrect, our business operations and financial results may be harmed.

Our internal computer systems, or those used by our CROs, CDMOs or other contractors or consultants, may fail or suffer security breaches.

Despite the implementation of security measures, our internal computer systems and those of our CROs, CDMOs and other contractors and consultants are vulnerable to damage from computer viruses and unauthorized access. While we have not experienced any such material system failure or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. For example, the loss of our preclinical data and clinical trial data from preclinical studies or clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data.

Likewise, we currently rely on third parties for the manufacture of our product candidates and rely on third parties to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed.

Our operations or those of the third parties upon whom we depend might be affected by the occurrence of a natural disaster, pandemic or other catastrophic event.

We depend on our employees, consultants, CDMOs and CROs, as well as regulatory agencies and other parties, for the continued operation of our business. While we maintain disaster recovery plans, they might not adequately protect us. Despite any precautions we take for natural disasters or other catastrophic events, these events, including terrorist attack, pandemics, hurricanes, fire, floods and ice and snowstorms, could result in significant disruptions to our research and development, preclinical studies, clinical trials, and, ultimately, commercialization of our products. Long-term disruptions in the infrastructure caused by events, such as natural disasters, the outbreak of war, the escalation of hostilities and acts of terrorism or other “acts of God,” particularly involving cities in which we have offices, manufacturing or clinical trial sites, could adversely affect our businesses. Although we carry business interruption insurance policies and typically have provisions in our contracts that protect us in certain events, our coverage might not respond or be adequate to compensate us for all losses that may occur. Any natural disaster or catastrophic event affecting us, our CDMOs or CROs, regulatory agencies or other parties with which we are engaged could have a significant negative impact on our operations and financial performance.

Risks Related to Ownership of Our Common Stock and Our Status as a Public Company

An active trading market for our common stock may not develop or be sustained.

Although our common stock is listed on the Nasdaq Global Select Market, an active trading market for our shares may never develop or be sustained. As a result, it may be difficult for our stockholders to sell their shares without depressing the market price for the shares or at all.

If securities analysts do not publish or cease publishing research or reports or publish misleading, inaccurate or unfavorable research about our business or if they publish negative evaluations of our stock, the price and trading volume of our stock could decline.

The trading market for our common stock relies, in part, on the research and reports that industry or financial analysts publish about us or our business. We do not have control over these analysts. There can be no assurance that existing analysts will continue to cover us or that new analysts will begin to cover us. There is also no assurance that any covering analyst will provide favorable coverage. Although we have obtained analyst coverage, if one or more of the analysts covering our business downgrade their evaluations of our stock or publish inaccurate or unfavorable research about our business, or provide more favorable relative recommendations about our competitors, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price and trading volume to decline.

The price of our common stock is likely to be volatile and fluctuate substantially, which could result in substantial losses for our stockholders.

Our stock price has been, and is likely to continue to be, volatile. The stock market in general and the market for smaller biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, our stockholders may not be able to sell their common stock at or above the price they paid for their shares. The market price for our common stock may be influenced by many factors, including:

- results of or developments in preclinical studies and clinical trials of our product candidates or those of our competitors or potential collaborators;
- timing of the results of our preclinical studies and clinical trials or those of our competitors;
- our success in commercializing our product candidates, if and when approved;
- developments with respect to competitive products or technologies;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other intellectual property or proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license products, product candidates, technologies, or data referencing rights, the costs of commercializing any such products and the costs of development of any such product candidates or technologies;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or the financial results of companies that are perceived to be similar to us;
- sales of common stock by us, our executive officers, directors or principal stockholders or others;
- changes in the structure of healthcare payment systems;
- market conditions in the biopharmaceutical and biotechnology sectors;
- general economic, industry and market conditions, such as the impact of the COVID-19 pandemic on our industry; and
- the other factors described in this “Risk Factors” section.

In the past, following periods of volatility in the market price of a company’s securities, securities class-action litigation has often been instituted against that company. Any lawsuit to which we are a party, with or without merit, may result in an unfavorable judgment. We also may decide to settle lawsuits on unfavorable terms. Any such negative outcome could result in payments of substantial damages or fines, damage to our reputation or adverse changes to our offerings or business practices.

Such litigation may also cause us to incur other substantial costs to defend such claims and divert management’s attention and resources.

Our executive officers, directors, and principal stockholders, if they choose to act together, have the ability to significantly influence all matters submitted to stockholders for approval.

As of April 30, 2021, our executive officers, directors and stockholders who own more than 5% of our outstanding common stock, in the aggregate, beneficially owned shares representing approximately 60.4% of our common stock. As a result, if these stockholders were to choose to act together, they would be able to significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these stockholders, if they choose to act together, would significantly influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets.

This concentration of ownership control may:

- delay, defer or prevent a change in control;
- entrench our management and board of directors; or
- delay or prevent a merger, consolidation, takeover or other business combination involving us that other stockholders may desire.

We have broad discretion in the use of our cash, cash equivalents and available-for-sale securities and may not use them effectively.

Our management has broad discretion in the application of cash, cash equivalents and available-for-sale securities and could spend them in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest these funds in a manner that does not produce income or that loses value.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be the sole source of gain for our stockholders.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders for the foreseeable future.

A significant portion of our total outstanding shares are eligible to be sold into the market in the near future, which could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. As of April 30, 2021, we had 24,901,931 shares of common stock outstanding. This includes the 7,662,000 shares sold in our IPO, which may be resold in the public market immediately without restriction, unless purchased by our affiliates or existing stockholders. The remaining shares are currently restricted as a result of securities laws or lock-up agreements but will become eligible to be sold at various times after the IPO. The representatives of the underwriters may release some or all of the shares of common stock subject to lock-up agreements at any time and without notice, which would allow for earlier sales of shares in the public market.

Moreover, beginning after August 10, 2021, holders of an aggregate of 16,709,180 shares of our common stock will have rights, subject to specified conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We also registered all shares of common stock that we may issue under our equity compensation plans.

These shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and the lock-up agreements entered into in connection with the IPO.

We are an "emerging growth company" and a "smaller reporting company," and the reduced disclosure requirements applicable to emerging growth companies and smaller reporting companies may make our common stock less attractive to investors.

We are an "emerging growth company," or EGC, as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. We may remain an EGC until December 31, 2026, although if the market value of our common stock that is held by non-affiliates exceeds $700 million as of any June 30 before that time or if we have annual gross revenues of $1.07 billion or more in any fiscal year, we would cease to be an EGC as of December 31 of the applicable year. We also would cease to be an EGC if we issue more than $1 billion of non-convertible debt over a three-year period. For so long as we remain an EGC, we are permitted and intend to rely

on exemptions from certain disclosure requirements that are applicable to other public companies that are not EGCs. These exemptions include:

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

Even after we no longer qualify as an emerging growth company, we may continue to qualify as a smaller reporting company, which would allow us to take advantage of many of the same exemptions from disclosure requirements, including reduced disclosure obligations regarding executive compensation. In addition, if we are a smaller reporting company with less than $100 million in annual revenue, we would not be required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404.

We may choose to take advantage of some, but not all, of the available exemptions.

In addition, the JOBS Act permits an EGC to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have elected to take advantage of such extended transition period, which means that when a standard is issued or revised and it has different application dates for public or private companies, we will adopt the new or revised standard at the time private companies adopt the new or revised standard and will do so until such time that we either irrevocably elect to "opt out" of such extended transition period or no longer qualify as an EGC. We may choose to early adopt any new or revised accounting standards whenever such early adoption is permitted for private companies.

We cannot predict whether investors will find our common stock less attractive if we rely on certain or all of these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

We have incurred and will continue to incur increased costs as a result of operating as a newly public company, and our management has devoted and will continue to be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, and particularly after we are no longer an EGC or a smaller reporting company, we have incurred and will continue to incur significant legal, accounting and other expenses that we did not previously incur as a private company. The Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote and will continue to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs, particularly as we hire additional financial and accounting employees to meet public company internal control and financial reporting requirements, and will make some activities more time-consuming and costly compared to when we were a private company.

We cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404, beginning with our filing with the SEC of our Annual Report on Form 10-K for the fiscal year ending December 31, 2021, we will be required to furnish a report by our management on our internal control over financial reporting. However, while we remain an EGC or a smaller reporting company with less than $100 million in annual revenue, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we are engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, including through hiring additional financial and accounting personnel, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue

steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses in our internal control over financial reporting, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

We previously identified a material weakness in our disclosure controls and procedures and our internal controls, which we believe has been fully remediated. If we have inadequately remediated this material weakness or if we otherwise fail to develop, implement and maintain appropriate internal controls in future periods, our ability to report our financial condition and results of operations accurately and on a timely basis could be adversely affected.

We previously identified a material weakness in our internal control over financial reporting. The specific material weakness and our remediation efforts are described in Item 9A, "Controls and Procedures" in our Annual Report on Form 10-K as filed with the SEC on March 29, 2021. A "material weakness" is a deficiency, or a combination of deficiencies, in internal controls, such that there is a reasonable possibility that a material misstatement of our annual or interim consolidated financial statements would not be prevented or detected. We cannot assure you that additional material weaknesses in our internal controls will not be identified in the future. Any failure to maintain or implement required new or improved controls, or any difficulties we encounter in their implementation, could result in additional material weaknesses, or could result in material misstatements in our financial statements. These misstatements could result in restatements of our financial statements, cause us to fail to meet our reporting obligations or cause investors to lose confidence in our reported financial information.

We have developed certain remediation steps to address the material weakness discussed above and to improve our internal controls. We believe the material weakness discussed above has been fully remediated. If we have inadequately remediated this material weakness, there will continue to be an increased risk that our future financial statements could contain errors that will be undetected. Further and continued determinations that there are material weaknesses in the effectiveness of our internal controls could reduce our ability to obtain financing or could increase the cost of any financing we obtain and require additional expenditures of resources to comply with applicable requirements. For more information relating to our internal controls and disclosure controls and procedures, and the remediation plan undertaken by us, see Item 9A, "Controls and Procedures" in our Annual Report on Form 10-K as filed with the SEC on March 29, 2021.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.

Effective internal control over financial reporting is necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, is designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal control over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could harm our business and have a negative effect on the trading price of our stock.

We are required to disclose changes made in our internal controls and procedures on a quarterly basis and our management is required to assess the effectiveness of these controls annually. However, for as long as we are an EGC under the JOBS Act or a smaller reporting company with less than $100 million in annual revenue, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal control over financial reporting pursuant to Section 404. We could be an EGC for up to five years. Our assessment of internal controls and procedures may not detect material weaknesses in our internal control over financial reporting. Undetected material weaknesses in our internal control over financial reporting could lead to financial statement restatements and require us to incur the expense of remediation, which could have a negative effect on the trading price of our stock.

Provisions in our corporate charter documents and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current directors and members of management.

Provisions in our certificate of incorporation and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which our stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of

directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that only one of three classes of directors is elected each year;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from our board of directors;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal specified provisions of our certificate of incorporation or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, or the DGCL, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Our certificate of incorporation designates the Court of Chancery of the State of Delaware and the federal district courts of the United States of America as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers and employees.

Our certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Court of Chancery of the State of Delaware does not have jurisdiction, the federal district court for the District of Delaware) will be the sole and exclusive forum for the following types of actions or proceedings under Delaware statutory or common law:

- any derivative action or proceeding brought on our behalf;
- any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, employees or stockholders to our company or our stockholders;
- any action asserting a claim arising pursuant to any provision of the DGCL or as to which the DGCL confers jurisdiction on the Court of Chancery of the State of Delaware; or
- any action asserting a claim arising pursuant to any provision of our certificate of incorporation or bylaws (in each case, as they may be amended from time to time) or governed by the internal affairs doctrine.

These choice of forum provisions will not apply to suits brought to enforce a duty or liability created by the Exchange Act. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all such Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims. To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States of America shall, to the fullest extent permitted by law, be the sole and exclusive forum for the resolution of any claims arising under the Securities Act. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our certificate of incorporation. This may require significant additional costs associated with resolving such action in other jurisdictions and there can be no assurance that the provisions will be enforced by a court in those other jurisdictions.

These exclusive forum provisions may limit the ability of our stockholders to bring a claim in a judicial forum that such stockholders find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees. If a court were to find either exclusive forum provision contained in our certificate of

incorporation to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with resolving such action in other jurisdictions, all of which could materially adversely affect our business, financial condition and results of operations.

General Risk Factors

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We are subject to certain reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, recorded, processed, summarized, and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people, or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements or insufficient disclosures due to error or fraud may occur and not be detected.

Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition.

Recent changes in tax law may adversely affect our business or financial condition. On December 22, 2017, the U.S. government enacted the Tax Cuts and Jobs Act, or TCJA, which significantly reformed the Internal Revenue Code of 1986, as amended, or the Code. The TCJA, among other things, contains significant changes to corporate taxation, including reducing the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limiting the tax deduction for net interest expense to 30% of adjusted taxable income (except for certain small businesses), limiting the deduction for NOLs arising in taxable years beginning after December 31, 2017 to 80% of current year taxable income and elimination of NOL carrybacks for losses arising in taxable years ending after December 31, 2017 (though any such NOLs may be carried forward indefinitely), imposing a one-time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, eliminating U.S. tax on foreign earnings (subject to certain important exceptions), allowing immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits.

As part of Congress' response to the COVID-19 pandemic, the Families First Coronavirus Response Act, or FFCR Act, was enacted on March 18, 2020, and the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act, was enacted on March 27, 2020. Both contain numerous tax provisions. In particular, the CARES Act retroactively and temporarily (for taxable years beginning before January 1, 2021) suspends application of the 80%-of-income limitation on the use of NOLs, which was enacted as part of the TCJA. It also provides that NOLs arising in any taxable year beginning after December 31, 2017, and before January 1, 2021 are generally eligible to be carried back up to five years. The CARES Act also temporarily (for taxable years beginning in 2019 or 2020) relaxes the limitation of the tax deductibility for net interest expense by increasing the limitation from 30% to 50% of adjusted taxable income.

Regulatory guidance under the TCJA, the FFCR Act and the CARES Act is and continues to be forthcoming, and such guidance could ultimately increase or lessen their impact on our business and financial condition. It is also likely that Congress will enact additional legislation in connection with the COVID-19 pandemic, some of which could have an impact on us. In addition, it is uncertain if and to what extent various states will conform to the TCJA, the FFCR Act or the CARES Act. We urge investors in our common stock to consult with their legal and tax advisors with respect to any recently enacted tax legislation, or proposed changes in law, and the potential tax consequences of investing in or holding our common stock.

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

On February 17, 2021, we closed our initial public offering, or IPO, in which we issued and sold 7,062,000 shares of our common stock at a public offering price of $18.00 per share, and on February 24, 2021, we issued and sold an additional 600,000 shares pursuant to the underwriters' partial exercise of their option to purchase additional shares, for aggregate gross proceeds of $137.9 million. Upon the closing of the IPO, all shares of Convertible Preferred Stock then outstanding converted into 16,662,011 shares of common stock. All of the shares of common stock issued and sold in our initial public offering were registered under the Securities Act pursuant to a registration statement on Form S-1 (Registration No. 333-252347), which was declared effective by the SEC on February 11, 2021.

The aggregate net proceeds to us from the public offering, inclusive of the over-allotment exercise, was approximately $124.8 million, after deducting underwriting discounts and commissions and other offering expenses payable by us of approximately $13.1 million. As of March 31, 2021, we have used approximately $9.0 million of the net proceeds from the IPO. There has been no material change in the planned use of IPO proceeds from that described in the final prospectus related to our IPO filed with the SEC pursuant to Rule 424(b)(4) under the Securities Act of 1933, as amended, on February 12, 2021.

Item 3. Defaults Upon Senior Securities.

None.

Item 4. Mine Safety Disclosures.

Not applicable.

Item 5. Other Information.

None.

Item 6. Exhibits.

Exhibit Number	Description
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1*	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2*	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

* Filed herewith.

† Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.

SIGNATURES

Pursuant to the requirements 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.

DECIBEL THERAPEUTICS, INC.

Date: May 13, 2021

By: /s/ Laurence Reid
Laurence Reid, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Date: May 13, 2021

By: /s/ Elisabeth Leiderman
Elisabeth Leiderman, M.D.
Chief Financial Officer and Head of Corporate Development
(Principal Financial Officer)

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Laurence Reid, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Decibel Therapeutics, 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(s) 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)) 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) 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

   (c) 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 13, 2021

By: /s/ Laurence Reid
Laurence Reid, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Elisabeth Leiderman, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Decibel Therapeutics, 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(s) 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)) 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) 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

   (c) 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(s) 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 13, 2021

By: /s/ Elisabeth Leiderman
Elisabeth Leiderman, M.D.
Chief Financial Officer and Head of Corporate Development
(Principal Financial Officer)

Exhibit 32.1

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

In connection with the Quarterly Report on Form 10-Q of Decibel Therapeutics, Inc. (the "Company") for the period ended March 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that, to my 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 result of operations of the Company.

Date: May 13, 2021

By: /s/ Laurence Reid

Laurence Reid, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

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 Decibel Therapeutics, Inc. (the "Company") for the period ended March 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that, to my 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 result of operations of the Company.

Date: May 13, 2021

By: /s/ Elisabeth Leiderman
Elisabeth Leiderman, M.D.
Chief Financial Officer and Head of Corporate Development
(Principal Financial Officer)