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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-Q

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

For the quarterly period ended March 31, 2022

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: 001-39343

AKOUOS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**81-1716654**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
645 Summer Street, Suite 200 **Boston, MA**	**02210**
(Address of principal executive offices)	(Zip code)

Registrant's telephone number, including area code: (857) 410-1818

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 Par Value per Share	**AKUS**	**Nasdaq Global Select Market**

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

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

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

Large accelerated filer ☐ Accelerated filer ☐ Non-accelerated filer ☒ Smaller reporting company ☒
Emerging growth company ☒

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

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

As of April 29, 2022, there were 34,626,156 shares of the registrant's common stock, $0.0001 par value per share, outstanding.

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q, or this Quarterly Report, contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act and Section 21E of the Securities Exchange Act of 1934, as amended, that involve substantial risks and uncertainties. All statements, other than statements of historical fact, contained in this Quarterly Report, 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," "contemplate," "continue," "could," "estimate," "expect," "intend," "may," "might," "plan," "potential," "predict," "project," "should," "target," "will," "would," or the negative of these words or other 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 include, among other things, statements about:

- the initiation, timing, progress, and results of our current and future nonclinical studies and clinical trials and our research and development programs, including the timing of when we will submit an investigational new drug application for our product candidates AK-OTOF, for otoferlin gene (*OTOF*)-mediated hearing loss, and AK-antiVEGF, for vestibular schwannoma, to the U.S. Food and Drug Administration;
- our estimates regarding expenses, future revenue, capital requirements, need for additional financing, and the period over which we believe that our existing cash, cash equivalents and marketable securities will be sufficient to fund our operating expenses and capital expenditure requirements;
- our plans to develop and, if approved, subsequently commercialize our product candidates;
- the timing of and our ability to submit applications for, and obtain and maintain regulatory approvals for, our product candidates;
- our expectations regarding our regulatory strategy;
- the potential advantages of our product candidates;
- the rate and degree of market acceptance and clinical utility of our product candidates;
- our estimates regarding the potential addressable patient population for our product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates;
- our intellectual property position;
- our ability to identify additional products, product candidates, or technologies with significant commercial potential that are consistent with our commercial objectives;
- the impact of government laws and regulations;
- our competitive position and expectations regarding developments and projections relating to our competitors and any competing therapies that are or become available;

- developments and expectations regarding developments and projections relating to our competitors and our industry;
- the impact of the COVID-19 pandemic on our business, results of operations, and financial condition;
- our ability to maintain and establish collaborations or obtain additional funding; and
- our expectations regarding the time during which we will be an emerging growth company under the Jumpstart Our Business Startups Act 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, particularly in the "Risk Factors" section, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Moreover, we operate in a competitive and rapidly changing environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, collaborations, joint ventures, or investments we may make or enter into.

You should read this Quarterly Report and the documents that we file with the Securities and Exchange Commission 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 are made as of the date of this Quarterly Report, 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.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this Quarterly Report, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete. Our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information.

SUMMARY OF RISK FACTORS

Our business is subject to numerous risks and uncertainties, including those highlighted in the section entitled "Risk Factors" in Part II, Item 1A of this Quarterly Report. These risks include, but are not limited to, the following:

- we have incurred significant losses during all fiscal periods since our inception, have no products approved for commercial sale, and we expect to incur substantial losses for the foreseeable future. Our net loss was $27.0 million for the quarter ended March 31, 2022 and $16.1 million for the quarter ended March 31, 2021;
- we have a limited operating history and are very early in our development efforts, all of our product candidates, including AK-OTOF and AK-antiVEGF, are still in preclinical development, and we may be unable to advance our product candidates to clinical development, obtain regulatory approval and ultimately commercialize our product candidates;
- we expect that we will need to raise additional funding before we can expect to complete clinical development of any product candidates or become profitable from any future sales of approved products;
- the manufacture of genetic medicine products is complex and difficult, and we could experience manufacturing problems that result in delays in our development or commercialization programs;

- we currently rely, and expect to continue to rely, on third-party manufacturers to produce nonclinical and clinical supply of our product candidates and we have experienced manufacturing delays, including delays related to the COVID-19 pandemic, at our third-party manufacturers, and we could experience further delays in the development or commercialization of our product candidates, including delays related to COVID-19, other natural disasters, or supply chain shortages or delays;
- the COVID-19 pandemic could continue to adversely impact our business, including our manufacturing activities, nonclinical studies, and planned clinical trials;
- we have not tested any of our product candidates in clinical trials, and the outcome of nonclinical studies and earlier-stage clinical trials may not be predictive of future results or the success of later-stage clinical trials or commercial success;
- preclinical and clinical development involve a lengthy and expensive process with an uncertain outcome, and we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our current product candidates or any future product candidates;
- if we do not achieve our projected development goals in the timeframes we announce and expect, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business;
- our product candidates are based on a relatively novel technology with which there is little clinical experience, which makes it difficult to predict the time and cost development and of subsequently obtaining regulatory approval, if at all;
- AK-OTOF and our other product candidates will be a biologic-device combination involving a novel delivery approach, which may result in additional regulatory and other risks;
- even if we complete the necessary nonclinical 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;
- the conditions we seek to treat have low prevalence and it may be difficult to identify patients with these diseases, which may lead to delays in enrollment for our trials or slower commercial revenue if approved;
- we may not be successful in our efforts to build a pipeline of additional product candidates;
- if we are unable to obtain and maintain patent protection for our products and technology, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to successfully commercialize our products and technology may be adversely affected;
- our product candidates may cause undesirable and unforeseen side effects, which could delay or prevent their advancement into clinical trials or regulatory approval, limit the commercial potential or result in significant negative consequences;
- if we fail to comply with our obligations under our existing or any future license agreements, we could lose intellectual property rights that are important to our business; and
- we may not be successful in our efforts to develop our product candidates or to build a pipeline of additional product candidates if we fail to retain and attract key personnel.

PART I
FINANCIAL INFORMATION

Item 1. Financial Statements

AKOUOS, INC.

CONDENSED CONSOLIDATED BALANCE SHEETS
(UNAUDITED)

(In thousands, except share and per share amounts)

	March 31, 2022	December 31, 2021
ASSETS		
Current Assets		
Cash and cash equivalents	$ 54,382	$ 121,907
Marketable securities	154,716	110,545
Prepaid expenses and other current assets	2,353	3,711
Total current assets	211,451	236,163
Property and equipment, net	21,849	19,803
Operating lease right-of-use assets	20,167	20,341
Restricted cash	2,448	2,448
Other assets	43	—
Total assets	$ 255,958	$ 278,755
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current Liabilities		
Accounts payable	$ 1,331	$ 1,280
Accrued expenses and other current liabilities	16,517	14,850
Operating lease liabilities	711	671
Total current liabilities	18,559	16,801
Operating lease liabilities, net of current portion	28,415	28,304
Total liabilities	46,974	45,105
Commitments and contingencies (See Note 11)		
Stockholders' Equity		
Common stock, $0.0001 par value: Authorized: 200,000,000 shares at March 31, 2022 and December 31, 2021. Issued and outstanding: 34,605,503 and 34,498,443 shares at March 31, 2022 and December 31, 2021, respectively.	3	3
Additional paid-in capital	405,094	402,244
Accumulated other comprehensive loss	(735)	(202)
Accumulated deficit	(195,378)	(168,395)
Total stockholders' equity	208,984	233,650
Total liabilities and stockholders' equity	$ 255,958	$ 278,755

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

AKOUOS, INC.

CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(UNAUDITED)

(In thousands, except share and per share amounts)

	Three Months Ended March 31,	
	2022	**2021**
Operating expenses:		
Research and development	$ 20,388	$ 11,258
General and administrative	6,646	4,890
Total operating expenses	27,034	16,148
Loss from operations	(27,034)	(16,148)
Other income (expense):		
Interest income	257	509
Other expense, net	(206)	(447)
Total other income, net	51	62
Net loss	$ (26,983)	$ (16,086)
Net loss per share attributable to common stockholders, basic and diluted	$ (0.78)	$ (0.47)
Weighted-average common shares outstanding, basic and diluted	34,528,992	34,284,419
Other comprehensive income (loss):		
Unrealized gain (loss) on marketable securities	(533)	28
Total other comprehensive income (loss)	(533)	28
Total comprehensive loss	$ (27,516)	$ (16,058)

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

AKOUOS, INC.

CONDENSED CONSOLIDATED STATEMENTS OF

STOCKHOLDERS' EQUITY
(UNAUDITED)

(In thousands, except share amounts)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balances at December 31, 2020	34,383,719	$ 3	$ 392,322	$ 13	$ (81,724)	$ 310,614
Issuance of common stock upon exercise of stock options	62,197	—	225	—	—	225
Vesting of restricted common stock from early-exercised stock options	—	—	21	—	—	21
Stock-based compensation expense	—	—	2,000	—	—	2,000
Net loss	—	—	—	—	(16,086)	(16,086)
Unrealized gain on marketable securities	—	—	—	28	—	28
Balances at March 31, 2021	34,445,916	$ 3	$ 394,568	$ 41	$ (97,810)	$ 296,802
Balances at December 31, 2021	34,498,443	$ 3	$ 402,244	$ (202)	$ (168,395)	$ 233,650
Issuance of common stock upon exercise of stock options	107,060	—	220	—	—	220
Vesting of restricted common stock from early-exercised stock options	—	—	4	—	—	4
Stock-based compensation expense	—	—	2,626	—	—	2,626
Net loss	—	—	—	—	(26,983)	(26,983)
Unrealized loss on marketable securities	—	—	—	(533)	—	(533)
Balances at March 31, 2022	34,605,503	$ 3	$ 405,094	$ (735)	$ (195,378)	$ 208,984

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

AKOUOS, INC.

CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
(UNAUDITED)

(In thousands)

	Three Months Ended March 31,	
	2022	2021
Cash flows from operating activities:		
Net loss	$ (26,983)	$ (16,086)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization expense	748	544
Net amortization of premiums and accretion of discounts on marketable securities	188	442
Amortization of operating lease right-of-use assets	174	96
Stock-based compensation expense	2,626	2,000
Loss on disposal of property and equipment	—	5
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	1,358	(1,796)
Accounts payable	51	97
Other assets	(43)	10
Operating lease liabilities	151	(163)
Accrued expenses and other current liabilities	1,671	(1,071)
Net cash used in operating activities	(20,059)	(15,922)
Cash flows from investing activities:		
Purchases of property and equipment	(2,794)	(4,107)
Purchases of marketable securities	(64,892)	(70,302)
Proceeds from sales or maturities of marketable securities	20,000	140,000
Net cash provided by (used in) investing activities	(47,686)	65,591
Cash flows from financing activities:		
Payments of finance lease obligations	—	(63)
Proceeds from exercise of stock options	220	246
Net cash provided by financing activities	220	183
Net increase (decrease) in cash, cash equivalents and restricted cash	(67,525)	49,852
Cash, cash equivalents and restricted cash at beginning of period	124,355	70,249
Cash, cash equivalents and restricted cash at end of period	$ 56,830	$ 120,101
Supplemental cash flow information:		
Cash paid for interest	$ —	$ 1
Supplemental disclosure of non-cash investing and financing information:		
Vesting of common stock subject to repurchase	$ 4	$ 21
Remeasurement of operating lease right-of-use asset for lease modification	$ —	$ 5,592
Reconciliation of cash, cash equivalents and restricted cash:		
Cash and cash equivalents	$ 54,382	$ 117,653
Restricted cash	2,448	2,448
Total cash, cash equivalents and restricted cash shown in the statement of cash flows	$ 56,830	$ 120,101

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

AKOUOS, INC.

NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS (UNAUDITED)

1. Nature of the Business and Basis of Presentation

Akouos, Inc., together with its consolidated subsidiary (the "Company" or "Akouos"), is a precision genetic medicine company dedicated to its mission of developing gene therapies with the potential to restore, improve, and preserve high-acuity physiologic hearing for individuals who live with disabling hearing loss worldwide. The Company was formed as a limited liability corporation under the laws of the Commonwealth of Massachusetts in March 2016 under the name Akouos, LLC and converted into a corporation under the laws of the State of Delaware in November 2016 under the name Akouos, Inc.

The Company is subject to risks and uncertainties common to early-stage companies in the biotechnology industry, including, but not limited to, development by competitors of new technological innovations, dependence on key personnel, protection of proprietary technology, compliance with government regulations, the impact of the COVID-19 pandemic, and the ability to secure additional capital to fund operations. Product candidates currently under development will require significant additional research and development efforts, including extensive preclinical and clinical testing and 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 development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

On June 30, 2020, the Company completed its initial public offering of its common stock and issued and sold 14,375,000 shares of its common stock, at a public offering price of $17.00 per share, for gross proceeds of $244.4 million, or net proceeds of $223.8 million after deducting underwriting discounts, commissions, and offering expenses.

In August 2021, the Company entered into a sales agreement ("the ATM Sales Agreement") with Cowen and Company, LLC, ("Cowen") to issue and sell, from time to time at prevailing market prices, shares of the Company's common stock having aggregate gross proceeds of up to $100.0 million. Sales of common stock under the ATM Sales Agreement may be made by any method that is deemed an "at the market" offering as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended. The Company agreed to pay Cowen a commission of 3.0% of the aggregate gross proceeds of any shares sold by Cowen under the ATM Sales Agreement. As of March 31, 2022, no sales have been made pursuant to the ATM Sales Agreement.

The accompanying condensed consolidated financial statements have been prepared on the basis of continuity of operations, realization of assets, and the satisfaction of liabilities and commitments in the ordinary course of business. The Company has primarily funded its operations with proceeds from sales of convertible preferred stock and proceeds from the Company's initial public offering of common stock. The Company has incurred losses and negative cash flows from operations since its inception. As of March 31, 2022, the Company had an accumulated deficit of $195.4 million.

The Company expects that its operating losses and negative cash flows will continue for the foreseeable future. The Company expects that its existing cash, cash equivalents and marketable securities will be sufficient to fund its operating expenses and capital expenditure requirements for at least 12 months from the issuance date of the interim condensed consolidated financial statements.

The Company expects to seek additional funding through public and private equity financings, debt financings, collaborations, licensing arrangements, and/or strategic alliances. The Company may not be able to obtain financing on acceptable terms, or at all, and the Company may not be able to enter into collaborations or other such arrangements. The terms of any financing may adversely affect the holdings or the rights of the Company's stockholders. If the Company is unable to obtain funding, the Company could be forced to delay, reduce, or eliminate some or all of its research and development programs, product portfolio expansion, or commercialization efforts, which could adversely affect its business prospects. Although management continues to pursue these plans, there is no assurance that the

Company will be successful in obtaining sufficient funding on terms acceptable to the Company to fund continuing operations, if at all.

Impact of the COVID-19 Pandemic

The COVID-19 pandemic has caused many governments to implement measures to slow the spread of the pandemic. The pandemic and government measures taken in response have had and will continue to have a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred, supply chains have been disrupted, and facilities and production have been suspended. The Company has experienced manufacturing delays at its third-party manufacturers, including delays related to the COVID-19 pandemic, and may experience additional delays in the future, including supply chain delays or shortages, which could further delay product development timelines. The future progression of the pandemic and its continued effects on the Company's business and operations are uncertain. The COVID-19 pandemic may affect the Company's ability to initiate and complete nonclinical studies, delay the initiation of its planned clinical trial or future clinical trials, disrupt regulatory activities, or have other adverse effects on its business and operations. In particular, the Company and its third-party manufacturers and contract research organizations may face additional disruptions that may affect the Company's ability to initiate and complete nonclinical studies, obtain nonclinical and clinical supplies, and initiate clinical trial sites. The pandemic may cause significant disruptions in the financial markets, which could impact the Company's ability to raise additional funds to support its operations. Moreover, the pandemic has significantly impacted economies worldwide, which could result in adverse effects on the Company's business and operations.

As described above, to date, the Company has experienced a business disruption at its third-party manufacturers, including delays related to the COVID-19 pandemic. The Company is continuing to monitor the impact of the COVID-19 pandemic on its business and financial statements. To date, the Company has not incurred impairment losses in the carrying values of its assets as a result of the pandemic and it is not aware of any specific related event or circumstance that would require it to revise its estimates reflected in these condensed consolidated financial statements. The extent to which the COVID-19 pandemic will continue to directly or indirectly impact the Company's business, results of operations and financial condition, including planned and future clinical trials and research and development costs, will depend on future developments that are highly uncertain, including as a result of new information that may emerge concerning COVID-19, the actions taken to contain or treat it, and the duration and intensity of the related effects.

Basis of Presentation

The accompanying condensed consolidated financial statements reflect the operations of the Company and its wholly owned, domestic subsidiary. Intercompany balances and transactions have been eliminated in consolidation. The accompanying condensed consolidated financial statements have been prepared in conformity with generally accepted accounting principles in the United States of America ("GAAP"). 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 Update ("ASU") of the Financial Accounting Standards Board ("FASB").

Use of Estimates

The preparation of the Company's consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements, and the reported amounts of revenue and expenses during the reporting periods. Significant estimates and assumptions reflected in these condensed consolidated financial statements include, but are not limited to, the accrual of research and development expenses. The Company bases its estimates on historical experience, known trends, and other market specific or other relevant factors that it believes to be reasonable under the circumstances. On an ongoing basis, management evaluates its estimates, as there are changes in circumstances, facts, and experience. Changes in estimates are recorded in the period in which they become known. Actual results may differ from those estimates or assumptions.

Unaudited Interim Financial Information

The accompanying condensed consolidated balance sheet as of March 31, 2022, the condensed consolidated statements of operations and comprehensive loss for the three months ended March 31, 2022 and 2021, the condensed consolidated statements of cash flows for the three months ended March 31, 2022 and 2021 and the condensed consolidated statements of stockholders' equity for the three months ended March 31, 2022 and 2021 are unaudited. 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 statement of the Company's financial position as of March 31, 2022 and the results of its operations for the three months ended March 31, 2022 and 2021 and its cash flows for the three months ended March 31, 2022 and 2021. The financial data and other information disclosed in these notes related to the three months ended March 31, 2022 and 2021 are also unaudited. The results for the three months ended March 31, 2022 and 2021 are not necessarily indicative of results to be expected for the year ending December 31, 2022, any other interim periods, or any future year or period. The accompanying balance sheet as of December 31, 2021 has been derived from the Company's audited financial statements for the year ended December 31, 2021. Certain information and footnote disclosures normally included in financial statements prepared in accordance with GAAP have been condensed or omitted pursuant to rules and regulations. However, the Company believes that the disclosures are adequate to make the information presented not misleading. The accompanying unaudited condensed consolidated financial statements and notes should be read in conjunction with the audited consolidated financial statements and related notes for the year ended December 31, 2021 included in the Company's Annual Report on Form 10-K for the year ended December 31, 2021 filed with the Securities and Exchange Commission (the "SEC") on March 29, 2022 (the "Annual Report on Form 10-K").

2. Summary of Significant Accounting Policies

Summary of Significant Accounting Policies

The significant accounting policies and estimates used in the preparation of the accompanying consolidated financial statements are described in the Company's audited consolidated financial statements included in the Annual Report on Form 10-K. There have been no material changes in the Company's significant accounting policies during the three months ended March 31, 2022.

Recently Adopted Accounting Pronouncements

In December 2019, the FASB issued ASU No. 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes ("ASU* 2019-12*")*. ASU 2019-12 simplifies the accounting for income taxes by eliminating certain exceptions to the guidance in ASC Topic 740, *Income Taxes* related to the approach for intraperiod tax allocation, the methodology for calculating income taxes in an interim period and the recognition of deferred tax liabilities for outside basis differences. ASU 2019-12 is effective for annual periods beginning after December 15, 2020, including interim periods within those fiscal years. Early adoption is permitted. The Company adopted ASU 2019-12 as of the required effective date of January 1, 2021, and the adoption did not have a material impact on the Company's consolidated financial statements.

Recently Issued Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the FASB or other standard-setting bodies that the Company adopts as of the specified effective date. The Company qualifies as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012 and has elected not to "opt out" of the extended transition period related to complying with new or revised accounting standards, which means that when a standard is issued or revised and it has different application dates for public and non-public companies, the Company can adopt the new or revised standard at the time non-public companies adopt the new or revised standard and can do so until such time that the Company either (i) irrevocably elects to "opt out" of such extended transition period or (ii) no longer qualifies as an

emerging growth company. The Company may choose to early adopt any new or revised accounting standards whenever such early adoption is permitted for non-public companies.

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments—Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* ("ASU 2016-13"), which requires the measurement and recognition of expected credit losses for financial assets held at amortized cost. ASU 2016-13 replaces the existing incurred loss impairment model with an expected loss model. It also eliminates the concept of other-than-temporary impairment and requires credit losses related to available-for-sale debt securities to be recorded through an allowance for credit losses rather than as a reduction in the amortized cost basis of the securities. These changes may result in earlier recognition of credit losses. In November 2018, the FASB issued ASU No. 2018-19, *Codification Improvements to Topic 326, Financial Instruments—Credit Losses*, which narrowed the scope and changed the effective date for non-public entities for ASU 2016-13. The FASB subsequently issued supplemental guidance within ASU No. 2019-05, *Financial Instruments—Credit Losses (Topic 326): Targeted Transition Relief* ("ASU 2019-05"). ASU 2019-05 provides an option to irrevocably elect the fair value option for certain financial assets previously measured at amortized cost basis. For public entities that are SEC filers, excluding entities eligible to be smaller reporting companies, ASU 2016-13 was effective for annual periods beginning after December 15, 2019, including interim periods within those fiscal years. For all other entities, ASU 2016-13 is effective for annual periods beginning after December 15, 2022, including interim periods within those fiscal years. Early adoption is permitted. The Company is currently evaluating the impact that the adoption of ASU 2016-13 will have on its consolidated financial statements.

3. Fair Value Measurements

The following tables present the Company's fair value hierarchy for its assets that are measured at fair value on a recurring basis and indicate the level within the fair value hierarchy of the valuation techniques the Company utilized to determine such fair value:

	Fair Value Measurements at March 31, 2022 Using:			
(in thousands)	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	$ 55,895	$ —	$ —	$ 55,895
Restricted cash:				
Money market funds	2,448	—	—	2,448
Marketable securities:				
U.S. Treasury notes	—	154,716	—	154,716
	$ 58,343	$ 154,716	$ —	$ 213,059

	Fair Value Measurements at December 31, 2021 Using:			
(in thousands)	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	$ 121,018	$ —	$ —	$ 121,018
Restricted cash:				
Money market funds	2,448	—	—	2,448
Marketable securities:				
U.S. Treasury notes	—	110,545	—	110,545
	$ 123,466	$ 110,545	$ —	$ 234,011

U.S. government money market funds were valued by the Company based on quoted market prices, which represent a Level 1 measurement within the fair value hierarchy.

As of March 31, 2022, the Company's marketable securities consisted of U.S. Treasury notes, which were valued based on Level 2 inputs. In determining the fair value of its U.S. Treasury notes, the Company relied on quoted prices for similar securities in active markets or other inputs that are observable or can be corroborated by observable market data.

During the three months ended March 31, 2022 and 2021, there were no transfers between Level 1, Level 2, and Level 3 of the fair value hierarchy.

4. Marketable Securities

As of March 31, 2022 and December 31, 2021, the fair value of available-for-sale marketable debt securities by type of security was as follows:

	March 31, 2022			
(in thousands)	Amortized Cost	Gross Unrealized Gain	Gross Unrealized Loss	Fair Value
Assets				
Marketable securities:				
U.S. Treasury notes	$ 155,451	$ —	$ (735)	$ 154,716
	$ 155,451	$ —	$ (735)	$ 154,716

	December 31, 2021			
(in thousands)	Amortized Cost	Gross Unrealized Gain	Gross Unrealized Loss	Fair Value
Assets				
Marketable securities:				
U.S. Treasury notes	$ 110,747	$ —	$ (202)	$ 110,545
	$ 110,747	$ —	$ (202)	$ 110,545

At March 31, 2022 and December 31, 2021, all available-for-sale marketable securities had contractual maturities of less than two years.

5. Property and Equipment, Net

Property and equipment, net consisted of the following:

(in thousands)	March 31, 2022	December 31, 2021
Laboratory equipment	$ 8,226	$ 7,595
Furniture and fixtures	611	600
Leasehold improvements	15,871	15,871
Construction in progress	2,668	516
	27,376	24,582
Less: Accumulated depreciation and amortization	(5,527)	(4,779)
	$ 21,849	$ 19,803

Depreciation and amortization expense for the three months ended March 31, 2022 and March 31, 2021 was approximately $0.7 million and $0.5 million, respectively.

6. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following:

(in thousands)	March 31, 2022	December 31, 2021
Accrued manufacturing expenses	$ 9,859	$ 8,039
Accrued employee compensation and benefits	1,325	3,234
Accrued external research and development expenses	3,671	2,507
Accrued professional fees	1,595	983
Other	67	87
	$ 16,517	$ 14,850

7. Stockholders' Equity

Common Stock

As of March 31, 2022 and December 31, 2021, the Company's certificate of incorporation, as amended and restated, authorized the Company to issue 200,000,000 shares of common stock, $0.0001 par value per share.

On June 30, 2020, the Company completed its initial public offering of its common stock and issued and sold 14,375,000 shares of common stock, at a public offering price of $17.00 per share, for gross proceeds of $244.4 million, or net proceeds of $223.8 million after deducting underwriting discounts, commissions, and offering expenses.

In August 2021, the Company entered into the ATM Sales Agreement with Cowen to issue and sell from time to time at prevailing market prices, up to $100.0 million in shares of the Company's common stock. As of March 31, 2022, the Company has not yet issued or sold any securities under the ATM Sales Agreement.

Preferred Stock

As of March 31, 2022 and December 31, 2021, the Company's certificate of incorporation, as amended and restated, authorized the Company to issue 5,000,000 shares of preferred stock, $0.0001 par value per share. As of March 31, 2022 and December 31, 2021, no shares of preferred stock were issued or outstanding.

8**. Stock-Based Compensation**

2016 Stock Plan

The Company's 2016 Stock Plan (the "2016 Plan") provides for the Company to grant incentive stock options or non-qualified stock options, restricted stock, restricted stock units, and other equity awards to employees, directors, and consultants of the Company. The 2016 Plan is administered by the board of directors or, at the discretion of the board of directors, by a committee of the board of directors. The board of directors may also delegate to one or more officers of the Company the power to grant awards to employees and certain officers of the Company. The exercise prices, vesting, and other restrictions are determined at the discretion of the board of directors, or its committee or any such officer if so delegated.

Stock options granted under the 2016 Plan with service-based vesting conditions generally vest over four years and expire after ten years.

As of March 31, 2022 and December 31, 2021, no shares remained available for future issuance under the 2016 Plan.

2020 Stock Plan

On May 28, 2020, the Company's board of directors adopted, and on June 17, 2020 its stockholders approved, the 2020 Stock Plan (the "2020 Plan"). The 2020 Plan provides for the grant of incentive stock options, non-statutory stock options, stock appreciation rights, restricted stock awards, restricted stock units, and other stock-based awards. The number of shares initially reserved for issuance under the 2020 Plan is the sum of 4,294,594, plus the number of shares (up to 3,622,691 shares) equal to the sum of (i) the number of shares remaining available for issuance under the 2016 Plan upon the effectiveness of the 2020 Plan and (ii) the number of shares of common stock subject to outstanding awards granted under the 2016 Plan that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right. The number of shares of common stock that may be issued under the 2020 Plan will automatically increase on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2021 and continuing for each fiscal year until, and including, the fiscal year ending December 31, 2030, equal to the lowest of (i) 2,728,610 shares, (ii) 4% of the number of shares of common stock outstanding on such date, and (iii) an amount determined by the Company's board of directors. On January 1, 2022, the number of shares reserved for issuance under the 2020 Plan increased, pursuant to the terms of the 2020 Plan, by an additional 1,379,937 shares, equal to 4% of the Company's then outstanding common stock. The shares of common stock underlying any awards that are forfeited, cancelled, held back upon exercise or settlement of an award to satisfy the exercise price or tax withholding, repurchased or are otherwise terminated by the Company under the 2020 Plan will be added back to the shares of common stock available for issuance under the 2020 Plan.

As of March 31, 2022, the total number of shares of common stock available for issuance under the 2020 Plan is 4,606,996 shares.

2020 Employee Stock Purchase Plan

On May 28, 2020, the Company's board of directors adopted, and on June 17, 2020 its stockholders approved, the 2020 Employee Stock Purchase Plan (the "2020 ESPP"). A total of 360,651 shares of common stock were initially reserved for issuance under this plan. The number of shares of common stock that may be issued under the 2020 ESPP will automatically increase on the first day of each fiscal year, beginning with the fiscal year commencing on January 1, 2021 and continuing for each fiscal year until, and including, the fiscal year commencing on January 1, 2031, equal to the lowest of (i) 640,630 shares, (ii) 1% of the number of shares of common stock outstanding on such date, and (iii) an amount determined by the Company's board of directors. On January 1, 2022, the number of shares reserved for issuance under the 2020 ESPP increased, pursuant to the terms of the 2020 ESPP, by an additional 344,984 shares, equal to 1% of the Company's then outstanding common stock.

As of March 31, 2022, the total number of shares of common stock available for issuance under the 2020 ESPP is 1,049,472.

Stock Option Valuation

The fair value of stock option grants is estimated using the Black-Scholes option-pricing model. The Company historically has been a private company and lacks company-specific historical and implied volatility information. Therefore, it estimates its expected stock volatility based on the historical volatility of a publicly traded set of peer companies and expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded stock price. For options with service-based vesting conditions, the expected term of the Company's stock options has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that the Company has never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future.

Stock Options

The following table summarizes the Company's stock option activity since December 31, 2021:

	Number of Shares	Weighted-Average Exercise Price	Weighted-Average Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2021	4,392,836	$ 11.71	8.3	$ 6,801
Granted	1,601,700	$ 5.80		
Exercised	(107,060)	$ 2.05		
Forfeited and cancelled	(158,863)	$ 13.98		
Outstanding as of March 31, 2022	5,728,613	$ 10.20	8.7	$ 1,976
Vested and expected to vest as of March 31, 2022	5,728,613	$ 10.20	8.7	$ 1,976
Options exercisable as of March 31, 2022	1,579,119	$ 9.87	7.9	$ 1,451

The weighted-average grant-date fair value of stock options granted during the three months ended March 31, 2022 and 2021 was $4.11 per share and $12.14 per share, respectively.

Early Exercise of Stock Options into Restricted Stock

Certain option grants permit option holders to elect to exercise unvested options in exchange for unvested common stock. The options that are exercised prior to vesting will continue to vest according to the respective option agreement, and such unvested shares are subject to repurchase by the Company at the optionee's original exercise price in the event the optionee's service with the Company voluntarily or involuntarily terminates.

A summary of the Company's unvested common stock from option early exercises that is subject to repurchase by the Company is as follows:

	Shares
Unvested restricted common stock as of December 31, 2021	14,070
Vested	(3,775)
Unvested restricted common stock as of March 31, 2022	10,295

Proceeds from the early exercise of options are recorded as a liability within accrued expenses and other current liabilities on the condensed consolidated balance sheet. The liability for unvested common stock subject to repurchase is then reclassified to additional paid-in capital as the Company's repurchase right lapses. The shares purchased by the employees and directors pursuant to the early exercise of stock options are not deemed, for accounting purposes, to be

outstanding until those shares have vested. As of March 31, 2022 and December 31, 2021, the liability related to the payments for unvested shares from early-exercised options was less than $0.1 million at each date.

Restricted Common Stock Awards

The Company has both (i) granted restricted stock awards, with the recipient not paying for the shares of common stock, and (ii) issued and sold restricted stock, with the recipient purchasing the common stock at its fair value per share. In both circumstances, the restricted shares of common stock have service-based vesting conditions and unvested shares are either subject to forfeiture by the employee or subject to repurchase by the Company, at the lesser of holder's original purchase price or fair value, in the event the holder's service with the Company voluntarily or involuntarily terminates. Service-based restricted stock awards generally vest over four years.

Proceeds from the issuance and sale of restricted common stock are recorded as a liability within accrued expenses and other current liabilities on the condensed consolidated balance sheet. The liability for unvested common stock subject to repurchase is then reclassified to additional paid-in capital as the Company's repurchase right lapses. Shares of restricted common stock granted or sold to employees and directors are not deemed, for accounting purposes, to be outstanding until those shares have vested.

The Company did not grant or sell restricted common stock awards during 2021 or the three months ended March 31, 2022. As of March 31, 2022, there was no remaining liability related to the payments received for shares of unvested restricted stock. As of December 31, 2021, the liability related to the payments received for shares of unvested restricted stock was less than $0.1 million.

The following table summarizes the Company's restricted common stock award activity for the three months ended March 31, 2022:

	Shares	Weighted-Average Grant-Date Fair Value
Unvested restricted common stock as of December 31, 2021	770	$ 0.85
Vested	(770)	0.85
Unvested restricted common stock as of March 31, 2022	—	$ —

The total fair value of restricted common stock vested during the three months ended March 31, 2022 was less than $0.1 million.

Stock-Based Compensation

The Company records compensation cost for all stock-based payment arrangements, including employee, director, and consultant stock options and restricted stock.

The Company recorded stock-based compensation expense in the following expense categories of its consolidated statements of operations and comprehensive loss (in thousands):

	Three Months Ended March 31,	
	2022	2021
Research and development expenses	$ 997	$ 954
General and administrative expenses	1,629	1,046
	$ 2,626	$ 2,000

As of March 31, 2022, there was $28.5 million of unrecognized compensation cost related to unvested stock options, which is expected to be recognized over a weighted-average period of 2.9 years.

9. License Agreements

License Agreement with Massachusetts Eye and Ear

In October 2017, the Company entered into a license agreement with Massachusetts Eye and Ear Infirmary and the Schepens Eye Research Institute, Inc. (collectively referred to as "MEE") (the "MEE License"). Under the MEE License, the Company received an exclusive, non-transferable, sublicensable, worldwide, royalty-bearing license to certain patent rights and know-how, including rights related to adeno-associated virus ("AAV") ancestral technology, including AAVAnc80, to use, research, develop, manufacture, and commercialize licensed products in the treatment, diagnosis, and prevention of any and all balance disorders, including hearing disorders of the inner ear, in each case, with a total prevalence in the United States of less than 3,000 patients, and an exclusive, non-transferable, sublicensable right and license under MEE's rights, title, and interest in certain patents co-owned by MEE and Children's Medical Center Corporation to use, research, develop, manufacture, and commercialize licensed products. The Company is obligated to use commercially reasonable efforts to develop and commercialize the MEE licensed products, including filing an investigational new drug application ("IND") in the United States or investigational medicinal product dossier ("IMPD") in any country in the European Union or an equivalent application in any country within 18 months of completion of specified toxicology studies for a licensed product.

Upon entering into the MEE License in 2017, the Company issued to MEE shares of the Company's common stock then having a fair value of $0.1 million. The Company is obligated to make aggregate milestone payments to MEE of up to $17.7 million upon the achievement of specified development, regulatory, and sales milestones. The Company is also obligated to pay tiered royalties of a mid to high single-digit percentage based on annual net sales of licensed products by the Company and any of its affiliates and sublicensees. Royalties will be paid by the Company on a licensed product-by-licensed product and country-by-country basis beginning after the first commercial sale of an MEE licensed product and lasting until the later of (i) the expiration of the last valid claim in the licensed patents or (ii) ten years after the first commercial sale of such MEE licensed product (the "MEE Royalty Term").

The MEE License remains in effect until the last expiration date of the last to expire MEE Royalty Term, unless terminated earlier. The Company has the right to terminate the MEE License at will, with or without cause, by 90 days' advance written notice to MEE or upon MEE's material breach of the MEE License, provided that MEE does not cure such material breach within a specified period. MEE has the right to terminate the MEE License in its entirety if (i) the Company fails to make any payment due within a specified period after MEE notifies the Company of such failure, (ii) the Company or its affiliates challenge the validity of the licensed patent rights, (iii) the Company fails to maintain required insurance, or (iv) the Company becomes insolvent or bankrupt. MEE also has the right to terminate the Company's rights to specific intellectual property rights it has licensed to the Company under the MEE License if the Company materially breaches certain diligence obligations and does not cure within a specified period after written notice from MEE.

During the three months ended March 31, 2022 and 2021, the Company did not make any payments to MEE or recognize any research and development expenses under the MEE License.

Sublicense Agreement with Lonza Houston, Inc.

In October 2017, the Company entered into a sublicense agreement with Lonza Houston, Inc. ("Lonza"), as amended in December 2018 (the "Lonza Sublicense"). Under the agreement, the Company received an exclusive, non-transferable, sublicensable, worldwide, royalty-bearing sublicense to certain patent rights and know-how related to AAV ancestral technology, including AAVAnc80, to use, research, develop, manufacture, and commercialize licensed products for the treatment, diagnosis, and prevention of any and all balance disorders or diseases pertaining to the inner ear and/or any and all hearing diseases or disorders, including hearing disorders of the inner ear, but excluding all such disorders or diseases with a total prevalence in the United States of less than 3,000 patients. The Company is obligated to use commercially reasonable efforts to develop and commercialize the Lonza sublicensed products, including filing an

IND in the United States or IMPD in any country in the European Union or an equivalent application in any country within 18 months of completion of specified toxicology studies for a licensed product.

Upon entering into the Lonza Sublicense in 2017, the Company issued to Lonza shares of the Company's common stock then having a fair value of $0.1 million. The Company is obligated to make aggregate milestone payments to Lonza of up to $18.5 million upon the achievement of specified development, regulatory, and sales milestones. The Company is also obligated to pay tiered royalties of a mid to high single-digit percentage based on annual net sales of licensed products by the Company and any of its affiliates and sublicensees as denoted in the Lonza Sublicense. Royalties will be paid by the Company on a licensed product-by-licensed product and country-by-country basis beginning after the first commercial sale of a Lonza sublicensed product and lasting until the later of (i) the expiration of the last valid claim in the patent or (ii) ten years after the first commercial sale of such Lonza sublicensed product (the "Lonza Royalty Term").

The Lonza Sublicense remains in effect until the last expiration date of the last to expire Lonza Royalty Term, unless terminated earlier. The Company has the right to terminate the Lonza Sublicense at will, with or without cause, by 90 days' advance written notice to Lonza or upon Lonza's material breach of the Lonza Sublicense, provided that Lonza does not cure such material breach within a specified period. Lonza has the right to terminate the Lonza Sublicense in its entirety if (i) the Company fails to make any payment due within a specified period after Lonza notifies the Company of such failure, (ii) the Company or its affiliates challenge the validity of the sublicensed patent rights, (iii) the Company fails to maintain required insurance, or (iv) the Company becomes insolvent or bankrupt. Lonza also has the right to terminate the Company's rights to specific intellectual property rights it has sublicensed to the Company under the Lonza Sublicense if the Company materially breaches certain diligence obligations and does not cure within a specified period after written notice from Lonza.

During the three months ended March 31, 2022 and 2021 the Company did not make any payments to Lonza or recognize any research and development expenses under the Lonza Sublicense.

10. Leases

The Company leases its office and laboratory facility in Boston, Massachusetts pursuant to a lease agreement entered into in December 2018 (the "2018 Lease"), which includes a lease incentive, fixed payment escalations, and a rent holiday. The 2018 Lease term commenced in May 2019, which was the point at which the Company obtained control of the leased premises, and expires in February 2028. Under the 2018 Lease, the Company is entitled to one option to extend the lease term for an additional five years. The option to extend the lease term was not included in the right-of-use asset and lease liability as it was not reasonably certain of being exercised. The Company classified the 2018 Lease as an operating lease under ASC 842, *Leases*. The initial annual base rent under the 2018 Lease is $2.3 million, with such base rent increasing annually during the initial term by 3% and with lease payments beginning in February 2020. Additionally, the 2018 Lease requires the Company to pay its portion of real estate taxes and costs related to the premises, including costs of operations, maintenance, repair, replacement, and management of the new leased premises. In connection with the 2018 Lease, the Company is required to maintain a letter of credit for the benefit of the landlord in an amount of approximately $1.3 million, based on a specified formula. The 2018 Lease included a landlord-provided tenant improvement allowance of up to $6.6 million to be applied to the costs of the construction of leasehold improvements. The Company determined that it owns the leasehold improvements related to the 2018 Lease and, as such, reflected the $6.6 million lease incentive as a reduction of the rental payments used to measure the operating lease liability, and, in turn, the operating lease right-of-use asset as of the lease commencement date in May 2019. Between the lease commencement date and December 31, 2019, the Company recorded increases of $6.6 million to the operating lease liability and to leasehold improvements as and when such leasehold improvements were paid for by the lessor.

The Company entered into an amendment in January 2021 to its 2018 Lease (the "Amended 2018 Lease"). Under the Amended 2018 Lease, the Company's leased space expanded the 2018 leased premises to include an additional 37,500 square feet for a total of approximately 75,000 square feet and extended the term of the 2018 Lease for a new ten-year term. The term extension of existing square feet under the 2018 Lease is accounted for as a lease modification, which resulted in the remeasurement of the existing right-of-use asset and lease liability of $5.9 million and $13.1 million, respectively, to $11.5 million and $18.7 million, respectively, in January 2021, the effective date of

the Amended 2018 Lease agreement, and is accounted for as an operating lease. The lease term of the additional leased premises commenced in April 2021, which was the point at which the Company obtained control of the leased premises. On commencement date the Company recorded a right-of-use asset and lease liability of $9.9 million, respectively, and is accounted for as an operating lease. The Amended 2018 Lease included a landlord-provided tenant improvement allowance of up to $7.1 million to be applied to the costs of the construction of leasehold improvements. The Company determined that it owns the leasehold improvements related to the amended 2018 Lease and, as such, reflected the $7.1 million lease incentive as a reduction of the rental payments used to measure the operating lease liability, and, in turn, the operating lease right-of-use asset as of the lease commencement date in April 2021. As of March 31, 2022, the Company has not yet received any payment reimbursements from the lessor for leasehold improvement costs related to the Amended 2018 Lease.

The components of the Company's lease expense are as follows:

(in thousands)	March 31, 2022
Operating lease cost	$ 1,116
Variable lease cost	$ 85

Supplemental disclosure of cash flow information related to leases was as follows:

(in thousands)	March 31, 2022
Cash paid for amounts included in the measurement of operating lease liabilities (operating cash flows)	$ 792

The weighted-average remaining lease term and discount rate were as follows:

	March 31, 2022	December 31, 2021
Weighted-average remaining lease term (in years) used for:		
Operating leases	9.75	10.00
Weighted-average discount rate used for:		
Operating leases	10.00 %	10.00 %

Because the interest rate implicit in the lease was not readily determinable, the borrowing rate was used to calculate the present value of the Amended 2018 Lease. In determining its incremental borrowing rate, the Company considered its credit quality and assessed interest rates available in the market for similar borrowings, adjusted for the impact of collateral over the term of the lease.

Future annual lease payments under the Amended 2018 Lease as of March 31, 2022 were as follows (in thousands):

Years Ending December 31,	Operating Leases
2022	$ (4,597)
2023	5,020
2024	5,611
2025	5,786
2026	5,959
Thereafter	34,419
Total future lease payments	52,198
Less: Imputed interest	(23,072)
Total lease liabilities	$ 29,126

The following table presents lease assets and liabilities and their classification on the consolidated balance sheet (in thousands):

Leases	Consolidated Balance Sheet Classification (unaudited)	March 31, 2022	December 31, 2021
Assets:			
Operating lease assets	Operating lease right-of-use assets	$ 20,167	$ 20,341
Total lease assets		$ 20,167	$ 20,341
Liabilities:			
Current:			
Operating lease liabilities	Operating lease liabilities	$ 711	$ 671
Non-current:			
Operating lease liabilities	Operating lease liabilities, net of current portion	28,415	28,304
Total lease liabilities		$ 29,126	$ 28,975

11. Commitments and Contingencies

401(k) Plan

The Company has a defined-contribution plan under Section 401(k) of the Internal Revenue Code of 1986 (the "401(k) Plan"). The 401(k) Plan covers all employees who meet defined minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pre-tax basis. The Company has made contributions to the 401(k) plan and recorded contribution expense of $0.2 million for the three months ended March 31, 2022. The Company did not make any contributions during the three month period ended March 31, 2021.

Indemnification Agreements

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, contract research organizations, business partners, and other parties with respect to certain matters including, but not limited to, losses arising out of breach of such agreements or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with members of its board of directors and certain of its executive officers that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is, in many cases, unlimited. The Company has not incurred any material costs as a result of such indemnifications and is not currently aware of any indemnification claims.

Legal Proceedings

The Company is not currently party to any material legal proceedings. At each reporting date, the Company evaluates whether or not a potential loss amount or a potential range of loss is probable and reasonably estimable under the provisions of the authoritative guidance that addresses accounting for contingencies. The Company expenses as incurred the costs related to such legal proceedings.

12. Net Loss per Share

Net Loss per Share

Basic and diluted net loss per share attributable to common stockholders was calculated as follows:

(in thousands, except share and per share data)	Three Months Ended March 31, 2022	2021
Numerator:		
Net loss attributable to common stockholders	$ (26,983)	$ (16,086)
Denominator:		
Weighted-average common shares outstanding, basic and diluted	34,528,992	34,284,419
Net loss per share attributable to common stockholders, basic and diluted	$ (0.78)	$ (0.47)

The Company's potential dilutive securities have been excluded from the computation of diluted net loss per share as the effect would be to reduce the net loss per share. Therefore, the weighted-average number of common shares outstanding used to calculate both basic and diluted net loss per share attributable to common stockholders is the same. The Company excluded the following potential common shares, presented based on amounts outstanding at each period end, from the computation of diluted net loss per share attributable to common stockholders for the periods indicated because including them would have had an anti-dilutive effect:

	March 31, 2022	2021
Unvested restricted common stock	10,295	90,844
Stock options to purchase common stock	5,728,613	4,356,486
	5,738,908	4,447,330

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our condensed consolidated financial statements and related notes appearing elsewhere in this Quarterly Report on Form 10-Q, or this Quarterly Report, and our audited financial statements and related notes for the year ended December 31, 2021 included in our Annual Report on Form 10-K, filed with the Securities and Exchange Commission, or SEC, on March 29, 2022. Some of the information contained in this discussion and analysis or set forth elsewhere in this Quarterly Report, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Quarterly Report, 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.

Overview

We are a precision genetic medicine company dedicated to our mission of developing gene therapies with the potential to restore, improve, and preserve high-acuity physiologic hearing for individuals who live with disabling hearing loss worldwide. We have built a precision genetic medicine platform that incorporates a proprietary vector library consisting of variants of a small virus commonly used in gene therapy, known as adeno-associated virus, or AAV, and a novel delivery approach. We are executing on our core strategic initiatives, which include the advancement of our lead product candidate, AK-OTOF; expansion of our pipeline to include programs focused on monogenic and inner ear conditions of complex etiology, such as AK-antiVEGF for vestibular schwannoma; and development of internal manufacturing capabilities and, ultimately, a commercial infrastructure. We believe the genetic medicines we

are developing have the potential to create a new standard of care for the treatment of disabling hearing loss, and to transform the lives of individuals and their families, with disabling hearing loss, by providing a meaningful alternative to the invasive and limited current non-pharmacologic treatments. Our aim is to leverage our capabilities to become a fully integrated biotechnology company. We believe our platform and our team together provide a unique advantage to efficiently develop potential genetic medicines for a variety of inner ear conditions.

Since our inception, we have focused substantially all of our resources on organizing and staffing our company, business planning, raising capital, conducting research and development activities, filing and prosecuting patent applications, identifying potential product candidates, soliciting input from regulators regarding development of these product candidates, and undertaking nonclinical studies. We do not have any products approved for sale and have not generated any revenue from product sales. To date, we have funded our operations primarily with proceeds from sales of preferred stock (including borrowings under convertible promissory notes, which converted into preferred stock in 2017) and, most recently, with proceeds from our initial public offering, or IPO. On June 30, 2020, we completed an IPO of our common stock and issued and sold 14,375,000 shares of common stock at a public offering price of $17.00 per share, resulting in net proceeds of $223.8 million after deducting underwriting discounts and commissions and offering expenses. Since our inception, we have incurred significant operating losses. Our ability to generate any product revenue or product revenue sufficient to achieve profitability will depend on the successful development and eventual commercialization of one or more of our product candidates.

We reported a net loss of $27.0 million for the three months ended March 31, 2022. As of March 31, 2022, we had an accumulated deficit of $195.4 million. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. We expect that our expenses and capital expenditures will increase substantially in connection with our ongoing activities, particularly if and as we:

- submit an investigational new drug application, or IND, and initiate a planned Phase 1/2 clinical trial of our lead product candidate, AK-OTOF, for the treatment of otoferlin gene (*OTOF*)-mediated hearing loss;
- conduct IND-enabling studies in preparation for an IND submission for our product candidate AK-antiVEGF for the treatment of vestibular schwannoma;
- continue our current research programs and our preclinical development of product candidates from our current research programs;
- advance additional product candidates into preclinical and clinical development;
- build a current good manufacturing practice manufacturing facility;
- expand the capabilities of our genetic medicine platform;
- expand our facilities;
- seek marketing approvals for any product candidates that successfully complete clinical trials;
- ultimately establish a sales, marketing, and distribution infrastructure; scale up manufacturing capabilities; and commercialize any products for which we may obtain marketing approval;
- expand, maintain, and protect our intellectual property portfolio;
- hire additional clinical, regulatory, manufacturing, and other scientific personnel to support our research, product development, and future commercialization efforts; and

- add operational, legal, compliance, financial, and management information systems personnel, including personnel to support our research, product development, and future commercialization efforts and support our operations as a public company.

We will not generate revenue from product sales unless and until we successfully complete clinical development and obtain regulatory approval for one or more of our product candidates. If we obtain regulatory approval for any of our product candidates, we expect to incur significant expenses related to developing our commercialization capability to support product sales, marketing, and distribution. Further, we expect to incur additional costs associated with operating as a public company.

As a result, we will need substantial additional funding to support our continuing operations and pursue our growth 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, collaborations, licensing arrangements, and strategic alliances. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as, and when, needed, we may have to significantly delay, scale back, or discontinue the development and commercialization of one or more of our product candidates.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve or maintain profitability. Even if we are able to generate 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.

The COVID-19 pandemic may affect our ability to initiate and complete nonclinical studies, delay the initiation of our planned clinical trial or future clinical trials, disrupt regulatory activities, or have other adverse effects on our business, results of operations, and financial condition. In addition, the pandemic has caused substantial disruption to supply chains and adversely impacted economies worldwide and could impact the financial markets, each of which could result in adverse effects on our business and operations and our ability to raise additional funds to support our operations.

To date, we have experienced a business disruption at our third-party manufacturers, specifically manufacturing delays, including delays related to the COVID-19 pandemic. We are continuing to monitor the impact of the COVID-19 pandemic on our business and financial statements. We have not incurred impairment losses in the carrying values of our assets as a result of the pandemic. We are following, and will continue to follow, recommendations from the U.S. Centers for Disease Control and Prevention as well as federal, state, and local governments regarding work-from-home practices for non-essential employees as well as return-to-work policies and procedures. As a result, we have modified our business practices, including implementing work-from-home and return-to-work policies for employees in accordance with guidance from, and requirements of, federal and state authorities. We expect to continue to take actions as may be required or recommended by government authorities or as we determine are in the best interests of our employees and other business partners in light of the 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.

Components of Our Results of Operations

Revenue

To date, we have not generated any revenue from any sources, including product sales, and do not expect to generate any revenue from the sale of products for the foreseeable future. If our development efforts for our product candidates are successful and result in regulatory approval or collaboration or license agreements with third parties, we may generate revenue in the future from product sales, payments from collaboration or license agreements that we may enter into with third parties, or any combination thereof.

Operating Expenses

Research and Development Expenses

Research and development expenses consist of costs incurred for our research activities, including our discovery efforts, and the development of our programs. These expenses include:

- employee-related expenses, including salaries, related benefits, and stock-based compensation expense for employees engaged in research and development functions;
- expenses incurred in connection with the preclinical development of our product candidates and research programs, including under agreements with third parties, such as consultants, contractors, and contract research organizations, or CROs;
- the cost of developing and scaling our manufacturing process and manufacturing drug products for use in our research and nonclinical studies, including under agreements with third parties, such as consultants, contractors, and third-party manufacturers;
- laboratory supplies and research materials;
- facilities, depreciation, and other expenses, which include direct and allocated expenses for rent and maintenance of facilities and insurance; and
- payments made under third-party licensing agreements.

We expense research and development costs as incurred. Non-refundable advance payments that we make for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. The prepaid amounts are expensed as the related goods are delivered or the services are performed, or when it is no longer expected that the goods will be delivered or the services rendered. Upfront payments under license agreements are expensed upon receipt of the license, and annual maintenance fees under license agreements are expensed in the period in which they are incurred. Milestone payments under license agreements are accrued, with a corresponding expense being recognized, in the period in which the milestone is determined to be probable of achievement and the related amount is reasonably estimable.

Our direct external research and development expenses are tracked on a program-by-program basis, including our early-stage programs, and consist of costs that include fees, reimbursed materials, and other costs paid to consultants, contractors, third-party manufacturers, and CROs in connection with our research, nonclinical, and manufacturing activities. We do not allocate employee costs, costs associated with our discovery efforts, laboratory supplies, and facilities expenses, including depreciation or other indirect costs, to specific product development programs because these costs are deployed across multiple programs and our platform and, as such, are not separately classified.

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 increase substantially in connection with our planned preclinical and clinical development activities in the near term and in the future. In particular, we expect that the research and development expenses of our AK-OTOF and AK-antiVEGF programs will increase substantially in the near term. These substantial increases in expenses relate to plans to submit an IND for AK-OTOF for OTOF-mediated hearing loss to the U.S. Food and Drug Administration, or FDA, in the first half of 2022, and to initiate a planned Phase 1/2 clinical trial of AK-OTOF, and to submit an IND for AK-antiVEGF for vestibular schwannoma to FDA in 2022. We also expect that the research and development expenses of our AK-CLRN1 and GJB2 programs will increase in the near term as we initiate IND-enabling activities for those product candidates. At this time, we cannot accurately estimate or know the nature, timing, and costs of the efforts that will be necessary to complete the preclinical and clinical development of any

of our product candidates. The successful development of our product candidates is highly uncertain. This is due to the numerous risks and uncertainties associated with product development, including the following:

- the timing and progress of nonclinical studies, including IND-enabling studies;
- the number and scope of preclinical and clinical programs we decide to pursue;
- raising additional funds necessary to complete clinical development of our product candidates;
- the timing of filing and acceptance of INDs or comparable foreign applications that allow commencement of our planned clinical trial or future clinical trials for our product candidates;
- the successful initiation, enrollment, and completion of clinical trials, including under current good clinical practices;
- our ability to achieve 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;
- the availability of specialty raw materials for use in production of our product candidates;
- our ability to establish arrangements through our own facilities or with third-party manufacturers for clinical supply;
- our ability to establish new licensing or collaboration arrangements;
- the receipt and related terms of regulatory approvals from FDA and other applicable regulatory authorities;
- our ability to establish and maintain patent, trademark, and trade secret protection or regulatory exclusivity for our product candidates;
- our ability to procure intellectual property protection and regulatory exclusivity and enforce and defend our intellectual property rights and claims; and
- our ability to maintain a continued acceptable safety, tolerability, and efficacy profile of our product candidates following approval.

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

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and personnel-related costs, including stock-based compensation, for our personnel in executive, legal, finance and accounting, human resources, and other administrative functions. General and administrative expenses also include legal fees relating to intellectual property and corporate matters; professional fees paid for accounting, auditing, consulting, and tax services; insurance costs; travel expenses; and facility costs not otherwise included in research and development expenses.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support our continued research activities and development of our programs and platform. We also anticipate that we will continue to incur increased accounting, audit, legal, regulatory, compliance, director and officer insurance, and investor and public relations expenses associated with operating as a public company.

Other Income (Expense)

Interest Income

Interest income consists of interest earned on our invested cash and marketable securities balances.

Other Income (Expense), Net

Other income (expense), net includes interest expense related to a finance lease, any realized gains or losses on the sale of marketable securities, and miscellaneous other income and expense unrelated to our core operations.

Income Taxes

Since our inception, we have not recorded any income tax benefits for the net losses we have incurred or for the research and development tax credits earned in each year and interim period, as we believe, based upon the weight of available evidence, that it is more likely than not that all of our net operating loss carryforwards and tax credit carryforwards will not be realized.

Results of Operations

Comparison of the three months ended March 31, 2022 and 2021

The following table summarizes our results of operations for the three months ended March 31, 2022 and 2021:

	Three Months Ended March 31,		
(In thousands)	**2022**	**2021**	**Change**
Operating expenses:			
Research and development	$ 20,388	$ 11,258	$ 9,130
General and administrative	6,646	4,890	1,756
Total operating expenses	27,034	16,148	10,886
Loss from operations	(27,034)	(16,148)	(10,886)
Other income (expense):			
Interest income	257	509	(252)
Other expense, net	(206)	(447)	241
Total other income, net	51	62	(11)
Net loss	$ (26,983)	$ (16,086)	$ (10,897)

Research and Development Expenses

	Three Months Ended March 31,		
(In thousands)	**2022**	**2021**	**Change**
Direct research and development expenses by program:			
AK-OTOF	$ 8,166	$ 2,256	$ 5,910
AK-antiVEGF	698	1,409	(711)
Other early-stage programs	228	506	(278)
Platform, research and discovery, and unallocated expenses:			
Platform-related external costs	1,020	244	776
Personnel related (including stock-based compensation)	6,926	4,508	2,418
Facility related and other	3,350	2,335	1,015
Total research and development expenses	$ 20,388	$ 11,258	$ 9,130

Research and development expenses were $20.4 million for the three months ended March 31, 2022, compared to $11.3 million for the three months ended March 31, 2021. The increase of $5.9 million in direct costs related to our AK-OTOF program was primarily due to increased manufacturing costs of $3.9 million and increased external research costs of $1.5 million. The decrease of $0.7 million in direct costs related to our AK-antiVEGF program was primarily

due to decreased nonclinical toxicology studies and manufacturing costs. The decrease of $0.3 million in research and development expenses for our other early-stage programs was primarily due to decreased spend related to the research of these programs.

The increase of $0.8 million in platform-related external costs was primarily related to increases in spending related to the development of our novel delivery approach. The increase of $2.4 million in personnel-related costs was primarily due to increased headcount in our research and development function. Personnel-related costs included stock-based compensation expense of $1.0 million for the three months ended March 31, 2022 and $1.0 million for the three months ended March 31, 2021. The increase of $1.0 million in facility related and other costs was primarily due to an increase in facility costs and laboratory costs related to our corporate headquarters, for which our lease amendment was entered into in January 2021.

General and Administrative Expenses

(In thousands)	Three Months Ended March 31, 2022	2021	Change
Personnel related (including stock-based compensation)	$ 4,573	$ 2,836	$ 1,737
Professional and consultant fees	874	1,103	(229)
Facility related and other	1,199	951	248
Total general and administrative expenses	$ 6,646	$ 4,890	$ 1,756

General and administrative expenses for the three months ended March 31, 2022 were $6.6 million, compared to $4.9 million for the three months ended March 31, 2021. Personnel-related costs increased by $1.7 million primarily as a result of the increase in headcount in our general and administrative function. Personnel-related costs included stock-based compensation expense of $1.6 million for the three months ended March 31, 2022 and $1.0 million for the three months ended March 31, 2021. The decrease of $0.2 million in professional and consultant fees was related to a decrease in professional fees related to legal and accounting services. The increase in facility-related and other expenses of $0.2 million was primarily due to an increase in facility costs and laboratory costs related to our corporate headquarters, for which our lease amendment was entered into in January 2021.

Other Income (Expense)

Interest Income. Interest income was $0.3 million and $0.5 million, respectively, for each of the three months ended March 31, 2022 and 2021, consisting of interest earned on invested cash balances.

Other Expense, Net. Other expense, net was $0.2 million and $0.4 million, respectively, for each of the three months ended March 31, 2022 and 2021, and was primarily related to net amortization of premiums and accretion of discounts on marketable securities.

Liquidity and Capital Resources

Since our inception, we have incurred significant operating losses. We expect to incur significant expenses and operating losses for the foreseeable future as we advance the preclinical and, if successful, the clinical development of our programs. To date, we have funded our operations with proceeds from sales of preferred stock (including borrowings under convertible promissory notes, which converted into preferred stock in 2017) and through proceeds from our IPO. As of March 31, 2022, we had cash, cash equivalents and marketable securities of $209.1 million.

On June 30, 2020, we completed our IPO and issued and sold 14,375,000 shares of our common stock, at a public offering price of $17.00 per share, for gross proceeds of $244.4 million, or net proceeds of $223.8 million after deducting underwriting discounts, commissions, and offering expenses.

In August 2021, we entered into a sales agreement, or the ATM Sales Agreement, with Cowen and Company, LLC, to issue and sell, from time to time at prevailing market prices, shares of the Company’s common stock having aggregate gross proceeds of up to $100.0 million. The shares that may be sold pursuant to the ATM Sales Agreement, if

any, will be issued and sold pursuant to our shelf registration statement on Form S-3 that was declared effective by the SEC on August 20, 2021. As of March 31, 2022, we have not yet issued or sold any securities under the ATM Sales Agreement.

Cash Flows

The following table summarizes our sources and uses of cash for each of the periods presented:

(In thousands)	Three Months Ended March 31, 2022	2021
Cash used in operating activities	$ (20,059)	$ (15,922)
Cash provided by (used in) investing activities	(47,686)	65,591
Cash provided by financing activities	220	183
Net increase (decrease) in cash, cash equivalents and restricted cash	$ (67,525)	$ 49,852

Operating Activities

During the three months ended March 31, 2022, operating activities used $20.1 million of cash, primarily resulting from our net loss of $27.0 million, partially offset by non-cash charges of $3.7 million and net cash provided by changes in our operating assets and liabilities of $3.2 million.

During the three months ended March 31, 2021, operating activities used $15.9 million of cash, primarily resulting from our net loss of $16.1 million, partially offset by non-cash charges of $3.1 million and net cash used by changes in our operating assets and liabilities of $2.9 million.

Changes in accounts payable, accrued expenses and other current liabilities, and prepaid expenses and other current assets in all periods were generally due to growth in our business, the advancement of our research programs, and the timing of vendor invoicing and payments.

Investing Activities

During the three months ended March 31, 2022, net cash used in investing activities was $47.7 million, related to purchases of marketable securities of $64.9 million and purchases of property and equipment of $2.8 million, partially offset by proceeds from sales or maturities of marketable securities of $20.0 million.

During the three months ended March 31, 2021, net cash provided by investing activities was $65.6 million, related to maturities of marketable securities of $140.0 million, partially offset by purchases of marketable securities of $70.3 million and purchases of property and equipment of $4.1 million.

Financing Activities

During the three months ended March 31, 2022, net cash provided by financing activities was $0.2 million, consisting of proceeds from the exercise of stock options.

During the three months ended March 31, 2021, net cash provided by financing activities was $0.2 million, consisting primarily of proceeds from the exercise of stock options.

Funding Requirements

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we advance the nonclinical activities and studies and initiate clinical trials for our product candidates in development. The timing and amount of our funding requirements will depend on many factors, including:

- the progress, costs, and results of our planned Phase 1/2 clinical trial of AK-OTOF and any future clinical development of AK-OTOF;
- the progress, costs, and results of our IND-enabling studies to support our planned IND submission for AK-antiVEGF, and any future clinical development of AK-antiVEGF;
- the scope, progress, costs, and results of preclinical and clinical development for our other product candidates and development programs;
- the number and development requirements of other product candidates that we pursue;
- the costs, timing, and outcome of regulatory review of our product candidates and device system;
- the cost and timing of completion of clinical and commercial-scale manufacturing activities;
- 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, which in turn depends on the sales price and the availability of coverage and adequate third-party reimbursement;
- the costs of operating as a public company;
- the costs to retain and attract our personnel;
- the costs and timing of preparing, filing, and prosecuting patent applications, maintaining and enforcing our intellectual property rights, and defending any intellectual property-related claims;
- the cash requirements of any future acquisitions or discovery of product candidates;
- the extent to which we may acquire or in-license other product candidates and technologies; and
- the severity, duration, and impact of the COVID-19 pandemic, which may adversely impact our business, including our planned Phase 1/2 clinical trials and manufacturing activities for AK-OTOF and AK-antiVEGF, and planned development activities for other product candidates.

We believe that our existing cash, cash equivalents and marketable securities will enable us to fund our operating expenses and capital expenditure requirements for at least 18 months from the issuance date of the consolidated financial statements. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we expect.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our operations through a combination of equity offerings, debt financings, collaborations, strategic alliances, and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of such stockholders. 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 acquisitions or capital expenditures, or declaring dividends. If we raise additional funds through collaborations, licensing arrangements, or strategic alliances 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, we may be required to delay, limit, reduce, or terminate our research, product development, or future commercialization efforts, or grant rights to develop and market drugs that we would otherwise prefer to develop and market ourselves.

Application of Critical Accounting Estimates

Our consolidated financial statements are prepared in accordance with generally accepted accounting principles in the United States. The preparation of our consolidated financial statements and related disclosures requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, costs and expenses, and the disclosure of contingent assets and liabilities in our consolidated financial statements. We base our estimates on historical experience, known trends and events, and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions.

During the three months ended March 31, 2022, there were no material changes to our critical accounting estimates. Our critical accounting policies are described in the notes to the consolidated financial statements and under the heading "Management's Discussion and Analysis of Financial Condition and Results of Operations—Critical Accounting Policies and Significant Judgments and Estimates" in our Annual Report on Form 10-K for the year ended December 31, 2021 filed with the SEC on March 29, 2022, and in the notes to the condensed consolidated financial statements appearing elsewhere in this Quarterly Report on Form 10-Q.

Recently Issued Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is disclosed in Note 2 to our condensed consolidated interim financial statements appearing elsewhere in this Quarterly Report.

Emerging Growth Company Status

The Jumpstart Our Business Startups Act of 2012 permits an "emerging growth company" such as us 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 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 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 (i) irrevocably elect to "opt out" of such extended transition period or (ii) no longer qualify as an emerging growth company. We may choose to early adopt any new or revised accounting standards whenever such early adoption is permitted for private companies.

Item 3. Quantitative and Qualitative Disclosures About Market Risk

We are a smaller reporting company as defined by Rule 12b-2 of the Securities Exchange Act of 1934, as amended, and are not required to provide the information under this item.

Item 4. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

The Company's management, with the participation of the Company's principal executive officer and principal financial officer, evaluated the effectiveness of the Company's disclosure controls and procedures as of March 31, 2022. The term "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, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits 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 a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of the Company's disclosure controls and procedures as of March 31, 2022, the Company's principal executive officer and principal financial officer concluded that, as of such date, the Company's disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Control Over Financial Reporting

No change in the Company's internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the fiscal quarter ended March 31, 2022 that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting.

PART II
OTHER INFORMATION

Item 1. Legal Proceedings

We are not currently subject to any material legal proceedings.

Item 1A. Risk Factors

Our business is subject to numerous risks. You should carefully consider the risks and uncertainties described below together with all of the other information contained in this Quarterly Report, including our consolidated financial statements and the related notes appearing elsewhere in this Quarterly Report, and our other public filings with the Securities and Exchange Commission, or SEC, in evaluating our business. 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, operating results and financial condition to suffer materially.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses during all fiscal periods since our inception, have no products approved for commercial sale, and we expect to incur substantial losses for the foreseeable future.

Since inception, we have incurred significant operating losses. Our net losses were $27.0 million for the three months ended March 31, 2022, and $86.7 million for the year ended December 31, 2021. As of March 31, 2022, we had an accumulated deficit of $195.4 million. To date, we have financed our operations with proceeds from the issuance of

common stock in our initial public offering, or IPO, and proceeds from the sales of preferred stock (including borrowings under convertible promissory notes, which converted into preferred stock in 2017). We have devoted substantially all of our financial resources and efforts to research and development, and our net losses have resulted principally from these research and development activities and from personnel expenses. We are still in the early stages of development of our product candidates, and we have not commenced or completed clinical development of any product candidates. We expect to continue to incur significant expenses and increasing 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 in the foreseeable future as we:

- submit an investigational new drug application, or IND, and initiate a planned Phase 1/2 clinical trial of our lead product candidate, AK-OTOF, for the treatment of the otoferlin gene (*OTOF*)-mediated hearing loss;
- conduct IND-enabling studies in preparation for an IND submission for our product candidate AK-antiVEGF for the treatment of vestibular schwannoma;
- continue our current research programs and our preclinical development of product candidates from our current research programs;
- advance additional product candidates into preclinical and clinical development;
- build a current good manufacturing practice, or cGMP, manufacturing facility;
- expand the capabilities of our genetic medicine platform;
- expand our facilities;
- seek marketing approvals for any product candidates that successfully complete clinical trials;
- ultimately establish a sales, marketing, and distribution infrastructure; scale up manufacturing capabilities; and commercialize any products for which we may obtain marketing approval;
- expand, maintain, and protect our intellectual property portfolio;
- hire additional clinical, regulatory, manufacturing, and other scientific personnel to support our research, product development, and future commercialization efforts; and
- add operational, legal, compliance, financial, and management information systems personnel, including personnel to support our research, product development, and future commercialization efforts and support our operations as a public company.

Even if we obtain regulatory approval of and are successful in commercializing one or more of our product candidates, we will continue 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 not initiated clinical development of any product candidate and 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 nonclinical testing, initiating and completing clinical trials of our product candidates, discovering additional product

candidates, obtaining regulatory approval for these product candidates, and manufacturing, marketing, and selling any products for which we may obtain regulatory 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 predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. 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 any comparable regulatory authority in other jurisdictions, 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.

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. In addition, we may encounter unforeseen expenses, difficulties, complications, delays, and other unknown factors that may adversely affect our revenues, expenses, and profitability.

Our failure to achieve or sustain profitability 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 are heavily dependent on the success of our product candidates, AK-OTOF and AK-antiVEGF.

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 AK-OTOF and AK-antiVEGF. Accordingly, our business currently depends heavily on the successful development, regulatory approval, and commercialization of AK-OTOF and AK-antiVEGF. We cannot be certain that AK-OTOF or AK-antiVEGF will receive regulatory approval or be successfully commercialized even if we receive regulatory approval. If we were required to discontinue development of AK-OTOF or AK-antiVEGF, or if either AK-OTOF or AK-antiVEGF 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.

We will need substantial additional capital to execute our business plan. If we are unable to raise capital when needed, we could be forced to delay, reduce, or eliminate our product 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 prepare for and initiate our planned Phase 1/2 clinical trial of AK-OTOF, conduct IND-enabling studies to support our planned IND for AK-antiVEGF, advance our genetic medicine platform, and continue research and development and initiate additional clinical trials of, and potentially seek marketing approval for, our other product candidates. Identifying potential product candidates and conducting nonclinical 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 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 expect 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.

As of March 31, 2022, we had cash, cash equivalents and marketable securities of $209.1 million. We believe that our existing cash, cash equivalents and marketable securities will enable us to fund our operating expenses and capital expenditure requirements for at least 18 months from the issuance date of the consolidated financial statements. 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. Furthermore, because the outcome of our planned Phase 1/2 clinical trials and future clinical trials is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of our product candidates. As a result, we could deplete our capital resources sooner than we currently expect.

The timing and amount of our funding requirements will depend on many factors, including:

- the progress, costs, and results of our planned Phase 1/2 clinical trial of AK-OTOF and any future clinical development of AK-OTOF;
- the progress, costs, and results of our IND-enabling studies to support our planned IND submission for AK-antiVEGF and any future clinical development of AK-antiVEGF;
- the scope, progress, costs, and results of preclinical and clinical development for our other product candidates and development programs;
- the number and development requirements of other product candidates that we pursue;
- the costs, timing, and outcome of regulatory review of our product candidates and device system;
- the cost and timing of completion of clinical and commercial-scale manufacturing activities;
- 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, which in turn depends on the sales price and the availability of coverage and adequate third-party reimbursement;
- the costs of operating as a public company;
- the costs to attract and retain our personnel;
- the costs and timing of preparing, filing, and prosecuting patent applications, maintaining and enforcing our intellectual property rights, and defending any intellectual property-related claims;
- the cash requirements of any future acquisitions or discovery of product candidates;
- the extent to which we may acquire or in-license other product candidates and technologies; and
- the severity, duration, and impact of the COVID-19 pandemic, which may adversely impact our business, including our planned Phase 1/2 clinical trials and manufacturing activities for AK-OTOF and AK-antiVEGF, and planned development activities for other product candidates.

We do not have any committed external source of funds and adequate additional financing may not be available to us on acceptable terms, or at all. In addition, we may seek additional capital due to favorable market conditions or

strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. If adequate funds are not available to us on a timely basis or on terms acceptable to us, we would be required to delay, limit, reduce, or terminate nonclinical studies, clinical trials, manufacturing, or other development activities for one or more product candidates or discovery stage programs or delay, limit, reduce, or terminate our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize any product candidates.

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 product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances, and licensing arrangements. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our stockholders. 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, declaring dividends or encumbering our assets to secure future indebtedness. Such restrictions could adversely impact our ability to conduct our operations and execute our business plan.

If we raise additional funds through collaborations, strategic alliances, 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 would 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 to evaluate the success of our business to date and to assess our future viability.

We commenced operations in 2016, and our operations to date have been limited to organizing and staffing our company, business planning, raising capital, conducting research and development activities, filing and prosecuting patent applications, identifying potential product candidates, soliciting input from regulators regarding development of these product candidates, and undertaking nonclinical and supportive clinical studies. All of our product candidates are still in preclinical development. We have not yet demonstrated our ability to successfully initiate or complete any clinical trials, obtain marketing approvals, manufacture a commercial-scale product, or partner with third-party manufacturers 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 genetic medicine 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, our stockholders should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

The COVID-19 pandemic may affect our ability to initiate and complete nonclinical studies, delay our ongoing manufacturing activities, delay the initiation of our planned clinical trial or future clinical trials, disrupt regulatory activities, or have other adverse effects on our business and operations. In addition, this pandemic has adversely impacted economies worldwide and could impact the financial markets, both of which could result in adverse effects on our business and operations.

The COVID-19 pandemic has caused many governments to implement measures to slow the spread of the pandemic through quarantines, travel restrictions, heightened border scrutiny, and other measures. The pandemic and government measures taken in response have also had and will continue to have a significant impact, both direct and indirect, 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 pandemic and its effects on our business and operations are uncertain. We and our third-party manufacturers and other contract research organizations, or CROs, have experienced a reduction in the capacity to undertake and execute some research activities and nonclinical studies, and we may face disruptions that may affect our ability to initiate and complete nonclinical studies, including disruptions in procuring items that are essential for our research and development activities, such as raw materials used in the manufacture of our product candidates, laboratory supplies used in our nonclinical studies, or animals that are used for nonclinical testing for which there are shortages because of ongoing efforts to address the pandemic, delays, or difficulties in securing manufacturing slots, and delays or difficulties in the buildout of our in-house manufacturing. We have experienced manufacturing delays at our third-party manufacturers, including delays related to the COVID-19 pandemic, and may experience additional delays in the future, which could delay our product development timelines. We and our third-party manufacturers and CROs, as well as clinical trial sites, may face disruptions related to our planned clinical trial or future clinical trials arising from delays in IND-enabling studies, manufacturing disruptions, and the ability to obtain necessary institutional review board, or IRB, institutional biosafety committee, or IBC, or other necessary site approvals, as well as other delays at clinical trial sites. 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 progress regulatory approvals and protect our intellectual property. In addition, we may face impediments to regulatory meetings and approvals due to measures intended to limit in-person interactions. The pandemic could cause significant disruptions in the financial markets, which could impact our ability to raise additional funds through public offerings and may also impact the volatility of our stock price and trading in our stock. Moreover, the pandemic has significantly impacted economies worldwide and could result in adverse effects on our business and operations. The 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 research, nonclinical studies, and clinical trials, which could lead to delays in our research and development efforts. 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.

Risks Related to the Development of our Product Candidates

We are very early in our development efforts. Our business is dependent on our ability to advance AK-OTOF, AK-antiVEGF, and our other current and future product candidates through nonclinical 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 and all of our product candidates are still in preclinical development. We expect to submit an IND to FDA with respect to our AK-OTOF program in the first half of 2022. We also expect to submit an IND to FDA with respect to our AK-antiVEGF program in 2022. Additionally, we have a portfolio of programs that are in even earlier stages of preclinical development and may never advance 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 and eventual commercialization of our product candidates, which may never occur. We currently generate no revenue from sales of any product, and we may never be able to develop or commercialize a marketable product.

Additionally, the research, testing, manufacturing, labeling, approval, sale, marketing, and distribution of genetic medicine products are and will remain subject to extensive regulation by FDA and other regulatory authorities in the United States and other countries that each have differing regulations. We are not permitted to market AK-OTOF, AK-antiVEGF, or any of our other current or future product candidates, in the United States until it receives approval of a biologics license application, or BLA, from FDA, or in any foreign countries until it receives the requisite approval from such countries. We have not submitted a BLA for AK-OTOF, AK-antiVEGF, or any other product candidate to FDA or comparable applications to other regulatory authorities and do not expect to be in a position to do so for the foreseeable future.

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

- timely and successful completion of nonclinical studies, including IND-enabling studies;
- effective INDs or comparable foreign applications that allow commencement of our planned clinical trial or future clinical trials for our product candidates;
- successful enrollment and completion of clinical trials, including under current Good Clinical Practices, or GCPs;
- 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 FDA and other applicable regulatory authorities;
- establishment of arrangements through our own facilities or with third-party manufacturers for clinical supply and, where applicable, commercial manufacturing capabilities;
- 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;
- establishment of a physician training system and network for administration of our product candidates by surgical procedure;
- successful development of a delivery device intended for use as part of a delivery system;
- 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 clinical outcomes, the regulatory review process, potential threats to our intellectual property rights, and the manufacturing, marketing and sales efforts of any future 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 commercialize our product candidates, which would materially harm our

business. If we are unable to advance our 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. As a company, we have not advanced any product candidates into clinical development. Our lack of experience in conducting clinical development activities for our product candidates may adversely impact the likelihood that we will be successful in advancing our programs. Further, any predictions about the future success or viability of our programs may not be as accurate as they could be if we had a history of conducting clinical trials.

Furthermore, because our other product candidates are based in part on similar technology to AK-OTOF, our most advanced product candidate, if AK-OTOF shows unexpected adverse events or a lack of efficacy in the indications we intend to treat, or if we experience other regulatory or developmental issues associated with AK-OTOF, our development plans and business could be significantly harmed. In addition, competitors may be developing product candidates with similar technology and may experience problems with their product candidates that could negatively impact the development of our product candidates and ultimately harm our business.

We may encounter substantial delays in commencement or completion of our clinical trials, or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities, which could prevent us from commercializing our current and future product candidates on a timely basis, if at all.

The risk of failure for each of our product candidates is high. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive regulatory approval. 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 initiated or completed a clinical trial of any of our product candidates. 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.

Before we can commence clinical trials for a product candidate, we must complete extensive nonclinical testing and studies that support our planned INDs and other regulatory filings. We cannot be certain of the timely completion or outcome of our nonclinical testing and studies and cannot predict if FDA will accept our proposed clinical programs or if the outcome of our nonclinical testing and studies will ultimately support the further development of any product candidates. As a result, we cannot be sure that we will be able to submit INDs for our preclinical programs on the timelines we expect, if at all, and we cannot be sure that submission of INDs will result in FDA allowing clinical trials to begin. Furthermore, product candidates are subject to continued nonclinical 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.

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 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.

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

- delays in reaching a consensus with regulatory authorities on trial design to support biologic-device combination development;
- delays in reaching agreement on acceptable terms with prospective CROs and clinical trial sites;
- delays related to COVID-19 disruptions at CROs, third-party manufacturers, and/or clinical trial sites;

- delays in opening clinical trial sites or obtaining required IRB or IBC approval, or the equivalent review groups for ex-U.S. sites, 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 GCP;
- failure by physicians to adhere to delivery 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;
- 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;
- ambiguous or negative interim results;
- 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; or
- lack of adequate funding to continue the clinical trial.

Any inability to successfully complete nonclinical 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 studies or 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.

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 our product candidates 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 are affected by factors including:

- perceived risks and benefits of genetic medicine-based approaches for the potential treatment of inner ear conditions, including an adeno-associated viral, or AAV, vector approach commonly used in gene therapy;
- size of the patient population and process for identifying potential trial participants;
- design of the trial;
- inclusion and exclusion criteria;
- perceived risks and benefits of the product candidate under study;
- 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;
- our inability to locate and appropriately train physicians to conduct such clinical trials;
- 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.

Genetic medicine programs are often initially targeting orphan diseases with relatively small populations, which limits the pool of potential participants for our genetic medicine clinical trials. Because genetic medicine trials generally require participants who have not previously received any other genetic medicine or potentially other pharmacological therapeutics for the same indication, we will also need to compete with others who are also developing genetic medicines 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 genetic medicines. 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.

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

Genetic medicine is an emerging field of drug development with a limited number of genetic medicines having received regulatory approval to date. Our genetic medicine 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, genetic medicines. 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 with our product candidates. We have begun to establish our own genetic medicine technical capabilities, but we will need to continue to expand those capabilities by either hiring internally or seeking assistance from outside service providers. Genetic medicine 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 genetic medicine 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 genetic medicine 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 product candidates that we develop. Failure to commence or complete, or delays in, our planned clinical trial or future clinical trials, could prevent us from or delay us in commercializing our product candidates.

As we prepare for the potential initiation of our first genetic medicine clinical trials, we will need to build our internal and external capabilities in designing and executing genetic medicine clinical trials. 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 nonclinical data. If we are unable to initiate and conduct our genetic medicine clinical trials in a manner that satisfies our expectations or regulatory requirements, the value of our genetic medicine programs may be diminished.

Our AAV genetic medicine product candidates 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 have concentrated our therapeutic product research and development efforts on our genetic medicine platform. Our future success is almost entirely dependent on this therapeutic approach. Because our genetic medicine candidates are based on relatively novel technology, development problems we experience in the future related to our genetic medicine 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.

In addition, the clinical trial requirements of the FDA, the EMA, and other regulatory agencies and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty, and intended use and market of the potential products. The regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other, better known or extensively studied therapeutic approaches or biopharmaceutical or other product candidates.

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.

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.

In past clinical trials that were conducted by others with gene therapy 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 vectors demonstrate a similar adverse effect, or other adverse events, we may be required to halt or delay further clinical development of our product candidates.

In addition to side effects caused by the product candidate itself, the administration procedure also can cause side effects. As part of our genetic medicine platform, we are developing a delivery device to administer our product candidates to the inner ear. The delivery device is intended to be used as part of a delivery system consisting of three components (the delivery device, a syringe, and a syringe pump) that allow for the controlled delivery of our product candidates. Although the delivery approach we have developed is based on common surgical techniques used in clinical practice, it requires training in order to administer. Moreover, 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 device and procedure on humans, we cannot be certain that our delivery approach will be successful. If side effects were to occur in connection with the surgical procedure during our planned clinical trial, or if we fail to successfully apply our delivery approach in humans, our clinical trial could be suspended or terminated.

If in the future we are unable to demonstrate that such side effects were not caused by our product candidates, or delivery approach, FDA 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 potential participant 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 genetic medicine for the prevention or treatment of human diseases or conditions. Public attitudes may be influenced by claims that genetic medicines 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 trial participants. 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.

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

The results of nonclinical studies may not be predictive of the results of clinical trials, and the results of any early-stage clinical trials we commence may not be predictive of the results of the later-stage clinical trials or of clinical trials for 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, even if successful, the results of our planned Phase 1/2 clinical trial of AK-OTOF may not be predictive of the results of further clinical trials of this product candidate or any of our other product candidates. Moreover, nonclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in nonclinical 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 genetic medicine 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 top-line 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 top-line 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 business prospects and may cause the trading price of our common stock to fluctuate significantly.

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 genetic medicine platform to address a broad array of targets and new therapeutic areas. The discovery activities that we are conducting may not be successful in identifying product candidates that are useful in restoring, improving, or preserving physiologic hearing. 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 is too complex and difficult to navigate successfully or economically.

In addition, we may choose to focus our efforts and resources on a potential product candidate that ultimately proves to be unsuccessful. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other product candidates or other diseases that may later prove to have greater commercial potential, or relinquish valuable rights to such product candidates through collaboration, licensing or other royalty arrangements in cases in which it would have been advantageous for us to retain sole development and commercialization rights. If we are unable to identify additional suitable product candidates for clinical development, this would adversely impact our business strategy, financial position, results of operations, prospects, and share price and could potentially cause us to cease operations.

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

We face an inherent risk of clinical trial and product liability exposure related to the testing of our 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 commence 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 genetic medicine 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 development or commercialization of product candidates.

Genetic medicine drug products are complex and difficult to manufacture. For our nonclinical studies of AK-OTOF, a third-party manufacturer has provided the supply of our product candidates. For our planned Phase 1/2 clinical trial of AK-OTOF, we plan to rely on third-party manufacturers and suppliers to provide clinical supply and certain other materials for the manufacturing process. We are establishing our own manufacturing facility for long-term clinical supply.

We believe that the high demand for clinical genetic medicine material and a scarcity of potential third-party manufacturers may cause long lead times for establishing manufacturing capabilities for genetic medicine 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. We have experienced manufacturing delays, including delays related to the COVID-19 pandemic, at our third-party manufacturer and may experience additional delays in the future. Any delay in the manufacturing of our nonclinical or clinical supplies, whether from an existing or alternative third-party manufacturers, transition to an alternative third-party manufacturer, or from our internal manufacturing capabilities, would likely further delay our product development timelines. 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 cGMP compliant. In particular, plasmids, cell lines and other starting materials for genetic medicine manufacture are usually sole sourced, as there are a limited number of qualified suppliers. The progress of our genetic medicine programs is highly dependent on these suppliers providing us or our third-party 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, or any damage to such starting materials, would likely 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 drugs 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 third-party 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, FDA and comparable regulatory authorities in other jurisdictions may require us to submit samples of any lot of any approved product together with the protocols showing the results of applicable tests at any time. Under some circumstances, 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 third-party manufacturers need to expend considerable time and resources to develop assays and other analytical tests for our genetic medicine product candidates, including assays to assess the titer and potency of our genetic medicine product candidates. Some assays need to be outsourced to specialized testing laboratories. Even when assays are developed, they need to be further tested, or 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 nonclinical studies to late-stage clinical trials towards potential approval and commercialization, it is common that various aspects of the development 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 genetic medicine 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 or delay 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 rely, and expect to continue to rely, on third parties to conduct some or all aspects of our product manufacturing, protocol development, research and nonclinical and clinical testing, and these third parties may not successfully perform their obligations to us.

We do not expect to independently conduct all aspects of our product manufacturing, protocol development, research and nonclinical and clinical testing. We currently rely, and expect to continue to rely, on third parties with respect to many of these items. While we are currently building our own cGMP manufacturing facility, we cannot be sure when this facility will be available for cGMP manufacturing, if at all, and, even if it is available for cGMP manufacturing, that we will be able to manufacture commercial material. In addition, we currently rely, and expect to continue to rely, on a third party for the manufacture of our delivery device.

Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it could delay our product development activities. Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibility to ensure compliance with all required regulations and study or trial protocols. For example, for product candidates that we develop and commercialize on our own, we will remain responsible for ensuring that each of our IND-enabling studies and clinical trials are conducted in accordance with the study plans and trial protocols. We compete with many other companies for the resources of these third parties. These third parties may have contractual relationships with other entities, some of which may be our competitors, which may draw time and resources from our product candidates. The third parties with whom we contract might not be diligent, careful, or timely in conducting our nonclinical studies or clinical trials, resulting in the nonclinical studies or clinical trials being delayed or unsuccessful.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines, or conduct our studies or trials in accordance with regulatory requirements or our stated study plans and trial protocols, we will not be able to complete, or may be delayed in completing, the nonclinical studies and clinical trials required to support IND submissions and future approval of our product candidates. Switching manufacturers may involve substantial costs and may result in a delay in our desired clinical and commercial timelines.

Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured the product candidates ourselves, including:

- the inability to negotiate manufacturing agreements with third parties under commercially reasonable terms;
- reduced control as a result of using third-party manufacturers for all aspects of manufacturing activities;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us; and
- disruptions to the operations of our third-party manufacturers or suppliers caused by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier.

Any of these events could lead to clinical trial delays or failure to obtain regulatory approval or impact our ability to successfully commercialize future products. Some of these events could be the basis for FDA action, including injunction, recall, seizure, or total or partial suspension of production.

We and our third-party 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 third-party 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 third-party manufacturers must supply all necessary documentation in support of a BLA on a timely basis and must adhere to FDA's good laboratory practices, or GLP, and cGMP regulations enforced by 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 manufacturers. 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, 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 a 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 expect 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 expect 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 will control only certain aspects of our CROs' activities. Nevertheless, we will be 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 will be 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. FDA enforces these GCPs through periodic inspections of sponsors, principal investigators, and clinical trial sites. If we or our CROs fail to comply with applicable GCPs, the clinical data generated in our future clinical trials may be deemed unreliable and FDA may require us to perform additional clinical trials before approving any marketing applications. Upon inspection, FDA may determine that our clinical trials did not comply with GCPs. In addition, our future 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, or HIPAA, as amended by Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, 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.

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 current 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 conditions 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.

While many companies focus on gene therapies targeting blood, eye, muscle, and neurologic disorders, we are aware of certain companies with active development programs in the hearing space. Decibel Therapeutics, Inc., or Decibel, is focused on hearing and balance disorders. Decibel's lead therapeutic candidate is being investigated for the prevention of ototoxicity associated with cisplatin chemotherapy. Decibel has announced a potential gene therapy for OTOF related hearing loss, DB-OTO, and has projected that it will file an IND or clinical trial application, or CTA, in 2022 and, subject to the acceptance of an IND or CTA, that it expects to initiate a Phase 1/2 clinical trial in 2022. Decibel is also pursuing additional preclinical gene therapy programs, AAV.103 and AAV.104, targeting hearing loss resulting from other monogenic forms of hearing loss. AAV.103 is a preclinical gene therapy program for hearing loss caused by a mutation in the *GJB2* gene and Decibel expects to identify a product candidate for AAV.103 in 2022. In

2021, Decibel announced its AAV.104 program is targeting the stereocilin gene in patients with autosomal recessive hearing disorders. Decibel has also announced that it is co-developing DB-OTO, AAV.103, and AAV.104 with Regeneron Pharmaceuticals, Inc., and that it retains worldwide commercial rights. In addition to pursuing gene therapies for monogenic forms of hearing loss, Decibel is also pursuing gene therapies for hair cell regeneration within the inner ear. Decibel has stated its plans to announce a target for a cochlear hair cell regeneration program in 2022.

Frequency Therapeutics, Inc., or Frequency, is developing small molecule therapeutics to selectively activate progenitor cells. Frequency's lead program is focused on regenerating hair cells through activation of progenitor cells for sensorineural hearing loss and is currently in Phase 2 trials. In 2019, Frequency announced a partnership with Astellas Pharma Inc., or Astellas, under which Astellas agreed to oversee development and commercialization of its lead program worldwide, except the United States, where Frequency will assume those responsibilities.

Otonomy, Inc. and Applied Genetic Technologies Corporation have entered into a strategic collaboration to co-develop and co-commercialize OTO-825, an AAV-based gene therapy, to restore hearing in individuals with sensorineural hearing loss caused by a mutation in the *GJB2* gene. Otonomy has announced that the pre-IND meeting for OTO-825 is complete and IND-enabling activities are underway with an IND filing anticipated in the first half of 2023.

Sensorion SA, or Sensorion, is focused on developing potential therapies for inner ear disorders. Sensorion has announced a collaboration with Institut Pasteur in gene therapy programs targeting hearing loss. Sensorion has three preclinical gene therapy programs targeting Usher Syndrome Type I, *OTOF* deficiency, and *GJB2* deficiency, and plans to file a CTA in the first half of 2023 for OTOF-GT and to make a candidate selection for GJB2-GT in mid-2022.

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.

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, nonclinical 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.

Even if any product candidate 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 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 hearing health 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 in the United States and the European Union. 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 approved, our product candidates that are licensed and regulated as biologics may face competition from biosimilars approved through an abbreviated regulatory pathway.

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, was enacted as part of the Patient Protection and Affordable Care Act, or the ACA, to establish an abbreviated pathway for the approval of biosimilar and interchangeable biological products. The regulatory pathway establishes legal authority for FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to an approved biologic. Under the BPCIA, a reference biological product is granted 12 years of data exclusivity from the time of first licensure of the product, and FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product. In addition, the licensure of a biosimilar product may not be made effective by FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still develop and receive approval of a competing biologic, so long as its BLA does not rely on the reference product or sponsor's data or submit the application as a biosimilar application. The law is complex and is still being interpreted and implemented by FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty, and any new policies or processes adopted by FDA could have a material adverse effect on the future commercial prospects for our biological products.

We believe that any of the product candidates we develop as a biological product under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that FDA will not consider the subject product candidates to be reference products for competing products, potentially creating the opportunity for biosimilar competition sooner than anticipated. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of the reference products in a way that is similar to traditional generic substitution for non-biological products will depend on a number of marketplace and regulatory factors that are still developing. Nonetheless, the approval of a biosimilar to our product candidates would have a material adverse impact on our business due to increased competition and pricing pressure.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain 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 ability to obtain and maintain intellectual property protection in the United States and other countries with respect to our proprietary product candidates and manufacturing technology. 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 may not be able to file, prosecute, maintain, 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 in the genetic medicine field 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.

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 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.

We may not be aware of all third-party intellectual property rights potentially relating to our product candidates. 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 that we 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.

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 patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of 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. Moreover, some of our owned and in-licensed patents and patent applications are, or may in the future be, co-owned with third parties. If we are unable to obtain an exclusive license to any such third-party co-owners' interest in such patents or patent applications, such 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. In addition, we or our licensors may need the cooperation of any such co-owners of our owned and in-licensed patents in order to enforce such patents against third parties, and such cooperation may not be provided to us or our licensors. 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 able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States 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 may not be able to obtain granted patents covering our product candidates in all countries outside the United States and, as a result, may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

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 of our patents or marketing of competing products in violation of our proprietary rights generally. For example, an April 2021 report from the Office of the United States Trade Representative identified a number of countries on their priority watch list, including China, Russia, Argentina, Chile, Saudi Arabia, Ukraine, Indonesia, Venezuela, and India, where challenges to the procurement and enforcement of patent rights have been reported. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

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 revenue could be reduced.

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 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 licensed patents and/or 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 business.

We may not be successful in obtaining necessary rights to our product candidates through acquisitions and in-licenses.

We currently have rights to certain intellectual property, through licenses from third parties, to develop our product candidates. Because our programs may require the use of proprietary 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 proprietary rights. In addition, with respect to any patents or patent applications we co-own with third parties, we may require licenses to such co-owners' interest in such patents or patent applications. 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.

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 fail to comply with our obligations under our existing license agreements, or under any future intellectual property licenses, 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 party to license agreements with the Massachusetts Eye and Ear Infirmary and The Schepens Eye Research Institute, Inc., which we refer to collectively as MEE, and Lonza, pursuant to which we have been granted an exclusive, non-transferable, sublicensable, worldwide, royalty-bearing license to certain patent rights related to AAV ancestral technology, including a proprietary ancestral AAV, known as AAVAnc80, to research, develop, make, have made, manufacture, use, sell, offer to sell, import, export, market, promote, distribute, register and otherwise commercially exploit the licensed product in the treatment, diagnosis, prevention and palliation of balance disorders, diseases pertaining to the inner ear, and/or any and all hearing diseases or disorders. We may enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future licenses will impose, specified diligence, milestone payment, royalty, and other obligations on us. Furthermore, the licensors have the right to terminate the agreement 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, thereby removing our ability to develop and commercialize product candidates and technology covered by these license agreements. If these in-licenses are terminated, or if the underlying intellectual property fails to provide the intended exclusivity, competitors could have the freedom to seek regulatory approval of, and to market, products and technologies identical to ours. This 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 ability to defend intellectual property and to enforce intellectual property rights against third parties;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the 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, license agreements are 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 financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, some of our in-licensed patents and patent applications are, and may in the future be, subject to third-party interests such as co-ownership or licenses. For example, a patent application directed to certain compositions and methods for several of our product candidates is co-owned by MEE and The Children's Medical Center Corporation, or BCH. At present, we have an exclusive license to MEE's ownership interest, however, we do not have a license to BCH's ownership interest. If we are unable to obtain an exclusive license to such third-party co-owners' interest in such patents or patent applications, such co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could potentially market competing products and technology if our exclusive licenses from MEE and Lonza for the AAV ancestral technology terminate or expire. In addition, we may need the cooperation of any such co-owners of our patents in order to enforce such patents against third parties, and such cooperation may not be provided to us. Any of the foregoing could have a material adverse effect on our competitive position, business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected technology and product candidates, which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Additionally, we do not have complete control in the preparation, filing, prosecution, maintenance, enforcement, and defense of patents and patent applications covering the technology that we license from third parties. For example, pursuant to our intellectual property licenses with MEE and Lonza, our licensors retain control of preparation, filing, prosecution, and maintenance, and, in certain circumstances, enforcement and defense of their patents and patent applications. It is possible that our licensors' 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 or may not be conducted in accordance with our best interests. 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 prosecute, maintain, enforce, and defend such patents, 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 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 from making, using, and selling competing products. Our licensors may have relied on third-party consultants or collaborators or on funds from third parties such that our licensors are not the sole and exclusive owners of the patents we in-licensed. If other third parties have ownership rights to our in-licensed patents, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. Any of these events could have a material adverse effect on our competitive position, business, financial condition, results of operations, and prospects.

Furthermore, inventions contained within some of our in-licensed patents and patent applications may have been made using U.S. government funding. We rely on our licensors to ensure compliance with applicable obligations arising from such funding, such as timely reporting, an obligation associated with our in-licensed patents and patent applications. The failure of our licensors to meet their obligations may lead to a loss of rights or the unenforceability of relevant patents. For example, the U.S. government could have certain rights in such in-licensed patents, 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 to third parties and to exercise march-in rights to use or allow third parties to use the technology we have licensed that was developed using U.S. government funding. The U.S. government may also 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. In addition, our rights in such in-licensed U.S. government-funded inventions may be subject to certain requirements to manufacture product candidates embodying such inventions in the United States. Any of the foregoing could harm our business, financial condition, results of operations, and prospects significantly.

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 initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid 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. 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. Such a loss of patent protection could harm our business.

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 and contractors. We cannot guarantee that we have entered into such agreements with each party that may have or have 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. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors.

Third parties may initiate legal proceedings alleging that we are infringing 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 the proprietary rights and intellectual property of third parties. The biotechnology and pharmaceutical industries are characterized by extensive and complex litigation regarding patents and other intellectual property rights. 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 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. 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 could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Competitors may challenge the validity and enforceability of our patents, infringe our patents or the patents of our licensing partners, or we may be required to defend against claims of infringement. To defend the validity of our patents, assert infringement or unauthorized use claims, or to defend against claims of infringement can be 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 adequately conduct such litigation or proceedings. 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 patent litigation or other proceedings could adversely affect our ability to compete in the marketplace.

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 personnel. 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 and contractors 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.

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 United States 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. 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. 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, such as exclusive ownership of, or right to use, intellectual property that is important to any product candidates. 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.

As of March 31, 2022, we have filed to register trademarks in the United States with the USPTO, and also have registered trademarks in certain jurisdictions outside of the United States, for the marks "Akouos", the Akouos logo, "Resonate", the Resonate by Akouos logo, "The Sing Registry," and the Sing logo. Our 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 financial condition or results of operations.

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 genetic medicine products that are similar to our product candidates but that are not covered by the claims of the patents that we license or may own 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 application that we license or may own 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 our owned or licensed intellectual property rights;
- it is possible that our pending patent applications or those that we may own 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 our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;
- the patents 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 significantly harm 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 pipeline, we must, at times, share our proprietary technology and confidential information, including trade secrets, 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. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how

and trade secrets, a competitor's discovery of our 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 nonclinical 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 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 nonclinical and clinical data and supporting information, including manufacturing information, to the various regulatory authorities for each therapeutic indication to establish the biologic product candidate's safety, purity, and potency. 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. 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 nonclinical, clinical, or other studies. In addition, varying interpretations of the data obtained from nonclinical and clinical testing could delay, limit, or prevent marketing approval of a product candidate. Moreover, 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.

Accordingly, 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 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 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 withdrawal of the United Kingdom from the European Union, commonly referred to as Brexit. The United Kingdom is no longer part of the European Single Market and European Union.

As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or the MHRA, became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law, whereas Northern Ireland will continue to be subject to European Union rules under the Northern Ireland Protocol. The MHRA will rely on the Human Medicines Regulations 2012 (SI 2012/1916) (as amended), or the HMR, as the basis for regulating medicines. The HMR has incorporated into the domestic law of the body of European Union law instruments governing medicinal products that pre-existed prior to the United Kingdom's withdrawal from the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may force us to restrict or delay efforts to seek regulatory approval in the United Kingdom for our product candidates, which could significantly and materially harm our business.

We expect that we will be subject to additional risks in commercializing any of our product candidates that receive marketing approval outside the United States, including tariffs, trade barriers and regulatory requirements; economic weakness, including inflation, or political instability in particular foreign economies and markets; compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country; and workforce uncertainty in countries where labor unrest is more common than in the United States.

Regulatory requirements governing genetic medicine 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.

FDA decides whether individual genetic medicine protocols may proceed and it can put an IND on a clinical hold. In addition, adverse developments in clinical trials of genetic medicine products conducted by others may cause FDA or other oversight bodies to change the requirements for approval of our product candidates. Similarly, EMA may issue new guidelines concerning the development and marketing authorization for genetic medicine products and require that we comply with these new guidelines.

In addition, ethical, social, and legal concerns about genetic medicine, 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.

Negative public opinion of gene therapy and increased regulatory scrutiny of gene therapy and genetic research may adversely impact public perception of our future product candidates.

Our potential therapeutic products involve introducing genetic material into patients' 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. Adverse events in our 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. 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. If any such adverse events occur, commercialization of our product candidates or further advancement of our clinical trials could be halted or delayed, which would have a negative impact on our business and operations.

We may in the future conduct, and intend to conduct, clinical trials for product candidates at sites outside the United States, and FDA may not accept data from trials conducted in such locations.

Although FDA may accept data from sites or clinical trials outside the United States, acceptance of these data is subject to conditions imposed by FDA. For example, the clinical trial must be well-designed and conducted and performed by qualified investigators in accordance with ethical principles. The trial population must also adequately represent the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that FDA deems clinically meaningful. In addition, while these clinical trials or trial sites are subject to the applicable local laws, FDA acceptance of the data will depend on its determination that the trials or trial sites also complied with all applicable U.S. laws and regulations, including GCP requirements. If FDA does not accept the data from any trial or trial site outside the United States, it would likely result in the need for additional trials, which would be costly and time-consuming and would delay or permanently halt our development of the applicable product candidates.

Other risks inherent in conducting international clinical trials or using international trial sites include:

- foreign regulatory requirements that could restrict or limit our ability to conduct our clinical trials;
- the administrative burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment;
- the failure of enrolled patients to adhere to clinical protocols or inadequate collection and assessment of clinical data as a result of differences in healthcare services or cultural customs;
- foreign exchange fluctuations;
- diminished or loss of protection of intellectual property in the relevant jurisdiction; and
- political, economic, environmental, and health risks relevant to specific foreign countries, including risks related to natural disasters or disease outbreaks, including the COVID-19 pandemic.

We have received a rare pediatric disease designation for AK-OTOF and may seek a rare pediatric disease designation for one or more of our other 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 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. 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. 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 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. In April 2021, we received a rare pediatric disease designation for AK-OTOF.

FDA may determine that a BLA for one or more of our product candidates does not meet the eligibility criteria for a priority review voucher upon approval. 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, 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. If we do not obtain approval of a BLA for a product candidate with this designation by these dates, and if the Priority Review Voucher Program is not further extended by congressional action, we would not receive a Priority Review Voucher.

Expedited review programs may not lead to a faster development or regulatory review or approval process and do not assure FDA approval of our product candidates.

If a product candidate is intended for the treatment of a serious or life-threatening condition and the product candidate demonstrates the potential to address unmet medical need for this condition, the sponsor may apply to FDA for fast track designation. For fast track products, sponsors may have greater interactions with FDA, and FDA may initiate review of sections of a fast track product's application before the application is complete. This rolling review may be available if FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a fast track product may be effective.

In addition, an applicant may seek designation of its product as a breakthrough therapy, which is a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and for which preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs and biologics that have been designated as breakthrough therapies, interaction and communication between FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of participants placed in ineffective control regimens.

Further, if FDA determines that a product candidate offers major advances in treatment or provides a treatment where no adequate therapy exists, FDA may designate the product candidate for priority review. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority review designation means that the goal for FDA to review an application is six months, rather than the standard review period of ten months.

An applicant may also seek designation of its product candidate as a regenerative medicine advanced therapy if it is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product candidate has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative medicine advanced therapy designation include early interactions with the FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for priority review and accelerated approval based on surrogate or intermediate endpoints.

We may seek these and other designations for our product candidates. FDA has broad discretion with respect to whether or not to grant these designations to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, FDA may decide not to grant it. Moreover, a fast track or breakthrough therapy designation does not necessarily mean a faster regulatory review process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. As a result, while we may seek and receive these designations for our product candidates, we may not experience a faster development process, review or approval compared to conventional FDA procedures. In addition, FDA may withdraw these designations if it believes that the designation is no longer supported by data from our clinical development program.

We may seek PRIME Designation in the European Union for one or more of our product candidates but we might not receive such designations and, even if we do, such designations may not lead to a faster development or regulatory review or approval process.

In the European Union, we may seek PRIority MEdicines, or PRIME, designation for our product candidates in the future. PRIME is a voluntary program aimed at enhancing the EMA's role to reinforce scientific and regulatory support in order to optimize development and enable accelerated assessment of new medicines that are of major public health interest with the potential to address unmet medical needs. The program focuses on medicines that target conditions for which there exists no satisfactory method of treatment in the European Union or even if such a method exists, it may offer a major therapeutic advantage over existing treatments. PRIME is limited to medicines under development and not authorized in the European Union and the applicant intends to apply for an initial marketing authorization application through the centralized procedure. To be accepted for PRIME, a product candidate must meet the eligibility criteria in respect of its major public health interest and therapeutic innovation based on information that is capable of substantiating the claims.

The benefits of a PRIME designation include the appointment of a Committee for Human Medicinal Products rapporteur to provide continued support and help to build knowledge ahead of a marketing authorization application, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review, meaning reduction in the review time for an opinion on approvability to be issued earlier in the application process. PRIME enables an applicant to request parallel EMA scientific advice and health technology assessment advice to facilitate timely market access. Even if we receive PRIME designation for any of our product candidates, the designation may not result in a materially faster development process, review or approval compared to conventional EMA procedures. Further, obtaining PRIME designation does not assure or increase the likelihood of EMA's grant of a marketing authorization.

We have received orphan drug designations for AK-OTOF but 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 FDA or EMA from approving other competing products.

Under the Orphan Drug Act, 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 FDA or 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 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. 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 FDA issued final guidance suggesting that it would not consider two genetic medicine 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, FDA can subsequently approve the same product for the same condition if 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 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. In April 2021, FDA granted orphan drug designation for AK-OTOF, and in July 2021, the European Commission granted orphan drug designation for AK-OTOF.

In 2017, Congress passed 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. Under Omnibus legislation signed by President Trump on December 27, 2020, the requirement for a product to show clinical superiority applies to drugs and biologics that received orphan drug designation before enactment of FDARA in 2017 but have not yet been approved or licensed by FDA.

FDA may further reevaluate the Orphan Drug Act and its regulations and policies. This may be particularly true in light of a decision from the Court of Appeals for the 11th Circuit in September 2021 finding that, for the purpose of determining the scope of exclusivity, the term "same disease or condition" means the designated "rare disease or condition" and could not be interpreted by FDA to mean the "indication or use." The court concluded that orphan drug exclusivity applies to the entire designated disease or condition rather than the "indication or use." We do not know if, when, or how 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 FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

FDA, EMA or other comparable foreign regulatory authorities could require the clearance or approval of a companion diagnostic device as a condition of approval for any product candidate that requires or would commercially benefit from such tests. Failure to successfully validate, develop and obtain regulatory clearance or approval for companion diagnostics on a timely basis or at all could harm our product development strategy and we may not realize the commercial potential of any such product candidate.

If safe and effective use of any of our other product candidates depends on an in vitro diagnostic, then FDA generally will require approval or clearance of that diagnostic, known as a companion diagnostic, at the same time that FDA approves our product candidates. The process of obtaining or creating such diagnostic is time consuming and costly. Companion diagnostics, which provide information that is essential for the safe and effective use of a corresponding therapeutic product, are subject to regulation by FDA, EMA and other comparable foreign regulatory authorities as medical devices and require separate regulatory approval from therapeutic approval prior to commercialization. FDA previously has required in vitro companion diagnostics intended to select the patients who will respond to a product candidate to obtain pre-market approval, or PMA, simultaneously with approval of the therapeutic candidate. The PMA process, including the gathering of preclinical and clinical data and the submission and review by the FDA, can take several years or longer. It involves a rigorous pre-market review during which the applicant must prepare and provide FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing, and labeling. After a device is placed on the market, it remains subject to significant regulatory requirements, including requirements governing development, testing, manufacturing, distribution, marketing, promotion, labeling, import, export, record-keeping, and adverse event reporting.

Given our limited experience in developing and commercializing diagnostics, we do not plan to develop companion diagnostics internally and thus will be dependent on the sustained cooperation and effort of third-party collaborators in developing and obtaining approval for these companion diagnostics. We may not be able to enter into arrangements with a provider to develop a companion diagnostic for use in connection with a registrational trial for our product candidates or for commercialization of our product candidates, or do so on commercially reasonable terms, which could adversely affect and/or delay the development or commercialization of our product candidates. We and our future collaborators may encounter difficulties in developing and obtaining approval for the companion diagnostics, including issues relating to selectivity/specificity, analytical validation, reproducibility, or clinical validation. Any delay or failure by our collaborators to develop or obtain regulatory approval of the companion diagnostics could delay or prevent approval of our product candidates. In addition, we, our collaborators or third parties may encounter production difficulties that could constrain the supply of the companion diagnostics, and both they and we may have difficulties gaining acceptance of the use of the companion diagnostics by physicians.

We believe that adoption of screening and treatment into clinical practice guidelines is important for payer access, reimbursement, utilization in medical practice and commercial success, but both our collaborators and we may have difficulty gaining acceptance of the companion diagnostic into clinical practice guidelines. If such companion diagnostics fail to gain market acceptance, it would have an adverse effect on our ability to derive revenues from sales, if any, of any of our product candidates that are approved for commercial sale. In addition, any companion diagnostic collaborator or third party with whom we contract may decide not to commercialize or to discontinue selling or manufacturing the companion diagnostic that we anticipate using in connection with development and commercialization of our product candidates, or our relationship with such collaborator or third party may otherwise terminate. We may not be able to enter into arrangements with another provider to obtain supplies of an alternative diagnostic test for use in connection with the development and commercialization of our product candidates or do so on commercially reasonable terms, which could adversely affect and/or delay the development or commercialization of our product candidates.

AK-OTOF and our other product candidates will be a biologic-device combination involving a novel delivery approach, which may result in additional regulatory and other risks.

We are developing AK-OTOF and our other product candidates as a biologic-device combination for administration directly to the cochlea, or the organ in the inner ear responsible for hearing, using our delivery approach. There are currently no approved fluids, drugs, or biologics that are delivered directly into the cochlea and, as such, no

delivery device is available to facilitate this route of delivery. We are developing a delivery device as part of our novel delivery approach. This approach also relies on ancillary delivery system components, including a syringe and a syringe pump to be used with the delivery device, which introduces additional regulatory and other risks. We may experience delays in obtaining regulatory approval of AK-OTOF and our other product candidates given the increased complexity of the review process when approval of a biologic and a delivery device is sought under a single marketing application. The delivery will be subject to FDA device requirements regarding design, performance and validation as well as human factors testing, among other things. AK-OTOF may be regulated as a biologic-device combination product, which requires coordination within FDA for review of the product candidate's device and biologic components. The determination whether a combination product requires a single marketing application or two separate marketing applications for each component is made by the FDA on a case-by-case basis. Although a single marketing application may be sufficient for the approval of a combination product, FDA may determine that separate marketing applications are necessary. This determination could significantly increase the resources and time required to bring our combination product to market. Although FDA has systems in place for the review and approval of combination products such as ours, we may experience delays in the development and commercialization of our product candidate due to regulatory timing constraints and uncertainties in the product development and approval process, as well as coordination between two different centers within FDA responsible for review of the different components of the combination product. Furthermore, we may elect to pursue the *de novo* pathway for our delivery device within the Center for Devices and Radiological Heath of FDA. The decision to seek a *de novo* pathway may cause us to experience regulatory delays that could adversely impact our development timelines.

Inadequate funding for the FDA, the SEC and other government agencies, including from government shut downs, or other disruptions to these agencies' operations, could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at FDA have fluctuated in recent years as a result. Disruptions at FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Separately, in response to the COVID-19 pandemic, a number of companies announced receipt of complete response letters due to FDA's inability to complete required inspections for their applications. As of May 26, 2021, FDA noted it was continuing to ensure timely reviews of applications for medical products during the ongoing COVID-19 pandemic in line with its user fee performance goals and conducting mission critical domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA quality standards. However, FDA may not be able to continue its current pace and review timelines could be extended, including where a pre-approval inspection or an inspection of clinical sites is required and due to the ongoing COVID-19 pandemic and travel restrictions, FDA is unable to complete such required inspections during the review period. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities.

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 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 BLA is obligated to monitor and report adverse events and any failure of a product to meet the specifications in the BLA. For genetic medicines that use AAV vectors as a delivery system, 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 BLA 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. 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.

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 third-party 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, operating results, 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.

Similar restrictions apply to the approval of our products in the European Union. The holder of a marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include compliance with the European Union's stringent pharmacovigilance or safety reporting rules, which can impose post-authorization studies and additional monitoring obligations; the manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory; and the marketing and promotion of authorized drugs, which are strictly regulated in the European Union and are also subject to laws of the European Union member states. The failure to comply with these and other EU requirements can also lead to significant penalties and sanctions.

Accordingly, 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.

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. 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 FDA and other federal and state enforcement agencies, including the Department of Justice. Violation of the Federal Food, Drug, and Cosmetic Act, or FDCA, 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, third-party 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, FDA could require us to adopt a Risk Evaluation and Mitigation Strategy, 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;
- HIPAA, as further amended by HITECH, 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, other healthcare providers, 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.

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

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.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA. In addition, other legislative changes have been proposed and adopted since the ACA 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 Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act, suspended the 2% Medicare sequester from May 1, 2020 through December 31, 2020, and extended the sequester by one year, through 2031. These Medicare sequester reductions have been suspended through the end of March 2022. From April 2022 through June 2022, a 1% sequester cut will be in effect, with the full 2% cut resuming thereafter. 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 ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, or the Tax Act, 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. Further, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the Tax Act, the remaining provisions of the ACA are invalid as well. The U.S. Supreme Court heard this case on November 10, 2020, and on June 17, 2021, dismissed this action after finding that the plaintiffs do not have standing to challenge the constitutionality of the ACA. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The Trump Administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden revoked those orders and issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care, and consider actions that will protect and strengthen that access. Under this Order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents. This Executive Order also directs the U.S. Department of Health and Human Services to create a special enrollment period for the Health Insurance Marketplace in response to the COVID-19 pandemic.

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 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. Accordingly, such reforms, if enacted, could have an

adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop or commercialize product candidates.

The prices of prescription pharmaceuticals in the United States and foreign jurisdictions is subject to considerable legislative and executive actions and could impact the prices we obtain for our products, if and when licensed.

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. There have been several recent U.S. congressional inquiries as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid. In 2020, President Trump issued several executive orders intended to lower the costs of prescription products and certain provisions in these orders have been incorporated into regulations. These include an interim final rule implementing a most favored nation model, for prices that would tie Medicare Part B payments for certain physician-administered pharmaceuticals to the lowest price paid in other economically advanced countries, effective January 1, 2021. That rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, the Centers for Medicare & Medicaid Services, or CMS, issued a final rule to rescind it. With issuance of this rule, CMS stated that it will explore all options to incorporate value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence-based care.

In addition, in October 2020, the U.S. Department of Health and Human Services, or HHS, and FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or SIP, to import certain prescription drugs from Canada into the United States. The final rule is currently the subject of ongoing litigation, but at least six states (Vermont, Colorado, Florida, Maine, New Mexico, and New Hampshire) have passed laws allowing for the importation of drugs from Canada with the intent of developing SIPs for review and approval by FDA. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed by the Biden administration until January 1, 2023.

On July 9, 2021, President Biden signed Executive Order 14063, which focuses on, among other things, the price of pharmaceuticals. The executive order directs HHS to create a plan within 45 days to combat "excessive pricing of prescription pharmaceuticals and enhance domestic pharmaceutical supply chains, to reduce the prices paid by the federal government for such pharmaceuticals, and to address the recurrent problem of price gouging." On September 9, 2021, HHS released its plan to reduce pharmaceutical prices. The key features of that plan are to (a) make pharmaceutical prices more affordable and equitable for all consumers and throughout the health care system by supporting pharmaceutical price negotiations with manufacturers; (b) improve and promote competition throughout the prescription pharmaceutical industry by supporting market changes that strengthen supply chains, promote biosimilars and generic drugs, and increase transparency; and (c) foster scientific innovation to promote better healthcare and improve health by supporting public and private research and making sure that market incentives promote discovery of valuable and accessible new treatments.

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 organizations 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 product candidates or additional pricing pressures.

In the European Union, similar political, economic and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In markets outside of the United States and the European Union, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. In some countries, particularly the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

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.

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 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 California Consumer Privacy 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). In March 2020, the California State Attorney General proposed varying versions of companion draft regulations which are not yet finalized. Despite the delay in adopting regulations, the California State Attorney General commenced enforcement actions against violators beginning July 1, 2020. 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.

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. For example, 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 and the UK Bribery Act 2010. Violation 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.

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.

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 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 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.

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

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, manufacturing, 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 regulatory 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 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.

Our operations might be affected by the occurrence of a natural disaster or other catastrophic event.

We depend on our employees, consultants, third-party manufacturers, 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, pandemic, hurricanes, fire, floods, and ice and snowstorms, could result in significant disruptions to our research and development, nonclinical studies, clinical trials, and, ultimately, commercialization of our products. Long-term disruptions in the infrastructure caused by events, such as natural disasters, military conflict (including the escalating military tension between Russia and Ukraine), 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 third-party manufacturers, our CROs, regulatory agencies, or other parties with which we are engaged could have a significant negative impact on our operations and financial performance.

Our internal computer systems, or those used by our CROs, third-party manufacturers, 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, third-party manufacturers, and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, or attacks by nation states, hackers or cyber criminals or breaches due to employee error, malfeasance or other disruptions, such as business email compromises, phishing and other cyber-related fraud. While we continuously seek to improve the security attributes of our information technology infrastructure, we cannot eliminate risk or ensure that we will not be harmed by cyberattacks, which could result in a material disruption of our development programs and our business operations. For example, the loss of our nonclinical data and clinical trial data from nonclinical 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 expect to 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 and the further development and commercialization of our product candidates could be delayed. Any significant security incidents could harm our reputation and cause us to incur legal liability and increased costs to address such events and related security concerns.

Risks Related to Ownership of Our Common Stock

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

Our shares began trading on the Nasdaq Global Select Market on June 26, 2020. Prior to June 26, 2020, there was no public market for our common stock and we cannot be certain an active trading market for our shares will continue to 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.

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

Our stock price is likely 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 paid for their shares. The market price for our common stock may be influenced by many factors, including:

- results of or developments in nonclinical studies and clinical trials of our product candidates or those of our competitors or potential collaborators;
- timing of the results of our nonclinical studies and clinical trials or those of our competitors;
- our success in commercializing any product candidates, if and when approved;
- the success of 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 our product candidates;
- 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; 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.

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. 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 provides 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.

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

As of April 29, 2022, our executive officers and directors and their affiliates, in the aggregate, beneficially owned shares representing approximately 34.8% 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.

This concentration of ownership may also adversely affect the market price of our common stock.

We have broad discretion in the use of our cash, cash equivalents and marketable securities and may not use them effectively.

Our management has broad discretion in the application of our cash, cash equivalents, and marketable securities, and could use the funds 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 cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest our cash, cash equivalents and marketable securities 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.

Future sales of shares of our common stock, including by us, employees, and significant stockholders, could negatively affect our stock price.

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. Persons who were our stockholders prior to our IPO continue to hold a substantial number of shares of our

common stock. If such persons sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline.

Moreover, holders of a substantial number of shares of our common stock 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 have also filed, and expect to continue to file, registration statements on Form S-8 to register shares of common stock that we may issue under our equity compensation plans. Shares registered under these registration statements on Form S-8 can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates, vesting arrangements and exercise of options.

We currently have on file with the SEC a universal shelf registration statement on Form S-3, or the Shelf Registration Statement, which allows us to offer and sell registered common stock, preferred stock, debt securities, units, depository shares, subscription rights, purchase contracts, and/or warrants from time to time pursuant to one or more offerings at prices and terms to be determined at the time of sale. In August 2021, we entered into a Sales Agreement, or the ATM Sales Agreement, with Cowen and Company, LLC pursuant to which, from time to time, we may offer and sell under the ATM Sales Agreement up to $100 million of the common stock registered under the Shelf Registration Statement pursuant to one or more "at the market" offerings as defined in Rule 415 under the Securities Act of 1933, as amended, or the Securities Act. As of March 31, 2022, we had not sold any shares of common stock pursuant to the ATM Sales Agreement. The extent to which we utilize the ATM Sales Agreement as a source of funding will depend on a number of factors, including the prevailing market price of our common stock, general market conditions, and the extent to which we are able to secure funds from other sources.

Sales of substantial amounts of shares of our common stock or other securities by our stockholders, by us under the Shelf Registration Statement, pursuant to the ATM Sales Agreement or through any other means, could also lower the market price of our common stock and impair our ability to raise capital through the sale of equity or equity-related securities.

We have incurred and will continue to incur increased costs as a result of operating as a 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 emerging growth company, or EGC, or a smaller reporting company, we will continue to incur significant legal, accounting, and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, 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, 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 of the Sarbanes-Oxley Act of 2002, or Section 404, we will be required to furnish a report by our management on our internal control over financial reporting beginning with our filing of an Annual Report on Form 10-K with the SEC for the year ended December 31, 2021. 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.

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 controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are 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 Jumpstart Our Business Startups Act of 2012 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.

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

As a public company, 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 individuals, 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.

Changes in tax laws may adversely affect our business or financial condition. On December 22, 2017, the U.S. government enacted the Tax Act, which significantly reformed the U.S. Internal Revenue Code of 1986, as amended, or the Code. The Tax Act, among other things, contained significant changes to corporate taxation, including a reduction of

the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, the limitation of the tax deduction for net interest expense to 30% of adjusted taxable income (except for certain small businesses),the limitation of the deduction for net operating losses, or 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), the imposition of a one-time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, the elimination of U.S. tax on foreign earnings (subject to certain important exceptions), the allowance of immediate deductions for certain new investments instead of deductions for depreciation expense over time, and the modification or repeal of 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, and COVID-19 relief provisions were included in the Consolidated Appropriations Act, 2021, or CAA, which was enacted on December 27, 2020. All 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 Tax Act. 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 Tax Act, the FFCR Act, the CARES Act, and the CAA is and continues to be forthcoming, and such guidance could ultimately increase or lessen the impact of these laws on our business and financial condition. It is also possible that Congress will enact additional legislation in connection with the COVID-19 pandemic, or otherwise, some of which could have an impact on our company. In addition, it is uncertain if and to what extent various states will conform to the Tax Act, the FFCR Act, the CARES Act, or the CAA.

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

We have incurred substantial losses since inception and do not expect to become profitable in the near future, if ever. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any. As of December 31, 2021, we had federal NOL carryforwards of $146.7 million, which may be available to offset future taxable income, of which $0.4 million begin to expire in 2036, while the remaining $146.3 million do not expire but are limited in their usage to an annual deduction equal to 80% of annual taxable income. In addition, as of December 31, 2021, we had state NOL carryforwards of $145.4 million, which may be available to offset future taxable income and expire at various dates beginning in 2036. Under Sections 382 and 383 of the Code, if a corporation 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 rolling three-year period, the corporation's ability to use its pre-change NOLs and other pre-change tax attributes (such as research tax credits) to offset its post-change income or taxes may be limited. We have not conducted a study to assess whether any such ownership changes have occurred. We may have experienced ownership changes in the past and may experience ownership changes in the future as a result of subsequent shifts in our stock ownership (some of which shifts are outside our control). As a result, if 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. Similar provisions of state tax law may also apply to limit our use of accumulated state tax attributes. 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 unused 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 Tax Act, as amended by the CARES Act, 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. In addition, state NOLs generated in one state cannot be used to offset income generated in another state. For these reasons, even if we attain profitability, we may be unable to use a material portion of our NOLs and other tax attributes.

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 state courts in the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could discourage lawsuits against the company and 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 proceedings:

- 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 Securities Act, the Exchange Act, or any other claim for which federal courts have exclusive jurisdiction. Furthermore, 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.

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. Alternatively, if a court were to find the choice of forum provisions contained in our certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could materially adversely affect our business, financial condition, and operating results. For example, under the Securities Act, federal courts have concurrent jurisdiction over all suits brought to enforce any duty or liability created by the Securities Act, and investors cannot waive compliance with the federal securities laws and the rules and regulations thereunder.

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

Use of Proceeds from Initial Public Offering

On June 30, 2020, we closed our initial public offering, or IPO, of common stock pursuant to a registration statement on Form S-1 (File No. 333-238977), which was declared effective by the Securities and Exchange Commission, or SEC, on June 25, 2020.

We received aggregate net proceeds from the IPO of approximately $223.8 million, after deducting $17.1 million of underwriting discounts and commissions and $3.4 million of other offering expenses payable by us. None of the underwriting discounts and commissions or offering expenses were paid directly or indirectly to any directors or officers of ours or their associates or to persons owning 10% or more of any class of equity securities or to any affiliates of ours.

As of March 31, 2022, we have invested the unused net proceeds from the IPO in cash equivalents and marketable securities. There has been no material change in our planned use of the net proceeds from our IPO as described in our final prospectus filed pursuant to Rule 424(b)(4) under the Securities Act with the SEC on June 26, 2020.

Item 6. Exhibits

Exhibit Number	Description
3.1	Restated Certificate of Incorporation of the registrant (incorporated by reference to Exhibit 3.1 to the registrant's Current Report on Form 8-K, filed with the Securities and Exchange Commission on June 30, 2020).
3.2	Amended and Restated Bylaws of the registrant (incorporated by reference to Exhibit 3.2 to the registrant's Current Report on Form 8-K, filed with the Securities and Exchange Commission on June 30, 2020).
10.1*	Summary of Amended and Restated Non-employee Director Compensation Program
31.1*	Certification of Principal Executive Officer Pursuant to Rule 13a-14(a) and Rule 15d-14(a) under the Securities Exchange Act of 1934, as amended, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2*	Certification of Principal Financial Officer Pursuant to Rule 13a-14(a) and Rule 15d-14(a) under the Securities Exchange Act of 1934, as amended, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1**	Certification of Principal Executive and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101.INS*	Inline XBRL Instance Document
101.SCH*	Inline XBRL Taxonomy Extension Schema Document
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (formatted as Inline XBRL with applicable taxonomy extension information contained in Exhibits 101)

* Filed herewith.

** The certification attached as Exhibit 32.1 that accompanies this Quarterly Report is deemed furnished and not filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Akouos, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Quarterly Report, irrespective of any general incorporation language contained in such filing.

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.

AKOUOS, INC.

Date: May 12, 2022

By: /s/ Emmanuel Simons

Emmanuel Simons, Ph.D., M.B.A.
President and Chief Executive Officer
(Principal Executive Officer)

Date: May 12, 2022

By: /s/ Sachiyo Minegishi

Sachiyo Minegishi, M.B.A.
Chief Financial Officer
(Principal Financial and Accounting Officer)

AKOUOS, INC.

AMENDED AND RESTATED NON-EMPLOYEE DIRECTOR COMPENSATION POLICY

Effective as of January 1, 2022, the non-employee directors of Akouos, Inc. (the "Company") shall receive the following compensation for their service as members of the Board of Directors (the "Board") of the Company.

Director Compensation

Our goal is to provide compensation for our non-employee directors in a manner that enables us to attract and retain outstanding director candidates and reflects the substantial time commitment necessary to oversee the Company's affairs. We also seek to align the interests of our directors and our stockholders and we have chosen to do so by compensating our non-employee directors with a mix of cash and equity-based compensation.

Cash Compensation

The fees that will be paid to our non-employee directors for service on the Board, and for service on each committee of the Board on which the director is then a member, and the fees that will be paid to the chairperson of the Board, if one is then appointed, and the chairperson of each committee of the Board will be as follows:

	Non-Chair Annual Fee	Chair Annual Fee
Board of Directors	$ 40,000	$ 65,000
Audit Committee	$ 7,500	$ 15,000
Compensation Committee	$ 5,000	$ 10,000
Nominating and Corporate Governance Committee	$ 4,000	$ 8,000

The foregoing fees will be payable in arrears in four equal quarterly installments on the last day of each quarter, provided that the amount of such payment will be prorated for any portion of such quarter that the director is not serving on the Board, on such committee or in such position. Additionally, the Board may establish other committees from time to time that include fees for both members and chairpersons, as well as per meeting fees.

Equity Compensation

Initial Grants. Upon initial election to the Board, each non-employee director will be granted, automatically and without the need for any further action by the Board, an initial equity award of an option to purchase 32,000 shares of our common stock. The initial award shall have a term of ten years from the date of the award, and shall vest and become exercisable as to one-third of the shares underlying such award at the end of each of the first, second, and third anniversaries of the date of grant, subject to the non-employee director's continued service to the Company through each applicable vesting date. The vesting shall accelerate as to 100% of the shares upon a change in control of the Company. The exercise price of the option shall be the closing price of our common stock on the date of grant.

Annual Grants. Each non-employee director who has served as a member of the Board for at least six months prior to the date of our annual meeting of stockholders for a particular year will be granted, automatically and without the need for any further action by the Board, an option to purchase 16,000 shares of our common stock on the date of the first Board meeting held after our annual meeting of stockholders for such year. The annual award shall have a term of ten years from the date of the award, and shall vest and become exercisable in full upon the earlier of the one-year anniversary of the grant date or the first annual meeting of stockholders occurring after the grant date, subject to the non-employee director's continued service to the Company through each applicable vesting date. The vesting shall accelerate as to 100% of the shares upon a change in control of the Company. The exercise price of the option shall be the closing price of our common stock on the date of grant.

The foregoing share amounts shall be automatically adjusted in the event of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spin-off or other similar change in

capitalization or event effecting our common stock, or any distribution to holders of our common stock other than an ordinary cash dividend.

The initial awards and the annual awards shall be subject to the terms and conditions of our 2020 Stock Plan, or any successor plan, and the terms of the option agreements entered into with each director in connection with such awards.

Expenses

Each non-employee director is reimbursed for reasonable travel and other expenses incurred in connection with attending Board and committee meetings.

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, Emmanuel Simons, Ph.D., M.B.A., certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Akouos, 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)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

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

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

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

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

5. The registrant's other certifying officer(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 12, 2022

By: /s/ Emmanuel Simons

Emmanuel Simons, Ph.D., M.B.A.
President and Chief Executive Officer
(Principal Executive Officer)

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, Sachiyo Minegishi, M.B.A., certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Akouos, 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)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

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

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

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

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

5. The registrant's other certifying officer(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 12, 2022

By: /s/ Sachiyo Minegishi
Sachiyo Minegishi, M.B.A.
Chief Financial Officer
(Principal Financial and Accounting Officer)

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 Akouos, Inc. (the "Company") for the period ending March 31, 2022, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to his or her knowledge:

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

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

Date: May 12, 2022

By: /s/ Emmanuel Simons
Emmanuel Simons, Ph.D., M.B.A.
President and Chief Executive Officer
(Principal Executive Officer)

Date: May 12, 2022

By: /s/ Sachiyo Minegishi
Sachiyo Minegishi, M.B.A.
Chief Financial Officer
(Principal Financial and Accounting Officer)