

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549**

FORM 10-Q

(Mark One)

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

For the quarterly period ended June 30, 2021

OR

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

For the transition period from _____ to _____

Commission File Number: 001-40489

VERVE THERAPEUTICS, INC.

(Exact Name of Registrant as Specified in its Charter)

Delaware

(State or other jurisdiction of
incorporation or organization)

82-4800132

(I.R.S. Employer
Identification No.)

**500 Technology Square, Suite 901
Cambridge, Massachusetts**

(Address of principal executive offices)

02139

(Zip Code)

Registrant's telephone number, including area code: (617) 603-0070

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common stock, par value \$0.001 per share	VERV	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
Non-accelerated filer

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 August 9, 2021, the registrant had 47,991,799 shares of common stock, par value \$0.001 per share, outstanding.

FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q includes forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical fact, contained in this Quarterly Report on Form 10-Q, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words “anticipate,” “believe,” “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 on Form 10-Q include, among other things, statements about:

- the initiation, timing, progress and results of our research and development programs and preclinical studies and clinical trials;
- the impact of the COVID-19 pandemic and our response to the pandemic;
- our estimates regarding expenses, future revenue, capital requirements, need for additional financing and the period over which we believe our existing cash, cash equivalents and marketable securities will be sufficient to fund our operating expenses and capital expenditure requirements;
- the timing of and our ability to submit applications for and obtain and maintain regulatory approvals for our current and future product candidates;
- the potential therapeutic attributes and advantages of our current and future product candidates;
- our expectations about the translatability of non-human primates results into humans;
- our plans to develop and, if approved, subsequently commercialize any product candidates we may develop;
- the rate and degree of market acceptance and clinical utility of our products, if approved;
- our estimates regarding the addressable patient population and potential market opportunity for our current and future product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our expectations regarding our ability to obtain and maintain intellectual property protection;
- 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 relating to our competitors and our industry;
- our ability to establish and maintain 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.

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

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

RISK FACTOR SUMMARY

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

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

- We will need substantial additional funding. 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;
 - Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability;
 - We are very early in our development efforts, and we have not yet completed investigational new drug application, or IND, -enabling studies or initiated clinical development of any product candidate. As a result, we expect it will be many years before we commercialize any product candidate, if ever. If we are unable to advance our current or future product candidates into and through clinical trials, obtain marketing approval and ultimately commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed;
 - Gene editing, including base editing, is a novel technology in a rapidly evolving field that is not yet clinically validated for human therapeutic use. The approaches we are taking to discover and develop novel therapeutics are unproven and may never lead to marketable products. We are focusing our research and development efforts on gene editing using base editing technology, but other gene editing technologies may be discovered that provide significant advantages over base editing, which could materially harm our business;
 - The outcome of preclinical studies and earlier-stage clinical trials may not be predictive of future results or the success of later preclinical studies and clinical trials;
 - If any of the product candidates we may develop, or the delivery modes we rely on to administer them, cause serious adverse events, undesirable side effects or unexpected characteristics, such events, side effects or characteristics could delay or prevent regulatory approval of the product candidates, limit the commercial potential or result in significant negative consequences following any potential marketing approval;
 - Adverse public perception of genetic medicines, and gene editing and base editing in particular, may negatively impact regulatory approval of, and/or demand for, our potential products;
 - Genetic medicines are complex and difficult to manufacture. We could experience delays in satisfying regulatory authorities or production problems that result in delays in our development programs, limit the supply of our product candidates we may develop, or otherwise harm our business;
 - We rely, and expect to continue to rely, on third parties to conduct some or all aspects of our product manufacturing, research and preclinical and clinical testing, and these third parties may not perform satisfactorily;
 - We have entered into collaborations, and may enter into additional collaborations, with third parties for the research, development, manufacture and commercialization of programs or product candidates. If these collaborations are not successful, our business could be adversely affected;
 - If we or our licensors are unable to obtain, maintain, defend and enforce patent rights that cover our gene editing technology and product candidates or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully develop and commercialize our technology and product candidates may be adversely affected;
 - If we fail to comply with our obligations in our intellectual property licenses arrangements with third parties, or otherwise experience disruptions to our business relationships with our licensors, we could lose intellectual property rights that are important to our business;
 - The intellectual property landscape around genome editing technology, including base editing, is highly dynamic, and third parties may initiate legal proceedings alleging that we are infringing, misappropriating, or otherwise violating their intellectual property rights, the outcome of which would be uncertain and may prevent, delay or otherwise interfere with our product discovery and development efforts;
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- We face substantial competition, which may result in others discovering, developing or commercializing products before us or more successfully than we do; and
 - The COVID-19 pandemic may affect our ability to initiate and complete preclinical studies, delay the initiation of 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, both of which could result in adverse effects on our business, operations and ability to raise capital.
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Part I – Financial Information

Item 1. Financial Statements

Verve Therapeutics, Inc.

Condensed consolidated balance sheets

(in thousands, except share and per share amounts) (unaudited)	June 30, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	\$ 387,446	\$ 8,993
Marketable securities	30,178	63,119
Prepaid expenses and other current assets	1,940	1,854
Total current assets	419,564	73,966
Property and equipment, net	6,417	3,984
Restricted cash	463	463
Other long term assets	74	—
Total assets	\$ 426,518	\$ 78,413
Liabilities, convertible preferred stock, and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	\$ 1,530	\$ 36
Accrued expenses	6,967	7,189
Deferred rent, current portion	152	90
Total current liabilities	8,649	7,315
Deferred rent, net of current portion	13	125
Success payment liability (See Notes 5, 8 and 14)	12,460	2,806
Antidilution rights liability (See Notes 5, 8 and 14)	—	6,916
Total liabilities	21,122	17,162
Commitments and contingencies (See Note 7 and Note 8)		
Convertible preferred stock (See Note 10)	—	125,160
Stockholders' equity (deficit):		
Common stock, \$0.001 par value; 200,000,000 and 255,000,000 shares authorized, 48,215,812 and 3,123,424 shares issued at June 30, 2021 and December 31, 2020, respectively; 47,946,996 and 2,585,789 shares outstanding at June 30, 2021 and December 31, 2020, respectively	48	3
Additional paid-in capital	538,109	2,616
Accumulated other comprehensive income	3	8
Accumulated deficit	(132,764)	(66,536)
Total stockholders' equity (deficit)	405,396	(63,909)
Total liabilities, convertible preferred stock, and stockholders' equity (deficit)	\$ 426,518	\$ 78,413

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

Verve Therapeutics, Inc.

Condensed consolidated statements of operations and comprehensive loss

(in thousands, except share and per share amounts) (unaudited)	Three months ended June 30,		Six months ended June 30,	
	2021	2020	2021	2020
Operating expenses:				
Research and development	\$ 13,423	\$ 5,654	\$ 24,768	\$ 12,177
General and administrative	3,541	1,032	6,257	1,878
Total operating expenses	16,964	6,686	31,025	14,055
Loss from operations	(16,964)	(6,686)	(31,025)	(14,055)
Other income (expense):				
Change in fair value of preferred stock tranche liability	-	-	-	2,507
Change in fair value of antidilution rights liability	(25,970)	(863)	(25,574)	(1,745)
Change in fair value of success payment liability	(10,036)	(81)	(9,654)	(17)
Interest income and other income (expense), net	5	50	25	127
Total other (expense) income, net	(36,001)	(894)	(35,203)	872
Net loss	\$ (52,965)	\$ (7,580)	\$ (66,228)	\$ (13,183)
Net loss per common share attributable to common stockholders, basic and diluted	\$ (6.66)	\$ (3.41)	\$ (12.46)	\$ (6.36)
Weighted-average common shares used in net loss per share attributable to common stockholders, basic and diluted	7,948,110	2,225,017	5,316,804	2,071,249
Comprehensive Loss:				
Net loss	\$ (52,965)	\$ (7,580)	\$ (66,228)	\$ (13,183)
Other comprehensive (loss) income:				
Unrealized gain (loss) on marketable securities	(4)	(19)	(5)	(8)
Comprehensive loss attributable to common stockholders	\$ (52,969)	\$ (7,599)	\$ (66,233)	\$ (13,191)

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

Verve Therapeutics, Inc.

Condensed consolidated statements of convertible preferred stock and stockholders' equity (deficit)

(in thousands, except share amounts) (unaudited)	Convertible preferred stock		Common stock				Accumulated other comprehensive income (loss)	Accumulated deficit	Total stockholders' equity (deficit)
	Shares	Amount	Shares	Amount	Additional paid-in capital				
Balance at December 31, 2019	51,421,404	\$ 25,480	1,854,438	\$ 2	\$ 1,268	\$ 9	\$ (20,832)	\$ (19,553)	
Issuance of Series A convertible preferred stock, net of issuance costs of \$22	49,749,167	36,792	—	—	—	—	—	—	
Issuance of common stock to licensor institutions	—	—	187,867	—	487	—	—	487	
Vesting of restricted common stock	—	—	134,409	—	—	—	—	—	
Exercise of stock options	—	—	2,025	—	3	—	—	3	
Unrealized gain on available-for-sale securities	—	—	—	—	—	11	—	11	
Stock-based compensation	—	—	—	—	95	—	—	95	
Net loss	—	—	—	—	—	—	(5,603)	(5,603)	
Balance at March 31, 2020	101,170,571	\$ 62,272	2,178,739	\$ 2	\$ 1,853	\$ 20	\$ (26,435)	\$ (24,560)	
Issuance of Series A-1 convertible preferred stock, net of issuance costs of \$112	78,348,461	62,888	—	—	—	—	—	—	
Vesting of restricted common stock	—	—	134,408	—	—	—	—	—	
Unrealized loss on available-for-sale securities	—	—	—	—	—	(19)	—	(19)	
Stock-based compensation	—	—	—	—	100	—	—	100	
Net loss	—	—	—	—	—	—	(7,580)	(7,580)	
Balance at June 30, 2020	179,519,032	\$ 125,160	2,313,147	\$ 2	\$ 1,953	\$ 1	\$ (34,015)	\$ (32,059)	
Balance at December 31, 2020	179,519,032	\$ 125,160	2,585,789	\$ 3	\$ 2,616	\$ 8	\$ (66,536)	\$ (63,909)	
Issuance of Series B convertible preferred stock, net of issuance costs of \$241	77,163,022	93,759	—	—	—	—	—	—	
Vesting of restricted common stock	—	—	134,409	—	—	—	—	—	
Exercise of stock options	—	—	48,745	—	72	—	—	72	
Unrealized loss on available-for-sale securities	—	—	—	—	—	(1)	—	(1)	
Stock-based compensation	—	—	—	—	670	—	—	670	
Net loss	—	—	—	—	—	—	(13,263)	(13,263)	
Balance at March 31, 2021	256,682,054	\$ 218,919	2,768,943	\$ 3	\$ 3,358	\$ 7	\$ (79,799)	\$ (76,431)	
Conversion of convertible preferred stock to common stock upon closing of initial public offering	(256,682,054)	(218,919)	27,720,923	28	218,891	—	—	218,919	
Issuance of common stock from initial public offering, net of issuance costs of \$25,098	—	—	16,141,157	16	281,568	—	—	281,584	
Issuance of common stock to licensor institutions	—	—	878,098	1	32,489	—	—	32,490	
Vesting of restricted common stock	—	—	134,408	—	—	—	—	—	
Exercise of stock options	—	—	303,467	—	452	—	—	452	
Unrealized loss on available-for-sale securities	—	—	—	—	—	(4)	—	(4)	
Stock-based compensation	—	—	—	—	1,351	—	—	1,351	
Net loss	—	—	—	—	—	—	(52,965)	(52,965)	
Balance at June 30, 2021	—	\$ —	47,946,996	\$ 48	\$ 538,109	\$ 3	\$ (132,764)	\$ 405,396	

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

Verve Therapeutics, Inc.

Condensed consolidated statements of cash flows

(unaudited, in thousands)	Six months ended June 30,	
	2021	2020
Cash flows from operating activities:		
Net loss	\$ (66,228)	\$ (13,183)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	651	451
Amortization of premium on marketable securities	356	66
Stock-based compensation	2,021	195
Change in fair value of preferred stock tranche liabilities	-	(2,507)
Change in fair value of antidilution rights	25,574	1,745
Change in fair value of success payments liabilities	9,654	17
Changes in operating assets and liabilities:		
Prepaid expenses and other assets	(159)	(591)
Accounts payable	1,283	(1,044)
Accrued expenses and other liabilities	(1,584)	914
Deferred rent liability	(50)	(29)
Net cash used in operating activities	(28,482)	(13,966)
Cash flows from investing activities:		
Purchases of property and equipment	(2,376)	(1,449)
Purchases of marketable securities	(11,176)	(73,128)
Maturities of marketable securities	43,755	14,281
Net cash provided by (used in) investing activities	30,203	(60,296)
Cash flows from financing activities:		
Proceeds from issuance of Preferred Stock, net	93,759	92,616
Proceeds from initial public offering, net of underwriting discount	285,214	-
Payment of initial public offering costs	(2,765)	-
Proceeds from exercise of stock options	524	3
Net cash provided by financing activities	376,732	92,619
Increase in cash, cash equivalents and restricted cash	378,453	18,357
Cash, cash equivalents and restricted cash—beginning of period	9,456	3,221
Cash, cash equivalents and restricted cash—end of period	\$ 387,909	\$ 21,578
Supplemental disclosure of noncash investing and financing activities:		
Property and equipment additions included in accounts payable and accrued expenses	\$ 794	\$ 98
Settlement of tranche right liability	\$ —	\$ 7,064
Initial public offering costs included in accounts payable and accrued liabilities	\$ 865	\$ —
Conversion of convertible preferred stock to common stock upon closing of initial public offering	\$ 218,919	\$ —
Settlement of antidilution rights liability by issuing common stock	\$ 32,490	\$ 487

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

Verve Therapeutics, Inc.

Notes to condensed consolidated financial statements (unaudited)

1. Nature of the business and basis of presentation

Organization

Verve Therapeutics, Inc. (the “Company” or “Verve”) is a genetic medicines company pioneering a new approach to the care of cardiovascular disease, transforming treatment from chronic management to single-course gene editing medicines. The Company was incorporated on March 9, 2018 as Endcadia, Inc., a Delaware corporation, and began operations shortly thereafter. In January 2019, the Company amended its certificate of incorporation to change its name to Verve Therapeutics, Inc. The Company’s principal offices are located in Cambridge, Massachusetts.

Liquidity and capital resources

Since its inception, the Company has devoted its efforts principally to research and development and raising capital. The Company is subject to risks and uncertainties common to early-stage companies in the biotechnology industry including, but not limited to, technical risks associated with the successful research, development and manufacturing of product candidates, development by competitors of new technological innovations, dependence on key personnel, protection of proprietary technology, compliance with government regulations and the ability to secure additional capital to fund operations. Current and future programs will require significant 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 21, 2021, the Company completed its initial public offering, or IPO, in which the Company issued and sold 16,141,157 shares of its common stock, including 2,105,368 shares pursuant to the full exercise of the underwriters’ option to purchase additional shares, at a public offering price of \$19.00 per share, for aggregate gross proceeds of \$306.7 million. The Company received approximately \$281.6 million in net proceeds after deducting underwriting discounts and estimated offering expenses payable by the Company. In connection with the IPO, all outstanding shares of convertible preferred stock converted into 27,720,923 shares of the Company’s common stock.

In connection with the Company’s IPO, the Company effected a one-for-9.2595 reverse stock split of the Company’s issued and outstanding common stock. Accordingly, all shares of common stock and per share amounts, as well as the conversion ratio of the Company’s outstanding convertible preferred stock, for all periods presented in the accompanying consolidated financial statements and notes thereto have been retroactively adjusted, where applicable, to reflect the reverse stock split, including reclassification of par and additional paid-in capital amounts as a result of the reverse stock split.

The accompanying condensed consolidated financial statements have been prepared on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities and commitments in the ordinary course of business. The Company expects that its cash, cash equivalents and marketable securities of \$417.6 million as of June 30, 2021 will be sufficient to fund its operations and capital expenditure requirements beyond the next 12 months. The Company will need additional financing to support its continuing operations and pursue its growth strategy. Until such time as the Company can generate significant revenue from product sales, if ever, it expects to finance its operations through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. The Company may be unable to raise additional funds or enter into such other agreements when needed on favorable terms or at all. The inability to raise capital as and when needed could have a negative impact on the Company’s financial condition and its ability to pursue its business strategy. The Company will need to generate significant revenue to achieve profitability, and it may never do so.

Basis of presentation

The accompanying condensed consolidated financial statements have been prepared in accordance with United States generally accepted accounting principles (“GAAP”) and pursuant to the rules and regulations of the Securities and Exchange Commission (“SEC”). 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”). Certain information and footnote disclosures normally included in

financial statements prepared in accordance with GAAP have been condensed or omitted pursuant to such rules and regulations.

The unaudited interim condensed consolidated financial statements have been prepared on the same basis as the audited consolidated financial statements. In the opinion of the Company's management, the accompanying unaudited interim condensed consolidated financial statements contain all adjustments that are necessary to present fairly the Company's financial position as of June 30, 2021, the results of its operations and other comprehensive loss for the three and six months ended June 30, 2021 and 2020, convertible preferred stock and stockholders' deficit for the three and six months ended June 30, 2021 and 2020 and cash flows for the six months ended June 30, 2021 and 2020. Such adjustments are of a normal and recurring nature. The results for the three and six months ended June 30, 2021 are not necessarily indicative of the results for the year ending December 31, 2021, or for any future period. These interim financial statements should be read in conjunction with the audited consolidated financial statements as of and for the year ended December 31, 2020, and the notes thereto, included in the Company's final prospectus for its initial public offering filed pursuant to Rule 424(b)(4) under the Securities Act with the SEC on June 17, 2021.

2. Summary of significant accounting policies

The Company's significant accounting policies are disclosed in Note 2, "Summary of significant accounting policies," in the audited consolidated financial statements for the year ended December 31, 2020, and notes thereto, included in the Company's final prospectus for its IPO filed pursuant to Rule 424(b)(4) under the Securities Act with the SEC on June 17, 2021. Since the date of those financial statements, there have been no changes to its significant accounting policies.

Cash, cash equivalents and restricted cash

Restricted cash represents collateral provided for a letter of credit issued as a security deposit in connection with the Company's lease of its corporate facilities. A reconciliation of the cash, cash equivalents, and restricted cash reported within the balance sheet that sum to the total of the same amounts shown in the statement of cash flows is as follows:

(in thousands)	June 30, 2021	June 30, 2020
Cash and cash equivalents	\$ 387,446	\$ 20,931
Restricted cash	463	647
Total cash, cash equivalents and restricted cash	\$ 387,909	\$ 21,578

3. Marketable securities

Marketable securities by security type consisted of the following:

(in thousands)	June 30, 2021			
	Amortized cost	Gross unrealized gains	Gross unrealized losses	Fair value
U.S. treasury bills and notes	\$ 25,173	\$ 3	\$ -	\$ 25,176
U.S. agency securities	5,002	-	-	5,002
Total	\$ 30,175	\$ 3	\$ -	\$ 30,178

(in thousands)	December 31, 2020			
	Amortized cost	Gross unrealized gains	Gross unrealized losses	Fair value
U.S. treasury bills and notes	\$ 32,221	\$ 3	\$ -	\$ 32,224
U.S. agency securities	30,890	5	-	30,895
Total	\$ 63,111	\$ 8	\$ -	\$ 63,119

The remaining contractual maturities of all marketable securities were less than one year as of June 30, 2021 and December 31, 2020.

4. Property and equipment, net

Property and equipment, net, consist of the following:

(in thousands)	June 30, 2021	December 31, 2020
Lab equipment	\$ 6,754	\$ 3,937
Leasehold improvements	432	259
Furniture and fixtures	535	481
Computer equipment	145	105
Total property and equipment	7,866	4,782
Less accumulated depreciation	(1,449)	(798)
Property and equipment, net	\$ 6,417	\$ 3,984

Depreciation expense for the three and six months ended June 30, 2021 was \$0.4 million and \$0.7 million, respectively. Depreciation expense for the three and six months ended June 30, 2020 was \$0.3 million and \$0.5 million, respectively.

5. Fair value of financial instruments

The Company's financial instruments that are measured at fair value on a recurring basis consist of money market funds, marketable securities, the preferred stock tranche liability as well as certain derivative liabilities (antidilution right liability and success payment liability) pursuant to the Harvard/Broad License Agreement and the Broad License Agreement.

The following tables set forth the fair value of the Company's financial instruments by level within the fair value hierarchy:

(in thousands)	As of June 30, 2021			
	Fair value	Level 1	Level 2	Level 3
Assets				
Money market funds	\$ 324,973	\$ 324,973	\$ -	\$ -
Marketable securities:				
U.S. treasury bills and notes	25,176	-	25,176	-
U.S. agency securities	5,002	-	5,002	-
Total assets	\$ 355,151	\$ 324,973	\$ 30,178	\$ -
Liabilities				
Success payment liability	12,460	-	-	12,460
Total liabilities	\$ 12,460	\$ -	\$ -	\$ 12,460

(in thousands)	As of December 31, 2020			
	Fair value	Level 1	Level 2	Level 3
Assets				
Money market funds	\$ 6,724	\$ 6,724	\$ -	\$ -
Marketable securities:				
U.S. treasury bills and notes	32,224	-	32,224	-
U.S. agency securities	30,895	-	30,895	-
Total assets	\$ 69,843	\$ 6,724	\$ 63,119	\$ -
Liabilities				
Success payment liability	\$ 2,806	\$ -	\$ -	\$ 2,806
Antidilution rights liability	6,916	-	-	6,916
Total liabilities	\$ 9,722	\$ -	\$ -	\$ 9,722

Cash Equivalents—Cash equivalents of \$325.0 million and \$6.7 million as of June 30, 2021 and December 31, 2020, respectively, consisted of money market funds and are classified within Level 1 of the fair value hierarchy because they are valued using quoted market prices in active markets.

Marketable Securities—The Company measures its marketable securities at fair value on a recurring basis and classifies those instruments within Level 2 of the fair value hierarchy. Marketable securities are classified within Level 2 of the fair value hierarchy because pricing inputs are other than quoted prices in active markets, which are either directly or indirectly observable as of the reporting date, and fair value is determined through the use of models or other valuation methodologies.

Antidilution Rights Liability—The antidilution rights liability represents the obligation to issue additional shares of common stock to Harvard and Broad following the completion of (1) a defined aggregate level of preferred stock financing and (2) either a sale of the Company's preferred stock, an initial public offering, or a company sale meeting a certain value threshold. The antidilution rights liability is stated at fair value and is considered Level 3 in the fair value hierarchy because its fair value measurement is based, in part, on significant inputs not observed in the market. The antidilution rights liability related to meeting a defined aggregate level of preferred stock financing was valued using a probability-weighted present value model that considered the probability of meeting the defined aggregate level of preferred stock financing, as well as the fair value of the Company's common stock. The antidilution rights liability related to the achievement of a specified valuation through either a sale of the Company's preferred stock, an initial public offering, or a company sale was valued using a Monte Carlo simulation model, which models the value of the liability based on several key variables, including probability of event occurrence, timing of event occurrence, as well as the fair value of the Company's common stock.

In June 2021, upon completion of its IPO, the Company settled the antidilution rights liability in full through the issuance of 878,098 shares of the Company's common stock for a settlement amount of \$32.5 million. Prior to settlement, the Company remeasured the liability with a corresponding increase of \$26.0 million and \$25.6 million to other expense for the three and six months ended June 30, 2021, respectively. The Company recorded an increase of \$0.9 million and \$1.7 million to other expense for three and six months ended June 30, 2020, respectively.

Success Payment Liability—The Company is obligated to pay to Harvard and Broad tiered success payments in the event its average market capitalization exceeds specified thresholds for a specified period of time ascending from a high nine-digit dollar amount to \$10.0 billion, or sale of the Company for consideration in excess of those thresholds. In the event of a change of control or a sale of the Company, the Company is required to pay success payments in cash within a specified period following such event. Otherwise, the success payments may be settled at the Company's option in either cash or shares of its common stock, or a combination of cash and shares of its common stock. The maximum aggregate success payments that could be payable by the Company is \$31.3 million (after termination of the Broad agreement).

The success payments liability is stated at fair value and is considered Level 3 because its fair value measurement is based, in part, on significant inputs not observed in the market. The Company used a Monte Carlo simulation model, which models the value of the liability based on several key variables, including probability of event occurrence, timing of event occurrence, as well as the value of the Company's common stock. The Company also estimated the likelihood that it would maintain both the Harvard/Broad License Agreement and the Broad License Agreement based on its on-going research efforts.

The Company remeasured the liability at fair value with corresponding increases of \$10.0 million and \$9.7 million recorded to other expense for the three and six months ended June 30, 2021, respectively, and increases of \$0.1 million and less than \$0.1 million recorded to other expense for the three and six months ended June 30, 2020, respectively. No settlements of the success payment liability occurred during the three and six months ended June 30, 2021 and 2020. The Company will continue to adjust the success payment liability for changes in fair value until the earlier of the achievement or expiration of the obligation.

The primary inputs used in valuing (i) the success payments liability and (ii) the antidilution rights liability associated with the Company's realization of a certain valuation threshold through either a sale of the Company's preferred stock, an initial public offering, or a company sale at June 30, 2021 (only applicable to success payments liability) and December 31, 2020, were as follows:

	At June 30, 2021	At December 31, 2020
Fair value of common stock (per share)	\$ 60.25	\$ 8.24
Equity volatility	78 %	105 %
Cumulative probability of triggering event	n/a	70 %
Expected term (in years)	n/a	0.50

At December 31, 2020, the fair value of the common stock was determined by management with the assistance of an independent third-party valuation specialist using methods consistent with the AICPA Valuation Guide. The computation of equity volatility was estimated using available information about the historical volatility of stocks of similar publicly traded companies for a period matching the expected term assumption. In addition, the Company incorporated the timing and probability of future events in the calculation of liabilities. The Company also estimated the likelihood that it would maintain both the Harvard/Broad License Agreement and the Broad License Agreement based on its on-going research efforts. The Company applied a 90% probability of termination of the Broad License Agreement at December 31, 2020.

In February 2021, the Company provided written notice to Broad of its election to terminate the Broad License Agreement, which termination became effective in June 2021. As a result, the Company applied a 100% probability of termination for the Broad License Agreement at March 31, 2021 and June 30, 2021.

The reconciliation of changes in the fair value of financial instruments based on Level 3 inputs for the six months ended June 30, 2021 is as follows:

(in thousands)	Antidilution rights liability	Success payment liability	Total
Balance at December 31, 2020	\$ 6,916	\$ 2,806	\$ 9,722
Issuance of common stock	(32,490)	-	(32,490)
Changes in fair value	25,574	9,654	35,228
Balance at June 30, 2021	\$ -	\$ 12,460	\$ 12,460

The reconciliation of changes in the fair value of financial instruments based on Level 3 inputs for the six months ended June 30, 2020 is as follows:

(in thousands)	Preferred stock tranche liability	Antidilution rights liability	Success payment liability	Total
Balance at December 31, 2019	\$ 9,571	\$ 2,044	\$ 419	\$ 12,034
Issuance of Series A Preferred Stock	(7,064)	-	-	(7,064)
Issuance of common stock	-	(487)	-	(487)
Changes in fair value	(2,507)	1,745	17	(745)
Balance at June 30, 2020	\$ -	\$ 3,302	\$ 436	\$ 3,738

6. Accrued expenses

Accrued expenses consist of the following:

(in thousands)	June 30, 2021	December 31, 2020
Employee compensation and related benefits	\$ 1,517	\$ 1,636
Accrued external research and development expenses	3,262	4,827
Professional fees	1,161	303
Other	1,027	423
Total	\$ 6,967	\$ 7,189

7. Commitments

Operating leases

The Company leases its facilities under non-cancelable operating leases that expire at various dates beginning in July 2022. All of the Company's leases contain escalating rent clauses, which require higher rent payments in future years, and as such rent expense is recognized on a straight-lined basis. See Note 7, "Commitments," in the audited consolidated financial statements for the year ended December 31, 2020, and notes thereto, included in the Company's final prospectus for its IPO filed pursuant to Rule 424(b)(4) under the Securities Act with the SEC on June 17, 2021 for additional information regarding the Company's operating leases.

8. License agreements

The Company's significant license agreements are disclosed in Note 8, "License Agreements," in the audited consolidated financial statements for the year ended December 31, 2020, and notes thereto, included in the Company's final prospectus for its IPO filed pursuant to Rule 424(b)(4) under the Securities Act with the SEC on June 17, 2021. Since the date of those financial statements, there have been no changes to its license agreements, except as noted below.

Harvard/Broad license agreement and Broad license agreement

In March 2019, the Company simultaneously entered into the Harvard/Broad License Agreement and Broad License Agreement (the "license agreements") for certain base editing technologies pursuant to which the Company received exclusive, worldwide, sublicensable, royalty-bearing licenses under specified patent rights to develop and commercialize

licensed products and nonexclusive, worldwide, sublicensable, royalty-bearing licenses under certain patent rights to research and develop licensed products. The Company agreed to use commercially reasonable efforts to develop licensed products in accordance with the development plans, to introduce any licensed products that gain regulatory approval into the commercial market, to market licensed products that have gained regulatory approval following such introduction into the market, and to make licensed products that have gained regulatory approval reasonably available to the public. The term of the agreements will continue until the expiration of the last to expire valid claim. The Company may terminate either of the license agreements without cause upon four months' prior written notice to Harvard and Broad, unless terminated earlier. In February 2021, the Company provided written notice to Broad of its intent to terminate the Broad License Agreement, which termination was effective in June 2021.

As partial consideration for the rights granted under the Harvard/ Broad License Agreement and Broad License Agreement, the Company paid \$0.3 million in non-refundable upfront license fees and also issued 276,075 shares of its common stock with a fair value of \$0.3 million. Additional consideration under the license agreements is as follows:

Antidilution Rights—The initial shares of common stock issued to Harvard and Broad are subject to antidilution provisions as further described in Note 5, Fair value of financial instruments. The antidilution rights associated with the Company achieving a defined aggregate level of preferred stock financing were partially satisfied in 2019 and fully satisfied in 2020, which settlement amounts totaled \$0.1 million and \$0.5 million, respectively, and which amounts were settled through issuances of 121,411 and 187,867 shares of common stock, respectively. The remaining antidilution rights obligation was fully satisfied in the three months ended June 30, 2021 with the Company's initial public offering. The settlement amount totaled \$32.5 million, and was settled through issuance of 878,098 shares of common stock.

Success Payments—The Company is required to make success payments under the license agreements as further described in Note 5, Fair value of financial instruments. As of and for the three and six months ended June 30, 2021 and 2020, no success payments were paid or due.

Other Payments—The Company agreed to pay an annual license maintenance fee ranging from low-to-mid five figures to low six figures, depending on the particular calendar year, for each of the license agreements. The Company is responsible for the payment of certain patent prosecution and maintenance costs incurred by Harvard and Broad related to licensed patents. To the extent achieved, the Company is obligated to pay up to an aggregate of \$46.2 million and \$108 million in development and sales-based milestones, respectively. If the Company undergoes a change of control during the term of the license agreements, then certain of the milestone payments would be increased by a mid-double-digit percentage. To the extent there are sales of a licensed product, the Company is required to pay low single digit royalties on net sales, for each of the license agreements. The Company is entitled to certain reductions and offsets on these royalties with respect to a licensed product in a given country.

Verily agreement

The Company elected to terminate its collaboration agreement with Verily Life Sciences LLC ("Verily"), effective June 26, 2020, and has no outstanding amounts due or payable to Verily as of June 30, 2021. The Company did not record any amounts as research and development expense in the three and six months ended June 30, 2021 related to this agreement and recorded \$0.2 million and \$1.5 million as research and development expense in the three and six months ended June 30, 2020, respectively, related to this agreement.

Beam license agreement

In April 2019, the Company and Beam Therapeutics, Inc. ("Beam") entered into a collaboration and license agreement. As partial consideration for the license rights granted by Beam under this agreement, the Company paid a one-time, nonrefundable fee through issuing 276,075 shares of its common stock with a fair value of \$0.3 million. To the extent achieved, for each licensed product, the Company is also obligated to pay up to \$11.3 million in development and regulatory-based milestones and \$15.0 million in sales-based milestones. To the extent there are sales of a licensed product, the Company is required to pay low-to-mid single digit royalties on net sales. To the extent achieved, for each collaboration product outside of the United States, the Company is obligated to pay up to \$5.6 million in development and regulatory-based milestones and \$7.5 million in sales-based milestones. To the extent there are ex-U.S. sales of a collaboration product, the Company is required to pay low-to-mid single digit royalties on net sales.

The Company has not triggered any milestone payments pursuant to its arrangement with Beam, and no expense has been recorded for milestones as of June 30, 2021. To the extent there are sales of a delivery technology product, each party will pay the other party low-to-mid single digit royalties based on the annual aggregate worldwide net sales resulting from the sale of each delivery technology product of such paying party; provided, however, that such royalty payments will not apply to net sales of the collaboration products or licensed products. The Company concluded the receipt of any milestone or royalty payments under the agreement was not probable as of June 30, 2021.

Beam materials exchange letter agreement

In October 2020, the Company and Beam entered into a materials exchange agreement wherein the parties agreed that Beam would provide certain mRNA, gRNA, and protein to the Company and that the Company would provide certain gRNAs to Beam at an agreed upon price per each material provided.

For the three and six months ended June 30, 2021, the Company did not purchase any materials from Beam. For the three and six months ended June 30, 2020, the Company purchased \$0.0 million and \$0.2 million, respectively, as a charge to research and development expense related to materials purchased from Beam.

For the three and six months ended June 30, 2021, the Company recognized \$0.0 million and \$0.2 million, respectively, as a reduction to research and development expense related to reimbursements received for materials sold to Beam. During the three and six months ended June 30, 2020, the Company recognized \$0.0 million and less than \$0.1 million, respectively, as a reduction to research and development expense related to reimbursements received for materials sold to Beam.

Acuitas agreements

Development and option agreement

In December 2019, the Company and Acuitas Therapeutics, Inc. ("Acuitas") entered into a development and collaboration agreement, which agreement was amended and restated in October 2020. The Company agreed to reimburse Acuitas on a quarterly basis for its services performed related to the program activities based on an agreed upon number of fulltime employees committed to work on the program at an annual rate per employee, including reimbursement of reasonable external costs. These services commenced during 2020 and the Company recognized research and development expense during the three and six months ended June 30, 2021 of \$0.3 million and \$0.6 million, respectively, related to the reimbursement of research and development services provided by Acuitas and technology maintenance fees and \$0.3 million and \$0.8 million for the three and six months ended June 30, 2020, respectively. In 2020 upon the one-year anniversary of the agreement the Company had exercised one of its options to enter into a non-exclusive license agreement, as further described below.

License agreement

In October 2020, the Company paid Acuitas a non-refundable, upfront license fee of \$2.0 million (less a previously paid target reservation fee) to exercise an option with respect to a licensed product and a licensed genome target and entered into a non-exclusive, worldwide license with Acuitas, with a right to sub-license through multiple tiers, under the licensed LNP technology to research, develop and commercialize the licensed products using the LNP technology in connection with the PCSK9 gene target for all human therapeutic or prophylactic uses.

To the extent achieved, the Company is also obligated to pay up to an aggregate of \$9.8 million in clinical and regulatory milestones and \$9.5 million in sales-based milestones. The milestones have not been achieved and no expense has been recorded for these milestones as of June 30, 2021.

9. Preferred stock tranche liability

Included in the terms of the Series A Preferred Stock purchase agreement were certain tranche rights whereupon the Company is obligated to issue, and the Series A Preferred investors have the obligation to purchase 49,749,167 shares of Series A Preferred Stock at \$0.598 per share upon the Company achieving additional scientific and non-scientific milestones ("third tranche").

In March 2020, the board of directors agreed to waive the final remaining milestones and determined the third tranche milestones, as modified, were achieved. In March 2020, the Company settled the third tranche by issuing 49,749,167 shares of Series A Preferred Stock at a price of \$0.598 per share for gross proceeds of \$29.8 million.

10. Preferred and common stock

In January 2021, the Company issued 77,163,022 shares of Series B Preferred Stock at a price of \$1.2182 per share for gross proceeds of \$94.0 million. The Company incurred issuance costs in connection with this transaction of \$0.2 million.

In June 2021, the Company amended and restated its certificate of incorporation to authorize 5,000,000 shares of preferred stock, which shares of preferred stock are currently undesignated, and 200,000,000 shares of common stock, \$0.001 par value per share.

In June 2021, the Company completed its IPO, pursuant to which the Company issued and sold 16,141,157 shares of its common stock, including 2,105,368 shares pursuant to the full exercise of the underwriters' option to purchase additional shares, at a public offering price of \$19.00 per share, for aggregate gross proceeds of \$306.7 million. The Company

received approximately \$281.6 million in net proceeds, after deducting underwriting discounts and estimated offering expenses payable by the Company.

Upon the closing of the IPO, all outstanding shares of the Company's preferred stock automatically converted into 27,720,923 shares of the Company's common stock.

In June 2021, the Company issued 878,098 shares of its common stock to Harvard and Broad as final settlement of its antidilution rights obligation.

The holders of common stock are entitled to one vote for each share of common stock.

11. Stock-based compensation

The 2018 Equity Incentive Plan, or the 2018 Plan, adopted by the board of directors in August 2018 provided for the grant of qualified incentive stock options, non-statutory stock options, stock appreciation rights, restricted stock and restricted stock units to the Company's employees, officers, directors, advisors, and outside consultants for the issuance or purchase of shares of the Company's common stock. The maximum number of shares of common stock that were authorized for issuance under the 2018 Plan was 6,885,653.

In June 2021, the Company's board of directors adopted, and the Company's stockholders approved, the 2021 Stock Incentive Plan, or the 2021 Plan, which became effective on June 16, 2021. The 2021 Plan provides for grant of qualified and nonqualified stock options, stock appreciation rights, restricted and unrestricted stock and stock units, performance awards, and other share-based awards to the Company's employees, directors, advisors and outside consultants. Upon effectiveness of the 2021 Plan, the number of shares of common stock that was reserved for issuance under the 2021 Plan is the sum of: (1) 3,466,530; plus (2) the number of shares as is equal to the sum of (x) the number of shares of common stock reserved for issuance under the 2018 Plan that remained available for grant under the 2018 Plan on June 16, 2021 and (y) the number of shares of common stock subject to outstanding awards granted under the 2018 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; plus (3) an annual increase, to be added on the first day of each fiscal year, commencing on January 1, 2022 and continuing until, and including, January 1, 2031, equal to the lesser of (i) 5% of the number of shares of common stock outstanding on such date and (ii) the number of shares of common stock determined by our board of directors. As of June 30, 2021 the Company had reserved 4,632,042 shares of the Company's common stock for issuance of stock options and restricted stock, of which 4,167,523 remained outstanding for future grant under the 2021 Plan. Upon effectiveness of the 2021 Plan, the Company ceased granting additional awards under the 2018 Plan.

Stock-based compensation expense recorded as research and development and general and administrative expenses in the consolidated statements of operations and comprehensive loss is as follows:

(in thousands)	Three months ended		Six months ended June 30,	
	June 30,		2021	
	2021	2020	2021	2020
Research and development	\$ 708	\$ 59	\$ 1,021	\$ 120
General and administrative	643	41	1,000	75
Total stock-based compensation expense	\$ 1,351	\$ 100	\$ 2,021	\$ 195

Stock options

There were no stock options granted during the six months ended June 30, 2020. A summary of option activity during the six months ended June 30, 2021 was as follows:

	Number of options	Weighted average exercise price per share	Weighted average remaining contractual life (in years)	Aggregate intrinsic value ⁽²⁾ (in thousands)
Outstanding at December 31, 2020	3,888,823	\$ 2.13		
Granted	2,224,012	10.61		
Exercised	(352,212)	1.49		
Forfeited	(39,636)	2.54		
Outstanding at June 30, 2021	5,720,987	\$ 5.48	9.1	\$ 313,348
Exercisable at June 30, 2021	817,954	\$ 1.51	8.0	\$ 48,048
Expected to vest after June 30, 2021 ⁽¹⁾	4,903,033	\$ 6.14	9.2	\$ 265,300

- (1) This represents the number of unvested options outstanding as of June 30, 2021 that are expected to vest in the future.
- (2) The aggregate intrinsic value is calculated as the difference between the exercise price of the underlying options and the estimated fair value of the common stock for the options that were in the money as of June 30, 2021.

As of June 30, 2021, there was \$25.9 million of unrecognized compensation cost related to unvested stock options, which is expected to be recognized over a weighted-average period of approximately 3.2 years.

Restricted stock

A summary of the status of and change in unvested restricted stock as of June 30, 2021 was as follows:

	Shares		Weighted-average grant date fair value per share
Unvested as of December 31, 2020	537,633	\$	0.0028
Vested	(268,817)	\$	0.0028
Unvested as of June 30, 2021	268,816	\$	0.0028

At June 30, 2021, there was less than \$0.1 million of unrecognized stock-based compensation expense related to restricted stock that is expected to vest. These costs are expected to be recognized over a weighted-average remaining vesting period of less than 1.0 year.

2021 Amended and Restated Employee Stock Purchase Plan

In June 2021, the board of directors adopted, and the Company's stockholders approved, the 2021 Employee Stock Purchase Plan, or the ESPP, which became effective on June 16, 2021. The Company has initially reserved 433,316 shares of common stock for sale under the ESPP. The aggregate number of shares reserved for sale under the ESPP will increase automatically on the first day of each fiscal year commencing on January 1, 2022 through January 1, 2031, by the number of shares equal to the least of (a) 1,083,290 shares, (b) 1% of the total outstanding shares of common stock on such date, and (c) a number of shares as may be determined by the board of directors in any particular year. The first offering period under the ESPP commenced on June 16, 2021 and will end on December 13, 2021. As of June 30, 2021, no shares have been purchased by employees under the ESPP.

12. Net loss per share attributable to common stockholders

The Company's potential dilutive securities, which include convertible preferred stock, unvested restricted stock and common stock options, have been excluded from the computation of diluted net loss per share as the effects would be anti-dilutive. 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 period end, from the computation of diluted net loss per share attributable to common stockholders for the period indicated because including them would have had an anti-dilutive effect:

	As of June 30,	
	2021	2020
Convertible preferred stock	-	19,387,544
Unvested restricted stock	268,816	806,451
Outstanding options to purchase common stock	5,720,987	1,927,030
Total	5,989,803	22,121,025

As part of the license agreements with Harvard and Broad, the Company is required to make success payments. The Company may elect to make these payments by issuing shares of the Company's common stock. As of June 30, 2021, no success payments have been paid or were due relating to these license agreements.

13. Income taxes

Deferred tax assets and deferred tax liabilities are recognized based on temporary differences between the financial reporting and tax basis of assets and liabilities using statutory rates. A valuation allowance is recorded against deferred tax assets if it is more likely than not that some or all of the deferred tax assets will not be realized. Due to the uncertainty

surrounding the realization of the favorable tax attributes in future tax returns, the Company has recorded a full valuation allowance against the Company's otherwise recognizable net deferred tax assets.

14. Related party transactions

For the three and six months ended June 30, 2021 and 2020, the Company made payments of \$0.1 million and \$0.2 million, respectively, to four of the founder shareholders for scientific consulting and other expenses. All five founders also vested in a total of 268,817 shares of restricted stock for the six months ended June 30, 2021.

An executive of Beam is a board member of the Company. In October 2020, the Company and Beam entered into a materials exchange agreement wherein the parties agreed that Beam would provide certain mRNA, gRNA, and protein to the Company and that the Company would provide certain gRNAs to Beam at an agreed upon price per each material provided. For the three and six months ended June 30, 2021, the Company recognized \$0.0 million and \$0.2 million, respectively, as a reduction to research and development expense related to reimbursements received for materials sold to Beam. See Note 8, License agreements.

An officer of the Company is affiliated with Massachusetts General Hospital ("MGH") as a physician. In February 2019 and November of 2019, the Company entered into an Option License Agreement and Patent License Agreement, respectively, with MGH. As part of the agreement, the Company recognizes an annual license fee of \$0.1 million.

An executive of Broad was a board member of the Company. The board member resigned, effective May 2021. In March 2019, the Company simultaneously entered into the Harvard/Broad License Agreement and Broad License Agreement for certain base editing technologies pursuant to which the Company received exclusive, worldwide, sublicensable, royalty-bearing licenses under specified patent rights to develop and commercialize licensed products and nonexclusive, worldwide, sublicensable, royalty-bearing licenses under certain patent rights to research and develop licensed products. Additional consideration under the license agreements include antidilution rights and success payments. See Note 8, License agreements.

15. Subsequent events

The Company considers events or transactions that occur after the balance sheet date but prior to the issuance of the financial statements to provide additional evidence relative to certain estimates or to identify matters that require additional disclosure.

In July 2021, the Company amended an existing sublease to extend the term for four months, resulting in an additional commitment of approximately \$0.7 million.

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 the related notes to those statements included elsewhere in this Quarterly Report on Form 10-Q and our final prospectus for our initial public offering filed pursuant to Rule 424(b)(4) under the Securities Act of 1933, as amended, or the Securities Act, with the Securities and Exchange Commission, or SEC, on June 17, 2021. In addition to historical financial information, the following discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of many factors, including those discussed in "Risk Factors" in Part II, Item 1A. You should carefully read the section entitled "Risk Factors" to gain an understanding of the important factors that could cause actual results to differ materially from our forward- looking statements.

Overview

We are a genetic medicines company pioneering a new approach to the care of cardiovascular disease, or CVD, transforming treatment from chronic management to single-course gene editing medicines. Despite advances in treatment over the last 50 years, CVD remains the leading cause of death worldwide. The current paradigm of chronic care is fragile—requiring rigorous patient adherence, extensive healthcare infrastructure and regular healthcare access—and leaves many patients without adequate care. Our goal is to disrupt the chronic care model for CVD by providing a new therapeutic approach with single-course in vivo gene editing treatments focused on addressing the root causes of this highly prevalent and life-threatening disease. Our initial two programs target PCSK9 and ANGPTL3, respectively, genes that have been extensively validated as targets for lowering blood lipids, such as low-density lipoprotein cholesterol, or LDL-C. We believe that single-course treatments could provide substantial health benefits that are sustained throughout the lifetimes of patients with or at risk for atherosclerotic cardiovascular disease, or ASCVD, the most common form of CVD.

We were incorporated in March 2018 and commenced operations shortly thereafter. Since our inception, we have devoted substantially all of our resources to building our gene editing capabilities and advancing development of our portfolio of programs, establishing and protecting our intellectual property, conducting research and development activities, organizing and staffing our company, business planning, raising capital and providing general and administrative support for these operations. To date, we have financed our operations primarily through the sales of our preferred stock and, most recently, common stock in our initial public offering, or IPO.

On June 21, 2021, we completed our IPO in which we issued and sold an aggregate of 16,141,157 shares of our common stock, including 2,105,368 shares of common stock sold pursuant to the underwriters' full exercise of their option to purchase additional shares, at a public offering price of \$19.00 per share, for aggregate net proceeds of \$281.6 million, after deducting underwriting discounts and estimated offering expenses payable by us. Upon completion of the IPO, all 256,682,054 shares of outstanding convertible preferred stock automatically converted into 27,720,923 shares of common stock. Through June 30, 2021, we had raised an aggregate of \$523.2 million in gross proceeds from the sale of our preferred stock in private placements and common stock in our IPO.

We are a development-stage company, and all of our programs are at a preclinical stage of development. To date, we have not generated any revenue and do not expect to generate revenue from the sale of products for the foreseeable future. Since our inception, we have incurred significant operating losses. Our net losses for the three and six months ended June 30, 2021 were \$53.0 million and \$66.2 million, respectively, and \$7.6 million and \$13.2 million for the three and six months ended June 30, 2020, respectively. Our net loss for the year ended December 31, 2020 was \$45.7 million. As of June 30, 2021, we had an accumulated deficit of \$132.8 million.

Since our inception, we have incurred significant operating losses. We expect to continue to incur significant expenses and increasing operating losses in connection with ongoing development activities related to our portfolio of programs as we continue our preclinical development of product candidates; advance these product candidates toward clinical development; further develop our base editing technology and manufacturing capabilities; seek to discover and develop additional product candidates; maintain, expand enforcement, defend, and protect our intellectual property portfolio; hire research and development and clinical personnel; ultimately establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval; establish a commercial manufacturing source and secure supply chain capacity sufficient to provide commercial quantities of any product candidates for which we may obtain regulatory approval; and add operational, legal, compliance, financial and management information systems and personnel to support our research, product development, future commercialization efforts and operations as a public company.

As a result, we will need substantial additional funding to support our continuing operations and pursue our strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of equity offerings, debt financings and other sources of capital, which may include collaborations or licensing arrangements with other companies or other strategic transactions. If we are unable to raise capital or obtain adequate funds when needed or on acceptable terms, we may be required to delay, limit, reduce or terminate our research and development programs or any future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve profitability. Even if we are able to generate revenue from product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

As of June 30, 2021, we had cash, cash equivalents and marketable securities of \$417.6 million. We believe that our existing cash, cash equivalents and marketable securities will enable us to fund our operating expenses and capital expenditure requirements into 2024. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. To finance our operations beyond that point we will need to raise additional capital, which cannot be assured. See "Liquidity and capital resources."

Impact of COVID-19 on our business

In March 2020, COVID-19 was declared a global pandemic by the World Health Organization and to date, the COVID-19 pandemic continues to present a substantial public health and economic challenge around the world. The length of time and full extent to which the COVID-19 pandemic may directly or indirectly impact our business, results of operations and financial condition will depend on future developments that are highly uncertain, subject to change and difficult to predict. We, our contract manufacturing organizations, or CMOs, and our contract research organizations, or CROs, experienced temporary reductions in the capacity to undertake research-scale production and to execute some preclinical studies. While these operations have since normalized, we, together with our CMOs and CROs, are closely monitoring the impact of the COVID-19 pandemic on these operations.

We also plan to continue to closely monitor the ongoing impact of the COVID-19 pandemic on our employees and our other business operations. In an effort to provide a safe work environment for our employees, we have, among other things, increased the cadence of sanitization of our office and lab facilities, implemented various social distancing measures in our offices and labs including replacing all in-person meetings with virtual interactions, and are providing personal protective equipment for our employees present in our office and lab facilities. We are continuing to monitor the impact and effects of the COVID-19 pandemic and our response to it, and 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.

While the COVID-19 pandemic did not significantly impact our business or results for the three and six months ended June 30, 2021 and 2020, the length and extent of the pandemic, its consequences, and containment efforts will determine the future impact on our operations and financial condition.

License and collaboration agreements

We have obligations under various license and collaboration agreements to make potentially significant milestone and success payments in the future and to pay royalties on sales of any product candidates covered by those agreements that eventually achieve regulatory approval and commercialization. For information regarding these agreements, see Note 8, License agreements to our condensed consolidated financial statements included in this Quarterly Report.

Components of our results of operations

Revenue

To date, we have not generated any revenue. We do not expect to generate any revenue from the sale of products in the near future and unless and until we successfully complete development and obtain regulatory approval for one or more of our product candidates. If our development efforts for our product candidates are successful and result in regulatory approval or we successfully enter into license or collaboration agreements with third parties, we may generate revenue in the future from product sales, payments from third-party collaboration or license agreements, or any combination thereof.

Operating expenses

Research and development expenses

Research and development expenses consist of costs incurred in performing research and development activities, which include:

- the cost to obtain and maintain licenses to intellectual property, such as those with the President and Fellows of Harvard College, or Harvard, The Broad Institute, Inc., or Broad, Beam Therapeutics Inc., or Beam, Acuitas Therapeutics, Inc., or Acuitas, and formerly Verily Life Sciences LLC (which agreement was terminated effective June 26, 2020), and related future payments should certain development and regulatory milestones be achieved;
- personnel-related expenses, including salaries, bonuses, benefits and stock-based compensation for employees engaged in research and development functions;
- expenses incurred in connection with the discovery and preclinical development of our research programs, including under agreements with third parties, such as consultants, contractors and CROs;
- the cost of developing and validating our manufacturing process for use in our preclinical studies and future clinical trials, including the cost of raw materials used in our research and development activities;
- the cost of laboratory supplies and research materials; and
- facilities, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities and insurance.

We expense research and development costs as incurred. Nonrefundable 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 benefits are consumed.

In the early phases of development, our research and development costs are often devoted to proof-of-concept studies that are not necessarily allocable to a specific target; therefore, we have not yet begun tracking our expenses on a program-by-program basis.

Research and development activities are central to our business model. We expect that our research and development expenses will continue to increase for the foreseeable future as we advance our programs and product candidates into and through clinical development, and as we continue to develop additional product candidates. We also expect our discovery research efforts and our related personnel costs will increase and, as a result, we expect our research and development expenses, including costs associated with stock-based compensation, will increase above historical levels. In addition, we may incur additional expenses related to milestone and royalty payments payable to third parties with whom we may enter into license, acquisition and option agreements to acquire the rights to future product candidates.

At this time, we cannot reasonably estimate or know the nature, timing and costs of the efforts that will be necessary to complete the preclinical and clinical development of, and obtain regulatory approval for, any of our product candidates or programs. 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 preclinical and clinical development activities;
- the number and scope of preclinical and clinical programs we decide to pursue;
- raising additional funds necessary to complete preclinical and clinical development of our product candidates;
- the timing of filing and acceptance of investigational new drug applications, or INDs, or comparable foreign applications that allow commencement of future clinical trials for our product candidates;
- the successful initiation, enrollment and completion of clinical trials;
- 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 in the intended patient populations of any product candidates we may develop;
- our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize, our product candidates for the expected indications and patient populations;
- our ability to hire and retain key research and development personnel;
- the costs associated with the development of any additional product candidates we develop or acquire through collaborations;

- our ability to establish and maintain agreements with third-party manufacturers for clinical supply for our clinical trials and commercial manufacturing, if our product candidates are approved;
- the terms and timing of any existing or future collaboration, license or other arrangement, including the terms and timing of any milestone payments thereunder;
- our ability to establish and obtain intellectual property protection and regulatory exclusivity for our product candidates and enforce and defend our intellectual property rights and claims;
- our ability to commercialize products, if and when approved, whether alone or in collaboration with others;
- our ability to maintain a continued acceptable safety, tolerability and efficacy profile of our product candidates following approval; and
- the effects of the COVID-19 pandemic.

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

General and administrative expenses

General and administrative expenses consist primarily of personnel-related costs, including salaries, benefits and stock-based compensation, for personnel in our executive, intellectual property, business development, and administrative functions. General and administrative expenses also include legal fees relating to intellectual property and corporate matters, professional fees for accounting, auditing, tax and consulting services, insurance costs, travel, and direct and allocated facility-related expenses and other operating costs.

We anticipate that our general and administrative expenses will increase in the future to support increased research and development activities. We also expect to incur increased costs associated with being a public company, including costs of accounting, audit, legal, regulatory and tax-related services associated with maintaining compliance with Nasdaq and SEC requirements, director and officer insurance costs, and investor and public relations costs.

Other income (expense)

Change in fair value of preferred stock tranche liability

Change in fair value of preferred stock tranche liability consists primarily of remeasurement gains or losses associated with changes in the fair value of the tranche rights associated with our Series A Preferred Stock. The preferred stock tranche liability was settled as of March 31, 2020, and therefore, there will be no further remeasurement.

Change in fair value of antidilution rights liability

Change in fair value of antidilution rights liability consists of remeasurement gains or losses associated with changes in the antidilution rights liability associated with our license agreements with Harvard and Broad, or the Harvard/Broad License Agreement, and Broad, or the Broad License Agreement.

The antidilution rights represent the obligation to issue additional shares of common stock to Harvard and Broad following the completion of preferred stock financings and other equity financings, which was fully satisfied upon the closing of our IPO. At the inception of the agreements, the liability for the antidilution rights was recorded at fair value with the cost recorded as research and development expense and will be remeasured at each reporting period with changes recorded in other income (expense) while the instruments are outstanding.

The antidilution rights liability was partially satisfied in 2019 and 2020 and was fully satisfied during the three months ended June 30, 2021 with the issuance of an aggregate of an additional 878,098 shares of common stock upon the closing of our IPO.

Change in fair value of success payment liability

We are also obligated to pay to Harvard and Broad tiered success payments in the event our average market capitalization exceeds specified thresholds ascending from a high nine-digit dollar amount to \$10.0 billion for a specified period of time, or sale of our company for consideration in excess of those thresholds. In the event of a change of control of our company or a sale of our company, we are required to pay any related success payment in cash within a specified period following such event. Otherwise, the success payments may be settled at our option in either cash or shares of our common stock, or a combination of cash and shares of our common stock. The maximum aggregate success payments that could be payable by us is \$31.3 million. At inception of the agreements, the success payment liabilities were recorded

at fair value with the cost recorded as research and development expense and will be remeasured at each reporting period with charges recorded in other income (expense) while the instrument is outstanding.

Depending on our valuation, the fair value of the antidilution rights and success payment liabilities, and the corresponding changes in fair value that we record in our statements of operations, could fluctuate significantly from period to period.

Interest and other income (expense), net

Interest and other income primarily consisted of interest earned on our marketable securities and other miscellaneous income and expenses unrelated to our core operations.

Income tax

During the three and six months ended June 30, 2021 and 2020, we recorded a full valuation allowance on federal and state deferred tax assets since management does not forecast that we will be in a taxable position in the near future.

Results of operations

Comparison of three months ended June 30, 2021 and 2020

The following table summarizes our results of operations for the three months ended June 30, 2021 and 2020:

(in thousands)	Three months ended		Change
	2021	June 30, 2020	
Operating expenses:			
Research and development	\$ 13,423	\$ 5,654	\$ 7,769
General and administrative	3,541	1,032	2,509
Total operating expenses	\$ 16,964	\$ 6,686	\$ 10,278
Other income (expense):			
Change in fair value of antidilution rights liability	(25,970)	(863)	(25,107)
Change in fair value of success payment liability	(10,036)	(81)	(9,955)
Interest income and other income (expense), net	5	50	(45)
Total other income (expense)	\$ (36,001)	\$ (894)	\$ (35,107)
Net loss	\$ (52,965)	\$ (7,580)	\$ (45,385)

Research and development expenses

The following table summarizes our research and development expenses for the three months ended June 30, 2021 and 2020:

(in thousands)	Three months ended	
	2021	June 30, 2020
Employee-related expenses	\$ 4,113	1,520
Raw material costs and external expenses associated with manufacturing activities, including third-party contract manufacturing organizations, or CMOs	2,990	-
External expenses associated with preclinical studies performed by outside consulting services, including third-party contract research organizations, or CROs	3,681	2,452
Lab supplies used in research and development activities	1,138	563
Facility-related costs (including depreciation)	821	474
License and milestone payments	25	292
Other research and development costs	655	353
Total research and development expenses	\$ 13,423	\$ 5,654

Research and development expenses were \$13.4 million for the three months ended June 30, 2021, compared to \$5.7 million for the three months ended June 30, 2020. The increase of approximately \$7.8 million was primarily due to the following:

- an increase in raw material costs and external expenses associated with developing and validating our manufacturing activities, including third-party CMOs, for use in our preclinical studies and future clinical trials of \$3.0 million;

- an increase in external expenses associated with preclinical studies (primarily animal-study costs) performed by outside consulting services, including third-party CROs, of \$1.2 million;
- an increase in personnel-related costs of \$2.6 million driven by an increase in headcount of employees involved in research and development activities;
- an increase in lab supplies of \$0.6 million due to increased headcount and company growth;
- an increase in facility-related costs (including depreciation) and other allocated miscellaneous expenses of \$0.4 million due to increased investment in research and development;
- an increase in other research and development costs of \$0.3 million, primarily due to an increase in professional fees and consulting fees in support of increased investment in research and development activities; and
- a decrease in research and development expense attributed to license and milestone payments of \$0.3 million.

We expect our research and development expenses will continue to increase as we continue our current research programs, initiate new research programs, continue our preclinical development of product candidates and conduct future clinical trials for any of our product candidates.

General and administrative expenses

General and administrative expenses were \$3.5 million for the three months ended June 30, 2021, compared to \$1.0 million for the three months ended June 30, 2020. The increase of approximately \$2.5 million was primarily attributable to the following:

- an increase of \$1.7 million in personnel, facility and other expenses stemming from an increase in headcount to support our growth;
- an increase of \$0.3 million in legal and professional service fees, primarily due to increased professional fees for audit, tax and consulting services; and
- an increase in other miscellaneous expenses of \$0.5 million.

Other income (expense)

Change in fair value of antidilution rights liability

The change in fair value for the antidilution rights liability was primarily due to the settlement of the liability during the three months ended June 30, 2021 with the issuance of 878,098 shares of our common stock. The settlement amount was \$32.5 million and resulted in a fair value adjustment to the antidilution rights liability of \$26.0 million due to an increase in the fair value of the shares being issued upon settlement.

Change in fair value of success payments liability

The change in fair value for the success payments liability was primarily due to the increase in the fair value of our common stock, which resulted in a fair value adjustment of \$10.0 million to other expense during the three months ended June 30, 2021. The success payment obligations are still outstanding as of June 30, 2021 and will continue to be revalued at the end of each reporting period.

Interest and other income (expense), net

The decrease of less than \$0.1 million in the three months ended June 30, 2021 compared to the three months ended June 30, 2020 was attributable to lower interest rates on our investments and an increase in loss on settlement of invoices in foreign currency compared to 2020.

Comparison of six months ended June 30, 2021 and 2020

The following table summarizes our results of operations for the six months ended June 30, 2021 and 2020:

(in thousands)	Six months ended		
	June 30,		Change
	2021	2020	
Operating expenses:			
Research and development	\$ 24,768	\$ 12,177	\$ 12,591
General and administrative	6,257	1,878	4,379
Total operating expenses	\$ 31,025	\$ 14,055	\$ 16,970
Other income (expense):			
Change in fair value of preferred stock tranche liability	-	2,507	(2,507)
Change in fair value of antidilution rights liability	(25,574)	(1,745)	(23,829)
Change in fair value of success payment liability	(9,654)	(17)	(9,637)
Interest income and other income (expense), net	25	127	(102)
Total other income (expense)	\$ (35,203)	\$ 872	\$ (36,075)
Net loss	\$ (66,228)	\$ (13,183)	\$ (53,045)

Research and development expenses

The following table summarizes our research and development expenses for the six months ended June 30, 2021 and 2020:

(in thousands)	Six months ended	
	2021	2020
Employee-related expenses	\$ 6,806	\$ 2,894
Raw material costs and external expenses associated with manufacturing activities, including third-party CMOs	5,385	-
External expenses associated with preclinical studies performed by outside consulting services, including third-party CROs	7,691	5,243
Lab supplies used in research and development activities	1,869	958
Facility-related costs (including depreciation)	1,600	831
License and milestone payments	80	1,622
Other research and development costs	1,337	629
Total research and development expenses	\$ 24,768	\$ 12,177

Research and development expenses were \$24.8 million for the six months ended June 30, 2021, compared to \$12.2 million for the six months ended June 30, 2020. The increase of \$12.6 million was primarily due to the following:

- an increase in raw material costs and external expenses associated with developing and validating our manufacturing activities, including third-party CMOs, for use in our preclinical studies and future clinical trials of \$5.4 million;
- an increase in external expenses associated with preclinical studies (primarily animal-study costs) performed by outside consulting services, including third-party CROs, of \$2.4 million;
- an increase in personnel-related costs of \$3.9 million driven by an increase in headcount of employees involved in research and development activities;
- an increase in facility-related costs (including depreciation) and other allocated miscellaneous expenses of \$0.8 million due to increased investment in research and development;
- an increase in lab supplies of \$0.9 million due to the increased headcount and company growth;
- an increase in other research and development costs of \$0.7 million, primarily due to an increase in professional fees and consulting fees in support of increased investment in research and development activities; and
- a decrease in research and development expense attributed to license and milestone payments of \$1.5 million, primarily due to a \$1.0 million milestone payment and \$0.5 million payment relating to a collaboration agreement both incurred during the six months ended June 30, 2020.

We expect our research and development expenses will continue to increase as we continue our current research programs, initiate new research programs, continue our preclinical development of product candidates and conduct future clinical trials for any of our product candidates.

General and administrative expenses

General and administrative expenses were \$6.3 million for the six months ended June 30, 2021, compared to \$1.9 million for the six months ended June 30, 2020. The increase of \$4.4 million was primarily attributable to the following:

- an increase of \$2.9 million in personnel, facility and other expenses stemming from an increase in headcount to support our growth;
- an increase of \$0.8 million in legal and professional service fees, primarily due to increased professional fees for audit, tax and consulting services;
- an increase in facility related costs of \$0.2 million; and
- an increase in other miscellaneous expenses of \$0.5 million.

Other income (expense)

Change in fair value of preferred stock tranche liability

The change in fair value of the preferred stock tranche liability was due to the modification of the remaining milestones and subsequent settlement of the preferred stock tranche liability in March 2020, resulting in the issuance of Series A Preferred Stock.

Change in fair value of antidilution rights liability

The change in fair value for the antidilution rights liability was primarily due to the settlement of the liability during the six months ended June 30, 2021 with the issuance of 878,098 shares of our common stock. The settlement amount was \$32.5 million and resulted in a fair value adjustment to the antidilution rights liability of \$25.6 million due to an increase in the fair value of the shares being issued upon settlement.

Change in fair value of success payments liability

The change in fair value for the success payments liability was primarily due to the increase in the fair value of our common stock which resulted in a fair value adjustment of \$9.7 million to other expense during the six months ended June 30, 2021. The success payment obligations are still outstanding as of June 30, 2021 and will continue to be revalued at the end of each reporting period.

Interest and other income (expense), net

The decrease of \$0.1 million in the six months ended June 30, 2021 compared to the six months ended June 30, 2020 was attributable to lower interest rates on our investments and an increase in loss on settlement of invoices in foreign currency compared to 2020.

Liquidity and capital resources

Sources of liquidity and capital

Since our inception in 2018, 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, clinical development of our programs. To date, we have funded our operations primarily through equity offerings. Through June 30, 2021, we had raised an aggregate of \$523.2 million in gross proceeds from sales of our preferred stock in private placements and common stock in our IPO. As of June 30, 2021, we had \$417.6 million in cash, cash equivalents and marketable securities.

In June 2021, we completed our IPO in which we issued 16,141,157 shares of our common stock, including 2,105,368 shares of common stock sold pursuant to the underwriters' full exercise of their option to purchase additional shares, at a public offering price of \$19.00 per share. We received net proceeds from our IPO of \$281.6 million, after deducting underwriting discounts and offering expenses payable by us. In June 2021, we issued 878,098 shares of our common stock to Harvard and Broad as final settlement of the antidilution rights liability.

Cash flows

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

(in thousands)	Six months ended June 30,	
	2021	2020
Cash used in operating activities	\$ (28,482)	\$ (13,966)
Cash provided by (used in) investing activities	30,203	(60,296)
Cash provided by financing activities	376,732	92,619
Net increase in cash, cash equivalents and restricted cash	\$ 378,453	\$ 18,357

Operating activities

For the six months ended June 30, 2021, net cash used in operating activities was \$28.5 million, consisting primarily of our net loss of \$66.2 million and a decrease in our operating assets and liabilities of \$0.5 million. These amounts were partially offset by the following non-cash changes: \$25.6 million associated with the fair value change in antidilution rights liability, \$9.7 million associated with the fair value change in success payments liability, stock-based compensation of \$2.0 million, depreciation expense of \$0.7 million and amortization of investment premiums of \$0.4 million.

For the six months ended June 30, 2020, net cash used in operating activities was \$14.0 million, consisting primarily of our net loss of \$13.2 million and non-cash items of \$2.5 million, primarily associated with the fair value change in the preferred stock tranche liability and a decrease in operating assets and liabilities of \$0.8 million. These amounts were partially offset by the following non-cash changes: change in fair value of antidilution rights liability of \$1.7 million, depreciation expense of \$0.5 million, stock-based compensation of \$0.2 million and amortization of investment premiums of \$0.1 million.

Investing activities

For the six months ended June 30, 2021, net cash provided by investing activities was \$30.2 million and consisted of maturities of marketable securities of \$43.8 million, offset partially by purchases of property and equipment of \$2.4 million, primarily related to lab equipment, and purchases of marketable securities of \$11.2 million.

For the six months ended June 30, 2020, net cash used in by investing activities was \$60.3 million and consisted of purchases of marketable securities of \$73.1 million and purchases of property and equipment of \$1.5 million, offset partially by maturities of marketable securities of \$14.3 million.

Financing activities

For the six months ended June 30, 2021, net cash provided by financing activities was \$376.7 million, consisting primarily of the net proceeds from the issuance of Series B Preferred Stock of \$93.8 million, net proceeds from our IPO of \$285.2 million and proceeds from exercises of stock options of \$0.5 million, offset partially by payment of IPO expenses of \$2.8 million.

For the six months ended June 30, 2020, net cash provided by financing activities was \$92.6 million, received as net proceeds from the issuance of Series A Preferred Stock and Series A-2 Preferred Stock.

Funding requirements

Our operating expenses and future funding requirements are expected to increase substantially as we continue to advance our portfolio of programs.

Specifically, our expenses will increase if and as we:

- continue our current research programs and our preclinical development of product candidates from our current research programs;
- seek to identify additional research programs and additional product candidates;
- advance our existing and future product candidates into clinical development;
- initiate preclinical studies and clinical trials for any additional product candidates we identify and develop or expand development of existing programs into additional patient populations;
- maintain, expand, enforce, defend and protect our intellectual property portfolio and provide reimbursement of third-party expenses related to our patent portfolio;

- seek regulatory and marketing approvals for any of our product candidates that we develop;
- seek to identify, establish and maintain additional collaborations and license agreements, and the success of those collaborations and license agreements;
- make milestone payments to Beam under our collaboration and license agreement with Beam, to Acuitas under our non-exclusive license agreement with Acuitas, under the Harvard/ Broad License Agreements, and under any additional future collaboration or license agreements that we obtain;
- ultimately establish a sales, marketing, and distribution infrastructure to commercialize any drug products for which we may obtain marketing approval, either by ourselves or in collaboration with others;
- generate revenue from commercial sales of product candidates we may develop for which we receive marketing approval;
- further develop our base editing technology;
- hire additional personnel including research and development, clinical and commercial personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development;
- acquire or in-license products, intellectual property, medicines and technologies;
- satisfy any post-marketing requirements, such as a cardiovascular outcomes trial;
- establish commercial-scale current good manufacturing practices, or cGMP, capabilities through a third-party or our own manufacturing facility; and
- operate as a public company.

As of June 30, 2021, we had cash, cash equivalents and marketable securities of \$417.6 million. We believe our existing cash, cash equivalents and marketable securities, will enable us to fund our operating expenses and capital expenditure requirements into 2024. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect.

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

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

Adequate additional funds may not be available to us on acceptable terms, or at all. We do not have any source of committed external funds. Market volatility resulting from the COVID-19 pandemic or other factors could also adversely impact our ability to access capital as and when needed. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders 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 or declaring dividends and may require the issuance of warrants, which could potentially dilute the ownership interest of our stockholders.

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

Contractual obligations

During the three months ended June 30, 2021, there were no material changes to our contractual obligations and commitments from those described under the heading “Management’s Discussion and Analysis of Financial Condition and Results of Operations—Contractual Obligations and Commitments” in our final prospectus for our IPO filed pursuant to Rule 424(b)(4) under the Securities Act with the SEC on June 17, 2021.

Emerging growth company and smaller reporting company status

As an emerging growth company, or EGC, under the Jumpstart Our Business Startups Act of 2012, or JOBS Act, we may delay the adoption of certain accounting standards until such time as those standards apply to private companies. Other exemptions and reduced reporting requirements under the JOBS Act for EGCs include presentation of only two years of audited financial statements in a registration statement for an initial public offering, or IPO, an exemption from the requirement to provide an auditor’s report on internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act of 2002, an exemption from any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation, and less extensive disclosure about our executive compensation arrangements.

In addition, the JOBS Act provides that an EGC can take advantage of an extended transition period for complying with new or revised accounting standards. This provision allows an EGC to delay the adoption of some accounting standards until those standards would otherwise apply to private companies. We have elected to use this extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date we (i) are no longer an emerging growth company or (ii) affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act. As a result, our consolidated financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates.

We may remain classified as an EGC until December 31, 2026, although if the market value of our common stock that is held by non-affiliates exceeds \$700 million as of any June 30 after we have filed an Annual Report on Form 10-K or if we have annual gross revenues of \$1.07 billion or more in any fiscal year, we would cease to be an emerging growth company as of December 31 of the applicable year. We also would cease to be an EGC if we issue more than \$1 billion of non-convertible debt over a three-year period.

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

Critical accounting policies and significant judgments

This management’s discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which we have prepared in accordance with U.S. generally accepted accounting principles. The preparation of these financial statements and related disclosures requires us to make estimates, judgments and assumptions that affect the reported amounts of assets, liabilities, 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 June 30, 2021, there were no material changes to our critical accounting policies from those described in our final prospectus for our IPO filed pursuant to Rule 424(b)(4) under the Securities Act with the SEC on June 17, 2021.

Off-balance sheet arrangements

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

Recently issued accounting pronouncements

See Note 2, “Summary of significant accounting policies – Recently issued accounting pronouncements” to our consolidated financial statements included in the final prospectus for our IPO filed pursuant to Rule 424(b)(4) under the Securities Act with the SEC on June 17, 2021.

Item 3. Quantitative and qualitative disclosures about market risk

We are exposed to market risk related to changes in interest rates. As of June 30, 2021, we had cash and equivalents of \$387.4 million, which consisted of standard checking accounts and money market account funds that invest primarily in the U.S. government-backed securities and treasuries. In addition, as of June 30, 2021, we also had marketable securities of \$30.2 million, which consist of U.S. treasury securities and agency securities. Interest income is sensitive to change in the general level of interest rates, however, due to the short-term maturities of our cash equivalents and the low risk profile of our marketable securities, an immediate 10% change in interest rates would not have a material effect on the fair market value of our cash equivalents and marketable securities.

We are not currently exposed to significant market risk related to changes in foreign currency exchange rates; however, we do contract with vendors that are located outside of the United States and may be subject to fluctuations in foreign currency rates. We may enter into additional contracts with vendors located outside of the United States in the future, which may increase our foreign currency exchange risk.

We do not believe that inflation had a material effect on our business, financial condition or results of operations during the three and six months ended June 30, 2021.

Item 4. Controls and procedures

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and our principal financial officer, evaluated, as of the end of the period covered by this Quarterly Report on Form 10-Q, the effectiveness of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act. The term “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under 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 our disclosure controls and procedures as of June 30, 2021, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures as of such date were effective at the reasonable assurance level.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the quarter ended June 30, 2021 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Part II – Other Information

Item 1. Legal proceedings

We are currently not a party to any material legal proceedings.

Item 1A. Risk factors

Our future operating results could differ materially from the results described in this Quarterly Report on Form 10-Q due to the risks and uncertainties described below. You should consider carefully the following information about risks below in evaluating our business. If any of the following risks actually occur, our business, financial conditions, results of operations and future growth prospects would likely be materially and adversely affected. In these circumstances, the market price of our common stock would likely decline. In addition, we cannot assure investors that our assumptions and expectations will prove to be correct. Important factors could cause our actual results to differ materially from those indicated or implied by forward-looking statements. See page i of this Quarterly Report on Form 10-Q for a discussion of some of the forward-looking statements that are qualified by these risk factors. Factors that could cause or contribute to such differences include those factors discussed below.

Risks related to our financial position and need for additional capital

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

Since our inception, we have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies, and have incurred significant operating losses. Our net losses were \$66.2 million for the six months ended June 30, 2021 and \$45.7 million for the year ended December 31, 2020. As of June 30, 2021, we had an accumulated deficit of \$132.8 million. To date, we have generated no revenue and have financed our operations primarily through private placements of our preferred stock and, most recently, from the sale of common stock in our initial public offering, or IPO. We have devoted all of our efforts to research and development, are still in the early stages of development of our research programs and have not commenced clinical development of any product candidates. We expect to continue to incur significant expenses and operating losses for the foreseeable future. Our operating expenses and net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially if and as we:

- continue our current research programs and our preclinical development of product candidates from our current research programs;
- seek to identify additional research programs and additional product candidates;
- advance our existing and future product candidates into clinical development;
- initiate preclinical studies and clinical trials for any additional product candidates we identify and develop or expand development of existing programs into additional patient populations;
- maintain, expand, enforce, defend and protect our intellectual property portfolio and provide reimbursement of third-party expenses related to our patent portfolio;
- seek regulatory and marketing approvals for any of our product candidates that we develop;
- seek to identify, establish and maintain additional collaborations and license agreements, and the success of those collaborations and license agreements;
- make milestone payments to Beam Therapeutics Inc., or Beam, under our collaboration and license agreement with Beam, or the Beam Agreement, milestone payments to Acuitas Therapeutics Inc., or Acuitas, under our non-exclusive license agreement with Acuitas, or the Acuitas Agreement, and milestone payments or success payments to The Broad Institute, Inc., or Broad, and the President and Fellows of Harvard College, or Harvard, under our license agreement with Broad and Harvard (as amended, the Cas9 License Agreement), and under any additional future collaboration or license agreements that we obtain;
- ultimately establish a sales, marketing, and distribution infrastructure to commercialize any drug products for which we may obtain marketing approval, either by ourselves or in collaboration with others;
- generate revenue from commercial sales of product candidates we may develop for which we receive marketing approval;

- further develop our base editing technology;
- hire additional personnel including research and development, clinical and commercial personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development;
- acquire or in-license products, intellectual property, medicines and technologies;
- satisfy any post-marketing requirements, such as a cardiovascular outcomes trial, or CVOT;
- establish commercial-scale current good manufacturing practices capabilities through a third-party or our own manufacturing facility; and
- operate as a public company.

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

- we are required by the U.S. Food and Drug Administration, or the FDA, the European Medicines Agency, or the EMA, or other regulatory authorities to perform trials or studies in addition to, or different than, those expected;
- there are any delays in completing our clinical trials or the development of any of our product candidates; or
- there are any third-party challenges to our intellectual property or we need to defend against any intellectual property-related claim.

Even if we obtain marketing approval for, and are successful in commercializing, one or more of our product candidates, we expect to incur substantial additional research and development and other expenditures to develop and market additional product candidates and/or to expand the approved indications of any marketed product. 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, obtaining the necessary regulatory approvals for and eventually commercializing a product or products that generate significant revenue. The ability to achieve this success will require us to be effective in a range of challenging activities, including:

- completing preclinical testing and clinical trials;
- identifying additional product candidates;
- obtaining marketing approval for these product candidates;
- manufacturing, marketing and selling any products for which we may obtain marketing approval; and
- achieving market acceptance of products for which we may obtain marketing approval as viable treatment options.

We are only in the preliminary stages of these activities and there is no assurance that we will be successful in these activities and, even if we are, may never generate revenues that are significant enough to achieve profitability. We are currently only in the preclinical stage of our research programs. 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 generate revenue or achieve profitability.

Even if we are able to generate revenue from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations. Our revenue will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to obtain coverage and reimbursement, and whether we own the commercial rights for that territory. If the number of our addressable patients is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect, or the treatment population is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales of such products, even if approved.

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

We expect to devote substantial financial resources to our ongoing and planned activities, particularly as we conduct research, development and preclinical testing, initiate clinical trials and potentially seek marketing approval for our current and any additional product candidates we may develop. We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we advance our preclinical activities and initiate clinical trials. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution. Furthermore, we have incurred and 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. If we are unable to raise capital or obtain adequate funds when needed or on acceptable terms, we may be forced to delay, limit, reduce or terminate our research and development programs or any future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

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

- the costs of acquiring licenses for the delivery modalities that will be used with our product candidates;
- the scope, progress, results and costs of discovery, preclinical and clinical development for any product candidates we may develop;
- the cost and timing of completion of commercial-scale manufacturing activities;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property and proprietary rights, and defending intellectual property-related claims, including claims of infringement, misappropriation or other violation of third-party intellectual property;
- the costs, timing and outcome of regulatory review of the product candidates we may develop;
- the costs of future commercialization activities, either by ourselves or in collaboration with others, including product sales, marketing, manufacturing, and distribution for any product candidates for which we receive marketing approval;
- the costs of satisfying any post-marketing requirements, such as a CVOT;
- the revenue, if any, received from commercial sales of product candidates we may develop for which we receive marketing approval;
- the success of our license agreements and our collaborations;
- our ability to establish and maintain additional collaborations on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments under any additional collaboration agreements we obtain;
- the extent to which we acquire or in-license products, intellectual property and technologies;
- the costs of operational, financial and management information systems and associated personnel; and
- the costs of operating as a public company.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, even if we successfully identify and develop product candidates and those are approved, we may not achieve commercial success. Our commercial revenues, if any, may not be sufficient to sustain our operations. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives.

As of June 30, 2021, we had cash, cash equivalents and marketable securities of approximately \$417.6 million. We believe that our existing cash, cash equivalents and marketable securities will enable us to fund our operating expenses and capital expenditure requirements into 2024. However, we have based this estimate on assumptions that may prove to be wrong, and our operating plan may change as a result of many factors currently unknown to us. As a result, we could deplete our capital resources sooner than we currently expect and could be forced to seek additional funding sooner than planned.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize any product candidates. We cannot be certain that additional funding will be available on acceptable terms, or at all. For example, while the potential impact and duration of the COVID-19 pandemic

on the global economy and our business in particular may be difficult to assess or predict, the pandemic has resulted in, and may continue to result in, significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. We have no committed source of additional capital and, if we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of our product candidates or other research and development initiatives. We could be required to seek collaborators for product candidates we may develop at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available or relinquish or license on unfavorable terms our rights to product candidates we may develop in markets where we otherwise would seek to pursue development or commercialization ourselves.

Any of the above events could significantly harm our business, prospects, financial condition and results of operations and cause the price of our common stock to decline.

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

Until such time, if ever, as we can generate substantial revenues from product sales, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. We do not have any source of committed external funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights as a common stockholder. Any 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.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed or on terms acceptable to us, we 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 for stockholders to evaluate the success of our business to date and to assess our future viability.

We commenced operations in 2018 and are an early-stage company. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, developing our technology, identifying potential product candidates, securing intellectual property rights and undertaking preclinical studies. All of our research programs are still in the research or preclinical stage of development, and their risk of failure is high. We have not yet demonstrated our ability to initiate or complete any clinical trials, obtain marketing approvals, manufacture a clinical development or commercial scale product or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. In part because of this lack of experience, we cannot be certain that our ongoing preclinical studies will be completed on time or if the planned preclinical studies and clinical trials will begin or be completed on time, if at all. Consequently, any predictions stockholders make 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 gene editing products.

Our limited operating history, particularly in light of the rapidly evolving genetic medicines field, may make it difficult to evaluate our technology and industry and predict our future performance. Our limited history as an operating company makes any assessment of our future success or viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by early-stage companies in rapidly evolving fields. If we do not address these risks successfully, our business will suffer.

In addition, as our business grows, we may encounter unforeseen expenses, restrictions, 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.

Our ability to use our net operating losses and research and development tax credit carryforwards to offset future taxable income or taxes may be subject to certain limitations.

We have a history of cumulative losses and anticipate that we will continue to incur significant losses in the foreseeable future; thus, we do not know whether or when we will generate taxable income necessary to utilize our net operating

losses, or NOLs, or research and development tax credit carryforwards. As of December 31, 2020, we had federal NOL carryforwards of \$49.2 million and state NOL carryforwards of \$41.6 million.

In general, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, and corresponding provisions of state law, a corporation that undergoes an “ownership change,” generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders over a three-year period, is subject to limitations on its ability to utilize its pre-change NOLs and research and development tax credit carryforwards to offset post-change taxable income or taxes. We have not conducted a study to assess whether any such ownership changes have occurred. We may have experienced such ownership changes in the past and may experience such ownership changes in the future as a result of subsequent changes in our stock ownership (which may be outside our control). As a result, if, and to the extent that, we earn net taxable income, our ability to use our pre-change NOLs and research and development tax credit carryforwards to offset such taxable income may be subject to limitations. Our NOLs or credits may also be impaired under state law.

There is also a risk that due to regulatory changes, such as suspensions on the use of NOLs, or other unforeseen reasons, our existing NOLs could expire or otherwise become unavailable to offset future income tax liabilities. As described below in “Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition,” the Tax Cuts and Jobs Act, or the Tax Act, as amended by the Coronavirus Aid, Relief, and Economic Security Act, or 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. For these reasons, even if we attain profitability, we may be unable to use a material portion of our NOLs and other tax attributes.

Risks related to discovery and development

We are very early in our development efforts, and we have not yet completed investigational new drug, or IND-, enabling studies or initiated clinical development of any product candidate. As a result, we expect it will be many years before we commercialize any product candidate, if ever. If we are unable to advance our current or future product candidates into and through clinical trials, obtain marketing approval and ultimately 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 have focused our research and development efforts to date on research efforts and preclinical development. Currently, all of our programs are in preclinical development or in discovery. Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful development, marketing approval and eventual commercialization of our product candidates, which may never occur. We have not yet generated revenue from product sales or otherwise, and we may never be able to develop or commercialize a marketable product.

Commencing clinical trials in the United States is subject to acceptance by the FDA of an IND and finalizing the trial design based on discussions with the FDA and other regulatory authorities. In the event that the FDA requires us to complete additional preclinical studies or we are required to satisfy other FDA requests prior to commencing clinical trials, the start of our first clinical trials may be delayed. Even after we receive and incorporate guidance from these regulatory authorities, the FDA or other regulatory authorities could disagree that we have satisfied their requirements to commence any clinical trial or change their position on the acceptability of our trial design or the clinical endpoints selected, which may require us to complete additional preclinical studies or clinical trials, delay the enrollment of our clinical trials or impose stricter approval conditions than we currently expect. There are equivalent processes and risks applicable to clinical trial applications in other countries, including countries in the European Union.

Commercialization of any product candidates we may develop will require preclinical and clinical development; regulatory and marketing approval in multiple jurisdictions, including by the FDA and the EMA; manufacturing supply, capacity and expertise; a commercial organization; and significant marketing efforts. The success of product candidates we may identify and develop will depend on many factors, including the following:

- timely and successful completion of preclinical studies, including toxicology studies, biodistribution studies and minimally efficacious dose studies in animals, where applicable;
- effective INDs or comparable foreign applications that allow commencement of our planned clinical trials or future clinical trials for any product candidates we may develop;
- successful enrollment and completion of clinical trials, including under the FDA's current Good Clinical Practices, or GCPs, current Good Laboratory Practices and any additional regulatory requirements from foreign regulatory authorities;
- positive results from our future clinical trials that support a finding of safety and effectiveness and an acceptable risk-benefit profile in the intended populations;

- receipt of marketing approvals from applicable regulatory authorities;
- establishment of arrangements through our own facilities or with third-party manufacturers for clinical supply and, where applicable, commercial manufacturing capabilities;
- establishment, maintenance, defense and enforcement of patent, trademark, trade secret and other intellectual property protection or regulatory exclusivity for any product candidates we may develop;
- commercial launch of any product candidates we may develop, if approved, whether alone or in collaboration with others;
- acceptance of the benefits and use of our product candidates we may develop, including method of administration, if and when approved, by patients, the medical community and third-party payers;
- effective competition with other therapies;
- maintenance of a continued acceptable safety, tolerability and efficacy profile of any product candidates we may develop following approval; and
- establishment and maintenance of healthcare coverage and adequate reimbursement by payers.

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 any product candidates we may develop, 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.

Gene editing, including base editing, is a novel technology that is not yet clinically validated for human therapeutic use. The approaches we are taking to discover and develop novel therapeutics are unproven and may never lead to marketable products.

We are focused on developing medicines utilizing gene editing technology, which is new and largely unproven. The base editing technologies that we have licensed and that we are utilizing with VERVE-101 and in our ANGPTL3 program have not yet been clinically tested, nor are we aware of any clinical trials for safety or efficacy having been completed by third parties using our base editing or similar technologies. The scientific evidence to support the feasibility of developing product candidates based on gene editing technologies is both preliminary and limited. Successful development of our product candidates will require us to safely deliver a gene editor into target cells, optimize the efficiency and specificity of such product candidates and ensure the therapeutic selectivity of such product candidates. There can be no assurance that base editing technology will lead to the development of genetic medicines or that we will be successful in solving any or all of these issues.

Our future success is highly dependent on the successful development of gene editing technologies, cellular delivery methods and therapeutic applications of that technology. We may decide to alter or abandon our initial programs as new data become available and we gain experience in developing gene editing therapeutics. We cannot be sure that our technologies will yield satisfactory products that are safe and effective, scalable or profitable in our initial indications or any other indication we pursue. Adverse developments in the clinical development efforts of other gene editing technology companies could adversely affect our efforts or the perception of our product candidates by both investors and regulatory authorities.

Similarly, another new gene editing technology that has not been discovered yet may be determined to be more attractive than base editing. Moreover, if we decide to develop gene editing technologies other than those involving base editing, we cannot be certain we will be able to obtain rights to such technologies. Although all of our founders who currently provide consulting and advisory services to us in the area of base editing technologies have assignment of inventions obligations to us with respect to the services they perform for us, these assignment of inventions obligations are subject to limitations and do not extend to their work in other fields or to the intellectual property arising from their employment with their respective academic and research institutions. To obtain intellectual property rights assigned by these founders to such institutions, we would need to enter into license agreements with such institutions, which may not be available on commercially reasonable terms or at all. Any of these factors could reduce or eliminate our commercial opportunity and could have a material adverse effect on our business, financial condition, results of operations and prospects.

Development activities in the field of gene editing are currently subject to a number of risks related to the ownership and use of certain intellectual property rights that are subject to patent interference proceedings in the United States and opposition proceedings in Europe. For additional information regarding the risks that may apply to our and our licensors' intellectual property rights, see the section entitled "—Risks related to our intellectual property" for more information.

Additionally, public perception and related media coverage relating to the adoption of new therapeutics or novel approaches to treatment, as well as ethical concerns related specifically to gene editing, may adversely influence the willingness of subjects to participate in clinical trials, or, if any therapeutic is approved, of physicians and patients to accept these novel and personalized treatments. Physicians, health care providers and third-party payors often are slow to adopt new products, technologies and treatment practices, particularly those that may also require additional upfront costs and training. Physicians may not be willing to undergo training to adopt these novel and potentially personalized therapies, may decide the particular therapy is too complex or potentially risky to adopt without appropriate training, and may choose not to administer the therapy. Further, due to health conditions, genetic profile or other reasons, certain patients may not be candidates for the therapies. In addition, responses by federal and state agencies, Congressional committees and foreign governments to negative public perception, ethical concerns or financial considerations may result in new legislation, regulations or medical standards that could limit our ability to develop or commercialize any product candidates, obtain or maintain regulatory approval or otherwise achieve profitability. 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. Based on these and other factors, health care providers and payors may decide that the benefits of these new therapies do not or will not outweigh their costs.

The gene editing field is relatively new and is evolving rapidly. We are focusing our research and development efforts on gene editing using base editing technology, but other gene editing technologies may be discovered that provide significant advantages over base editing, which could materially harm our business.

To date, we have focused our efforts on gene editing technologies using base editing. Other companies have previously undertaken research and development of gene editing technologies using zinc finger nucleases, engineered meganucleases and transcription activator-like effector nucleases, but to date none have obtained marketing approval for a product candidate. There can be no certainty that base editing technology will lead to the development of genetic medicines or that other gene editing technologies will not be considered better or more attractive for the development of medicines. For example, Feng Zhang's group at the Massachusetts Institute of Technology, or MIT, and Broad, and, separately, Samuel Sternberg's group at Columbia University recently announced the discovery of the use of transposons, or "jumping genes." Transposons can insert themselves into different places in the genome and can be programmed to carry specific DNA sequences to specific sites, without the need for making double-stranded breaks in DNA. Beam uses prime editing technology, which utilizes a CRISPR protein to target a mutation site in DNA and to nick a single strand of the target DNA. Guide RNA allows the CRISPR protein to recognize a DNA sequence that is complementary to the guide RNA and also carries a primer for reverse transcription and a replacement template. The reverse transcriptase copies the template sequence in the nicked site, installing the edit. A number of alternative approaches are being developed by others, including, for example, Intellia Therapeutics, Inc., which recently reported clinical data from a Phase 1 trial of a CRISPR/Cas9-based gene editing product candidate for the treatment of hereditary transthyretin amyloidosis with polyneuropathy. Similarly, another new gene editing technology that has not been discovered yet may be determined to be more attractive than base editing. Moreover, if we decide to develop gene editing technologies other than those involving base editing, we cannot be certain we will be able to obtain rights to such technologies. Any of these factors could reduce or eliminate our commercial opportunity, and could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may not be successful in our efforts to identify and develop potential product candidates. If these efforts are unsuccessful, we may never become a commercial stage company or generate any revenues.

The success of our business depends primarily upon our ability to identify, develop and commercialize product candidates based on our approach to gene editing. All of our product development programs are still in the research or preclinical stage of development and we have not yet completed IND-enabling studies for any product candidate. Our research programs may fail to identify potential product candidates for clinical development for a number of reasons. Our research methodology may be unsuccessful in identifying additional potential product candidates, our potential product candidates may be shown to have harmful side effects in preclinical *in vitro* experiments or animal model studies, they may not show promising signals of therapeutic effect in such experiments or studies or they may have other characteristics that may make the product candidates impractical to manufacture, unmarketable or unlikely to receive marketing approval.

If any of these events occur, we may be forced to abandon our research or development efforts for a program or programs, which would have a material adverse effect on our business, financial condition, results of operations and prospects. Research programs to identify new product candidates require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful, which would be costly and time-consuming.

The COVID-19 pandemic may affect our ability to initiate and complete preclinical studies, delay the initiation of 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, both of which could result in adverse effects on our business, operations and ability to raise capital.

In December 2019, a novel strain of coronavirus, SARS-CoV-2, causing a disease referred to as COVID-19, emerged in China. Since then, COVID-19 has spread to multiple countries worldwide, including the United States. In March 2020, the World Health Organization declared the COVID-19 outbreak a pandemic. The COVID-19 pandemic is causing 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 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 contract manufacturing organizations, or CMOs, and contract research organizations, or CROs, have experienced a reduction in the capacity to undertake research-scale production and to execute some preclinical studies, and we have faced and may face disruptions that affect our ability to initiate and complete preclinical studies, and disruptions in procuring items that are essential for our research and development activities, including:

- raw materials and supplies used in the production and purification of messenger RNA, or mRNA, nucleic acids as well as lipids used in the production of lipid nanoparticles, or LNPs;
- raw materials and supplies used in the manufacture of any product candidates we may develop;
- laboratory supplies used in our preclinical studies; and
- animals that are used for preclinical testing for which there are shortages because of ongoing efforts to address the pandemic.

We and our CROs and CMOs may also face disruptions related to our future IND-enabling studies and clinical trials arising from delays in preclinical 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 also 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, for example by causing interruption or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines. We have experienced delays with the FDA as a result of the COVID-19 pandemic. In addition, we may face impediments or delays to regulatory meetings and approvals due to measures intended to limit in-person interactions. The pandemic has already caused significant disruptions in worldwide financial markets, and may continue to cause such disruptions, 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. We cannot be certain what the overall impact of the COVID-19 pandemic will be on our business, although for the reasons described above it has the potential to adversely affect our business, financial condition, results of operations and prospects.

Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. If we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.

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 marketing approval. The time required to obtain approval from the FDA, EMA or other comparable foreign regulatory authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of regulatory authorities. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. We have not yet begun or completed a clinical trial of any product candidate. Clinical trials may fail to demonstrate that our product candidates are safe for humans and effective for indicated uses. Even if initial clinical trials in any of our product candidates we may develop are successful, these product candidates we may develop may fail to show the desired safety and efficacy in later stages of clinical development despite having successfully advanced through preclinical studies and initial clinical trials. There is a high failure rate for drugs and biologics proceeding through clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later stage clinical trials even after achieving promising results in earlier stage clinical

trials. Furthermore, 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 preclinical testing and studies that support our planned INDs and other regulatory filings in the United States and abroad. We cannot be certain of the timely completion or outcome of our preclinical testing and studies and cannot predict if the outcome of our preclinical testing and studies will ultimately support the further development of our current or future product candidates or whether regulatory authorities will accept our proposed clinical programs. As a result, we may not be able to submit applications to initiate clinical development on the timelines we expect, if at all, and the submission of these applications may not result in regulatory authorities allowing clinical trials to begin. Furthermore, product candidates are subject to continued preclinical safety studies, which may be conducted concurrently with our clinical testing. The outcomes of these safety studies may delay the launch of or enrollment in future clinical trials and could impact our ability to continue to conduct our clinical trials.

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

Preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. Furthermore, the failure of any of our product candidates to demonstrate safety and efficacy in any clinical trial could negatively impact the perception of our other product candidates and/or cause the FDA, EMA or other regulatory authorities to require additional testing before approving any of our product candidates.

Our current and future product candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA, EMA or other foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA, EMA or other foreign regulatory authorities that a product candidate is safe, pure and potent or effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA, EMA or other foreign regulatory authorities for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA, EMA or other foreign regulatory authorities may disagree with our interpretation of data from clinical trials or preclinical studies;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of a Biologics License Application, or BLA, to the FDA, or similar foreign submission to the EMA or other foreign regulatory authority, to obtain approval in the United States, the European Union or elsewhere;
- the FDA, EMA or other foreign regulatory authorities may find deficiencies with or fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA, EMA or other foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process as well as the unpredictability of clinical trial results may result in our failing to obtain regulatory approval to market any product candidate we develop, which would significantly harm our business, financial condition, results of operations and prospects.

The FDA, EMA and other comparable foreign regulatory authorities have substantial discretion in the approval process and determining when or whether regulatory approval will be obtained for any product candidate that we develop. Even if we believe the data collected from future clinical trials of our product candidates are promising, such data may not be sufficient to support approval by the FDA, EMA or any other comparable foreign regulatory authorities.

Even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may grant approval contingent on the performance of costly post-marketing clinical trials or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for

the successful commercialization of that product candidate. Additionally, outside of the United States, regulatory authorities may not approve the price we intend to charge for our products. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

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

We are in the early stage of research in the development of our programs and have not conducted any clinical trials. As a result, our belief in the potential capabilities of our programs is based on early research and preclinical studies. However, the results of preclinical studies may not be predictive of the results of later preclinical studies or clinical trials, and the results of any early-stage clinical trials may not be predictive of the results of later clinical trials. In addition, initial success in clinical trials may not be indicative of results obtained when such trials are completed. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. Our future clinical trials may not ultimately be successful or support further clinical development of any product candidates we may develop. There is a high failure rate for product candidates proceeding through clinical trials. 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 and results of operations.

We may incur unexpected costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- regulators or IRBs, or independent ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- regulators may decide that longer follow-up data are needed before they will consider our marketing application, which would delay our ability to obtain approval;
- regulators may decide the design of our clinical trials is flawed, for example if regulators do not agree with our chosen primary endpoints;
- regulators may decide to slow patient enrollment, resulting in delays to our ability to meet our timelines;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- preclinical testing may produce results based on which we may decide, or regulators may require us, to conduct additional preclinical studies before we proceed with certain clinical trials, limit the scope of our clinical trials, halt ongoing clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- regulators, IRBs or ethics committees may require us to perform additional or unanticipated clinical trials to obtain approval or we may be subject to additional post-marketing testing requirements to maintain regulatory approval, such as a CVOT;
- regulators may revise the requirements for approving our product candidates, or such requirements may not be as we anticipate;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;

- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators, IRBs or ethics committees to suspend or terminate the trials; and
- regulators may withdraw their approval of a product or impose restrictions on its distribution, such as in the form of a risk evaluation and mitigation strategy, or REMS.

We could encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are conducted or their ethics committees, by the data review committee or data safety monitoring board for such trial or by the FDA, EMA or other foreign regulatory authorities. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA, EMA or other foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, including those relating to the class of products to which our product candidates belong.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling or a REMS that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

Our development costs will also increase if we experience delays in preclinical studies or clinical trials or in obtaining marketing approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. We may also determine to change the design or protocol of one or more of our clinical trials, including to add additional patients or arms, which could result in increased costs and expenses and/or delays. Significant preclinical study or 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 and impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

Preclinical drug development is uncertain. Some or all of our preclinical programs may experience delays or may never advance to clinical trials, which would adversely affect our ability to obtain marketing approvals or commercialize these product candidates on a timely basis or at all, which would have an adverse effect on our business.

In order to obtain FDA approval to market a new biological product, we must demonstrate product purity (or product quality) as well as proof of safety and potency or efficacy in humans. To satisfy these requirements, we will have to conduct adequate and well-controlled clinical trials. Before we can commence clinical trials for a product candidate, we must complete extensive preclinical testing and studies that support an IND in the United States. We have not yet submitted an IND to the FDA for any of our product candidates. We cannot be certain of the timely completion or outcome of our preclinical testing and studies, and we cannot predict if the FDA will accept our proposed clinical programs or if the outcome of our preclinical testing and studies will ultimately support the further development of these product candidates. As a result, we cannot be sure that we will be able to submit INDs or similar applications for any preclinical programs on the timelines we expect, if at all, and we cannot be sure that submission of INDs or similar applications will result in the FDA or other regulatory authorities allowing clinical trials to begin.

Conducting preclinical testing is a lengthy, time-consuming and expensive process. The length of time may vary substantially according to the type, complexity, novelty and intended use of the product candidate, and often can be several years or more per product candidate. Delays associated with product candidates for which we are conducting preclinical testing and studies ourselves may cause us to incur additional operating expenses. Moreover, we may be affected by delays associated with the preclinical testing and studies of certain product candidates conducted by our potential partners over which we have no control. The commencement and rate of completion of preclinical studies and clinical trials for a product candidate may be delayed by many factors, including, for example:

- inability to generate sufficient preclinical or other *in vivo* or *in vitro* data to support the initiation of clinical trials; and
- delays in reaching a consensus with regulatory agencies on study design.

Moreover, even if we do initiate clinical trials for other product candidates, our development efforts may not be successful, and clinical trials that we conduct or that third parties conduct on our behalf may not demonstrate product purity (or quality) as well as proof of safety and potency or efficacy necessary to obtain the requisite marketing approvals for any of our product candidates or product candidates employing our technology. Even if we obtain positive results from preclinical studies or initial clinical trials, we may not achieve the same success in future trials.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

Identifying and qualifying patients to participate in clinical trials for our product candidates is critical to our success. Successful and timely completion of clinical trials will require that we enroll a sufficient number of patients who remain in the trial until its conclusion. We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside of the United States. Given the large patient population for atherosclerotic cardiovascular disease, or ASCVD, if we expand clinical development of VERVE-101 for the treatment of patients with established ASCVD, the number of patients that may be required for clinical trials could be high, we may not be able to enroll a sufficient number of patients and we may not be able to initiate or complete clinical trials of VERVE-101 for the treatment of patients with established ASCVD. Because of the small patient population for homozygous familial hypercholesterolemia, or HoFH, we may have difficulty enrolling patients and we may not be able to initiate or complete clinical trials for our ANGPTL3 program for the treatment of HoFH.

Patient enrollment is affected by a variety of other factors, including:

- the prevalence and severity of the disease under investigation;
- the eligibility criteria for the trial in question;
- the perceived risks and benefits of the product candidate under trial;
- the requirements of the trial protocols, which for products targeting cardiovascular disease, or CVD, could include up to 15 years of long-term patient follow-up;
- the availability of existing treatments for the indications for which we are conducting clinical trials;
- the ability to recruit clinical trial investigators with the appropriate competencies and experience;
- the efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- the proximity and availability of clinical trial sites for prospective patients;
- perceived negative public perception of gene editing;
- the conduct of clinical trials by competitors for product candidates that treat the same indications or address the same patient populations as our product candidates; and
- the cost to, or lack of adequate compensation for, prospective patients.

Other pharmaceutical and biotechnology companies have reported experiencing delays in enrollment in their ongoing clinical trials as a result of the COVID-19 pandemic, and we could also experience such delays. Our inability to locate and enroll a sufficient number of patients for our clinical trials would result in significant delays, could require us to abandon one or more clinical trials altogether and could delay or prevent our receipt of necessary regulatory approvals. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

Even if we are able to enroll a sufficient number of patients for our future clinical trials, we may have difficulty maintaining patients in our clinical trials. Many of the patients who end up receiving placebo may perceive that they are not receiving the product candidate being tested, and they may decide to withdraw from our clinical trials to pursue alternative therapies rather than continue the trial. If we have difficulty enrolling or maintaining a sufficient number of patients to conduct our clinical trials, we may need to delay, limit or terminate clinical trials, any of which would harm our business, financial condition, results of operations and prospects.

If any of the product candidates we may develop, or the delivery modes we rely on to administer them, cause serious adverse events, undesirable side effects or unexpected characteristics, such events, side effects or

characteristics could delay or prevent regulatory approval of the product candidates, limit the commercial potential or result in significant negative consequences following any potential marketing approval.

We have not evaluated any product candidates in human clinical trials. Moreover, there have been only a limited number of clinical trials involving the use of gene editing technologies and none involving base editing technology similar to our technology. Furthermore, there has not been any gene editing product candidate that has received regulatory approval for use in humans. It is impossible to predict when or if any product candidates we may develop will prove safe in humans. There can be no assurance that gene editing technologies will not cause undesirable side effects, as improper editing of a patient's DNA could lead to lymphoma, leukemia or other cancers or other aberrantly functioning cells.

A significant risk in any gene editing product candidate is that "off-target" edits may occur, which could cause serious adverse events, undesirable side effects or unexpected characteristics. We cannot be certain that off-target editing will not occur in any of our planned or future clinical studies, and the lack of observed side effects in preclinical studies does not guarantee that such side effects will not occur in human clinical studies. There is also the potential risk of delayed or late presentation of adverse events following exposure to gene editors due to the potential permanence of edits to DNA or due to other components of product candidates used to carry the genetic material. Further, because gene editing makes a permanent change, the therapy cannot be withdrawn, even after a side effect is observed.

We intend to use LNPs to deliver our gene editors to the liver. LNPs have recently been used to deliver mRNA in humans, including the COVID-19 vaccines developed by Pfizer Inc., or Pfizer, and BioNTech SE and by Moderna, Inc., and LNPs are being used to deliver mRNA for therapeutic use in clinical trials. LNPs have the potential to induce liver injury and/or initiate a systemic inflammatory response, either of which could potentially be fatal. While we aim to continue to optimize our LNPs, there can be no assurance that our LNPs will not have undesired effects. Our LNPs could contribute, in whole or in part, to one or more of the following: liver injury, immune reactions, infusion reactions, complement reactions, opsonization reactions, antibody reactions including IgA, IgM, IgE or IgG or some combination thereof, or reactions to the polyethylene glycol, or PEG, from some lipids or PEG otherwise associated with the LNP. Certain aspects of our investigational medicines may induce immune reactions from either the mRNA or the lipid as well as adverse reactions within liver pathways or degradation of the mRNA or the LNP, any of which could lead to significant adverse events in one or more of our future clinical trials. Some of these types of adverse effects have been observed for other LNPs. There may be uncertainty as to the underlying cause of any such adverse event, which would make it difficult to accurately predict side effects in future clinical trials and would result in significant delays in our programs.

If any product candidates we develop are associated with serious adverse events, undesirable side effects or unexpected characteristics, we may need to abandon their development or limit development to certain uses or subpopulations in which the serious adverse events, undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective, any of which would have a material adverse effect on our business, financial condition, results of operations and prospects.

If in the future we are unable to demonstrate that any of the above adverse events were caused by factors other than our product candidate, the FDA, the EMA or other regulatory authorities could order us to cease further development of, or deny approval of, any product candidates we are able to develop for any or all targeted indications. They could also revoke a marketing authorization if a serious safety concern is identified in any post-marketing follow up studies. Even if we are able to demonstrate that all future serious adverse events are not product-related, such occurrences could affect patient recruitment or the ability of enrolled patients to complete the trial. Moreover, if we elect, or are required, to delay, suspend or terminate any clinical trial of any product candidate we may develop, 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 identify and develop product candidates, and may harm our business, financial condition, result of operations, and prospects significantly.

Adverse public perception of genetic medicines, and gene editing and base editing in particular, may negatively impact regulatory approval of, and/or demand for, our potential products.

Our programs involve editing the human genome. The clinical and commercial success of our product candidates will depend in part on public understanding and acceptance of the use of gene editing therapy for the prevention or treatment of human diseases. Public attitudes may be influenced by claims that gene editing is unsafe, unethical or immoral, and, consequently, our product candidates 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.

In addition, gene editing technology is subject to public debate and heightened regulatory scrutiny due to ethical concerns.

More restrictive government regulations or negative public opinion would have a negative effect on our business or financial condition and may delay or impair our development and commercialization of product candidates or demand for any product candidates we may develop. Adverse events in our preclinical studies or clinical trials or those of our licensors, partners or competitors or of academic researchers utilizing gene editing technologies, even if not ultimately attributable to product candidates we may identify and develop, and the resulting publicity could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of potential product candidates we may identify and develop, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates. Use of gene editing technology by a third party or government to develop biological agents or products that threaten U.S. national security could similarly result in such negative impacts to us.

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

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

Genetic medicines are complex and difficult to manufacture. We could experience delays in satisfying regulatory authorities or production problems that result in delays in our development programs, limit the supply of our product candidates we may develop, or otherwise harm our business.

Any product candidates we may develop will likely require processing steps that are more complex than those required for most chemical pharmaceuticals. Moreover, unlike chemical pharmaceuticals, the physical and chemical properties of a biologic such as the product candidates we intend to develop generally cannot be fully characterized. As a result, assays of the finished product candidate may not be sufficient to ensure that the product candidate will perform in the intended manner. Problems with the manufacturing process, 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 or insufficient inventory or potentially delay progression of our potential IND filings. If we successfully develop product candidates, we may encounter problems achieving adequate quantities and quality of clinical-grade materials that meet FDA, EMA or other comparable applicable foreign standards or specifications with consistent and acceptable production yields and costs. In addition, the product candidates we may develop will require complicated delivery modalities, such as LNPs, which will introduce additional complexities in the manufacturing process.

In addition, the FDA, the EMA and other regulatory authorities 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, the FDA, the EMA or other regulatory authorities may require that we not distribute 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 or product recalls. Lot failures or product recalls could cause us to delay clinical trials or product launches, which could be costly to us and otherwise harm our business, financial condition, results of operations and prospects.

We also may encounter problems hiring and retaining the experienced scientific, quality control and manufacturing personnel needed to manage our manufacturing process, which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements.

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.

Any problems in our manufacturing process or the facilities with which we contract could make us a less attractive collaborator for potential partners, including larger pharmaceutical companies and academic research institutions, which could limit our access to additional attractive development programs. Problems in third-party manufacturing process or facilities also could restrict our ability to ensure sufficient clinical material for any clinical trials we may be conducting or are planning to conduct and meet market demand for any product candidates we develop and commercialize.

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

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

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

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

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

Because we have limited financial and managerial resources, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. Failure to allocate resources or capitalize on strategies in a successful manner will have an adverse impact on our business, financial condition and results of operations.

We may conduct clinical trials at sites outside the United States. The FDA may not accept data from trials conducted in such locations, and the conduct of trials outside the United States could subject us to additional delays and expense.

We may conduct one or more of our clinical trials with one or more trial sites that are located outside the United States. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of these data is subject to conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and be

performed by qualified investigators in accordance with ethical principles. The FDA must be able to validate the data from the trial through an onsite inspection, if necessary. 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 the FDA deems clinically meaningful. In addition, while these clinical trials are subject to the applicable local laws, whether the FDA accepts the data will depend on its determination that the trials also complied with all applicable U.S. laws and regulations. There can be no assurance that the FDA will accept data from trials conducted outside of the United States. If the FDA does not accept the data from any trial that we conduct outside the United States, it would likely result in the need for additional trials, which would be costly and time-consuming and could delay or permanently halt our development of the applicable product candidates.

In addition, conducting clinical trials outside the United States could have a significant adverse impact on us. Risks inherent in conducting international clinical trials include:

- clinical practice patterns and standards of care that vary widely among countries;
- non-U.S. regulatory authority requirements that could restrict or limit our ability to conduct our clinical trials;
- administrative burdens of conducting clinical trials under multiple non-U.S. regulatory authority schema;
- foreign exchange fluctuations; and
- diminished protection of intellectual property in some countries.

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, research and preclinical and clinical testing, and these third parties may not perform satisfactorily.

We do not expect to independently conduct all aspects of our product manufacturing, research and preclinical and clinical testing. We currently rely, and expect to continue to rely, on third parties with respect to many of these items, including CMOs for the manufacturing of any product candidates we test in preclinical or clinical development, as well as CROs for the conduct of our animal testing and research. 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 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 plan and protocols.

Although we intend to design the clinical trials for any product candidates we may develop, CROs will conduct some or all of the clinical trials. As a result, many important aspects of our development programs, including their conduct and timing, will be outside of our direct control. Our reliance on third parties to conduct future preclinical studies and clinical trials will also result in less direct control over the management of data developed through preclinical studies and clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may:

- have staffing difficulties;
- fail to comply with contractual obligations;
- experience regulatory compliance issues;
- undergo changes in priorities or become financially distressed; or
- form relationships with other entities, some of which may be our competitors.

These factors may materially adversely affect the willingness or ability of third parties to conduct our preclinical studies and clinical trials and may subject us to unexpected cost increases that are beyond our control. If the CROs and other third parties do not perform preclinical studies and future clinical trials in a satisfactory manner, breach their obligations to us or fail to comply with regulatory requirements, the development, regulatory approval and commercialization of any product candidates we may develop may be delayed, we may not be able to obtain regulatory approval and commercialize our product candidates or our development programs may be materially and irreversibly harmed. If we are unable to rely on preclinical and clinical data collected by our CROs and other third parties, we could be required to

repeat, extend the duration of or increase the size of any preclinical studies or clinical trials we conduct and this could significantly delay commercialization and require greater expenditures.

If third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our studies in accordance with regulatory requirements or our stated study plans and protocols, we will not be able to complete, or may be delayed in completing, the preclinical studies and clinical trials required to support future IND submissions and approval of any product candidates we may develop.

Manufacturing biologic products is complex and subject to product loss for a variety of reasons. We contract with third parties for the manufacture of our product candidates for preclinical and clinical testing and expect to continue to do so for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We rely, and expect to continue to rely, on third parties for the manufacture of VERVE-101 and our other product candidates for preclinical and clinical testing, as well as for commercial manufacture if any of our product candidates receive marketing approval. We also rely on these third parties for packaging, labeling, sterilization, storage, distribution and other production logistics. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts. We may be unable to establish any agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

We or our third-party manufacturers may encounter shortages in the raw materials or active pharmaceutical ingredients, or API, necessary to produce our product candidates in the quantities needed for our clinical trials or, if our product candidates are approved, in sufficient quantities for commercialization or to meet an increase in demand, as a result of capacity constraints or delays or disruptions in the market for the raw materials or API, including shortages caused by the purchase of such raw materials or API by our competitors or others. The failure of us or our third-party manufacturers to obtain the raw materials or API necessary to manufacture sufficient quantities of our product candidates may have a material adverse effect on our business.

Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical trials must be manufactured in accordance with cGMP. Our third-party manufacturers are subject to inspection and approval by regulatory authorities before we can commence the manufacture and sale of any of our product candidates, and thereafter subject to ongoing inspection from time to time. Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside of the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in regulatory actions, such as the issuance of FDA Form 483 notices of observations, warning letters or sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products.

Manufacturing biologic products, such as VERVE-101, is complex, especially in large quantities. Biologic products must be made consistently and in compliance with a clearly defined manufacturing process. Accordingly, it is essential to be able to validate and control the manufacturing process to assure that it is reproducible. The manufacture of biologics is extremely susceptible to product loss due to contamination, equipment failure or improper installation or operation of equipment, vendor or operator error, inconsistency in yields, variability in product characteristics and difficulties in scaling the product process. We have not yet scaled up the manufacturing process for any of our product candidates for potential commercialization. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects and other supply disruptions. If microbial, viral or other contaminations are discovered in our product candidates or in the manufacturing facilities in which our product candidates are made, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination, which could harm our results of operations and cause potential reputational damage. Our product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. As a result, we

may not obtain access to these facilities on a priority basis or at all. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply or a source for bulk drug substance nor do we have any agreements with third-party manufacturers for long-term commercial supply. If any of our future contract manufacturers cannot perform as agreed, we may be required to replace such manufacturers. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we may incur added costs and delays in identifying and qualifying any such replacement or be unable to reach agreement with an alternative manufacturer.

Our current and anticipated future dependence upon others for the manufacture of our product candidates or products may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

If any third-party manufacturer of our product candidates is unable to increase the scale of its production of our product candidates, and/or increase the product yield of its manufacturing, then our costs to manufacture the product candidate may increase and commercialization may be delayed.

In order to produce sufficient quantities to meet the demand for clinical trials and, if approved, subsequent commercialization of any current or future product candidates that we may develop, our third-party manufacturers will be required to increase their production and optimize their manufacturing processes while maintaining the quality of the product. The transition to larger scale production could prove difficult. In addition, if our third-party manufacturers are not able to optimize their manufacturing processes to increase the product yield for our product candidates, or if they are unable to produce increased amounts of our product candidates while maintaining the quality of the product, then we may not be able to meet the demands of clinical trials or market demands, which could decrease our ability to generate profits and have a material adverse impact on our business and results of operation.

We have entered into collaborations, and may enter into additional collaborations, with third parties for the research, development, manufacture and commercialization of programs or product candidates. If these collaborations are not successful, our business could be adversely affected.

As part of our strategy, we have entered into collaborations and intend to seek to enter into additional collaborations with third parties for one or more of our programs or product candidates. For example, in April 2019, we entered into the Beam Agreement to exclusively license certain of Beam's base editing, gene editing and delivery technology against certain cardiovascular targets for use in our product candidates, and in October 2020, we entered into the Acuitas Agreement to license from Acuitas its LNP delivery technology. Our likely collaborators for any other collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. We have under the Beam Agreement, and we may have under any other arrangements that we may enter into with any third parties, limited control over the amount and timing of resources that collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenue from these arrangements may depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations that we enter into may not be successful, and any success will depend heavily on the efforts and activities of such collaborators. Collaborations pose a number of risks, including the following:

- collaborators have significant discretion in determining the amount and timing of efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development of our product candidates or may elect not to continue or renew development programs based on results of clinical trials or other studies, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may not pursue commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew commercialization programs based on results of clinical trials or other studies, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that may divert resources or create competing priorities;
- collaborators may delay preclinical studies and clinical trials, provide insufficient funding for a preclinical study or clinical trial program, stop a preclinical study or clinical trial or abandon a product candidate, repeat or conduct new preclinical studies or clinical trials or require a new formulation of a product candidate for preclinical or clinical testing;

- we may not have access to, or may be restricted from disclosing, certain information regarding product candidates being developed or commercialized under a collaboration and, consequently, may have limited ability to inform our stockholders about the status of such product candidates on a discretionary basis;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates and products if the collaborators believe that the competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator may fail to comply with applicable regulatory requirements regarding the development, manufacture, distribution or marketing of a product candidate or product;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over intellectual property or proprietary rights, contract interpretation or the preferred course of development, might cause delays or terminations of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly obtain, maintain, enforce, defend or protect our intellectual property or proprietary rights or may use our proprietary information in such a way as to potentially lead to disputes or legal proceedings that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- disputes may arise with respect to the ownership of intellectual property developed pursuant to our collaborations;
- collaborators may infringe, misappropriate or otherwise violate the intellectual property or proprietary rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated for the convenience of the collaborator, and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

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

Collaboration agreements may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our existing stockholders, or disrupt our management and business. For example, upon execution of the Beam Agreement, we issued 276,075 shares of our common stock to Beam. In addition, under the Cas9 License Agreement, we issued 138,037 shares of our common stock to Broad and Harvard. Broad and Harvard also had anti-dilution rights, pursuant to which we issued Broad and Harvard an additional 309,278 shares of our common stock in the aggregate following the completion of preferred stock financings. We also issued 878,098 additional shares of common stock to Broad and Harvard upon the closing of our initial public offering pursuant to the Cas9 License Agreement. We are also obligated to pay to Harvard and Broad tiered success payments in the event our average market capitalization exceeds specified thresholds ascending from a high nine-digit dollar amount to \$10.0 billion, or sale of our company for consideration in excess of those thresholds. In the event of a change of control of our company or a sale of our company, we are required to pay any related success payment in cash within a specified period following such event. Otherwise, the success payments may be settled at our option in either cash or shares of our common stock, or a combination of cash and shares of our common stock.

We could face significant competition in seeking appropriate collaborators, and the negotiation process is time-consuming and complex. Our ability to reach a definitive collaboration agreement will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration, and the proposed collaborator's evaluation of several factors. If we license rights to any product candidates we or our collaborators may develop, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture.

Additionally, subject to its contractual obligations to us, if a collaborator of ours is involved in a business combination, the collaborator might deemphasize or terminate the development or commercialization of any product candidate licensed to it

by us. If one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception in the business and financial communities could be adversely affected.

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

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

We may also be restricted under existing or future license agreements from entering into agreements on certain terms with potential collaborators.

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

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

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

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

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

Risks related to our intellectual property

If we or our licensors are unable to obtain, maintain, defend and enforce patent rights that cover our gene editing technology and product candidates or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully develop and commercialize our technology and product candidates may be adversely affected.

Our success depends in large part on our ability to obtain, maintain, defend, and enforce protection of the intellectual property we may own solely and jointly with others or may license from others, particularly patents, in the United States and other countries with respect to proprietary technology and product candidates we develop. It is difficult and costly to protect our gene editing technologies and product candidates, and we may not be able to ensure their protection. Our ability to stop unauthorized third parties from making, using, selling, offering to sell, importing or otherwise commercializing our product candidates we may develop, or operatively similar products, is dependent upon the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities.

We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our product candidates that are important to our business and by in-licensing intellectual property related to our technologies and product candidates. If we are unable to obtain or maintain patent protection with respect to any proprietary technology or product candidate, our business, financial condition, results of operations and prospects could be materially harmed. Failure to obtain protection including patent protection, may be a result of specific legal and factual circumstances that may preclude the availability of protection for our product candidates in the United States or any given country. For example, inadequate, faulty or erroneous patent prosecution may result in diminution, loss or unavailability of patent rights that adequately cover our products. Patent disclosures and claims that are intended to cover our product candidates that are sufficient or allowable in one country may not be sufficient or allowable in another country. The requirements for filing a patent application in the United States may not be sufficient to support a patent filing in a country or region outside the United States.

The patent prosecution process is expensive, time-consuming and complex, and we may not be able to file, prosecute, maintain, defend or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. In addition, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our inventions and the prior art allow our inventions to be patentable over the prior art. 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. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain, enforce and defend the patents, covering technology that we license from third parties. Therefore, these in-licensed patents and applications may not be prepared, filed, prosecuted, maintained, defended and enforced in a manner consistent with the best interests of our business.

The patent position of pharmaceutical and biotechnology companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. The field of gene editing especially has been the subject of extensive patenting activity and litigation. In addition, the scope of patent protection outside of the United States is uncertain and laws of foreign countries may not protect our rights to the same extent as the laws of the United States or vice versa. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does.

With respect to both owned and in-licensed patent rights, we cannot predict whether the patent applications we and our licensors are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors. Further, we may not be aware of all third-party intellectual property rights potentially relating to our product candidates.

In addition, publications of discoveries in the scientific literature often lag behind 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 published at all. Therefore, neither we nor our licensors can know with certainty whether either we or our licensors were the first to make the inventions claimed in the patents and patent applications we own or in-license now or in the future, or that either we or our licensors were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our owned and in-licensed patent rights are highly uncertain. Moreover, our owned and in-licensed pending and future patent applications may not result in patents being issued which protect our technology and product candidates, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. 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 and our ability to obtain, protect, maintain, defend and enforce our patent rights, narrow the scope of our patent protection and, more generally, could affect the value or narrow the scope of our patent rights.

Moreover, we or our licensors may be subject to a third-party preissuance submission of prior art to the United States Patent and Trademark Office, or USPTO, or become involved in opposition, derivation, revocation, reexamination, *inter partes* review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize drugs without infringing third-party patent rights. If the breadth or strength of protection provided by our patents and patent applications is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Additionally, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if our owned and in-licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and in-licensed 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 freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and product candidates. Such proceedings also may result in substantial cost and require significant time from our management and employees, even if the eventual outcome is favorable to us. 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. Furthermore, our competitors may be able to circumvent our owned or in-licensed patents by developing similar or alternative technologies or products in a non-infringing manner. As a result, our owned and in-licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing technology and products similar or identical to any of our technology and product candidates.

Our rights to develop and commercialize our gene editing technology and product candidates are subject, in part, to the terms and conditions of licenses granted to us by others.

We depend on intellectual property licensed from third parties, and our licensors may not always act in our best interest. If we fail to comply with our obligations under our intellectual property licenses, if the licenses are terminated, or if disputes regarding these licenses arise, we could lose significant rights that are important to our business.

We have licensed and are dependent on certain patent rights and proprietary technology from third parties that are important or necessary to the development of our gene editing technology and product candidates. For example, we are a party to the Beam Agreement, the Cas9 License Agreement, the Acuitas Agreement and other license agreements, pursuant to which we in-license key patents and patent applications for our gene editing technology, LNP technology and product candidates. These license agreements impose various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with these obligations, our licensors may have the right to terminate our license, in which event we would not be able to develop or market our gene editing technology or product candidates covered by the intellectual property licensed under these agreements.

These and other licenses may not provide exclusive rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our gene editing technology and product candidates in the future. Some licenses granted to us are expressly subject to certain preexisting rights held by the licensor or certain third parties. As a result, we may not be able to prevent competitors from developing and commercializing competitive products in certain territories or fields. If we determine that rights to such excluded fields are necessary to commercialize our product candidates or maintain our competitive advantage, we may need to obtain a license from such third party in order to continue developing, manufacturing or marketing our product candidates. We may not be able to obtain such a license on an exclusive basis, on commercially reasonable terms, or at all, which could prevent us from commercializing our product candidates or allow our competitors or others the chance to access technology that is important to our business.

In addition, pursuant to the Cas9 License Agreement, under certain specific circumstances, Harvard and Broad may grant a license to the patents that are the subject of such license agreements to a third party in the same field as such patents are licensed to us. Such third party may then have full rights that are the subject of the Cas9 License Agreement, which could impact our competitive position and enable a third party to commercialize products similar to our potential future product candidates and technology. Any grant of rights to a third party in this scenario would narrow the scope of our exclusive rights to the patents and patent applications we have in-licensed from Harvard and Broad.

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. 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, the license granted to us in jurisdictions where the consent of a co-owner is necessary to grant such a license may not be valid and such co-owners may be able to license such patents to our competitors, and our competitors could market competing products and technology. In addition, our rights to our in-licensed patents and patent applications are dependent, in part, on inter-institutional or other operating agreements between the joint owners of such in-licensed patents and patent applications. If one or more of such joint owners breaches such inter-institutional or operating agreements, our rights to such in-licensed patents and patent applications may be adversely affected. Any of these events could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects.

Furthermore, inventions contained within some of our in-licensed patents and patent applications were 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.

In the event any of our third-party licensors determine that, in spite of our efforts, we have materially breached a license agreement or have failed to meet certain obligations thereunder, it may elect to terminate the applicable license agreement or, in some cases, one or more license(s) under the applicable license agreement, and such termination would result in us no longer having the ability to develop and commercialize product candidates and technology covered by that license agreement or license. In the event of such termination of a third-party in-license, or if the underlying patents under a third-party in-license fail to provide the intended exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, products identical to ours. Any of these events could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects.

Our owned patent applications and in-licensed patents and patent applications and other intellectual property may be subject to priority or inventorship disputes, interferences and similar proceedings. If we or our licensors are unsuccessful in any of these proceedings, we may be required to obtain licenses from third parties, which may not be available on commercially reasonable terms or at all, or to cease the development, manufacture, and commercialization of one or more of the product candidates we may develop, which could have a material adverse impact on our business.

Certain of the U.S. patents and one U.S. patent application to which we hold an option are co-owned by Broad and MIT, and in some cases co-owned by Broad, MIT and Harvard, which we refer to together as the Boston Licensing Parties, and were involved in U.S. Interference No. 106,048 with one U.S. patent application co-owned by the University of California, the University of Vienna, and Emmanuelle Charpentier, which we refer to together as CVC. On September 10, 2018, the Court of Appeals for the Federal Circuit, or the CAFC, affirmed the Patent Trial and Appeal Board of the USPTO's, or PTAB's, holding that there was no interference-in-fact. An interference is a proceeding within the USPTO to determine priority of invention of the subject matter of patent claims filed by different parties.

On June 24, 2019, the PTAB declared an interference (U.S. Interference No. 106,115) between 10 U.S. patent applications that are co-owned by CVC, and 13 U.S. patents and one U.S. patent application (that are co-owned by the Boston Licensing Parties). In the declared interference, CVC has been designated as the junior party and the Boston Licensing Parties have been designated as the senior party.

On December 20, 2020, the PTAB declared an interference (U.S. Interference No. 106,126) between one U.S. patent application owned by Toolgen, Inc. and 14 U.S. patents and two U.S. patent applications that are co-owned by the Boston Licensing Parties. In the declared interference, Boston Licensing Parties have been designated as the junior party and Toolgen, Inc. has been designated as the senior party.

As a result of the declaration of interference, an adversarial proceeding in the USPTO before the PTAB has been initiated, which is declared to ultimately determine priority, specifically and which party was first to invent the claimed subject matter. An interference is typically divided into two phases. The first phase is referred to as the motions or preliminary motions phase while the second is referred to as the priority phase. In the first phase, each party may raise issues including but not limited to those relating to the patentability of a party's claims based on prior art, written description, and enablement. A party also may seek an earlier priority benefit or may challenge whether the declaration of interference was proper in the first place. Priority, or a determination of who first invented the commonly claimed invention, is determined in the second phase of an interference. Although we cannot predict with any certainty how long each phase will actually take, each phase may take approximately a year or longer before a decision is made by the PTAB. It is possible for motions filed in the preliminary motions phase to be dispositive of the interference proceeding, such that the second priority phase is not reached.

There can be no assurance that the U.S. interference will be resolved in favor of the Boston Licensing Parties. If the 106,115 or 106,126 interference resolves in favor of CVC or Toolgen, Inc. respectively, or if the Boston Licensing Parties' patents and patent application are narrowed, invalidated, or held unenforceable, we will lose the ability to license the optioned patents and patent application and our ability to commercialize our product candidates may be adversely affected if we cannot obtain a license to relevant third-party patents that cover our product candidates. 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 nonexclusive, 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. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, we may be unable to commercialize our gene editing technology or product candidates or such commercialization efforts may be significantly delayed, which could in turn significantly harm our business.

We or our licensors may also be subject to claims that former employees, collaborators, or other third parties have an interest in our owned patent applications or in-licensed patents or patent applications or other intellectual property as an inventor or co-inventor. If we are unable to obtain an exclusive license to any such third-party co-owners' interest in such patent applications, such co-owners rights may be subject, or in the future subject, to assignment or license to other third parties, including our competitors. In addition, we may need the cooperation of any such co-owners to enforce any patents that issue from such patent applications against third parties, and such cooperation may not be provided to us.

If we or our licensors are unsuccessful in any interference proceedings or other priority, validity (including any patent oppositions) or inventorship disputes to which we or they are subject, we may lose valuable intellectual property rights through the loss of one or more of our owned, licensed or optioned patents, or such patent claims may be narrowed, invalidated or held unenforceable, or through loss of exclusive ownership of or the exclusive right to use our owned or in-licensed patents. In the event of loss of patent rights as a result of any of these disputes, we may be required to obtain and maintain licenses from third parties, including parties involved in any such interference proceedings or other priority or inventorship disputes. Such licenses may not be available on commercially reasonable terms or at all, or may be non-exclusive. If we are unable to obtain and maintain such licenses, we may need to cease the development, manufacture and commercialization of one or more of the product candidates we may develop. The loss of exclusivity or the narrowing of our patent claims could limit our ability to stop others from using or commercializing similar or identical technology and product candidates. Even if we or our licensors are successful in an interference proceeding, other similar priority disputes, or inventorship or ownership disputes, it could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could result in a material adverse effect on our business, financial condition, results of operations or prospects.

If we fail to comply with our obligations in our intellectual property licenses arrangements with third parties, or otherwise experience disruptions to our business relationships with our licensors, we could lose intellectual property rights that are important to our business.

We are party to agreements, and we may enter into additional arrangements, with third parties that may impose diligence, development and commercialization timelines, milestone payment, royalty, insurance and other obligations on us. We

have existing agreements, pursuant to which we are obligated to pay royalties on net product sales of product candidates or related technologies to the extent they are covered by the agreements. If we fail to comply with such obligations under current or future agreements, our counterparties may have the right to terminate these agreements or require us to grant them certain rights. Such an occurrence could materially adversely affect the value of any product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology, which would have a material adverse effect on our business, financial condition, results of operations and prospects. While we still face all of the risks described herein with respect to those agreements, we cannot prevent third parties from also accessing those technologies. In addition, our licenses may place restrictions on our future business opportunities.

Disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the agreement and other interpretation related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the 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 licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, the agreements under which we currently license intellectual property or technology from third parties 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, 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 conditions, results of operations and prospects.

Our current or future 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 intellectual property or intellectual property rights we in-license. If other third parties have ownership rights to intellectual property or intellectual property rights we in-license, they may be able to license such intellectual property or intellectual property rights to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects.

In spite of our best efforts, our 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 would 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.

If we are unable to obtain licenses from third parties on commercially reasonable terms or fail to comply with our obligations under such agreements, our business could be harmed.

We currently have rights to intellectual property, through licenses from third parties, to identify and develop product candidates, and we expect to seek to expand our product candidate pipeline in part by in-licensing the rights to key technologies. Although we have succeeded in licensing technologies from third-party licensors including Harvard, Broad, Beam, and Acuitas in the past, we cannot assure our stockholders that we will be able to in-license or acquire the rights to any product candidates or technologies from third parties on acceptable terms or at all.

Various third parties practice in competitive technology areas and may have issued patents or patent applications that will issue as patents in the future, which could impede or preclude our ability to commercialize our product candidates. For any third-party patents that could be relevant to our product candidates, we rely in part on the “safe harbor” or research exemption under 35 U.S.C. § 271(e)(1), which exempts from patent infringement activities related to pursuing FDA approval for a drug product. However, while U.S. patent law provides such a “safe harbor” to our clinical product

candidates under this provision, that exemption expires when an IND or BLA is submitted. Given the uncertainty of clinical trials, we cannot be certain of the timing of their completion and it is possible that we may submit a BLA for one of our product candidates at a time when one or more relevant third-party patents is in force.

It may therefore be necessary for us to use the patented or proprietary technology of third parties to commercialize our products, in which case we would be required to obtain a license from these third parties. If we are unable to license such technology, or if we are forced to license such technology on unfavorable terms, our business could be materially harmed. If we are unable to obtain a necessary license, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales or an obligation on our part to pay royalties and/or other forms of compensation. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us.

Furthermore, there has been extensive patenting activity in the field of gene editing, and pharmaceutical companies, biotechnology companies, and academic institutions are competing with us or are expected to compete with us in the field of gene editing technology and filing patent applications potentially relevant to our business, and there may be third-party patent applications that, if issued, may allow the third party to circumvent our patent rights. Because of the large number of patents issued and patent applications filed in our field, these and other third parties could allege they have patent rights encompassing our product candidates, technologies or methods. In order to market our product candidates, we may find it necessary or prudent to obtain licenses from such third-party intellectual property holders. 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 product candidates and gene editing technology we may develop. We may also require licenses from third parties for certain gene editing technologies including certain delivery and gene editing compositions and methods that we are evaluating, or may in the future evaluate, for use with product candidates we may develop. In addition, some of our owned patent applications and in-licensed patents and patent applications may be determined to be co-owned with third parties. With respect to any patents co-owned with third parties, we may require licenses to such co-owners' interest to such patents. 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 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.

Additionally, we may collaborate with academic institutions to accelerate our preclinical research or development under written agreements with these institutions. In certain cases, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Even if we hold such an option, we may be unable to negotiate a license from the institution 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 others, potentially blocking our ability to pursue our program.

In addition, the licensing or acquisition of third-party intellectual property rights is a highly competitive area, and a number of more established companies are also pursuing strategies to license or acquire third party intellectual property rights that we may consider attractive or necessary. 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 or at all. 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 have to abandon development of the relevant program or product candidate, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

If we are unable to 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 technology, 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 technology and product candidates, which could harm our business, financial condition, results of operations and prospects significantly.

Additionally, if we fail to comply with our obligations under license agreements, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market, or may be forced to cease developing, manufacturing or marketing, any product that is covered by these agreements or may face other penalties under such agreements. Such an occurrence could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our

rights under these agreements, or restrictions on our ability to freely assign or sublicense our rights under such agreements when it is in the interest of our business to do so, may result in our having to negotiate new or reinstated agreements with less favorable terms, cause us to lose our rights under these agreements, including our rights to important intellectual property or technology or impede, or delay or prohibit the further development or commercialization of one or more product candidates that rely on such agreements.

The intellectual property landscape around genome editing technology, including base editing, is highly dynamic, and third parties may initiate legal proceedings alleging that we are infringing, misappropriating, or otherwise violating their intellectual property rights, the outcome of which would be uncertain and may prevent, delay or otherwise interfere with our product discovery and development efforts.

Our commercial success depends upon our ability and the ability of our collaborators to research, develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property rights of third parties. The field of genome editing, especially in the area of base editing technology, is still in its infancy, and no such product candidates have reached the market. Due to the intense research and development that is taking place by several companies, including us and our competitors, in this field, the intellectual property landscape is evolving and in flux, and it may remain uncertain for the coming years. The biotechnology and pharmaceutical industries are characterized by extensive and complex litigation regarding patents and other intellectual property rights as well as administrative proceedings for challenging patents, including interference, derivation, *inter partes* review, post grant review, and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. There may be significant intellectual property related litigation and proceedings relating to our owned and in-licensed, and other third party, intellectual property and proprietary rights in the future. We may be subject to and may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our gene editing platform technology and any product candidates we may develop, including interference proceedings, post-grant review, *inter partes* review, and derivation proceedings before the USPTO and similar proceedings in foreign jurisdictions such as oppositions before the European Patent Office. Numerous U.S. and foreign issued patents and pending patent applications that are owned by third parties exist in the fields in which we are developing our product candidates and they may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit.

As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our gene editing technology and product candidates may give rise to claims of infringement of the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of therapies, products or their methods of use or manufacture. We are aware of certain third-party patent applications that, if issued, may be construed to cover our gene editing technology and product candidates. There may also be third-party patents of which we are currently unaware with claims to technologies, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents.

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

Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. There is a risk that third parties may choose to engage in litigation with us to enforce or to otherwise assert their patent rights against us. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, which could adversely affect our ability to commercialize our product candidates or any other of our product candidates or technologies covered by the

asserted third-party patents. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent.

Numerous third-party U.S. and foreign issued patents and pending patent applications exist in the fields in which we are developing product candidates. Our product candidates make use of CRISPR-based gene editing technology, which is a field that is highly active for patent filings. The extensive patent filings related to CRISPR and Cas make it difficult for us to assess the full extent of relevant patents and pending applications that may cover our gene editing technology and product candidates and their use or manufacture. There may be third-party patents or patent applications, including patents held or controlled by our competitors with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our gene editing technology and product candidates.

If we are found to infringe, misappropriate or otherwise violate a third party's valid and enforceable intellectual property rights, we could be required to obtain a license from such third party to continue developing, manufacturing and marketing our product candidates and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. We could be forced, including by court order, to cease developing, manufacturing and commercializing the infringing technology or product candidates. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right indemnify our customers or collaborators. A finding of infringement could prevent us from manufacturing and commercializing our product candidates or force us to cease some of our business operations, which could harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business, financial condition, results of operations and prospects.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Patents have a limited lifespan. The terms of individual patents depend upon the legal term for patents in the countries in which they are granted. In most countries, including the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest non-provisional filing date in the applicable country. However, the actual protection afforded by a patent varies from country to country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including biosimilars. 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 owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Our product candidates may face competition from biosimilars approved through an abbreviated regulatory pathway.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-approved reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first approved by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first approved. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of the other company's product. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty.

We believe that any of our product candidates approved 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 the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for biosimilar competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. Moreover, the extent

to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

If we do not obtain patent term extension in the United States under the Hatch-Waxman Act and in foreign countries under similar legislation, thereby potentially extending the term of our marketing exclusivity for any product candidates we may develop, our business may be materially harmed.

In the United States, the patent term of a patent that covers an FDA-approved drug may be eligible for limited patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under clinical development and regulatory review. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, and only one patent applicable to and that covers an approved drug may be extended. Similar provisions are available in Europe, such as supplementary protection certificates, and certain other non-United States jurisdictions to extend the term of a patent that covers an approved drug. While, in the future, if and when our product candidates receive FDA approval, we expect to apply for patent term extensions on patents covering those product candidates, there is no guarantee that the applicable authorities will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions. We may not be granted patent term extension either in the United States or in any foreign country because of, 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 term of extension, as well as the scope of patent protection during any such extension, afforded by the governmental authority could be less than we request. If we are unable to obtain any patent term extension or the term of any such extension is less than we request, our competitors may obtain approval of competing products following the expiration of our patent rights, and our business, financial condition, results of operations and prospects could be materially harmed.

It is possible that we will not obtain patent term extension under the Hatch-Waxman Act for a U.S. patent covering any of our product candidates that we may identify even where that patent is eligible for patent term extension, or if we obtain such an extension, it may be for a shorter period than we had sought.

Changes to patent laws in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our gene editing platform technology and product candidates.

As is the case with other biotech and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain.

Changes in either the patent laws or interpretation of patent laws in the United States, 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. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action.

Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith Act, the United States transitioned to a first-to-file system in which, assuming that the other statutory requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. As such, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our patent rights and our ability to protect, defend and enforce our patent rights in the future. For example, in the case, *Assoc. for Molecular Pathology v. Myriad Genetics, Inc.*, the U.S. Supreme Court held that claims to certain DNA molecules are not patentable. More recently, in *Amgen Inc. v. Sanofi*, the Federal Circuit held that claims with functional language may pose high hurdles in fulfilling the enablement requirement for claims with broad functional language. We cannot predict how this and future decisions by the courts, the U.S. Congress or the USPTO may impact the value of our patents. Any similar adverse changes in the patent laws of other jurisdictions could also have a material adverse effect on our business, financial condition, results of operations and prospects.

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

If we or one of our licensing partners initiates 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, written description or non-enablement. In addition, patent validity challenges may, under certain circumstances, be based upon non-statutory obviousness-type double patenting, which, if successful, could result in a finding that the claims are invalid for obviousness-type double patenting or the loss of patent term, including a patent term adjustment granted by the USPTO, if a terminal disclaimer is filed to obviate a finding of obviousness-type double patenting. 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, post grant review, *inter partes* review and equivalent 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 have a material adverse impact on 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.

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

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately.

Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and may also have an advantage in such proceedings due to their more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of intellectual property litigation or other proceedings could compromise our ability to compete in the marketplace.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance, renewal and annuity fees and various other government fees on any issued patent and pending patent application must be paid to the USPTO and foreign patent agencies in several stages or annually over the lifetime of our owned and in-licensed patents and patent applications. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In certain circumstances, we may rely on our licensing partners to pay these fees to, or comply with the procedural and documentary rules of, the relevant patent agency. With respect to our patents, we rely on outside firms and outside counsel to remind us of the due dates and to make payment after we instruct them to do so. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, potential competitors might be able to enter the market with similar or identical products or technology. If we or our licensors fail to maintain the patents and patent applications covering our product candidates, it would have a material adverse effect on our business, financial condition, results of operations and prospects.

We have limited foreign intellectual property rights and may not be able to protect our intellectual property and proprietary rights throughout the world.

We have limited intellectual property rights outside the United States. Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and the laws of foreign countries may not protect our rights to the same extent as the laws of 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, and even where such protection is nominally available, judicial and governmental enforcement of such intellectual property rights may be lacking. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection or licenses but enforcement is not as strong as that in the United States. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our intellectual property and proprietary rights generally. In addition, certain jurisdictions do not protect to the same extent or at all inventions that constitute new methods of treatment.

Proceedings to enforce our intellectual property and proprietary 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, could put 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 and proprietary 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 are 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.

We may be subject to claims by third parties asserting that our employees, consultants or contractors have wrongfully used or disclosed confidential information of third parties, or we have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees, consultants and contractors were previously employed at universities or other pharmaceutical or biotechnology companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and contractors 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.

In addition, while it is our policy to require our employees, consultants and contractors who may be involved in the 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 develops intellectual property that we regard as our own. Our intellectual property assignment agreements with them may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial conditions, results of operations and prospects.

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could have a material adverse effect on our competitive business position and prospects. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products, which license may not be available on commercially reasonable terms, or at all, or such license may be non-exclusive. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our management and employees.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for our some of our technology and product candidates, we also rely on trade secrets and confidentiality agreements to protect our unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect our trade secrets and other proprietary technology, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, CROs, CMOs, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants, but we cannot guarantee that we have entered into such agreements with each party that may have or has had access to our trade secrets or proprietary technology. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Detecting the disclosure or misappropriation of a trade secret and enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable.

In addition to contractual measures, we try to protect the confidential nature of our proprietary information through other appropriate precautions, such as physical and technological security measures. However, trade secrets and know-how can be difficult to protect. These measures may not, for example, in the case of misappropriation of a trade secret by an employee or third party with authorized access, provide adequate protection for our proprietary information. Our security measures may not prevent an employee or consultant from misappropriating our trade secrets and providing them to a competitor, and any recourse we might take against this type of misconduct may not provide an adequate remedy to protect our interests fully. In addition, trade secrets may be independently developed by others in a manner that could prevent us from receiving legal recourse. If any of our confidential or proprietary information, such as our trade secrets, were to be disclosed or misappropriated, or if any of that information was independently developed by a competitor, our competitive position could be harmed.

In addition, some courts inside and outside of the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our competitive position would be materially and adversely harmed.

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

Any registered trademarks or trade names may be challenged, 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:

- any product candidates we may develop will eventually become commercially available in generic or biosimilar product forms;
- others may be able to make gene editing product that are similar to ours but that are not covered by the claims of the patents that we own;
- we, or our license partners or current or future collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent applications that we license or 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 in-licensed intellectual property rights;
- it is possible that our pending owned and in-licensed patent applications or those we may own or in-license in the future will not lead to issued patents;
- it is possible that there are prior public disclosures that could invalidate our owned or in-licensed patents, or parts of our owned or in-licensed patents;
- it is possible that there are unpublished applications or patent applications maintained in secrecy that may later issue with claims covering our product candidates or technology similar to ours;
- it is possible that our owned or in-licensed patents or patent applications omit individual(s) that should be listed as inventor(s) or include individual(s) that should not be listed as inventor(s), which may cause these patents or patents issuing from these patent applications to be held invalid or unenforceable;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors;
- the laws of foreign countries may not protect our proprietary rights or the proprietary rights of license partners or current or future collaborators to the same extent as the laws of the United States;
- the inventors of our owned or in-licensed patents or patent applications may become involved with competitors, develop products or processes that design around our patents, or become hostile to us or the patents or patent applications on which they are named as inventors;
- 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 have engaged in scientific collaborations in the past and will continue to do so in the future and our collaborators may develop adjacent or competing products that are outside the scope of our patent rights;

- we cannot ensure that any of our patents, or any of our pending patent applications, if issued, or those of our licensors, will include claims having a scope sufficient to protect our product candidates;
- we cannot ensure that any patents issued to us or our licensors will provide a basis for an exclusive market for our commercially viable product candidates or will provide us with any competitive advantages;
- we cannot ensure that our commercial activities or product candidates will not infringe upon the patents of others;
- we cannot ensure that we will be able to successfully commercialize our product candidates on a substantial scale, if approved, before our relevant patents that we own or license expire;
- we may not develop additional proprietary technologies that are patentable;
- the patents of others may harm our business; and
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

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

Risks related to commercialization

Even if any of our current or future product candidates receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success, and the market opportunity for any of such product candidates, if approved, may be smaller than we estimate.

If any of our current or future product candidates receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. For example, current CVD treatments such as statins, ezetimibe, bempedoic acid, lomitapide, mipomersen and icosapent ethyl are well-established in the medical community, and physicians may continue to rely on these treatments. Efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may not be successful. If our current or future 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 current or future product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and potential advantages of such product candidates compared to the advantages and relative risks of alternative treatments;
- the effectiveness of sales and marketing efforts;
- the cost of treatment in relation to alternative treatments, including any similar biosimilar treatments;
- our ability to offer our products, if approved, for sale at competitive prices;
- 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; and
- any restrictions on the use of our products, if approved, together with other medications.

Our assessment of the potential market opportunity for our current or future product candidates is based on industry and market data that we obtained from industry publications, research, surveys and studies conducted by third parties and our analysis of these data, research, surveys and studies. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. While we believe these industry publications and third-party research, surveys and studies are reliable, we have not independently verified such data. Our estimates of the potential market opportunities for our product candidates include a number of key assumptions based on our industry knowledge,

industry publications and third-party research, surveys and studies, which may be based on a small sample size and fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions. If any of our assumptions or estimates, or these publications, research, surveys or studies prove to be inaccurate, then the actual market for any of our product candidates may be smaller than we expect, and as a result our revenues from product sales may be limited and it may be more difficult for us to achieve or maintain profitability.

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

The development and commercialization of new drug or biologic products is highly competitive. It is particularly competitive with respect to new products for CVD, for which the standard of care is well-established. We face competition with respect to our current product candidates, and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, 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 disease indications for which we are developing our product candidates. Some of these competitive products and therapies are based on scientific approaches that are 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.

There are several approved products for low-density lipoprotein cholesterol, or LDL-C, lowering or cardiovascular risk reduction, such as statins, ezetimibe, bempedoic acid, lomitapide, mipomersen and icosapent ethyl.

There are several approved products that target PCSK9 protein as a mechanism to lower LDL-C and reduce the risk of ASCVD. Evolocumab, a monoclonal antibody, or mAb, marketed as Repatha by Amgen, is approved by the FDA for the treatment of patients with heterozygous familial hypercholesterolemia, or HeFH, patients with HoFH and in patients with ASCVD. Alirocumab, a mAb marketed as Praluent by Sanofi and Regeneron Pharmaceuticals, Inc., or Regeneron, is approved by the FDA for the treatment of patients with ASCVD and for the treatment of patients with primary hyperlipidemia, including HeFH. Regeneron has sole U.S. rights to alirocumab and Sanofi has sole ex-U.S. rights to alirocumab. The approved mAb treatments act through extracellular inhibition of PCSK9 protein. Inclisiran, a small interfering RNA, or siRNA, marketed as Leqvio by Novartis AG, is approved in Europe for the treatment of patients with hypercholesterolemia, including HeFH, or mixed dyslipidemia. Inclisiran acts by inhibiting the synthesis of PCSK9 within liver cells, which is distinct from extracellular protein inhibition.

We are aware of several product candidates in clinical development that target PCSK9 protein as a mechanism to lower LDL-C and reduce the risk of ASCVD, including peptide-based anti PCSK9 vaccination, small molecule oral PCSK9 inhibitors, small binding proteins, and antisense oligonucleotides. In 2021, Esperion in-licensed an oral small molecule PCSK9 inhibitor from Serometrix LLC for which it plans to submit an IND in 2021.

We are aware of one other gene editing program targeting the PCSK9 gene in preclinical development. Precision Biosciences, Inc. has published preclinical data showing long-term stable reduction of LDL-C levels in non-human primates following *in vivo* gene editing of the PCSK9 gene using its gene editing platform.

Evinacumab, a mAb targeting ANGPTL3 protein that is marketed by Regeneron, is approved by the FDA for the treatment of patients with HoFH. Evinacumab is also being evaluated by Regeneron in Phase 2 development for severe hypertriglyceridemia.

We are aware of several product candidates in clinical development that target ANGPTL3 protein as a mechanism to lower LDL-C and reduce the risk of ASCVD, including vupanorsen, an antisense oligonucleotide therapy being evaluated in a Phase 2 clinical trial by Ionis Pharmaceuticals, Inc. and Pfizer for the treatment of patients with elevated non-high-density lipoprotein cholesterol and triglycerides. In addition, ARO-ANG3, a siRNA targeting ANGPTL3 protein, is being evaluated in a Phase 1/2 clinical trial by Arrowhead Pharmaceuticals, Inc., or Arrowhead. In 2021, Arrowhead filed an IND for a Phase 2b trial of ARO-ANG3 for the treatment of patients with mixed dyslipidemia.

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 any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of biosimilar products. If our product candidates achieve marketing approval, we expect that they will be priced at a significant premium over competitive biosimilar products.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do.

Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

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 current and future product candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience as a company with the commercialization of 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, if and when they are approved. There are 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.

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 obtain access to physicians or persuade adequate numbers of physicians to prescribe any future products;
- the inability of reimbursement professionals to negotiate arrangements for coverage, 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; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

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. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

We expect to rely on CMOs to manufacture our product candidates. If we are unable to enter into such arrangements as expected or if such organizations do not meet our supply requirements, development and/or commercialization of our product candidates may be delayed.

We expect to rely on third parties to manufacture clinical supplies of our product candidates and commercial supplies of our products, if and when approved for marketing by applicable regulatory authorities, as well as for packaging, sterilization, storage, distribution and other production logistics. If we are unable to enter into such arrangements on the

terms or timeline we expect, development and/or commercialization of our product candidates may be delayed. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or manufacture our product candidates in accordance with regulatory requirements, if there are disagreements between us and such parties or if such parties are unable to expand capacities to support commercialization of any of our product candidates for which we obtain marketing approval, we may not be able to fulfill, or may be delayed in producing sufficient product candidates to meet, our supply requirements. These facilities may also be affected by pandemics, including the ongoing COVID-19 pandemic, natural disasters, such as floods or fire, or such facilities could face manufacturing issues, such as contamination or regulatory concerns following a regulatory inspection of such facility. In such instances, we may need to locate an appropriate replacement third-party facility and establish a contractual relationship, which may not be readily available or on acceptable terms, which would cause additional delay and increased expense, including as a result of additional required FDA approvals, and may have a material adverse effect on our business.

Our third-party manufacturers will be subject to inspection and approval by the FDA before we can commence the manufacture and sale of any of our product candidates, and thereafter subject to FDA inspection from time to time. Failure by our third-party manufacturers to pass such inspections and otherwise satisfactorily complete the FDA approval regimen with respect to our product candidates may result in regulatory actions such as the issuance of FDA Form 483 notices of observations, warning letters or injunctions or the loss of operating licenses.

We or our third-party manufacturers may also encounter shortages in the raw materials or API necessary to produce our product candidates in the quantities needed for our clinical trials or, if our product candidates are approved, in sufficient quantities for commercialization or to meet an increase in demand, as a result of capacity constraints or delays or disruptions in the market for the raw materials or API, including shortages caused by the purchase of such raw materials or API by our competitors or others. The failure of us or our third-party manufacturers to obtain the raw materials or API necessary to manufacture sufficient quantities of our product candidates may have a material adverse effect on our business.

Even if we are able to commercialize any product candidates, the products may become subject to unfavorable pricing regulations, third-party coverage or reimbursement practices or healthcare reform initiatives, which could harm our business.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

Our ability to commercialize any product candidates successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

In the United States, there is no uniform policy of coverage and reimbursement for products exists among third-party payors. As a result, obtaining coverage and reimbursement approval of a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost-effectiveness data for the use of our products on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. The availability and adequacy of coverage and reimbursement by governmental healthcare programs such as Medicare and Medicaid, private health insurers and other third-party payors

are essential for most patients to be able to afford our product candidates, if approved. Our ability to achieve acceptable levels of coverage and reimbursement for our product candidates, if approved, by governmental authorities, private health insurers and other organizations will have an effect on our ability to successfully commercialize, our product candidates. Assuming we obtain coverage for a given product by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require patient out-of-pocket costs that patients find unacceptably high.

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Coverage and reimbursement may not be available for any product that we commercialize and, even if these are available, the level of reimbursement may not be satisfactory. Reimbursement may affect the demand for, or the price of, any product candidate for which we obtain marketing approval. Obtaining and maintaining adequate reimbursement for our products may be difficult. We may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies. If coverage and adequate reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar regulatory authorities outside of the United States. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution expenses. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

There can be no assurance that our product candidates, even if they are approved for sale in the United States or in other countries, will be considered medically reasonable and necessary for a specific indication or cost-effective by third-party payors, or that coverage and an adequate level of reimbursement will be available or that third-party payors' reimbursement policies will not adversely affect our ability to sell our product candidates profitably.

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

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

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

- reduced protection of intellectual property rights in some foreign countries, and related prevalence of biosimilar alternatives to therapeutics;
- foreign currency exchange rate fluctuations and currency controls;
- differing foreign reimbursement landscapes;
- uncertain and potentially inadequate reimbursement of our products; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

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

Clinical trial and product liability lawsuits against us could divert our resources and could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We will face an inherent risk of clinical trial and product liability exposure related to the testing of our product candidates in human 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 in clinical trials or that have been approved for commercial sale, the 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 any product candidates or products that we may develop;
- termination of clinical trials;
- 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 any products that we may develop.

We currently do not hold any clinical trial liability insurance coverage. We may need to obtain insurance coverage as we expand our clinical trials or if we commence commercialization of our product candidates. Insurance coverage is increasingly expensive. We may not be able to obtain and 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 regulatory approval and other legal compliance matters

Gene editing is novel and the regulatory landscape that will govern any product candidates we may develop is uncertain and may change. As a result, we cannot predict the time and cost of obtaining regulatory approval, if we receive it at all, for any product candidates we may develop.

The regulatory requirements that will govern any novel gene editing product candidates we develop are not entirely clear and may change. Within the broader genetic medicines field, we are aware of a limited number of gene therapy products that have received marketing authorization from the FDA and the EMA. Even with respect to more established products that fit into the categories of gene therapies or cell therapies, the regulatory landscape is still developing. Regulatory requirements governing gene therapy products and cell therapy products have changed frequently and will likely continue to change in the future. Moreover, there is substantial, and sometimes uncoordinated, overlap in those responsible for regulation of existing gene therapy products and cell therapy products. For example, in the United States, the FDA has established the Office of Tissues and Advanced 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. Gene therapy clinical trials may also be subject to review and oversight by an IBC, a local institutional committee that reviews and oversees basic and clinical research conducted at the institution participating in the clinical trial. Although the FDA decides whether individual gene therapy protocols may

proceed, the review process and determinations of other reviewing bodies can impede or delay the initiation of a clinical trial, even if the FDA has reviewed the trial and approved its initiation.

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

Adverse developments in post-marketing experience or in clinical trials conducted by others of gene therapy products, cell therapy products, or products developed through the application of a base editing or other gene editing technology may cause the FDA, the EMA, and other regulatory bodies to revise the requirements for development or approval of any product candidates we may develop or limit the use of products utilizing base editing technologies, either of which could materially harm our business. In addition, the clinical trial requirements of the FDA, the EMA, and other regulatory authorities 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 the product candidates we may develop can be more expensive and take longer than for other, better known, or more extensively studied pharmaceutical or other product candidates. Regulatory agencies administering existing or future regulations or legislation may not allow production and marketing of products utilizing base editing technology in a timely manner or under technically or commercially feasible conditions. In addition, regulatory action or private litigation could result in expenses, delays, or other impediments to our research programs or the commercialization of resulting products.

The regulatory review committees and advisory groups described above and the new guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies or trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates, or lead to significant post-approval limitations or restrictions. As we advance our research programs and develop future product candidates, we will be required to consult with these regulatory and advisory groups and to comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of any product candidates we identify and develop.

Because we are developing product candidates in the field of genetic medicines, a field that includes gene therapy and gene editing, in which there is little clinical experience, there is increased risk that the FDA, the EMA, or other regulatory authorities may not consider the endpoints of our clinical trials to provide clinically meaningful results and that these results may be difficult to analyze.

During the regulatory review process, we will need to identify success criteria and endpoints such that the FDA, the EMA, or other regulatory authorities will be able to determine the clinical efficacy and safety profile of any product candidates we may develop. As we are seeking to identify and develop product candidates to treat diseases in which there is no clinical experience using a gene editing approach, there is heightened risk that the FDA, the EMA, or other regulatory authorities may not consider the clinical trial endpoints that we propose to provide clinically meaningful results (reflecting a tangible benefit to patients). In addition, the resulting clinical data and results may be difficult to analyze. Even if the FDA does find our success criteria to be sufficiently validated and clinically meaningful, we may not achieve the pre-specified endpoints to a degree of statistical significance. Further, even if we do achieve the pre-specified criteria, we may produce results that are unpredictable or inconsistent with the results of the non-primary endpoints or other relevant data. The FDA also weighs the benefits of a product against its risks, and the FDA may view the efficacy results in the context of safety as not being supportive of regulatory approval. Other regulatory authorities in the EU and other countries may make similar comments with respect to these endpoints and data. Any product candidates we may develop will be based on a novel technology that makes it difficult to predict the time and cost of development and of subsequently obtaining regulatory approval. No gene editing therapeutic product has been approved in the United States or in Europe.

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of any product candidates we develop. If we are not able to obtain, or if there are delays in

obtaining, required regulatory approvals, we will not be able to commercialize, or will be delayed in commercializing, product candidates we develop, and our ability to generate revenue will be materially impaired.

Any product candidates we develop and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory authorities in the United States and by comparable authorities in other countries. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate in a given jurisdiction. We have not received approval to market any product candidates from regulatory authorities in any jurisdiction. We have no experience as a company in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party CROs to assist us in this process. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information, including manufacturing information, to the various regulatory authorities for each therapeutic indication to establish the biologic product candidate's safety, purity and potency. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Any product candidates we develop may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining marketing approvals, both in the United States and abroad, 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. Of the large number of products in development, only a small percentage successfully complete the FDA or foreign regulatory approval processes and are commercialized. Even if any product candidates we may develop 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. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Finally, disruptions at the FDA and other agencies may prolong the time necessary for new drugs 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 the FDA, have had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

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.

Obtaining and maintaining marketing approval or commercialization of our product candidates in the United States does not mean that we will be successful in obtaining marketing approval of our product candidates in other jurisdictions. 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 may develop in the European Union and many other foreign jurisdictions, we or our collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We or these third parties may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to

file for marketing approvals and may not receive necessary approvals to commercialize our product candidates in any jurisdiction, which would materially impair our ability to generate revenue.

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

Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of the Trade and Cooperation Agreement or otherwise, would prevent us from commercializing any product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or the European Union for any product candidates we may develop, which could significantly and materially harm our business.

A fast track, breakthrough therapy or priority review designation by the FDA may not lead to a faster development or regulatory review or approval process and does 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 the FDA for fast track designation. For fast track products, sponsors may have greater interactions with the FDA and the 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 the 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 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 the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens.

Further, if the FDA determines that a product candidate offers major advances in treatment or provides a treatment where no adequate therapy exists, the FDA may designate the product candidate for priority review. 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 the FDA to review an application is six months, rather than the standard review period of ten months.

We may seek these and other designations for our product candidates. The 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, the 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, the FDA may withdraw these designations if it believes that the designation is no longer supported by data from our clinical development program.

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

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

longer meets the criteria for orphan drug designation, in particular if the product is sufficiently profitable so that market exclusivity is no longer justified.

In order for the FDA to grant orphan drug exclusivity to one of our products, the agency must find that the product is indicated for the treatment of a condition or disease with a patient population of fewer than 200,000 individuals annually in the United States. The FDA may conclude that the condition or disease for which we seek orphan drug exclusivity does not meet this standard. Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different products can be approved for the same condition. In particular, the concept of what constitutes the "same drug" for purposes of orphan drug exclusivity remains in flux in the context of gene therapies, and the FDA has issued recent draft 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. In addition, even after an orphan drug is approved, the FDA can subsequently approve the same product for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusivity may also be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of the patients with the rare disease or condition.

In 2017, the Congress passed the FDA Reauthorization Act of 2017, or the 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. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

Negative public opinion of gene editing and increased regulatory scrutiny of gene editing 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 editing and gene regulation for the prevention or treatment of human diseases. Public attitudes may be influenced by claims that gene editing 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 editing and we cannot assure that it will not occur in any of our planned or future clinical trials. 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.

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 product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to quality control, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval

may be subject to limitations on the indicated uses for which the product 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 product.

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

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 products, when and if any of them are approved.

The FDA and other regulatory agencies closely regulate the post-approval marketing and promotion of medicines to ensure that they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. Although physicians may prescribe products for uses not described in the product's labeling, known as off-label uses, in their professional medical judgment, the FDA and other regulatory agencies impose stringent restrictions on manufacturers' communications regarding off-label use, and if we market our products, if approved, in a manner inconsistent with their approved labeling, we may be subject to enforcement action for off-label marketing by the FDA and other federal and state enforcement agencies, including the Department of Justice, or DOJ. Violation of the Federal Food, Drug, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription products may also lead to investigations or allegations of violations of federal and state health care fraud and abuse laws and state consumer protection laws.

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

- restrictions on such products, 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.

Any relationships we may have with customers, healthcare providers and professionals, and third-party payors, among others, will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to penalties, including criminal sanctions, civil penalties, contractual

damages, reputational harm, fines, disgorgement, exclusion from participation in government healthcare programs, curtailment or restricting of our operations, and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any products for which we are able to obtain marketing approval. Any arrangements we have with healthcare providers, third-party payors and customers will subject us to broadly applicable fraud and abuse and other healthcare laws and regulations. The laws and regulations may constrain the business or financial arrangements and relationships through which we conduct clinical research, market, sell and distribute any products for which we obtain marketing approval. These 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 civil and criminal false claims laws, including the federal False Claims Act, which can be enforced through civil whistleblower or qui tam actions, and civil monetary penalty laws impose civil and criminal penalties against individuals or entities for knowingly presenting or causing to be presented, to the federal government, claims for payment or approval from Medicare, Medicaid or other government payers that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which prohibits, among other things, knowingly and willfully executing, or attempting to execute, a scheme or artifice to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private), and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false, fictitious or fraudulent statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters;
- HIPAA, as further amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, which imposes certain requirements, including mandatory contractual terms, on covered entities subject to the rule, such as health plans, healthcare clearinghouses and certain healthcare providers, as well as their respective business associates and their subcontractors that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security, and transmission of such individually identifiable health information;
- 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, or HHS, information related to payments and other transfers of value to physicians, as defined by such law, and teaching hospitals and ownership and investment interests held by physicians (as defined by such law) and their immediate family members and applicable group purchasing organizations, and, beginning in 2022, will require applicable manufacturers to report information regarding payments and other transfers of value provided during the previous year to physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists, anesthesiologist assistants, and certified nurse midwives; 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 payers, 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 drug pricing and payments to physicians and other healthcare providers or marketing expenditures and state and local laws that require the registration of sales representatives; and state and foreign laws governing the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that any business arrangements we have with third parties, and our business generally, 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, individual imprisonment, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with

these laws, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, reputational harm, and the curtailment or restructuring of our operations. Defending against any such actions can be costly, time-consuming and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. Further, if any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Current and future legislation may increase the difficulty and cost for us and any collaborators to obtain marketing approval 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 collaborators, to profitably sell or commercialize any product candidate 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 collaborators, may receive for any approved products.

In March 2010, President Obama signed into law 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 2030, with the exception of a temporary suspension from May 1, 2020 through December 31, 2021, unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Since enactment of the 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 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 inseparable feature of the ACA, and therefore because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. On December 18, 2019, the Court of Appeals for the Fifth Circuit court affirmed the lower court's ruling that the individual mandate portion of the ACA is unconstitutional and it remanded the case to the district court for reconsideration of the severability question and additional analysis of the provisions of the ACA. Thereafter, the U.S. Supreme Court agreed to hear this case. Oral argument in the case took place on November 10, 2020. On February 10, 2021, the Biden administration withdrew the federal government's support for overturning the ACA. A ruling by the Court is expected sometime this year. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The former Trump presidential 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 Executive 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 HHS to create a special enrollment period for the Health Insurance Marketplace in response to the COVID-19 pandemic.

We expect that these healthcare reform measures, 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. It is also possible that additional governmental action will be taken in response to the COVID-19 pandemic.

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. To date, 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 drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for products. To those ends, President Trump issued several executive orders intended to lower the costs of prescription drug products. Certain of these orders are reflected in recently promulgated regulations, including an interim final rule implementing President Trump's most favored nation model, but such final rule is currently subject to a nationwide preliminary injunction. It remains to be seen whether these orders and resulting regulations will remain in force during the Biden administration. Further, on September 24, 2020, the former Trump presidential administration finalized a rule allowing states or certain other non-federal government entities to submit importation program proposals to the FDA for review and approval. Applicants are required to demonstrate that their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. The FDA has issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

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 health care 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 health care 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.

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 or transfer such data across borders, and the failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Union, including personal health data, is subject to the EU General Data Protection Regulation, or the GDPR,

which took effect across all member states of the European Economic Area, or EEA, in May 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR would increase 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 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. 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 certain 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.

The GDPR also imposes strict rules on the transfer of personal data to countries outside the EEA, including the United States, unless the parties to the transfer have implemented safeguards to protect the transferred personal information. The Court of Justice of the European Union, or CJEU, recently raised questions in a decision that has been dubbed Schrems II about whether the European Commission's Standard Contractual Clauses, one of the primary mechanisms used by companies to import personal information from Europe, complies with the GDPR. The Schrems II decision also invalidated the EU-U.S. Privacy Shield, a mechanism used by numerous companies to transfer personal data from the European Union to the United States. While the CJEU upheld the validity of the Standard Contractual Clauses, the CJEU ruled that the underlying data transfers must be assessed on a case-by-case basis by the data controller to determine whether the personal information will be adequately protected. Further, the European Commission recently proposed updates to the Standard Contractual Clauses. At present, there are few if any viable alternatives to the Standard Contractual Clauses and, therefore, there is uncertainty regarding how to ensure that transfers of personal information from Europe to the United States comply with the GDPR. As such, any transfers by us, or our vendors, of personal information from Europe may not comply with European data protection laws and may increase our exposure to the GDPR's heightened sanctions for violations of its cross-border data transfer restrictions. Loss of our ability to transfer personal information from Europe may also require us to increase our data processing capabilities in those jurisdictions at significant expense.

Further, the United Kingdom's withdrawal from the European Union and EEA on January 31, 2020 has created uncertainty with regard to data protection regulation in the United Kingdom. As of January 1, 2021, companies are subject to the UK GDPR and UK Data Protection Act of 2018, which retains the GDPR in the United Kingdom's national law. In particular, the collection, use, storage, disclosure, transfer, or other processing of personal data (including health data processed in the context of clinical trials) regarding data subjects in the United Kingdom and/or carried out in the context of the activities of our establishment in the United Kingdom is subject to the UK GDPR and the UK Data Protection Act of 2018. However, it is still unclear whether the transfer of personal information from the EEA to the United Kingdom will remain lawful under the GDPR.

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, or CCPA—which went into effect on January 1, 2020—is creating similar risks and obligations as those created by GDPR, though the CCPA 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 addition, California voters approved a new privacy law, the California Privacy Rights Act, or CPRA, in the November 3, 2020 election. Effective starting on January 1, 2023, the CPRA will significantly modify the CCPA, including by expanding consumers' rights with respect to certain sensitive personal information. The CPRA also creates a new state agency that will be vested with authority to implement and enforce the CCPA and the CPRA. It remains unclear, however, how the CCPA and CPRA will be interpreted.

New legislation proposed or enacted in Illinois, Massachusetts, Nevada, New Jersey, New York, Rhode Island, Virginia, Washington and other states, and a proposed right to privacy amendment to the Vermont Constitution, imposes, or has the potential to impose, additional obligations on companies that collect, store, use, retain, disclose, transfer and otherwise process confidential, sensitive and personal information, and will continue to shape the data privacy environment nationally. For example, Virginia became the second state to enact a comprehensive privacy law when it

recently passed the Consumer Data Protection Act, or CDPA, which will take effect on January 1, 2023. The CDPA contains provisions that require businesses subject to the legislation to conduct data protection assessments in certain circumstances and that require opt-in consent from Virginia consumers to process certain sensitive personal information.

Overall, state laws are changing rapidly and may be more stringent or broader in scope, or offer greater individual rights, with respect to confidential, sensitive and personal information than federal, international or other state laws, and such laws may differ from each other, which may complicate compliance efforts. There is also discussion in Congress of a new federal data protection and privacy law to which we would become subject if it is enacted. All of these evolving compliance and operational requirements impose significant costs that are likely to increase over time, may require us to modify our data processing practices and policies, divert resources from other initiatives and projects, and could restrict the way products and services involving data are offered, all of which could significantly harm our business, financial condition, results of operations and prospects.

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.

In addition, any breach of privacy laws or data security laws, particularly resulting in a significant security incident or breach involving the misappropriation, loss or other unauthorized use or disclosure of sensitive or confidential patient or consumer information, could have a material adverse effect on our business, reputation and financial condition. As a data controller, we will be accountable for any third-party service providers we engage to process personal data on our behalf, including our CROs. We attempt to mitigate the associated risks but there is no assurance that privacy and security-related safeguards will protect us from all risks associated with the third-party processing, storage and transmission of such information.

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

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

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

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

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

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

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

If we or any third-party manufacturer we engage now or in the future fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs or liabilities that could have a material adverse effect on our business.

We and third-party manufacturers we engage now are, and any third-party manufacturer we may engage in the future will be, subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain general liability insurance as well as workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or commercialization efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Further, with respect to the operations of our current and any future third-party contract manufacturers, it is possible that if they fail to operate in compliance with applicable environmental, health and safety laws and regulations or properly dispose of wastes associated with our products, we could be held liable for any resulting damages, suffer reputational harm or experience a disruption in the manufacture and supply of our product candidates or products. In addition, our supply chain may be adversely impacted if any of our third-party contract manufacturers become subject to injunctions or other sanctions as a result of their non-compliance with environmental, health and safety laws and regulations.

Risks related to employee matters and managing growth

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 Sekar Kathiresan, M.D., our chief executive officer, Andrew Ashe, J.D., our president, chief operating officer and general counsel, and Andrew Bellinger, M.D., Ph.D., our chief scientific officer, as well as the other principal members of our management, scientific and clinical teams. Although we have entered into employment agreements with our executive officers, each of them may terminate their employment with us at any time. We do not maintain “key person” insurance for any of our executives or other employees. Recruiting and retaining qualified scientific, clinical, manufacturing, accounting, legal and sales and marketing personnel will also be critical to our success.

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

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

As our development progresses, 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, manufacturing and quality control and, if any of our product candidates receive 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.

Future acquisitions or strategic alliances could disrupt our business and harm our financial condition and results of operations.

We may acquire additional businesses, technologies or assets, form strategic alliances or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new products or product candidates resulting from a strategic alliance or

acquisition that may delay or prevent us from realizing their expected benefits or enhancing our business. We cannot assure our stockholders that, following any such acquisition, we will achieve the expected synergies to justify the transaction. The risks we face in connection with acquisitions include:

- diversion of management time and focus from operating our business to addressing acquisition integration challenges;
- coordination of research and development efforts;
- retention of key employees from the acquired company;
- changes in relationships with collaborators as a result of product acquisitions or strategic positioning resulting from the acquisition;
- cultural challenges associated with integrating employees from the acquired company into our organization;
- the need to implement or improve controls, procedures and policies at a business that prior to the acquisition may have lacked sufficiently effective controls, procedures and policies;
- liability for activities of the acquired company before the acquisition, including intellectual property infringement claims, violation of laws, commercial disputes, tax liabilities and other known liabilities;
- unanticipated write-offs or charges; and
- litigation or other claims in connection with the acquired company, including claims from terminated employees, customers, former stockholders or other third parties.

Our failure to address these risks or other problems encountered in connection with our past or future acquisitions or strategic alliances could cause us to fail to realize the anticipated benefits of these transactions, cause us to incur unanticipated liabilities and harm the business generally. There is also a risk that future acquisitions will result in the incurrence of debt, contingent liabilities, amortization expenses or incremental operating expenses, any of which could harm our financial condition or results of operations.

Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Our internal computer systems and those of any collaborators, contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. If our privacy protection, data protection, or information security measures (or those of any third parties that handle our sensitive information) are inadequate or are breached as a result of third-party action, employee or contractor error, malfeasance, malware, system error, software bugs or defects in our products, trickery, process failure or otherwise, third parties gaining access to employee accounts using stolen or inferred credentials, computer malware, viruses, spamming, phishing attacks or other means, and deliberate attacks and attempts to gain unauthorized access to computer systems and networks, and, as a result, there is improper disclosure of, or someone obtains unauthorized access to sensitive information, including personally identifiable information or protected health information, or if we suffer a ransomware or advanced persistent threat attack, or if any of the foregoing is reported or perceived to have occurred, our reputation and business could be damaged, we could incur significant costs associated with remediation and the implementation of additional security measures, we may incur significant liability and financial loss, and be subject to regulatory scrutiny, investigations, proceedings, lawsuits and penalties.

Cyber-attacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyber-attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, unauthorized access to or deletion of files, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. We cannot guarantee that the measures we have taken to date, and actions we may take in the future, will be sufficient to remediate any future breaches. Cyber-attacks also could include phishing attempts or e-mail fraud to cause payments or information to be transmitted to an unintended recipient.

To the extent we experience a material system failure, accident, cyber-attack or security breach, it could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed.

While we have not experienced any material system failures, accidents or security breaches to date, if such an event were to occur and cause interruptions in our operations, it could result in a disruption of our drug development programs. These threats pose a risk to the security of our, our collaborators', our CROs', third-party logistics and service providers', distributors' and other contractors' and consultants' systems and networks, and the confidentiality, availability and integrity of our data. There can be no assurance that we will be successful in preventing cyber-attacks or successfully mitigating their effects. Any cyber-attack, data breach or destruction, inaccessibility, or loss of data could result in a violation of applicable U.S. and international privacy, data protection and other laws, and subject us to litigation and governmental investigations and proceedings by federal, state and local regulatory entities in the United States and by international regulatory entities, resulting in exposure to material civil and/or criminal liability. Further, our general liability insurance and corporate risk program may not cover all potential claims to which we are exposed and may not be adequate to indemnify us for all liability that may be imposed; and could have a material adverse effect on our business and prospects. For example, the loss of clinical trial data from completed, ongoing or planned clinical trials for any of our product candidates could result in delays in our development and regulatory approval efforts and significantly increase our costs to recover or reproduce the data. In addition, we may suffer reputational harm or face litigation or adverse regulatory action as a result of cyber-attacks or other data security breaches and may incur significant additional expense to implement further data protection measures.

Risks related to ownership of our common stock and our status as a public company

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

Our executive officers and directors and their affiliates, in the aggregate, beneficially owned shares representing approximately 26.0% of our common stock as of August 9, 2021. As a result, if these stockholders were to choose to act together, they would effectively be able to significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, 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.

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.

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

Our common stock began trading on the Nasdaq Global Select Market on June 17, 2021. Given the limited trading history of our common stock, there is a risk that an active trading market for our shares may not continue to develop or be sustained. If an active market for our common stock does not continue to develop or is not sustained, it may be difficult for our stockholders to sell their shares without depressing the market price for the shares, or at all.

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

The trading market for our common stock relies, in part, on the research and reports that industry or financial analysts publish about us or our business. There can be no assurance that existing analysts will continue to cover us or that new analysts will begin to cover us. There is also no assurance that any covering analyst will provide favorable coverage. Although we have obtained analyst coverage, if one or more of the analysts covering our business downgrade their evaluations of our stock or publish inaccurate or unfavorable research about our business, or 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.

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

- timing and results of or developments in preclinical studies and clinical trials of our product candidates or those of our competitors or potential collaborators;
- adverse regulatory decisions, including failure to receive regulatory approvals for any of our product candidates;
- our success in commercializing our product candidates, if and when approved;
- developments with respect to competitive products or technologies;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other intellectual property or proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license products, product candidates, technologies, 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 pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions, such as the impact of the COVID-19 pandemic on our 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. Furthermore, negative public announcements of the results of hearings, motions or other interim proceedings or developments could have a negative effect on the market price of our common stock.

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

Our management has broad discretion in the application of our cash and cash equivalents and could use such 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 have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest these funds in a manner that does not produce income or that loses value.

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

Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. As of August 9, 2021, we had 47,991,799 shares of common stock outstanding. This includes the 16,141,157 shares that we sold in our IPO, which may be resold in the public market immediately without restriction, unless purchased by our affiliates. The remaining shares are currently restricted as a result of securities laws or lock-up agreements but will become eligible to be sold at various times after the expiration of the applicable lock-up period. The lock-up agreements are subject to certain specified exceptions and the representatives of the underwriters may release some or all of the shares of common stock subject to lock-up agreements at any time in their sole discretion and without notice, which would allow for earlier sales of shares in the public market.

In addition, certain of our executive officers, directors and affiliated stockholders may enter into Rule 10b5-1 plans providing for sales of shares of our common stock from time to time. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the executive officer, director or affiliated stockholder when entering into the plan, without further direction from the executive officer, director or affiliated stockholder. A Rule 10b5-1 plan may be amended or terminated in some circumstances. Our executive officers, directors and affiliated stockholders also may buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material, nonpublic information.

Moreover, beginning on December 18, 2021, holders of an aggregate of 27,996,998 shares of our common stock will have rights, subject to specified conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves. We have also filed a registration statement on Form S-8 to register shares of common stock that we may issue under our equity compensation plans. Shares registered under this registration statement on Form S-8 can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates, vesting arrangements, exercise of options, and the lock-up agreements entered into in connection with our IPO.

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

We are an “emerging growth company,” or EGC, as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. We may remain an EGC until December 31, 2026, although if the market value of our common stock that is held by non-affiliates exceeds \$700 million as of any June 30 after we have filed an Annual Report on Form 10-K or if we have annual gross revenues of \$1.07 billion or more in any fiscal year, we would cease to be an EGC as of December 31 of the applicable year. We also would cease to be an EGC if we issue more than \$1 billion of non-convertible debt over a

three-year period. For so long as we remain an EGC, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not EGCs. These exemptions include:

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

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

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

In addition, the JOBS Act permits an EGC to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have elected 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 EGC or a smaller reporting company.

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 EGC or a smaller reporting company, we will incur significant legal, accounting and other expenses that we did not previously 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 need to continue to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs, particularly as we hire additional financial and accounting employees to meet public company internal control and financial reporting requirements, and will make some activities more time-consuming and costly compared to when we were a private company.

We are evaluating these rules and regulations and 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, 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, 2022. 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.

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

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 our stockholders' sole source of gain for the foreseeable future.

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

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

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

These choice of forum provisions will not apply to suits brought to enforce a duty or liability created by the Securities Exchange Act of 1934, as amended, or the Exchange Act. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all such Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims. To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States of America shall, to the fullest extent permitted by law, be the sole and exclusive forum for the resolution of any claims arising under the Securities Act. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our certificate of incorporation. This may require significant additional costs associated with resolving such action in other jurisdictions and there can be no assurance that the provisions will be enforced by a court in those other jurisdictions.

These exclusive forum provisions may limit the ability of our stockholders to bring a claim in a judicial forum that such stockholders find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees. If a court were to find either exclusive forum provision contained in our certificate of incorporation to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with resolving such action in other jurisdictions, all of which could materially adversely affect our business, financial condition and results of operations.

General risk factors

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

We are subject to certain reporting requirements of the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, recorded, processed, summarized, and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute,

assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people, or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements or insufficient disclosures due to error or fraud may occur and not be detected.

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

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

As part of Congress' response to the COVID-19 pandemic, the Families First Coronavirus Response Act, or FFCR Act, was enacted on March 18, 2020, and the CARES Act was enacted on March 27, 2020. Both contain numerous tax provisions. In particular, the CARES Act retroactively and temporarily (for taxable years beginning before January 1, 2021) suspends application of the 80%-of-income limitation on the use of NOLs, which was enacted as part of the 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 and the CARES Act is and continues to be forthcoming, and such guidance could ultimately increase or lessen their impact on our business and financial condition. It is also likely that Congress will enact additional legislation in connection with the COVID-19 pandemic, some of which could have an impact on us. In addition, it is uncertain if and to what extent various states will conform to the Tax Act, the FFCR Act or the CARES Act. We urge prospective investors in our common stock to consult with their legal and tax advisors with respect to any recently enacted tax legislation, or proposed changes in law, and the potential tax consequences of investing in or holding our common stock.

Unfavorable global economic conditions could adversely affect our business, financial condition, stock price and results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. For example, the 2008 global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn resulting from the COVID-19 pandemic could result in a variety of risks to our business, including weakened demand for any product candidates we may develop and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption. If the current equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly, and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could impair our ability to achieve our growth strategy, could harm our financial performance and stock price and could require us to delay or abandon clinical development plans. In addition, there is a risk that our current or future service providers, manufacturers or other collaborators may not survive such difficult economic times, which could directly affect our ability to attain our operating goals on schedule and on budget. We cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

Item 2. Unregistered sales of equity securities and use of proceeds

Recent sales of unregistered securities

From April 1, 2021 through June 30, 2021, we issued and sold an aggregate of 303,474 shares of common stock to our employees, advisors and consultants upon the exercise of stock options under our 2018 Equity Incentive Plan at a weighted-average per share exercise price of \$1.49.

The common stock issued upon the exercise of options described above were issued under our 2018 Equity Incentive Plan in reliance on the exemption provided by Rule 701 promulgated under the Securities Act. The recipients of securities in these transactions had adequate access, through employment, business or other relationships, to information about us. The foregoing transactions did not involve any underwriters, underwriting discounts or commissions, or any public offering.

On June 21, 2021, in connection with the closing of our initial public offering, or IPO, we issued an aggregate of 878,098 shares of common stock to The Broad Institute, Inc., or Broad, and the President and Fellows of Harvard College, or Harvard, in satisfaction of certain contractual obligations under a license and collaboration agreement, based on the IPO price of \$19.00 per share. The shares of common stock issued to Harvard and Broad were exempt from registration pursuant to Section 4(a)(2) of the Securities Act because the issuance did not involve a public offering and was not accompanied by any general advertisement or general solicitation.

Use of proceeds from registered securities

On June 21, 2021, we completed our IPO in which we issued and sold 16,141,157 shares of our common stock, including 2,105,368 shares of common stock sold pursuant to the underwriters' full exercise of their option to purchase additional shares, at a public offering price of \$19.00 per share, for aggregate gross proceeds of \$306.7 million. All of the shares issued and sold in the IPO were registered under the Securities Act pursuant to a Registration Statement on Form S-1 (File No. 333-256608), which was declared effective by the SEC on June 16, 2021 and Form S-1 (File No. 333-257158), which was filed pursuant to Rule 462(b) of the Securities Act and was declared effective by the SEC on June 16, 2021. J.P. Morgan Securities LLC, Jefferies LLC, Guggenheim Securities, LLC, and William Blair & Company, L.L.C. acted as joint book-running managers of the IPO.

The net offering proceeds to us, after deducting underwriting discounts and offering expenses payable by us of \$25.1 million, were \$281.6 million. No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning 10.0% or more of any class of our equity securities or to any other affiliates. As of June 30, 2021, we had not used any of the net proceeds from the IPO. We have invested the net proceeds from the offering in money market funds and short-term investments. There has been no material change in our planned use of the net proceeds from our IPO as described in our final prospectus, dated June 16, 2021, filed with the SEC pursuant to Rule 424(b).

Item 6. Exhibits

Exhibit Number	Description
3.1	Restated Certificate of Incorporation of Verve Therapeutics, Inc. (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K, filed with the SEC on June 21, 2021).
3.2	Amended and Restated Bylaws of Verve Therapeutics, Inc. (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K, filed with the SEC on June 21, 2021).
10.1	2021 Stock Incentive Plan (incorporated by reference to Exhibit 10.4 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1, filed with the SEC on June 14, 2021).
10.2	Form of Stock Option Agreement under the 2021 Stock Incentive Plan (incorporated by reference to Exhibit 10.5 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1, filed with the SEC on June 14, 2021).

10.3	<u>Form of Restricted Stock Unit Agreement under the 2021 Stock Incentive Plan (incorporated by reference to Exhibit 10.6 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1, filed with the SEC on June 14, 2021).</u>
10.4	<u>Amended and Restated 2021 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.7 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1, filed with the SEC on June 14, 2021).</u>
10.5	<u>Summary of Non-Employee Director Compensation Program (incorporated by reference to Exhibit 10.8 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1, filed with the SEC on June 14, 2021).</u>
10.6	<u>Form of indemnification agreement by and between the Registrant and each of its executive officers and directors (incorporated by reference to Exhibit 10.17 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1, filed with the SEC on June 14, 2021).</u>
10.7	<u>Employment Agreement, dated as of June 11, 2021, between the Registrant and Sekar Kathiresan, M.D. (incorporated by reference to Exhibit 10.18 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1, filed with the SEC on June 14, 2021).</u>
10.8	<u>Employment Agreement, dated as of June 11, 2021, between the Registrant and Andrew Ashe, J.D. (incorporated by reference to Exhibit 10.19 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1, filed with the SEC on June 14, 2021).</u>
10.9	<u>Employment Agreement, dated as of June 11, 2021, between the Registrant and Andrew Bellinger, M.D., Ph.D. (incorporated by reference to Exhibit 10.20 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1, filed with the SEC on June 14, 2021).</u>
31.1*	<u>Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.</u>
31.2*	<u>Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.</u>
32.1 ⁺	<u>Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.</u>
32.2 ⁺	<u>Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.</u>
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 (embedded within the Inline XBRL document)

* Filed herewith.

+ Furnished herewith.

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.

VERVE THERAPEUTICS, INC.

Date: August 12, 2021

By: _____ /s/ Sekar Kathiresan

Sekar Kathiresan, M.D.
Chief Executive Officer
Principal Executive Officer

Date: August 12, 2021

By: _____ /s/ Andrew Ashe

Andrew Ashe, J.D.
President and Chief Operating Officer
Principal Financial 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, Sekar Kathiresan, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Verve Therapeutics, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:
 - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - (c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: August 12, 2021

By: _____
/s/ Sekar Kathiresan
Sekar Kathiresan, M.D.
Chief Executive Officer
(Principal Executive 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 Verve Therapeutics, Inc. (the "Company") for the period ending June 30, 2021, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Sekar Kathiresan, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

- (1) The Report fully complies with the requirements of Section 13(a) or 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 result of operations of the Company.

Date: August 12, 2021

By: _____
/s/ Sekar Kathiresan
Sekar Kathiresan, M.D.
Chief Executive Officer
(Principal Executive 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 Verve Therapeutics, Inc. (the "Company") for the period ending June 30, 2021, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Andrew Ashe, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

- (1) The Report fully complies with the requirements of Section 13(a) or 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 result of operations of the Company.

Date: August 12, 2021

By: _____ /s/ Andrew Ashe
Andrew Ashe, J.D.
President and Chief Operating Officer
(Principal Financial Officer)
