UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-Q

(Mark One)

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

For the quarterly period ended March 31, 2020

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: 001-38433

Homology Medicines, Inc.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**47-3468154**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
One Patriots Park Bedford, MA	**01730**
(Address of principal executive offices)	**(Zip Code)**

(781) 301-7277
(Registrant's telephone number, including area code)

N/A
(Former name, former address, and former fiscal year, if changed since last report)

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	FIXX	Nasdaq Global Select Market

Securities registered pursuant to Section 12(g) of the Act: **None**

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

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

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

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

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

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

As of May 1, 2020, the registrant had 45,213,368 shares of common stock, $0.0001 par value per share, outstanding.

FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q contains forward-looking statements. We intend such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). All statements other than statements of historical facts contained in this Quarterly Report, including statements regarding our future results of operations and financial position, the anticipated impact of the novel coronavirus ("COVID-19") pandemic on our business, business strategy, prospective products, product approvals, research and development costs, anticipated timing and likelihood of success of clinical trials, expected timing of the release of clinical trial data, the plans and objectives of management for future operations and future results of anticipated products, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential", or "continue" or the negative of these terms or other similar expressions. The forward-looking statements in this Quarterly Report are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this Quarterly Report and are subject to a number of important factors that could cause actual results to differ materially from those in the forward-looking statements, including the factors described under the sections in this Quarterly Report titled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations."

Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties.

You should read this Quarterly Report and the documents that we reference in this Quarterly Report completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

Table of Contents

PART I—FINANCIAL INFORMATION

Item 1. Financial Statements.

HOMOLOGY MEDICINES, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share amounts)
(UNAUDITED)

	As of	
	March 31, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 143,372	$ 53,774
Short-term investments	91,557	208,614
Prepaid expenses and other current assets	3,404	4,189
Total current assets	238,333	266,577
Property and equipment, net	42,566	42,716
Right-of-use assets	6,615	—
Restricted cash	1,274	1,274
Total assets	$ 288,788	$ 310,567
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 7,398	$ 2,608
Accrued expenses and other liabilities	6,949	7,644
Operating lease liabilities	2,331	—
Deferred rent	—	1,313
Deferred revenue	774	809
Total current liabilities	17,452	12,374
Non-current liabilities:		
Operating lease liabilities, net of current portion	14,821	—
Deferred rent, net of current portion	—	9,544
Deferred revenue, net of current portion	29,974	30,142
Total liabilities	62,247	52,060
Commitments and contingencies (Note 7)		
Stockholders’ equity:		
Preferred stock, $0.0001 par value, 10,000,000 shares authorized; no shares issued and outstanding	—	—
Common stock, $0.0001 par value; 200,000,000 shares authorized; 45,212,190 and 45,138,408 shares issued as of March 31, 2020 and December 31, 2019, respectively; and 45,206,066 and 45,116,742 shares outstanding as of March 31, 2020 and December 31, 2019, respectively	4	4
Additional paid-in capital	461,561	457,994
Accumulated other comprehensive gain (loss)	(19)	183
Accumulated deficit	(235,005)	(199,674)
Total stockholders’ equity	226,541	258,507
Total liabilities and stockholders' equity	$ 288,788	$ 310,567

See notes to condensed consolidated financial statements.

HOMOLOGY MEDICINES, INC.

CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(in thousands, except share and per share amounts)
(UNAUDITED)

	Three months ended March 31,	
	2020	2019
Collaboration revenue	$ 588	$ 270
Operating expenses:		
Research and development	29,310	20,536
General and administrative	7,770	4,857
Total operating expenses	37,080	25,393
Loss from operations	(36,492)	(25,123)
Other income:		
Interest income	1,161	1,271
Total other income	1,161	1,271
Net loss	$ (35,331)	$ (23,852)
Net loss per share-basic and diluted	$ (0.78)	$ (0.64)
Weighted-average common shares outstanding-basic and diluted	45,151,265	37,384,507

See notes to condensed consolidated financial statements.

HOMOLOGY MEDICINES, INC.

CONDENSED CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(in thousands)
(UNAUDITED)

	Three months ended March 31,	
	2020	**2019**
Net loss	$ (35,331)	$ (23,852)
Other comprehensive gain (loss):		
Change in unrealized gain (loss) on available for sale securities, net	(202)	83
Total other comprehensive gain (loss)	(202)	83
Comprehensive loss	$ (35,533)	$ (23,769)

See notes to condensed consolidated financial statements.

HOMOLOGY MEDICINES, INC.

CONDENSED CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(in thousands, except share and per share amounts)
(UNAUDITED)

	Common Stock $0.0001 Par Value		Additional Paid-in Capital	Accumulated Other Comprehensive Gain (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at January 1, 2019	37,358,526	$ 3	$ 292,187	$ (77)	$ (95,758)	$ 196,355
Vesting of common stock from option exercises	31,584	—	18	—	—	18
Issuance of common stock from option exercises	18,876	—	21	—	—	21
Issuance of common stock pursuant to employee stock purchase plan	28,311	—	396	—	—	396
Stock-based compensation	—	—	1,243	—	—	1,243
Other comprehensive gain	—	—	—	83	—	83
Net loss	—	—	—	—	(23,852)	(23,852)
Balance at March 31, 2019	37,437,297	$ 3	$ 293,865	$ 6	$ (119,610)	$ 174,264

	Common Stock $0.0001 Par Value		Additional Paid-in Capital	Accumulated Other Comprehensive Gain (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at January 1, 2020	45,116,742	$ 4	$ 457,994	$ 183	$ (199,674)	$ 258,507
Vesting of common stock from option exercises	15,542	—	12	—	—	12
Issuance of common stock from option exercises	34,311	—	135	—	—	135
Issuance of common stock pursuant to employee stock purchase plan	39,471	—	537	—	—	537
Stock-based compensation	—	—	2,883	—	—	2,883
Other comprehensive loss	—	—	—	(202)	—	(202)
Net loss	—	—	—	—	(35,331)	(35,331)
Balance at March 31, 2020	45,206,066	$ 4	$ 461,561	$ (19)	$ (235,005)	$ 226,541

See notes to condensed consolidated financial statements.

HOMOLOGY MEDICINES, INC.

CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)
(UNAUDITED)

	Three months ended March 31,	
	2020	**2019**
Cash flows from operating activities:		
Net loss	$ (35,331)	$ (23,852)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	1,907	1,266
Amortization of right-of-use assets	221	—
Stock-based compensation expense	2,883	1,243
Amortization of premium on short-term investments	(175)	(661)
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	1,087	4,413
Accounts payable	4,841	(85)
Accrued expenses and other liabilities	(535)	(1,404)
Deferred revenue	(203)	(92)
Deferred rent	—	1,301
Operating lease liabilities	(541)	—
Net cash used in operating activities	(25,846)	(17,871)
Cash flows from investing activities:		
Purchases of short-term investments	—	(84,467)
Maturities of short-term investments	117,030	114,600
Purchases of property and equipment	(2,033)	(10,466)
Net cash provided by investing activities	114,997	19,667
Cash flows from financing activities:		
Proceeds from issuance of common stock pursuant to employee stock purchase plan	537	396
Proceeds from issuance of common stock from option exercises	135	21
Payment of deferred offering costs	(225)	(92)
Net cash provided by financing activities	447	325
Net change in cash, cash equivalents and restricted cash	89,598	2,121
Cash, cash equivalents and restricted cash, beginning of period	55,048	39,992
Cash, cash equivalents and restricted cash, end of period	$ 144,646	$ 42,113
Supplemental disclosures of noncash investing and financing activities:		
Reclassification of liability for common stock vested	$ 12	$ 18
Property and equipment additions included in accounts payable	$ 405	$ 5,274
Property and equipment additions included in accrued expenses and other liabilities	$ 23	$ —
Unrealized gain on available for sale securities, net	$ (202)	$ —
Deferred offering costs included in accounts payable and accrued expenses	$ 77	$ 174

See notes to condensed consolidated financial statements.

1. NATURE OF BUSINESS AND BASIS OF PRESENTATION

Nature of Business—Homology Medicines, Inc. (the "Company") is a clinical stage biopharmaceutical company dedicated to translating proprietary gene editing and gene therapy technology into novel treatments for patients with rare genetic diseases with significant unmet medical needs by curing the underlying cause of the disease. The Company was founded in March 2015 as a Delaware corporation. Its principal offices are in Bedford, Massachusetts.

Since its inception, the Company has devoted substantially all of its resources to recruiting personnel, developing its technology platform and advancing its pipeline of product candidates, developing and implementing manufacturing processes, building out manufacturing and research and development space, and maintaining and building its intellectual property portfolio. The Company is subject to a number of risks similar to those of other companies conducting high-risk, early-stage research and development of product candidates. Principal among these risks are dependency on key individuals and intellectual property, competition from other products and companies, and the technical risks associated with the successful research, development and manufacturing of its product candidates. The Company's success is dependent upon its ability to continue to raise additional capital in order to fund ongoing research and development, obtain regulatory approval of its products, successfully commercialize its products, generate revenue, meet its obligations, and, ultimately, attain profitable operations.

On April 2, 2018, the Company completed its initial public offering ("IPO") with the sale of 10,350,000 shares of its common stock, including shares issued upon the exercise in full of the underwriters' over-allotment option, at a public offering price of $16.00 per share, resulting in net proceeds of $150.8 million, after deducting underwriting discounts and commissions and offering expenses. Upon the closing of the IPO, all of the Company's outstanding shares of convertible preferred stock automatically converted into 24,168,656 shares of common stock at the applicable conversion ratio then in effect.

On April 12, 2019, the Company completed a follow-on public offering of its common stock. The Company sold 5,555,556 shares of its common stock at a public offering price of $22.50 per share and received net proceeds of $116.9 million, after deducting underwriting discounts and commissions and offering expenses. In addition, on April 26, 2019 and May 7, 2019, in connection with the exercise in full of the underwriters' option to purchase additional shares, the Company issued an aggregate of 833,333 shares of its common stock at a public offering price of $22.50 per share and received net proceeds of $17.6 million, after deducting underwriting discounts and commissions.

On March 12, 2020, the Company filed a Registration Statement on Form S-3 (File No. 333-237131) (the "Shelf") with the Securities and Exchange Commission ("SEC") in relation to the registration of common stock, preferred stock, debt securities, warrants and/or units of any combination thereof for a period up to three years from the date of the filing. The Shelf became effective on March 12, 2020. The Company also simultaneously entered into a sales agreement with Cowen and Company, LLC ("Cowen"), as sales agent, providing for the offering, issuance and sale by the Company of up to an aggregate $150.0 million of its common stock from time to time in "at-the-market" offerings under the Shelf (the "ATM"). The Company did not sell any shares of common stock pursuant to the ATM during the three months ended March 31, 2020. At March 31, 2020, there remained $150.0 million of common stock available for sale under the ATM. Simultaneous with the filing of the Shelf, the previous Registration Statement on Form S-3 (File No. 333-230664) filed with the SEC on April 1, 2019, and a prior sales agreement with Cowen providing for the offering, issuance and sale by the Company of up to an aggregate $100.0 million of its common stock from time to time in "at-the-market" offerings, with $76.8 million of remaining capacity, were terminated.

To date, the Company has not generated any revenue from product sales and does not expect to generate any revenue from the sale of product in the foreseeable future. Through March 31, 2020, the Company has financed its operations primarily through public offerings of its common stock, the issuance of convertible preferred stock, and with proceeds from its collaboration and license agreement with Novartis Institutes of BioMedical Research, Inc. ("Novartis") (see Note 10). During the three months ended March 31, 2020, the Company incurred a net loss of $35.3 million and as of March 31, 2020, had $235.0 million in accumulated deficit. The Company expects to incur additional operating losses and negative operating cash flows for the foreseeable future.

Based on current projections, management believes that existing cash, cash equivalents and short-term investments will enable the Company to continue its operations into the fourth quarter of 2021. In the absence of a significant source of recurring revenue, the continued viability of the Company beyond that point is dependent on its ability to continue to raise additional capital to finance its operations. There can be no assurance that the Company will be able to obtain sufficient capital to cover its costs on acceptable terms, if at all.

Basis of Presentation— The accompanying unaudited condensed consolidated financial statements have been prepared by the Company in conformity with accounting principles generally accepted in the United States of America ("U.S. GAAP") and pursuant to the rules and regulations of the SEC for interim financial statements. Certain information and footnote disclosures normally included in financial statements prepared in accordance with U.S. GAAP have been condensed or omitted pursuant to such rules and regulations. However, the Company believes that the disclosures are adequate to make the information presented not misleading. These condensed consolidated financial statements should be read in conjunction with the Company's audited consolidated financial statements and the notes thereto for the year ended December 31, 2019, included in the Company's Annual Report on Form 10-K on file with the SEC.

The unaudited interim condensed consolidated financial statements have been prepared on the same basis as the audited consolidated financial statements. In the opinion of management, the accompanying unaudited interim condensed consolidated financial statements contain all adjustments which are necessary for a fair statement of the Company's financial position as of March 31, 2020, and consolidated results of operations for the three months ended March 31, 2020 and 2019, and cash flows for the three months ended March 31, 2020 and 2019. Such adjustments are of a normal and recurring nature. The results of operations for the three months ended March 31, 2020 are not necessarily indicative of the results of operations that may be expected for the year ending December 31, 2020.

2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Principles of Consolidation—The Company's condensed consolidated financial statements include the accounts of the Company and its subsidiary, Homology Medicines Securities Corporation, a wholly owned Massachusetts corporation, for the sole purpose of buying, selling, and holding securities on the Company's behalf. All intercompany balances and transactions have been eliminated in the condensed consolidated financial statements.

Use of Estimates—The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenue, and expenses, and the disclosure of contingent assets and liabilities as of and during the reporting period. The Company bases its estimates and assumptions on historical experience when available and on various factors that it believes to be reasonable under the circumstances. Significant estimates and assumptions reflected in these condensed consolidated financial statements include, but are not limited to, revenue recognition, accrued research and development expenses and useful lives assigned to property and equipment. The Company assesses estimates on an ongoing basis; however, actual results could materially differ from those estimates.

Comprehensive Income (Loss) —Comprehensive income (loss) is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. The Company's only element of other comprehensive income (loss) is unrealized gains and losses on available-for-sale investments.

Cash and Cash Equivalents and Restricted Cash—Cash and cash equivalents consist of standard checking accounts, money market accounts and certain investments. The Company considers all highly liquid investments with original or remaining maturities at the time of purchase of 90 days or less to be cash equivalents. Restricted cash consists of cash serving as collateral for letters of credit issued for security deposits for the Company's facility leases in Bedford, Massachusetts.

The following table provides a reconciliation of cash, cash equivalents and restricted cash to amounts shown in the condensed consolidated statements of cash flows:

	March 31,	
	2020	2019
	(in thousands)	
Cash and cash equivalents	$ 143,372	$ 40,839
Restricted cash	1,274	1,274
Total cash, cash equivalents and restricted cash	$ 144,646	$ 42,113

Short-Term Investments—Short-term investments represent holdings of available-for-sale marketable securities in accordance with the Company's investment policy and cash management strategy. Short-term investments mature within one-year from the balance sheet date. Investments in marketable securities are recorded at fair value, with any unrealized gains and losses reported within accumulated other comprehensive income as a separate component of stockholders' equity until realized or until a determination is made that an other-than-temporary decline in market value has occurred. The amortized cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization and accretion, together with interest on securities, are included in interest income on the Company's condensed consolidated statements of operations. The cost of marketable securities sold is determined based on the specific identification method and any realized gains or losses on the sale of investments are reflected as a component of other income.

Deferred Offering Costs—The Company capitalizes incremental legal, professional accounting and other third-party fees that are directly associated with equity financings as other current assets until the transactions are completed. After equity financings are complete, these costs are recorded in stockholders' equity as a reduction of additional paid-in capital generated as a result of the offering.

Leases— In February 2016, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2016-02, *Leases* (Topic 842) ("ASU 2016-02"), which eliminated the tests for lease classification under prior U.S. GAAP and requires lessees to recognize right-of-use assets and related lease liabilities on the balance sheet. The FASB subsequently issued the following amendments to ASU 2016-02 that have the same effective date and transition date: ASU No. 2018-01 - *Leases* (Topic 842): *Land Easement Practical Expedient for Transition to Topic 842*, ASU No. 2018-10 - *Codification Improvements to Topic* 842, *Leases*, ASU No. 2018-11 – *Leases* (Topic 842): *Targeted Improvements*, ASU No. 2018-20 – *Leases* (Topic 842): *Narrow-Scope Improvements for Lessors*, and ASU No. 2019-01 – *Leases* (Topic 842): *Codification Improvements*. The Company adopted these amendments with ASU 2016-02 (collectively, the new leasing standards) effective January 1, 2020.

The Company adopted the new leasing standards using the modified retrospective approach, as of January 1, 2020, with no restatement of prior periods or cumulative adjustments to retained earnings. The Company elected the package of practical expedients permitted under the transition guidance within the new standard, which, among other things, allows the Company to carry forward the historical lease classification. In addition, the Company elected the practical expedient not to apply the recognition requirements in the leasing standards to short-term leases (a lease that at commencement date has a lease term of 12 months or less and does not contain a purchase option that it is reasonably certain to exercise) and the practical expedient that permits lessees to make an accounting policy election (by class of underlying asset) to not separate lease components of a contract from non-lease components.

The Company determines if an arrangement is a lease at contract inception. The Company's contracts are determined to contain a lease when all of the following criteria based on the specific circumstances of the arrangement are met: (1) there is an identified asset for which there are no substantive substitution rights; (2) the Company has the right to obtain substantially all of the economic benefits from the identified asset; and (3) the Company has the right to direct the use of the identified asset.

At the commencement date, operating lease liabilities and their corresponding right-of-use assets are recorded based on the present value of future lease payments over the expected lease term. The Company's lease agreements do not provide an implicit rate. As a result, the Company utilizes an estimated incremental borrowing rate to discount lease payments, which is based on the rate of interest the Company would have to pay to borrow a similar amount on a collateralized basis over a similar term. Certain adjustments to the right-of-use asset may be required for items such as initial direct costs paid or lease incentives received. Operating lease cost is recognized over the expected term on a straight-line basis. Variable lease cost is recognized as incurred.

The Company acts as sublessor related to a sublease of the Company's former headquarters. Fixed sublease payments received are recognized on a straight-line basis over the sublease term. Right-of-use assets are periodically evaluated for impairment.

The expected lease term for those leases commencing prior to January 1, 2020 did not change with the adoption of the new leasing standards. The expected lease term for leases commencing after the adoption of the new leasing standards includes noncancelable lease periods and, when applicable, periods covered by an option to extend the lease if the Company is reasonably certain to exercise that option, as well as periods covered by an option to terminate the lease if the Company is reasonably certain not to exercise that option.

As a result of the adoption of the new leasing standards, on January 1, 2020, the Company recorded a right-of-use asset of $6.8 million, operating lease liabilities of $17.7 million and the derecognition of deferred rent of $10.9 million originally accounted for under legacy guidance. The adoption did not have a material impact on the condensed consolidated statement of operations. For additional information on the adoption of the new leasing standards, refer to Note 7.

	January 1, 2020 (in thousands)		
	Prior to adoption of new leasing standards	Adjustment for adoption of new leasing standards	As Adjusted
Right-of-use assets (1)(2)	$ —	$ 6,835	$ 6,835
Deferred rent (2)	$ 1,313	$ (1,313)	$ —
Deferred rent, net of current portion (2)	$ 9,544	$ (9,544)	$ —
Operating lease liabilities (3)	$ —	$ 2,251	$ 2,251
Operating lease liabilities, net of current portion (3)	$ —	$ 15,441	$ 15,441

(1) Represents capitalization of operating right-of-use assets
(2) Represents reclassification of deferred rent and incentives as a reduction to operating right-of-use assets
(3) Represents recognition of operating lease liabilities

Research and Development Costs—Research and development costs are charged to expense as incurred. Research and development expense consists of expenses incurred in performing research and development activities, including salaries and benefits, materials and supplies, preclinical and clinical expenses, stock-based compensation expense, depreciation of equipment, contract services, and other outside expenses.

Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information provided to the Company by its vendors on their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the consolidated financial statements as prepaid expense or accrued research and development expense.

Revenue Recognition—Revenue is recognized in accordance with FASB Accounting Standards Codification (“ASC”) Topic 606, *Revenue from Contracts with Customers* (“ASC 606”). On January 1, 2019, the Company adopted ASC 606 using the full retrospective transition method.

Under ASC 606, the Company recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine the appropriate amount of revenue to be recognized for arrangements determined to be within the scope of ASC 606, the Company performs the following five steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation. The Company only applies the five-step model to contracts when it is probable that the entity will collect consideration it is entitled to in exchange for the goods or services it transfers to the customer.

The promised goods or services in the Company’s arrangements would likely consist of a license, rights to the Company’s intellectual property or research, development and manufacturing services. Performance obligations are promised goods or services in a contract to transfer a distinct good or service to the customer and are considered distinct when (i) the customer can benefit from the good or service on its own or together with other readily available resources and (ii) the promised good or service is separately identifiable from other promises in the contract. In assessing whether promised goods or services are distinct, the Company considers factors such as the stage of development of the underlying intellectual property, the capabilities of the customer to develop the intellectual property on its own or whether the required expertise is readily available and whether the goods or services are integral or dependent to other goods or services in the contract.

The Company estimates the transaction price based on the amount expected to be received for transferring the promised goods or services in the contract. The consideration may include fixed consideration and variable consideration. At the inception of each arrangement that includes variable consideration, the Company evaluates the amount of consideration to which the Company expects to be entitled to. The Company utilizes either the most likely amount method or expected value method to estimate the amount expected to be received based on which method best predicts the amount expected to be received. The amount of variable consideration that is included in the transaction price may be constrained and is included in the transaction price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period.

The Company's contracts may include development and regulatory milestone payments that are assessed under the most likely amount method and constrained until it is probable that a significant revenue reversal would not occur. Milestone payments that are not within the Company's control, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. At the end of each reporting period, the Company re-evaluates the probability of achievement of such development and regulatory milestones and any related constraint, and if necessary, adjust its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration revenue in the period of adjustment.

For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any royalty revenue resulting from the Company's collaboration arrangement.

The Company allocates the transaction price based on the estimated standalone selling price of each performance obligation. The Company must develop assumptions that require judgment to determine the stand-alone selling price for each performance obligation identified in the contract. The Company utilizes key assumptions to determine the stand-alone selling price, which may include other comparable transactions, pricing considered in negotiating the transaction and the estimated costs. Variable consideration is allocated specifically to one or more performance obligations in a contract when the terms of the variable consideration relate to the satisfaction of the performance obligation and the resulting amounts allocated are consistent with the amounts the Company would expect to receive for the satisfaction of each performance obligation.

The consideration allocated to each performance obligation is recognized as revenue when control is transferred for the related goods or services. For performance obligations which consist of licenses and other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress. The Company evaluates the measure of progress for its over-time arrangements at each reporting period and, if necessary, updates the measure of progress and revenue recognized.

Net Loss per Share—Basic net loss per share is computed by dividing net loss by the weighted-average number of common shares outstanding during the period. Diluted net loss per share is computed using the weighted-average number of common shares outstanding during the period and, if dilutive, the weighted-average number of potential shares of common stock. The weighted-average number of common shares included in the computation of diluted net loss gives effect to all potentially dilutive common equivalent shares, including outstanding stock options and unvested shares of common stock.

Common stock equivalent shares are excluded from the computation of diluted net loss per share if their effect is antidilutive. In periods in which the Company reports a net loss attributable to common stockholders, diluted net loss per share attributable to common stockholders is generally the same as basic net loss per share attributable to common stockholders since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive.

Recent Accounting Pronouncements—The Jumpstart Our Business Startups Act of 2012 permits an emerging growth company 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. As an emerging growth company, the Company has elected to take advantage of this extended transition period.

In February 2016, the FASB issued new leasing standards to increase transparency and comparability among organization related to their leasing activities. For additional information on the adoption of the new leasing standards, please refer to section titled "Leases" above, and Note 7.

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* ("ASU 2016-13") to improve financial reporting by requiring more timely recording of credit losses on loans and other financial instruments held by financial institutions and other organizations. ASU 2016-13 requires the measurement of all expected credit losses for financial assets held at the reporting date based on historical experience, current conditions and reasonable and supportable forecasts. ASU 2016-13 also requires enhanced disclosures to help investors and other financial statement users better understand significant estimates and judgments used in estimating credit losses, as well as the credit quality and underwriting standards of an organization's portfolio. ASU 2016-13 is effective for the Company beginning January 1, 2023, with early application permitted. The Company is currently evaluating the impact the adoption of this standard will have on its condensed consolidated financial statements.

In June 2018, the FASB issued ASU No. 2018-07, *Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting* ("ASU 2018-07"), which changes certain aspects of the accounting for share-based payments granted to nonemployees. Under ASU 2018-07, most of the guidance on such payments to nonemployees would be aligned with the requirements for share-based payments granted to employees. The Company adopted ASU 2018-07 on January 1, 2020. The adoption of ASU 2018-07 did not have a material impact on the Company's condensed consolidated financial statements and related disclosures.

3. SHORT-TERM INVESTMENTS

The Company invests its excess cash in fixed income instruments denominated and payable in U.S. dollars including U.S. treasury securities, commercial paper, corporate debt securities and asset-backed securities in accordance with the Company's investment policy that primarily seeks to maintain adequate liquidity and preserve capital.

The Company has designated all investments as available-for-sale and therefore such investments are reported at fair value. Unrealized gains or losses on investments are recorded in accumulated other comprehensive income or loss, a component of stockholders' equity, on the Company's condensed consolidated balance sheets.

The following table summarizes the Company's investments, which are included in cash equivalents and short-term investments:

As of March 31, 2020	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
		(in thousands)		
Asset-backed securities	$ 4,500	$ —	$ —	$ 4,500
Money market mutual funds	143,122	—	—	143,122
Commercial paper	25,913	—	—	25,913
U.S. Treasury securities	15,991	45	—	16,036
Corporate debt securities	45,172	—	(64)	45,108
Total	$ 234,698	$ 45	$ (64)	$ 234,679

As of December 31, 2019	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
		(in thousands)		
Repurchase agreements	$ 14,000	$ —	$ —	$ 14,000
Asset-backed securities	14,866	10	—	14,876
Money market mutual funds	39,524	—	—	39,524
Commercial paper	41,259	—	—	41,259
U.S. Treasury securities	59,926	45	—	59,971
Corporate debt securities	92,380	128	—	92,508
Total	$ 261,955	$ 183	$ —	$ 262,138

The Company utilizes the specific identification method in computing realized gains and losses. The Company had no realized gains and losses on its available-for-sale securities for the three months ended March 31, 2020 and 2019. The contractual maturity dates of all of the Company's investments are less than one year.

4. FAIR VALUE MEASUREMENTS

The Company's financial instruments consist of cash and cash equivalents, short-term investments, restricted cash and accounts payable. The carrying amount of cash, restricted cash and accounts payable are each considered a reasonable estimate of fair value due to the short-term maturity.

Assets measured at fair value on a recurring basis were as follows:

Description	March 31, 2020	Quoted Prices (Unadjusted) in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
		(in thousands)		
Cash equivalents:				
Money market mutual funds	$ 143,122	$ 143,122	$ —	$ —
Total cash equivalents	$ 143,122	$ 143,122	$ —	$ —
Short-term investments:				
Asset-backed securities	$ 4,500	$ —	$ 4,500	$ —
Commercial paper	25,913	—	25,913	—
U.S. Treasury securities	16,036	—	16,036	—
Corporate debt securities	45,108	—	45,108	—
Total short-term investments	$ 91,557	$ —	$ 91,557	$ —
Total financial assets	$ 234,679	$ 143,122	$ 91,557	$ —

Description	December 31, 2019	Quoted Prices (Unadjusted) in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
		(in thousands)		
Cash equivalents:				
Money market mutual funds	$ 39,524	$ 39,524	$ —	$ —
Repurchase agreements	14,000	—	14,000	—
Total cash equivalents	$ 53,524	$ 39,524	$ 14,000	$ —
Short-term investments:				
Asset-backed securities	$ 14,876	$ —	$ 14,876	$ —
Commercial paper	41,259	—	41,259	—
U.S. Treasury securities	59,971	—	59,971	—
Corporate debt securities	92,508	—	92,508	—
Total short-term investments	$ 208,614	$ —	$ 208,614	$ —
Total financial assets	$ 262,138	$ 39,524	$ 222,614	$ —

Short-term securities are valued using models or other valuation methodologies that use Level 2 inputs. These models are primarily industry-standard models that consider various assumptions, including time value, yield curve, volatility factors, default rates, current market and contractual prices for the underlying financial instruments, as well as other relevant economic measures. Substantially all of these assumptions are observable in the marketplace, can be derived from observable data or are supported by observable levels at which transactions are executed in the marketplace.

There were no transfers between fair value measure levels during the three months ended March 31, 2020 and 2019.

5. PROPERTY AND EQUIPMENT, NET

Property and equipment, net consists of the following:

	As of	
	March 31, 2020	December 31, 2019
	(in thousands)	
Laboratory equipment	$ 11,697	$ 10,837
Manufacturing equipment	7,479	4,911
Computers and purchased software	1,215	640
Furniture and fixtures	1,363	1,363
Leasehold improvements	29,961	30,862
Assets not yet in service	1,168	2,513
Property and equipment, at cost	52,883	51,126
Less: accumulated depreciation and amortization	(10,317)	(8,410)
Property and equipment, net	$ 42,566	$ 42,716

Depreciation expense for the three months ended March 31, 2020 was approximately $1.9 million, compared to $1.3 million for the three months ended March 31, 2019. There were no disposals of property and equipment during the three months ended March 31, 2020 and 2019. Leasehold improvements consist primarily of costs associated with the buildout of the Company's research and development, manufacturing and general office space in Bedford, Massachusetts.

6. ACCRUED EXPENSES AND OTHER LIABILITIES

Accrued expenses and other liabilities consist of the following:

	As of	
	March 31, 2020	December 31, 2019
	(in thousands)	
Accrued research and development expenses	$ 3,808	$ 2,258
Accrued compensation and benefits	2,254	4,551
Accrued professional fees	642	542
Accrued unvested common stock subject to repurchase	25	37
Accrued other	220	256
Total accrued expenses and other liabilities	$ 6,949	$ 7,644

7. COMMITMENTS AND CONTINGENCIES

Operating Leases—In September 2016, the Company entered into a noncancelable operating lease beginning in November 2016 for office, laboratory and manufacturing space in Bedford, Massachusetts, that expires in October 2021, with an option for an additional three-year term. On August 13, 2018, the Company entered into a sublease agreement for the entire leased premises. The rent commencement date of the sublease was December 2018, and the sublease will terminate on the scheduled termination date of the original lease. Under the terms of the sublease, the subtenant is obligated to pay the Company aggregate base rent of approximately $2.7 million over the term of the sublease in addition to passthrough of operating expenses and real estate taxes charged by the landlord.

In December 2017, the Company entered into a noncancelable operating lease for approximately 67,000 square feet of research and development, manufacturing and general office space in Bedford, Massachusetts. The lease expires in February 2027 with an option for an additional five-year term. Rent became due under the lease in two phases; rent on the first 46,000 square feet started in September 2018 and rent on the remaining 21,000 square feet started in March 2019. The initial annual base rent is $39.50 per square foot and will increase by three percent annually. The Company is obligated to pay, on a pro-rata basis, real estate taxes and operating costs related to the premises. The lease agreement entered into in December 2017 allowed for a tenant improvement allowance not to exceed $10.9 million, which the Company received in full, to be applied to the total cost of tenant improvements to the leased premises. The unamortized balance of the tenant improvement allowance was included in deferred rent and has been recorded as a reduction to the operating right-of-use asset upon the adoption of the new leasing standards.

The Company maintains letters of credit, secured by restricted cash, for security deposits totaling $1.3 million as of March 31, 2020 and December 31, 2019, respectively, in conjunction with its current leases.

The following table summarizes operating lease costs as well as sublease income for the three months ended March 31, 2020:

Three months ended March 31, 2020	Amount (in thousands)
Operating lease costs	$ 623
Sublease income	(228)
Net lease cost	$ 395

Rent expense, net of amortization of the deferred rent incentives was $0.2 million for the three months ended March 31, 2019.

The maturities of our operating lease liabilities and minimum lease payments as of March 31, 2020 were as follows:

For the Years Ending December 31,	Amount (in thousands)
2020	$ 2,863
2021	3,834
2022	2,987
2023	3,077
2024	3,169
Thereafter	7,197
Total undiscounted lease payments	$ 23,127
Less: imputed interest	(5,975)
Present value of operating lease liabilities	$ 17,152

The following table summarizes the lease term and discount rate as of March 31, 2020:

	As of March 31, 2020
Weighted-average remaining lease term (years)	
Operating leases	6.4
Weighted-average discount rate	
Operating leases	9.9%

The following table summarizes cash paid for amounts included in the measurement of the Company's operating lease liabilities for the three months ended March 31, 2020.

Three months ended March 31, 2020	Amount (in thousands)
Cash paid for amounts included in the measurement of lease liabilities	$ 943
Operating cash flows from operating leases	$ 943

8. STOCK INCENTIVE PLANS

2015 Stock Incentive Plan

In December 2015, the Company's Board of Directors adopted the 2015 Stock Incentive Plan (the "2015 Plan"), which provided for the grant of qualified incentive and nonqualified stock options or restricted stock awards to the Company's employees, officers, directors, advisors, and outside consultants. Stock options generally vest over a four-year period and expire ten years from the date of grant. Certain options provide for accelerated vesting if there is a change in control, as defined in the 2015 Plan. At March 31, 2020, there were no additional shares available for future grant under the 2015 Plan.

2018 Incentive Award Plan

In March 2018, the Company's Board of Directors adopted and the Company's stockholders approved the Homology Medicines, Inc. 2018 Incentive Award Plan (the "2018 Plan" and, together with the 2015 Plan, the "Plans"), which became effective on the day prior to the first public trading date of the Company's common stock. Upon effectiveness of the 2018 Plan, the Company ceased granting new awards under the 2015 Plan.

The 2018 Plan provides for the grant of incentive stock options, nonqualified stock options, restricted stock awards, restricted stock units, stock appreciation rights and other stock or cash-based awards to employees and consultants of the Company and directors of the Company. The number of shares of common stock initially available for issuance under the 2018 Plan was 3,186,205 shares of common stock plus the number of shares subject to awards outstanding under the 2015 Plan that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by the Company on or after the effective date of the 2018 Plan. In addition, the number of shares of common stock available for issuance under the 2018 Plan is subject to an annual increase on the first day of each calendar year beginning on January 1, 2019 and ending on and including January 1, 2028 equal to the lesser of (i) 4% of the Company's outstanding shares of common stock on the final day of the immediately preceding calendar year and (ii) such smaller number of shares of common stock as determined by the Company's Board of Directors, provided that not more than 20,887,347 shares of common stock may be issued under the 2018 Plan upon the exercise of incentive stock options. Therefore, on January 1, 2020, an additional 1,804,670 shares were added to the 2018 Plan, representing 4% of total common shares outstanding at December 31, 2019. At March 31, 2020, there were 2,802,656 shares available for future grant under the 2018 Plan.

2018 Employee Stock Purchase Plan

In March 2018, the Company's Board of Directors adopted and the Company's stockholders approved the Homology Medicines, Inc. 2018 Employee Stock Purchase Plan (the "2018 ESPP"). The 2018 ESPP allows employees to buy Company stock through after-tax payroll deductions at a discount from market value. The 2018 ESPP is intended to qualify as an "employee stock purchase plan" under Section 423 of the Internal Revenue Code. The number of shares of common stock initially available for issuance under the 2018 ESPP was 353,980 shares of common stock plus an annual increase on the first day of each calendar year beginning on January 1, 2019 and ending on and including January 1, 2028 equal to the lesser of (i) 1% of the Company's outstanding shares of common stock on the final day of the immediately preceding calendar year and (ii) such smaller number of shares of common stock as determined by the Company's Board of Directors, provided that not more than 4,778,738 shares of common stock may be issued under the 2018 ESPP. Therefore, on January 1, 2020, an additional 451,167 shares were added to the 2018 ESPP, representing 1% of total common shares outstanding at December 31, 2019. At March 31, 2020, there were 1,084,028 shares available for future issuance under the 2018 ESPP.

Under the 2018 ESPP, employees may purchase common stock through after-tax payroll deductions at a price equal to 85% of the lower of the fair market value on the first trading day of an offering period or the last trading day of an offering period. The 2018 ESPP generally provides for offering periods of six months in duration that end on the final trading day of each February and August. In accordance with the Internal Revenue Code, no employee will be permitted to accrue the right to purchase stock under the 2018 ESPP at a rate in excess of $25,000 worth of shares during any calendar year during which such a purchase right is outstanding (based on the fair market value per share of the Company's common stock as of the first day of the offering period).

During the three months ended March 31, 2020, 39,471 shares were issued under the 2018 ESPP for aggregate proceeds to the Company of $0.5 million. During the three months ended March 31, 2019, 28,311 shares were issued under the 2018 ESPP for aggregate proceeds to the Company of $0.4 million. The Company did not record any stock-based compensation pursuant to the 2018 ESPP during the three months ended March 31, 2020 and 2019, as the amounts estimated were insignificant in each such period.

Stock-based compensation expense

The Company recognizes compensation expense for awards to employees based on the grant date fair value of stock-based awards on a straight-line basis over the period during which an award holder provides service in exchange for the award, which is generally the vesting period. The fair value of each option award is estimated on the date of grant using the Black-Scholes option- pricing model, with the assumptions noted in the table below. Expected volatility for the Company's common stock was determined based on an average of the historical volatility of a peer group of publicly traded companies that are similar to the Company. The expected term of options granted to employees was calculated using the simplified method, which represents the average of the contractual term of the option and the weighted-average vesting period of the option. The Company uses the simplified method because it does not have sufficient historical option exercise data to provide a reasonable basis upon which to estimate expected term. The contractual life of the options was used for the expected term of options granted to non-employees. The assumed dividend yield is based upon the Company's expectation of not paying dividends in the foreseeable future. The risk-free rate is based on the U.S. Treasury yield curve in effect at the time of grant for periods commensurate with the expected term of the award. The Company recognizes forfeitures as they occur.

The assumptions used in the Black-Scholes option pricing model are as follows:

	Three months ended March 31,	
	2020	2019
Expected volatility	63.2% — 63.5%	64.0% — 64.7%
Weighted-average risk-free interest rate	0.74% — 1.73%	2.48% — 2.60%
Expected dividend yield	— %	— %
Expected term (in years)	6.25	6.25
Underlying common stock fair value	$17.00 — $21.75	$21.43 — $28.13

The Company recorded stock-based compensation expense related to stock options and shares purchased under the 2018 ESPP as follows:

	Three months ended March 31,	
	2020	2019
	(in thousands)	
Research and development	$ 1,313	$ 558
General and administrative	1,570	685
	$ 2,883	$ 1,243

As of March 31, 2020, there was $36.6 million of unrecognized compensation expense related to unvested employee and non-employee share-based compensation arrangements granted under the Plans. The unrecognized compensation expense is estimated to be recognized over a period of 2.9 years at March 31, 2020.

A summary of option activity under the Plans during the three months ended March 31, 2020 is as follows:

	Number of Options	Weighted-Average Exercise Price per Share	Weighted-Average Remaining Contractual Term (in Years)	Aggregate Intrinsic Value
				(in thousands)
Outstanding at January 1, 2020	4,843,018	$ 14.78	8.5	$ 33,809
Granted	666,550	$ 21.40		
Exercised	(34,311)	$ 3.93		
Cancelled/Forfeited	(27,442)	$ 19.57		
Outstanding at March 31, 2020	5,447,815	$ 15.63	8.5	$ 19,541
Vested and expected to vest at March 31, 2020	5,447,815	$ 15.63	8.5	$ 19,541
Exercisable at March 31, 2020	1,925,388	$ 10.05	7.5	$ 14,249

The total intrinsic value of options exercised during the three months ended March 31, 2020 and 2019 was $0.5 million and $0.4 million, respectively. The weighted-average grant date fair value per share of options granted during the three months ended March 31, 2020 and 2019 was $12.47 and $15.80, respectively.

Stock options granted pursuant to the 2015 Plan permit option holders to elect to exercise unvested options in exchange for unvested common stock. Options granted under the 2015 Plan that are exercised prior to vesting will continue to vest according to the respective option agreement, and such unvested shares are subject to repurchase by the Company at the optionee’s original exercise price in the event the optionee’s service with the Company voluntarily or involuntarily terminates.

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

	Shares
Unvested shares - January 1, 2020	21,666
Vested	(15,542)
Issued	—
Repurchased	—
Unvested shares - March 31, 2020	6,124

As of March 31, 2020 and December 31, 2019, 6,124 shares and 21,666 shares, respectively, remained subject to a repurchase right by the Company, with a related liability included in accrued expenses and other liabilities in the condensed consolidated balance sheets of less than $0.1 million as of March 31, 2020 and December 31, 2019.

9. NET LOSS PER SHARE

The Company's potential dilutive securities, which include unvested common stock from the early-exercise of stock options and outstanding common stock options, have been excluded from the computation of diluted net loss per share as the effect would be to reduce the net loss per share. Therefore, the weighted average number of common shares outstanding used to calculate both basic and diluted net loss per share attributable to common stockholders is the same. The Company excluded the following potential common shares, presented based on amounts outstanding at March 31, 2020 and 2019, from the computation of diluted net loss per share attributable to common stockholders because including them would have had an anti-dilutive effect:

	As of March 31,	
	2020	2019
Unvested common stock from early exercise of options	6,124	119,705
Stock options to purchase common stock	5,447,815	3,632,821
Total	5,453,939	3,752,526

10. COLLABORATION AND LICENSE AGREEMENT

Summary of Agreement

In November 2017, the Company entered into a collaboration and license agreement (the "Collaboration Agreement") with Novartis Institutes of BioMedical Research, Inc. ("Novartis") for the research, development, manufacturing and commercialization of products using the Company's gene-editing technology for the treatment of certain ophthalmic targets and sickle cell disease. In February 2019, Novartis elected to discontinue the sickle cell disease program under the Collaboration Agreement effective in August 2019. The Company continues to work with Novartis to identify new targets for the partnership based on the existing exploratory research component of the agreement and the collaboration on ophthalmic programs also continues.

Under the terms of the Collaboration Agreement, taking into account Novartis' election to discontinue the sickle cell disease program, the Company granted Novartis a research license, a development and commercialization license, and a manufacturing license, under certain of its intellectual property rights to research, develop, manufacture and commercialize the ophthalmic targets. Upon entering into the Collaboration Agreement, the Company received an upfront, nonrefundable payment of $35.0 million and issued additional shares of its Series B preferred stock to Novartis for consideration of $10.0 million. The Company recorded the Series B preferred stock at its estimated fair value of $11.7 million, including $1.7 million of the upfront payment, and allocated the remaining $33.3 million of the upfront payment to the Collaboration Agreement.

The Collaboration Agreement consists of a research term, where the Company and Novartis are collaborating to perform research and conduct preclinical development to identify candidates that modulate the ophthalmic targets. The Collaboration Agreement also includes exploratory work on the applicability of the gene-editing technology with respect to other gene targets. The Company's obligation to perform such exploratory research concludes in November 2020. Novartis may select up to two ophthalmic targets, with limited substitution rights. The Company is responsible for the manufacturing of proprietary research grade human hematopoietic stem cell derived adeno-associated virus vectors ("AAVHSCs") during the research term. Research activities performed by the Company are being reimbursed at a full-time equivalent rate ("FTE") and manufacturing activities will be reimbursed at cost, up to a maximum of $17.0 million during the research term, as specified and defined in the Collaboration Agreement. Novartis is

required to pay the Company a target fee of $5.0 million for each target that meets certain success criteria during the research term (the "target fee trigger date"), up to a maximum of two targets. The research term will continue for five years from the effective date of the Collaboration Agreement. Pursuant to the Collaboration Agreement, the Company will also participate on a joint steering committee and a joint manufacturing subcommittee, with equal representation from both the Company and Novartis.

Novartis has the exclusive right to develop and commercialize up to two candidates or products arising from the research activities. Subject to certain limitations pursuant to the terms of the Collaboration Agreement, Novartis will fund all development and commercialization costs. The Company will be responsible for manufacturing candidates and products for Novartis during the development and commercialization terms. The Company's manufacturing activities will be reimbursed at cost during the development term and at cost plus a margin during the commercialization term, as defined in the Collaboration Agreement. If the Company is not able to manufacture candidates or products that meet the quality or quantity requirements of Novartis, then Novartis shall have the right to designate a third-party contract manufacturer or manufacture such candidates or products itself.

In accordance with the Collaboration Agreement, taking into consideration Novartis' election to discontinue the sickle cell disease program, the Company is also eligible to receive up to a total of $530.0 million in milestone payments, including up to $180.0 million in development milestone payments, up to $170.0 million in regulatory milestone payments and up to $180.0 million in commercial milestone payments, with respect to the licensed products. The Company is also eligible to earn tiered royalties on net sales of licensed products by Novartis, its affiliates or sublicensees, ranging from mid single-digit, to sub-teen double-digit percentages, and such royalties are potentially subject to various reductions and offsets. If any of the exploratory research efforts are advanced into formal research and development programs, the parties will negotiate the economics including potential milestone payments for such programs at that time.

Unless earlier terminated, the Collaboration Agreement will continue on a target-by-target basis until the expiration of all applicable royalty terms with respect to all products that modulate such target on a country-by-country-basis. Either party may terminate the agreement on a target-by-target basis for the other party's material breach with respect to such target, or in the event of the other party's bankruptcy. Novartis may terminate the agreement for convenience on a target-by-target basis. The Company may terminate the agreement if Novartis files, or joins a third party in filing or maintaining, a patent challenge against certain of the patent rights licensed to Novartis under the terms of the agreement. There are no performance, cancellation, termination or refund provisions in the arrangement that contain material financial consequences to the Company.

Revenue Recognition

The Company determined that the (1) research, development and commercialization and manufacturing licenses, (2) the research activities performed by the Company (3) service on the joint committees and (4) manufacturing during the research and development terms represented a single performance obligation under the Collaboration Agreement. Since the option for Novartis to obtain manufacturing during the commercialization term from the Company is at a price that would reflect the standalone selling price, the option does not provide Novartis with a material right and is therefore not a performance obligation under the contract.

The Company has concluded that the research, development and commercialization and manufacturing licenses are not distinct from the research activities and manufacturing during the research and development term as Novartis cannot benefit from the licenses without the Company performing the research and manufacturing services. These services are so specialized and rely on the Company's expertise in gene editing technologies not available in the marketplace. As a result, these licenses have been combined with the research activities, service on the joint committees and the manufacturing during the research and development terms as a single performance obligation.

The transaction price consists of the $33.3 million non-refundable upfront payment, net of amounts classified as equity, and projected reimbursable research and manufacturing activities, which have been estimated using the expected value method. None of the target fees or development and regulatory milestone payments have been included in the transaction price, as all are fully constrained. As part of the evaluation of the constraint, the Company considered numerous factors, including the fact that achievement of the milestones is outside of the Company's control and is contingent upon the success of the Company's preclinical studies, clinical trials, Novartis' efforts and the receipt of regulatory approval. In addition, the Company has determined that the commercial milestones and sales-based royalties will be recognized when the related sales occur as they were determined to relate predominately to the licenses transferred to Novartis, and therefore have also been excluded from the transaction price. The Company will re-evaluate the transaction price, including estimated variable consideration included in the transaction price and all constrained amounts, in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

The Company identified only one performance obligation in the Collaboration Agreement. Therefore, the Company will allocate the transaction price at the onset of the contract to the single performance obligation.

The Company recognizes revenue over time using a cost-to-cost method, which it believes best depicts the transfer of control to the customer. Under the cost-to-cost method, the extent of progress towards completion is measured based on the ratio of actual costs incurred to the total estimated costs expected upon satisfying the identified performance obligation. Under this method, revenue is recorded over the performance period as a percentage of the estimated transaction price based on the extent of progress towards completion. As of March 31, 2020, the aggregate amount of the transaction price related to the unsatisfied portion of the performance obligation is $30.7 million, and the Company will recognize this revenue as the research and manufacturing activities are performed, which is expected to occur over a period of time that is estimated will conclude in 2027. The Company does not expect collaboration revenue to be recognized evenly over this period as it will be recognized on a percentage of completion basis as the Company performs the research, development and manufacturing services, which will likely vary from period to period.

In estimating the total costs to satisfy its single performance obligation pursuant to the Novartis agreement, the Company is required to make significant estimates including the expected time it will take to fulfill the performance obligation, which currently is expected to be approximately ten years from the date the Collaboration Agreement was entered into, and the expected costs associated with manufacturing during the research and development terms for a novel manufacturing process as well as the probability of success of a target to move into the development phase. The Company has made estimates of such costs utilizing its experience with similar product candidates, however not identical to those in the Collaboration Agreement. In making such estimates, significant judgment is required to evaluate those key assumptions related to cost estimates. The cumulative effect of revisions to the total estimated costs to complete the Company’s single performance obligation will be recorded in the period in which the changes are identified and amounts can be reasonably estimated. While such revisions will have no impact on the Company’s reported cash flows, a significant change in these assumptions and estimates could have a material impact on the timing and amount of revenue recognized in future periods.

During the three months ended March 31, 2020, the Company recognized revenue under the Collaboration Agreement of $0.6 million, of which $0.2 million was included in deferred revenue at the beginning of the period. During the three months ended March 31, 2019, the Company recognized revenue under the Collaboration Agreement of $0.3 million, of which $0.1 million was included in deferred revenue at the beginning of the period. As of March 31, 2020 and December 31, 2019, there was approximately $30.7 million and $31.0 million of deferred revenue related to the Collaboration Agreement, respectively. In addition, as of March 31, 2020 and December 31, 2019, the Company has recorded accounts receivable of $0.4 million related to reimbursable research and development costs under the Collaboration Agreement, which are included in prepaid expenses and other current assets on the condensed consolidated balance sheets as of each such date.

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our condensed consolidated financial statements and related notes appearing elsewhere in this Quarterly Report on Form 10-Q. Some of the information contained in this discussion and analysis or set forth elsewhere in this Quarterly Report on Form 10-Q, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. As a result of many important factors, including those set forth in the "Risk Factors" section of this Quarterly Report on Form 10-Q, our actual results could differ materially from the results described in, or implied, by these forward-looking statements.

Overview

We are a genetic medicines company dedicated to transforming the lives of patients suffering from rare genetic diseases with significant unmet medical needs by curing the underlying cause of the disease. Our proprietary platform is designed to utilize our human hematopoietic stem cell derived adeno-associated virus vectors, or AAVHSCs, to precisely and efficiently deliver single administration genetic medicines *in vivo* either through gene therapy or nuclease-free gene editing across a broad range of genetic disorders. Our diverse set of AAVHSCs allows us to precisely target, via a single injection, a wide range of disease-relevant tissues, including the liver, central nervous system, or CNS, bone marrow, muscle and eye. Our genetic medicines platform is designed to provide us the flexibility to choose the method we believe is best suited from either gene therapy or gene editing for each disease we pursue, based on such factors as the targeted disease biology, the biodistribution of our AAVHSCs to key tissues, and the rate of cell division the tissues exhibit. Our product development strategy is to continue to develop in parallel both gene therapy and gene editing, while initially leveraging the experience from our gene therapy product candidates to further advance our gene editing. We believe our dual technology platform will allow us to provide transformative cures using either modality.

The unique properties of our proprietary suite of 15 novel AAVHSCs enable us to focus on a method of gene editing called gene integration, through the replacement of an entire diseased gene in the genome with a whole functional copy by harnessing the naturally occurring deoxyribonucleic acid, or DNA, repair process of homologous recombination, or HR. We believe our HR-driven gene editing approach will allow us to efficiently perform gene editing at therapeutic levels without unwanted on- and off-target modifications, and to directly measure and confirm those modifications in an unbiased manner to ensure only the intended changes are made. By utilizing the body's natural mechanism of correcting gene defects, we also avoid the need for exogenous nucleases, or bacteria-derived enzymes used in other gene editing approaches to cut DNA, that are known to significantly increase the risk of unwanted modifications.

We are currently in the dose-escalation portion of our Phase 1/2 pheNIX clinical trial with our first and lead product candidate, HMI-102, a gene therapy for the treatment of phenylketonuria, or PKU. Once a dose is chosen, we plan to initiate the randomized, concurrently controlled Part B of the trial, which has the potential to be converted to a registrational trial. In December 2019, in accordance with a corporate goal that we had established in early 2018, we reported encouraging initial clinical data from the pheNIX trial from Cohort 1 (low dose, n=2) and Cohort 2 (mid-dose, n=1) based on the data cutoff date of December 2, 2019. Preliminary safety data from three subjects in Cohorts 1 and 2 showed HMI-102 was well-tolerated with no treatment-emergent adverse events, or TEAEs, or serious TEAEs. Efficacy data from the first patient in Cohort 2 suggested a dose-response effect with an observed reduction in phenylalanine, or Phe, levels from baseline and a corresponding increase in tyrosine, or Tyr, which translated to an overall reduction in the phenylalanine to tyrosine ratio, or Phe/Tyr ratio, suggestive of increased enzymatic activity. Phe levels have been evaluated as a primary registrable endpoint in previous PKU clinical trials, Tyr is a product of Phe metabolism and a precursor to neurotransmitters, and the Phe/Tyr ratio is a clinically relevant diagnostic measurement for PKU.

We are in IND-enabling studies with HMI-202, our lead gene therapy CNS product development candidate for the treatment of metachromatic leukodystrophy, or MLD. This represents our first CNS program as we are leveraging the ability of our AAVHSCs to cross the blood-brain-barrier as well as the blood-nerve-barrier.

We are in IND-enabling studies with HMI-103, our lead gene editing product development candidate for the treatment of PKU in pediatric patients. We have generated *in vivo* preclinical data demonstrating achievement of gene integration efficiencies in the liver that correspond with Phe correction in a PKU murine model, are significantly greater than other adeno-associated virus, or AAV, based approaches and we believe are at a therapeutic level in the preclinical model.

We have internal process development and Good Manufacturing Practices, or GMP, manufacturing capabilities, including a 25,000 square foot GMP manufacturing facility to support our clinical development programs in both gene therapy and gene editing. We have a commercial manufacturing process. We are currently operating three 500-liter bioreactors in our internal manufacturing facility and have successfully produced GMP material at the 500-liter scale for multiple pipeline candidates. Additionally, we have executed our manufacturing platform at the 2,000-liter bioreactor scale.

Our management team has a successful track record of discovering, developing and commercializing therapeutics with a particular focus on rare diseases. We have a robust intellectual property portfolio with issued composition of matter patents in the United States for our suite of 15 AAVHSCs and we believe the breadth and depth of our intellectual property is a strategic asset that has the potential to provide us with a significant competitive advantage. We continue to build on our intellectual property estate through our ongoing product and platform development efforts.

Since our inception in 2015, we have raised approximately $444.2 million in aggregate net proceeds through our initial public offering, or IPO, in April 2018, a follow-on public offering of common stock in April 2019, proceeds from the sale of common stock under an “at-the-market” sales agreement and preferred stock financings. We received $50.0 million from Novartis, our collaboration partner, including an up-front payment of $35.0 million and a $15.0 million equity investment. We will require additional capital in order to advance HMI-102 and our other product candidates through clinical development and commercialization. We believe that our compelling preclinical data, encouraging initial clinical data with HMI-102, scientific expertise, product development strategy, manufacturing capabilities, and robust intellectual property position us as a leader in the development of genetic medicines.

We were incorporated and commenced operations in 2015. Since our incorporation, we have devoted substantially all of our resources to organizing and staffing our company, business planning, raising capital, developing our technology platform, advancing our lead product candidate, HMI-102 for the treatment of PKU, through IND-enabling studies and into a Phase 1/2 clinical trial, advancing HMI-103 and HMI-202 into IND-enabling studies, researching and identifying additional product candidates, developing and implementing manufacturing processes and internal manufacturing capabilities, building out our manufacturing and research and development space, enhancing our intellectual property portfolio, and providing general and administrative support for these operations. To date, we have financed our operations primarily through the sale of common stock, through the sales of preferred stock, and through funding from our collaboration partner.

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products in the foreseeable future, if at all. We recognized $0.6 million and $0.3 million in collaboration revenue for the three months ended March 31, 2020 and 2019, respectively. Since inception, we have incurred significant operating losses. Our net losses for the three months ended March 31, 2020 and 2019 were $35.3 million and $23.9 million, respectively. As of March 31, 2020, we had an accumulated deficit of $235.0 million.

Our total operating expenses were $37.1 million and $25.4 million for the three months ended March 31, 2020 and 2019, respectively. Our operating expenses for the three months ended March 31, 2020 included substantial advance purchases of raw materials procured for future manufacturing needs to mitigate any possible supply chain interruptions as a result of the COVID-19 pandemic. We expect our operating expenses to continue to increase substantially in connection with our ongoing development activities related to our product candidates. Specifically, we anticipate that our expenses will increase substantially due to costs associated with our Phase 1/2 pheNIX clinical trial with HMI-102, development activities including IND-enabling studies associated with our other gene therapy and gene editing product candidates, including HMI-202, our gene therapy product candidate for MLD, and HMI-103, our gene editing product candidate for PKU, research activities in additional therapeutic areas to expand our pipeline, hiring additional personnel in manufacturing, research, clinical and regulatory, quality and other functional areas, increased expenses incurred with contract manufacturing organizations, or CMOs, to supply us with product for our clinical studies, costs to manufacture product for preclinical and clinical studies in our internal manufacturing facility and other costs including the maintenance and expansion of our intellectual property portfolio. In addition, we expect to incur additional costs associated with operating as a public company.

We have incurred significant capital expenditures for the buildout of a facility we have leased, including research and development labs, office space and manufacturing suites and the procurement of equipment and furniture for this facility and in support of our product development candidates and research initiatives. We expect to incur additional capital expenditures in 2020 and beyond in support of our research and development activities and our manufacturing facility.

Because of the numerous risks and uncertainties associated with the development of our current and any future product candidates and our platform and technology and because the extent to which we may enter into collaborations with third parties for development of any of our product candidates is unknown, we are unable to predict the timing and amount of increased operating expenses and capital expenditures associated with completing the research and development of our product candidates. Our future capital requirements will depend on many factors, including:

- the costs, timing, and results of our ongoing research and development efforts, including clinical trials, for HMI-102;
- the costs, timing, and results of our ongoing research and development efforts for HMI-103 and HMI-202, both of which are in IND-enabling studies;
- the costs, timing, and results of our research and development efforts for current and future product candidates in our gene therapy and gene editing pipeline;
- the costs and timing of process development and manufacturing scale-up activities, and the adequacy of supply of our product candidates for preclinical studies and clinical trials through CMOs and internal manufacturing;
- the costs and timing of capital expenditures for potential additional manufacturing capacity and related equipment and furniture;
- the costs and timing of preparing, filing, and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims, including any claims by third parties that we are infringing upon their intellectual property rights;
- the effect of competitors and market developments; and
- our ability to establish and maintain strategic collaborations, licensing or other agreements and the financial terms of such agreements for our product candidates.

We believe that our existing cash, cash equivalents and short-term investments will enable us to fund our current projected operating expenses and capital expenditures into the fourth quarter of 2021. We have based these estimates on assumptions that may prove to be imprecise, and we may use our available capital resources sooner than we currently expect. See “Liquidity and Capital Resources.” Adequate additional funds may not be available to us on acceptable terms, or at all. For example, the trading prices for our and other biopharmaceutical companies’ stock have been highly volatile as a result of the COVID-19 pandemic. As a result, we may face difficulties raising capital through sales of our common stock and any such sales may be on unfavorable terms. See “Risk Factors—The COVID-19 pandemic caused by the novel strain of coronavirus could adversely impact our business, including our preclinical studies and clinical trials.” in Part II, Item 1A of this Quarterly Report on Form 10-Q. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our shareholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect rights as a shareholder. Any future debt financing or preferred equity or other financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends and may require the issuance of warrants, which could potentially dilute the ownership interests of our shareholders.

If we raise additional funds through collaborations, strategic alliances, or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce, or terminate our product 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 drug development, we are unable to predict when or if we will be able to achieve or maintain 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.

Impact of COVID-19 Pandemic

We are closely monitoring how the spread of the COVID-19 pandemic is affecting our employees, Phase 1/2 pheNIX clinical trial, preclinical studies, manufacturing and overall operations. In response to the spread of COVID-19, we have taken steps to minimize the impact on our operations.

Operations – To protect the health of our employees and the third parties with whom we interact, we have instructed all office-based employees to work from home, while ensuring essential staffing levels in our operations remain in place, including maintaining key personnel in our laboratories and manufacturing facility. For those employees on-site, we have developed a modified office layout and traffic flow pattern to increase spacing capabilities, reduce inter-office risks and allow for business continuity. We have increased cleaning protocols throughout our entire facility, limited visitors to only those who are critical to our ongoing operations and have cancelled all business travel.

Phase 1/2 pheNIX clinical trial – We are currently continuing our Phase 1/2 pheNIX clinical trial and are working with trial sites to mitigate potential COVID-19-related disruptions in order to help ensure the safety of patients and healthcare professionals. In addition, we have deployed home-health services which include home visits for patient monitoring and reporting, as well as the utilization of a centralized laboratory for testing enrolled patients. Despite our best efforts, disruptions caused by the COVID-19 pandemic may result in difficulties or delays in enrolling, conducting or completing this trial and the incurrence of unforeseen costs as a result of clinical trial delays. We will continue to evaluate the impact of the ongoing global pandemic on the pheNIX trial and will make adjustments, as needed.

Preclinical studies – IND-enabling studies are continuing in support of our HMI-202 and HMI-103 programs and we have made operational changes to mitigate the risk of potential disruptions caused by the COVID-19 pandemic. All of our ongoing and planned preclinical studies at external CROs are progressing and we have accelerated shipments of reagents and supplies to avoid any disruption of activities. However, it is possible that the COVID-19 pandemic may have an impact in the future on our CROs' ability to complete critical studies required for the progression of these programs. In addition, any planned or potential meetings with the FDA or other regulatory authorities about any of our development programs could be delayed as these regulatory bodies respond to the ongoing pandemic.

Manufacturing – We continue to operate our manufacturing facility at or near normal levels. We have on-hand all of the drug product needed for the ongoing dose-escalation and planned Part B expansion phases of the pheNIX clinical trial. In addition, during the first quarter of 2020, we accelerated the procurement of raw materials for future manufacturing, research and development needs to minimize potential supply chain interruptions. While we currently do not anticipate any interruptions in our manufacturing process, it is possible that the COVID-19 pandemic and response efforts may have an impact in the future on our and/or our third-party suppliers and CMOs' ability to manufacture our product candidates or materials needed for our preclinical studies and clinical trials.

At this time, there is significant uncertainty relating to the trajectory of the COVID-19 pandemic and impact of related responses and as a result, we expect that the COVID-19 pandemic may impact our business, revenues, results of operations and financial condition. The impact of COVID-19 on our future results will largely depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the pandemic, travel restrictions and social distancing in the United States and other countries, business closures or business disruptions, the ultimate impact of COVID-19 on financial markets and the global economy, and the effectiveness of actions taken in the United States and other countries to contain and treat the disease. See "Risk Factors— The COVID-19 pandemic caused by the novel strain of coronavirus could adversely impact our business, including our preclinical studies and clinical trials." in Part II, Item 1A of this Quarterly Report on Form 10-Q.

Components of Our Results of Operations

Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products in the foreseeable future. We recorded $0.6 million in collaboration revenue for the three months ended March 31, 2020 (see Note 10 to our condensed consolidated financial statements included elsewhere in this Quarterly Report on Form 10-Q for additional information regarding Novartis revenue recognition discussion).

Operating Expenses

Our operating expenses since inception have consisted solely of research and development costs and general and administrative costs.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our discovery efforts, and the development of our product candidates, and include:

- salaries, benefits and other related costs, including stock-based compensation expense, for personnel engaged in research and development functions;
- expenses incurred under agreements with third parties, including contract research organizations, or CROs, and other third parties that conduct research, preclinical activities and clinical trials on our behalf as well as CMOs and our internal technical operations team that manufacture our product candidates for use in our preclinical testing, our Phase 1/2 pheNIX clinical trial and additional potential future clinical trials;
- costs of outside consultants, including their fees and related travel expenses;
- the costs of laboratory supplies and acquiring, developing and manufacturing preclinical study and clinical trial materials; and
- facility-related expenses, which include direct depreciation costs and allocated expenses for rent and maintenance of facilities and other operating costs.

We expense research and development costs as incurred.

We typically use our employee and infrastructure resources across our development programs. We track outsourced development costs by product candidate or development program, but we do not allocate personnel costs, license payments made under our licensing arrangements or other internal costs to specific development programs or product candidates. These costs are included in other research and development expenses in the table below.

The following table summarizes our research and development expenses by product candidate or development program:

	Three months ended March 31,		
(in thousands)	**2020**	**2019**	**Change**
HMI-102 external development costs	$ 11,433	$ 8,153	$ 3,280
Other development-stage programs' external development costs	5,814	2,662	3,152
Employee-related costs	10,158	6,459	3,699
Other research and development costs	1,905	3,262	(1,357)
Total research and development expenses	$ 29,310	$ 20,536	$ 8,774

Research and development activities are central to our business model. We expect that our research and development expenses will continue to increase substantially for the foreseeable future as we advance clinical trials of HMI-102 for the treatment of PKU, including our Phase 1/2 pheNIX clinical trial, continue to advance both HMI-103 and HMI-202 through IND-enabling studies and into clinical trials and continue to discover and develop additional product candidates.

We cannot determine with certainty the duration and costs of future clinical trials of HMI-102 and IND-enabling studies and future clinical trials of our other product candidates in development or any other future product candidate we may develop or if, when, or to what extent we will generate revenue from the commercialization and sale of any product candidate for which we obtain marketing approval. We may never succeed in obtaining marketing approval for any product candidate. The duration, costs and timing of clinical trials and development of HMI-102, our other product candidates in development and any other future product candidate we may develop will depend on a variety of factors, including:

- the scope, rate of progress, expense and results of clinical trials of HMI-102, HMI-103, HMI-202, as well as of any future clinical trials of other product candidates and other research and development activities that we may conduct;
- uncertainties in clinical trial design and patient enrollment rates;
- any delays in clinical trials as a result of the COVID-19 pandemic;
- the actual probability of success for our product candidates, including the safety and efficacy results, early clinical data, competition, manufacturing capability and commercial viability;
- significant and changing government regulation and regulatory guidance;

- the timing and receipt of any marketing approvals; and
- the expense of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the FDA or another regulatory authority were to require us to conduct clinical trials beyond those that we anticipate will be required for the completion of clinical development of a product candidate, or if we experience significant delays in our clinical trials due to patient enrollment or other reasons, we would be required to expend significant additional financial resources and time on the completion of clinical development.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in our executive, finance, human resources, 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 expenses; and facility-related expenses, which include direct depreciation costs, rent expense, maintenance of facilities and other operating costs.

We expect that our general and administrative expenses will increase in the future as we increase our personnel headcount to support increased research and development activities relating to HMI-102, HMI-103, HMI-202, and any other product candidate we may develop. We also have incurred and expect to continue to incur increased expenses associated with being a public company, including costs of accounting, audit, compliance with the Sarbanes-Oxley Act of 2002, 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.

Interest Income

Interest income consists of interest income earned on our cash, cash equivalents and short-term investments. Our interest income has decreased due to lower yields on invested funds during the three months ended March 31, 2020 as compared to the same period in 2019. Market volatility resulting from the COVID-19 pandemic has and may continue to adversely impact our interest income.

Critical Accounting Policies and Use of Estimates

This discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States. The preparation of our consolidated financial statements and related disclosures requires us to make estimates, assumptions and judgements that affect the reported amount of assets, liabilities, revenue, costs and expenses, and related disclosures. 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.

Our critical accounting policies are described under the heading “Management’s Discussion and Analysis of Financial Condition and Results of Operations— Critical Accounting Policies and Significant Judgments and Estimates” in our Annual Report on Form 10-K for the year ended December 31, 2019 and the notes to the condensed consolidated financial statements appearing elsewhere in this Quarterly Report on Form 10-Q. There were no material changes to our critical accounting policies through March 31, 2020 from those discussed in our Annual Report on Form 10-K for the year ended December 31, 2019.

Results of Operations

Comparison of Three Months Ended March 31, 2020 and 2019

The following table summarizes our results of operations for the periods presented:

(in thousands)	Three months ended March 31, 2020	2019	Change
Collaboration revenue	$ 588	$ 270	318
Operating expenses:			
Research and development	29,310	20,536	8,774
General and administrative	7,770	4,857	2,913
Total operating expenses	37,080	25,393	11,687
Loss from operations	(36,492)	(25,123)	(11,369)
Other income:			
Interest income	1,161	1,271	(110)
Net loss	$ (35,331)	$ (23,852)	$ (11,479)

Collaboration Revenue

Collaboration revenue for the three months ended March 31, 2020 was $0.6 million, compared to $0.3 million for the three months ended March 31, 2019. We recognize revenues consistent with the pattern of performance of our research and development activities under our collaboration agreement with Novartis, taking into consideration all upfront payments and research funding payments under this arrangement together as a single performance obligation. We expect the level of effort to substantially increase when and if we begin manufacturing during the development term of the collaboration agreement, which is dependent on the success of the research and Novartis' decision to take a candidate into development. Collaboration revenue recognized in a given period is based on actual costs incurred during that period as a percentage of total estimated costs to complete the single performance obligation under the arrangement. We would not expect collaboration revenue to be consistent period to period as it will fluctuate as we perform the research, development and manufacturing services over the term of our collaboration agreement with Novartis.

Research and Development Expenses

(in thousands)	Three months ended March 31, 2020	2019	Change
HMI-102 external development costs	$ 11,433	$ 8,153	$ 3,280
Other development-stage programs' external development costs	5,814	2,662	3,152
Employee-related costs	10,158	6,459	3,699
Other research and development costs	1,905	3,262	(1,357)
Total research and development expenses	$ 29,310	$ 20,536	$ 8,774

Research and development expenses for the three months ended March 31, 2020 were $29.3 million, compared to $20.5 million for the three months ended March 31, 2019. The increase of $8.8 million was primarily due to an increase of $3.3 million in direct research expenses, including costs related to manufacturing preclinical study and clinical trial materials, as well as costs incurred with our CRO to conduct and manage our Phase 1/2 pheNIX clinical trial, a $3.2 million increase in direct research expenses related to HMI-202 and HMI-103 external development costs as we advance through IND-enabling studies and a $3.7 million increase due to additional employee headcount to support our ongoing development programs, research initiatives, technology platform and manufacturing capabilities resulting in increases in salaries, payroll taxes, stock-based compensation expense and recruiting costs. Partially offsetting these increases was a $1.4 million decrease in other research and development costs related to laboratory supplies, research materials and services for our early-stage research programs.

General and Administrative Expenses

General and administrative expenses for the three months ended March 31, 2020 were $7.8 million, compared to $4.9 million for the three months ended March 31, 2019. The increase of $2.9 million was due to an increase in employee-related expenses of $1.3 million, which included $0.9 million of increased stock-based compensation expense, an increase in consulting expense of $0.8 million, an increase in facility costs of $0.6 million and an increase in recruiting costs of $0.2 million.

Interest Income

Interest income for the three months ended March 31, 2020 was $1.2 million, compared to $1.3 million for the three months ended March 31, 2019. The decrease was the result of lower yields on invested funds in cash, cash equivalents and short-term investment balances for the three months ended March 31, 2020 compared to the three months ended March 31, 2019.

Net Loss

Net loss for the three months ended March 31, 2020 was $35.3 million, compared to $23.9 million for the three months ended March 31, 2019. The increase in net loss was primarily due to the increases in research and development and general and administrative expenses discussed above.

Liquidity and Capital Resources

Since our inception, we have incurred significant operating losses. We expect to incur significant expenses and operating losses for the foreseeable future as we advance the preclinical and clinical development of our product candidates. We expect that our research and development and general and administrative costs and our capital expenditures will increase in connection with conducting preclinical studies and clinical trials for our product candidates, contracting with CMOs and producing material in our internal manufacturing facility to support preclinical studies and clinical trials, expanding our research and development laboratories, expanding our intellectual property portfolio, and providing general and administrative support for our operations. As a result, we will need additional capital to fund our operations, which we may obtain from additional equity or debt financings, collaborations, licensing arrangements, or other sources.

We do not currently have any approved products and have never generated any revenue from product sales. To date, we have financed our operations primarily through the sale of common stock, and the sale of preferred stock and through an up-front payment from a collaboration partner. Since our inception in 2015, we have raised approximately $444.2 million in aggregate net proceeds through our IPO, a follow-on public offering of common stock in April 2019, proceeds from the sale of common stock under an “at-the-market” sales agreement and preferred stock financings. We received an up-front payment of $50.0 million from a collaboration partner, comprised of $35.0 million in cash and a $15.0 million equity investment, the latter of which is included in the proceeds from the sale of preferred stock. As of March 31, 2020, we had $236.2 million in cash, cash equivalents, short-term investments and restricted cash and an accumulated deficit of $235.0 million.

In April 2019, we completed a follow-on public offering of our common stock. We sold 5,555,556 shares of our common stock at a public offering price of $22.50 per share and received net proceeds of $116.9 million, after deducting underwriting discounts and commissions and offering expenses. In addition, in April and May 2019, in connection with the exercise in full of the underwriters’ option to purchase additional shares, we issued an aggregate of 833,333 shares of our common stock at a public offering price of $22.50 per share and received net proceeds of $17.6 million, after deducting underwriting discounts and commissions.

In March 2020, we entered into a sales agreement, or the Sales Agreement, with Cowen and Company, LLC, or Cowen, as sales agent, pursuant to which we may, from time to time, issue and sell common stock with an aggregate value of up to $150 million in "at-the-market" offerings, or the ATM, under our Registration Statement on Form S-3 (File No. 333-237131) filed with the SEC on March 12, 2020. Sales of common stock, if any, pursuant to the Sales Agreement, may be made in sales deemed to be an “at the market offering” as defined in Rule 415(a) of the Securities Act, including sales made directly through the Nasdaq Global Market or on any other existing trading market for our common stock. No securities were issued pursuant to the Sales Agreement during the three months ended March 31, 2020. As of March 31, 2020, there was $150.0 million of common stock remaining available for sale under the ATM. Simultaneous with the filing of the registration statement in March 2020, our previous Registration Statement on Form S-3 (File No. 333-230664) filed with the SEC on April 1, 2019 and our prior sales agreement with Cowen providing for the offering, issuance and sale of up to an aggregate $100.0 million of our common stock from time to time in “at-the-market” offerings were terminated.

Cash Flows

Our cash, cash equivalents, short-term investments and restricted cash totaled $236.2 million and $263.7 million as of March 31, 2020 and December 31, 2019, respectively. We had no indebtedness as of March 31, 2020 and December 31, 2019.

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

	Three months ended March 31,	
(in thousands)	**2020**	**2019**
Net cash used in operating activities	$ (25,846)	$ (17,871)
Net cash provided by investing activities	114,997	19,667
Net cash provided by financing activities	447	325
Net change in cash, cash equivalents and restricted cash	$ 89,598	$ 2,121

Cash Flows for the Three Months ended March 31, 2020

Operating Activities

Net cash used in operating activities for the three months ended March 31, 2020 was $25.8 million, driven primarily by our net loss of $35.3 million as we incurred expenses associated with research and development activities on HMI-102, HMI-103 and HMI-202, including the Phase 1/2 pheNIX trial for our HMI-102 program, and research activities on other applications for our technology. The funding of our net loss was partially offset by net non-cash expenses of $4.8 million, including $2.9 million of stock-based compensation expense and $1.9 million of depreciation expense and a decrease in working capital of $5.4 million, including $4.8 million in increased accounts payable.

Investing Activities

Net cash provided by investing activities for the three months ended March 31, 2020 was $115.0 million, attributable to maturities of short-term investments of $117.0 million, partially offset by purchases of property and equipment of $2.0 million.

Financing Activities

Net cash provided by financing activities for the three months ended March 31, 2020 was $0.5 million, primarily due to proceeds from the issuance of common stock pursuant to the employee stock purchase plan.

Cash Flows for the Three Months ended March 31, 2019

Operating Activities

Net cash used in operating activities for the three months ended March 31, 2019 was $17.9 million, driven primarily by our net loss of $23.9 million as we incurred expenses associated with research activities on HMI-102, HMI-103 and HMI-202, and research activities on other applications for our technology. The funding of our net loss was partially offset by net non-cash expenses of $1.8 million, an increase in deferred rent of $1.3 million and a decrease in working capital of $2.9 million.

Investing Activities

Net cash provided by investing activities for the three months ended March 31, 2019 was $19.7 million, attributable to maturities of short-term investments of $114.6 million, partially offset by $84.5 million in purchases of short-term investments and $10.5 million in purchases of property and equipment.

Financing Activities

Net cash provided by financing activities for the three months ended March 31, 2019 was $0.3 million, primarily due to proceeds from the issuance of common stock pursuant to our employee stock purchase plan.

Funding Requirements

Our operating expenses increased substantially in 2019 and in the first quarter of 2020 and are expected to increase substantially for the remainder of 2020 and in future years in connection with our ongoing activities, particularly as we advance our Phase 1/2 pheNIX clinical trial with HMI-102, advance our preclinical activities including IND enabling studies, scale-up manufacturing processes, engage with CMOs, manufacture materials for preclinical and clinical activities in our internal manufacturing facility and initiate additional human clinical trials. In addition, we have incurred, and expect to continue to incur additional costs associated with operating as a public company. We also expect our capital expenditures to increase substantially as we expand our operations.

Specifically, our operating expenses and capital expenditures will increase as we:

- pursue the preclinical and clinical development of HMI-102 including the ongoing pheNIX Phase 1/2 clinical trial, HMI-103 and HMI-202;
- pursue the preclinical and clinical development of other product candidates based on our gene therapy and gene editing technology;
- further scale-up our internal manufacturing processes and capabilities, manufacture materials in our internal manufacturing facility and contract with CMOs to support our preclinical studies and clinical trials of our product candidates;
- further expand our manufacturing capacity;
- operate our business in our facility with expanded research and development labs and manufacturing suites and purchase additional equipment for our operations;
- in-license or acquire the rights to other products, product candidates or technologies;
- maintain, expand and protect our intellectual property portfolio;
- hire additional personnel in research, manufacturing and regulatory and clinical development as well as management personnel; and
- expand our operational, financial and management systems and increase personnel, including personnel to support our operations as a public company.

We believe that our existing cash, cash equivalents and short-term investments will enable us to fund our operating expenses and capital expenditure requirements into the fourth quarter of 2021. We have based these estimates on assumptions that may prove to be imprecise, and we could utilize our available capital resources sooner than we expect.

Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical drugs, it is difficult to estimate with certainty the amount of our working capital requirements. Our future funding requirements will depend on many factors, including:

- the progress, costs and results of our preclinical development and initial clinical trials for HMI-102 including the pheNIX Phase 1/2 clinical trial, HMI-103 and HMI-202;
- the progress, costs and results of our additional research and preclinical development programs in gene therapy and gene editing;
- the costs and timing of internal process development and manufacturing scale-up activities, the production of materials in our internal manufacturing facility, and outsourcing activities with CMOs associated with our lead product development programs and other programs we advance through preclinical and clinical development;
- our ability to establish and maintain strategic collaborations, licensing or other agreements and the financial terms of such agreements;
- the scope, progress, results and costs of any product candidates that we may derive from our platform technology or any other product candidates that we may develop;
- the extent to which we in-license or acquire rights to other products, product candidates or technologies; and
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against any intellectual property-related claims.

In addition, the magnitude and duration of the COVID-19 pandemic and its impact on our liquidity and future funding requirements is uncertain as of the filing date of this Quarterly Report on Form 10-Q, as the pandemic continues to evolve globally. See “Impact of COVID-19 Pandemic” above and “Risk Factors— The COVID-19 pandemic caused by the novel strain of coronavirus could adversely impact our business, including our preclinical studies and clinical trials.” in Part II, Item 1A of this Quarterly Report on Form 10-Q for a further discussion of the possible impact of the COVID-19 pandemic on our business.

Until such time, if ever, that we can generate product revenue sufficient to achieve profitability, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaboration agreements, other third-party funding, strategic alliances, licensing arrangements and marketing and distribution arrangements.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our shareholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our shareholders as common stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through other third-party funding, collaboration agreements, strategic alliances, licensing arrangements or marketing and distribution arrangements, 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 when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves. We currently have no credit facility or committed sources of capital.

Contractual Obligations

There have been no material changes to our contractual obligations during the three months ended March 31, 2020 from those previously disclosed in our Annual Report on Form 10-K for the year ended December 31, 2019.

Off-Balance Sheet Arrangements

We have not entered into any off-balance sheet arrangements and do not have any holdings in variable interest entities.

Item 3. Quantitative and Qualitative Disclosures About Market Risk.

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities. Our interest-earning assets consist of cash, cash equivalents, and short-term investments of $234.9 million, or 81.3% of our total assets at March 31, 2020, and $262.4 million, or 84.5% of our total assets at December 31, 2019. Interest income earned on these assets was $1.2 million and $1.3 million for the three months ended March 31, 2020 and 2019, respectively. Our interest income is sensitive to changes in the general level of interest rates, primarily U.S. interest rates. If a 10% change in interest rates were to have immediately occurred on March 31, 2020, this change would not have had a material effect on the fair value of our investment portfolio as of that date. At March 31, 2020, our cash equivalents consisted of bank deposits and money market funds, and our short-term investments included interest-earning securities. Such interest-earning instruments carry a degree of interest rate risk; however, historical fluctuations in interest income have not been significant for us. We had no debt outstanding as of March 31, 2020 and December 31, 2019.

Item 4. Controls and Procedures.

Limitations on Effectiveness of Controls and Procedures

In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief 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). Based on such evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of March 31, 2020.

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 three months ended March 31, 2020 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting, except as noted below.

During the three months ended March 31, 2020, we completed the first phase of our implementation of a Company-wide enterprise resource planning system. We have assessed and continue to monitor the impact of this implementation on our processes and procedures, as well as the impact on our internal control over financial reporting. Where appropriate, we have made changes to our internal controls to address system changes.

Also during the three months ended March 31, 2020, we implemented internal controls to ensure we adequately evaluated our lease arrangements and properly assessed the impact of ASC Topic 842, *Leases*, in connection with our adoption of this new standard on January 1, 2020. In addition, we implemented certain additional controls in connection with the ongoing accounting for our lease arrangements under ASC 842.

PART II—OTHER INFORMATION

Item 1. Legal Proceedings.

We are not party to any material legal proceedings.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. You should consider carefully the risks described below, together with the other information included or incorporated by reference in this Quarterly Report on Form 10-Q. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected. In these circumstances, the market price of our common stock could decline. Other events that we do not currently anticipate or that we currently deem immaterial may also affect our business, prospects, financial condition and results of operations.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses since inception and anticipate that we will incur continued losses for the foreseeable future. If we are unable to achieve and sustain profitability, the market value of our common stock will likely decline. We may never achieve or maintain profitability.

We are a clinical-stage genetic medicines company with a limited operating history. We have never been profitable and do not expect to be profitable in the foreseeable future. We have incurred net losses in each year since beginning to develop our product candidates, including net losses of approximately $35.3 million and $23.9 million for the three months ended March 31, 2020 and 2019, respectively. As of March 31, 2020, we had an accumulated deficit of approximately $235.0 million. In addition, we have not commercialized any products and have never generated any revenue from product sales. We have devoted most of our financial resources to research and development, including our preclinical development activities.

We expect to continue to incur significant additional operating losses for the foreseeable future as we seek to advance product candidates through preclinical and clinical development, expand our research and development activities, develop new product candidates, complete clinical trials, seek regulatory approval and, if we receive FDA approval, commercialize our products. Furthermore, the costs of advancing product candidates into each succeeding clinical phase tend to increase substantially over time. The total costs to advance any of our product candidates to marketing approval in even a single jurisdiction would be substantial. Because of the numerous risks and uncertainties associated with genetic medicine product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to begin generating revenue from the commercialization of products or achieve or maintain profitability. Our expenses will also 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, assess, acquire and/or develop additional research programs and additional product candidates;
- initiate preclinical testing and clinical trials for any product candidates we identify and develop;
- establish a sales, marketing and distribution infrastructure to commercialize any product candidates for which we may obtain marketing approval;
- maintain, expand and protect our intellectual property portfolio;
- further develop our genetic medicines platform;
- hire additional clinical, scientific and commercial personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts, as well as to support our operations as a public reporting company;
- acquire or in-license other commercial products, product candidates and technologies;
- make royalty, milestone or other payments under current and any future in-license agreements; and
- further expand our GMP manufacturing capacity.

Furthermore, our ability to successfully develop, commercialize and license our products and generate product revenue is subject to substantial additional risks and uncertainties. Each of our programs and product candidates will require additional preclinical and clinical development, potential regulatory approval in multiple jurisdictions, securing manufacturing supply, capacity and expertise, building of a commercial organization, substantial investment and significant marketing efforts before we generate any revenue from product sales. These risks are further described under "—Risks Related to Discovery, Development, Clinical Testing, Manufacturing and Regulatory Approval" and "—Risks Related to Commercialization." As a result, we expect to continue to incur net losses and negative cash flows for the foreseeable future. These net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital. The amount of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenues. If we are unable to develop and commercialize one or more of our product candidates either alone or with collaborators, or if revenues from any product candidate that receives marketing approval are insufficient, we will not achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability. If we are unable to achieve and then maintain profitability, the value of our equity securities will be materially and adversely affected.

We will require additional capital to fund our operations, and if we fail to obtain necessary financing, we may not be able to complete the development and commercialization of our product candidates.

We expect to spend substantial amounts to complete the development of, seek regulatory approvals for and commercialize our lead product candidate, HMI-102. We will require additional capital, which we may raise through equity offerings, debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or other sources to enable us to complete the development and potential commercialization of HMI-102, HMI-103, HMI-202 and any other product candidates. In addition, we may not be able to enter into any collaborations that will generate significant cash. Adequate additional financing may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative effect on our financial condition and our ability to pursue our business strategy. In addition, attempting to secure additional financing may divert the time and attention of our management from day-to-day activities and harm our product candidate development efforts.

Based upon our current operating plan, we believe that our existing cash, cash equivalents and short-term investments will enable us to fund our operating expenses and capital expenditure requirements into the fourth quarter of 2021, including, subject to the impact of the COVID-19 pandemic on our business, additional data readouts from our Phase 1/2 pheNIX clinical trial with HMI-102, the advancement of our lead gene editing product candidate, HMI-103, and our lead CNS gene therapy product candidate, HMI-202, the scale-up of our manufacturing processes and the expansion of our intellectual property portfolio. This estimate is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Changing circumstances could cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more than currently expected because of circumstances beyond our control. Because the length of time and activities associated with successful development of HMI-102, HMI-103, HMI-202 and any other product candidates is highly uncertain, we are unable to estimate the actual funds we will require for development and any approved marketing and commercialization activities. Our future funding requirements, both near and long-term, will depend on many factors, including, but not limited to:

- the initiation, progress, timing, costs and results of our planned clinical trials for HMI-102 and our other product candidates;
- the outcome, timing and cost of meeting regulatory requirements established by the FDA and other comparable foreign regulatory authorities;
- the cost of filing, prosecuting, defending and enforcing our patent claims and other intellectual property rights;
- the cost of defending potential intellectual property disputes, including patent infringement actions brought by third parties against us or HMI-102, HMI-103, HMI-202 or any of our product candidates;
- the effect of competing technological and market developments;
- the cost and timing of completion of commercial-scale manufacturing activities;
- the costs of operating as a public company;
- the extent to which we in-license or acquire other products and technologies;
- the cost of establishing sales, marketing and distribution capabilities for HMI-102, HMI-103, HMI-202 or any of our product candidates in regions where we choose to commercialize our products; and
- the initiation, progress, timing and results of our commercialization of HMI-102, HMI-103, HMI-202 or any of our product candidates, if approved for commercial sale.

We cannot be certain that additional funding will be available on acceptable terms, or at all. Moreover, market volatility resulting from the COVID-19 pandemic or other factors could also adversely impact our ability to access capital as and when needed. 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 HMI-102, HMI-103, HMI-202 or other product candidates or potentially discontinue operations.

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 revenue, we may finance our cash needs through a combination of equity offerings, debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements. We do not currently have any committed external source of funds. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, including under our effective Registration Statement on Form S-3, the ownership interests of our shareholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may be required to relinquish valuable rights to our technologies, future revenue streams 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 when needed, 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.

We have a limited operating history and no history of commercializing genetic medicine products, which may make it difficult to evaluate the prospects for our future viability.

We were established and began operations in 2015. Our operations to date have been limited to financing and staffing our company, developing our technology and identifying and developing our product candidates. We have not yet demonstrated an ability to successfully complete any clinical trials, including large-scale, pivotal clinical trials, obtain marketing approval, manufacture a 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. Typically, it takes about six to ten years to develop a new drug from the time it enters Phase 1 clinical trials to when it is approved for treating patients, but in many cases, it may take longer. Consequently, predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing genetic medicine products.

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

As we continue to build our business, we expect our financial condition and operating results may fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any particular quarterly or annual period as indications of future operating performance.

We are heavily dependent on the success of HMI-102, our most advanced product candidate, and if HMI-102 does not receive regulatory approval or is not successfully commercialized, our business may be harmed.

To date, we have invested a significant portion of our efforts and financial resources in the development of HMI-102. Our future success and ability to generate product revenue is substantially dependent on our ability to successfully develop, obtain regulatory approval for and successfully commercialize this product candidate. We currently have no products that are approved for commercial sale and may never be able to develop marketable products. We expect that a substantial portion of our efforts and expenditures over the next few years will be devoted to HMI-102, which will require additional clinical development, management of clinical and manufacturing activities, regulatory approval in multiple jurisdictions, securing manufacturing supply, building of a commercial organization, substantial investment and significant marketing efforts before we can generate any revenues from any commercial sales. Accordingly, our business currently depends heavily on the successful development, regulatory approval and

commercialization of HMI-102, which may never occur. We cannot be certain that HMI-102 will be successful in clinical trials, receive regulatory approval or be successfully commercialized even if we receive regulatory approval. Even if we receive approval to market HMI-102 from the FDA or other regulatory bodies, we cannot be certain that our product candidate will be successfully commercialized, widely accepted in the marketplace or more effective than other commercially available alternatives. Additionally, the research, testing, manufacturing, labeling, approval, sale, marketing and distribution of genetic medicine products are and will remain subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries that each have differing regulations. We are not permitted to market HMI-102 in the United States until it receives approval of a biologics license application, or BLA from the FDA, or in any foreign countries until it receives the requisite approval from such countries.

We have not submitted a BLA to the FDA or comparable applications to other regulatory authorities and do not expect to be in a position to do so for the foreseeable future.

HMI-102 is our most advanced product candidate, and because our other product candidates are based on similar technology, if HMI-102 shows unexpected adverse events or a lack of efficacy in the indications we intend to treat, or if we experience other regulatory or developmental issues, our development plans and business could be significantly harmed. Further, competitors may be developing products with similar technology and may experience problems with their products that could identify problems that would potentially harm our business.

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

Part of our strategy involves identifying novel product candidates. The process by which we identify product candidates may fail to yield product candidates for clinical development for a number of reasons, including those discussed in these risk factors and also:

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

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

We will need to expand our organization, and we may experience difficulties in managing this growth, which could disrupt our operations.

As of May 1, 2020, we had 195 employees. We will need to significantly expand our organization, and we may have difficulty identifying, hiring and integrating new personnel. Future growth would impose significant additional responsibilities on our management, including the need to identify, recruit, maintain, motivate and integrate additional employees, consultants and contractors. Also, our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenues could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize our product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

Many of the biotechnology companies that we compete against for qualified personnel and consultants have greater financial and other resources, different risk profiles and a longer history in the industry than we do. If we are unable to continue to attract and retain high-quality personnel and consultants, the rate and success at which we can discover and develop product candidates and operate our business will be limited.

We may be required to make significant payments in connection with our license agreements with each of the City of Hope and the California Institute of Technology.

Under our license agreements with each of City of Hope Medical Center, or COH, and California Institute of Technology, or Caltech, we are subject to significant obligations, including payment obligations upon achievement of specified milestones and royalties on product sales, as well as other material obligations, including potential payments to COH if we were to sublicense the COH technology to additional strategic collaborators. If these payments become due, we may not have sufficient funds available to meet our obligations or we may have to direct funds from other development efforts, and as a result, our development efforts may be materially harmed.

Risks Related to Discovery, Development, Clinical Testing, Manufacturing and Regulatory Approval

We intend to identify and develop product candidates based on our novel genetic medicines platform, which makes it difficult to predict the time and cost of product candidate development. No products that utilize gene editing technology have been approved in the United States or in Europe, and there have only been a limited number of human clinical trials involving a gene editing product candidate. Moreover, none of those trials has involved our nuclease-free gene editing technology.

We have concentrated our research and development efforts on our genetic medicines platform, which uses both nuclease-free gene editing and gene therapy technologies. Our future success depends on the successful development of this novel therapeutic approach. To date, no product that utilizes gene editing has been approved in the United States or Europe. There have been a limited number of clinical trials of gene editing technologies, however no product candidates have been approved, and none of these clinical trials involved product candidates that utilize our novel gene correction editing technology. In addition, because our programs are all in the research or preclinical stage, we have not yet been able to assess safety in humans, and there may be long-term effects from treatment with any of our future product candidates that we cannot predict at this time. Any gene correction editing product candidates we may develop will act at the level of DNA, and, because animal DNA differs from human DNA, it will be difficult for us to test our future product candidates in animal models for either safety or efficacy. Also, animal models may not exist for some of the diseases we expect to pursue. Our genetic medicines platform is based on a suite of 15 proprietary AAVHSCs which we can deploy with either gene editing or gene therapy constructs. Both applications rely on a unique ability of our AAVHSCs to efficiently target multiple tissues in the body. The mechanism of action by which these vectors target particular tissues is still not completely understood. Therefore, it is difficult for us to determine that our vectors will be able to properly integrate corrective DNA in or deliver gene transfer constructs to enough tissue cells to reach therapeutic levels. We cannot be certain that our AAVHSCs will be able to meet safety and efficacy levels needed to be therapeutic in humans or that they will not cause significant adverse events or toxicities. Furthermore, recent work conducted by a third party in non-human primates suggests that intravenous delivery of certain AAV vectors at very high doses may result in severe toxicity. To date, we have not observed the severe toxicities described in these publications after intravenous administration in non-human primates with our naturally occurring AAVHSC vectors, and we have not seen these toxicities in our product candidates. However, we cannot be certain that we will be able to avoid triggering toxicities in our future preclinical or clinical studies. Any such results could impact our ability to develop a product candidate. As a result of these factors, it

is more difficult for us to predict the time and cost of product candidate development, and we cannot predict whether the application of our genetic medicines platform, or any similar or competitive gene therapy or gene editing platforms, will result in the identification, development, and regulatory approval of any medicines, or that other genetic medicine technologies will not be considered better or more attractive for the development of medicines. There can be no assurance that any development problems we experience in the future related to our genetic medicines platform or any of our research programs will not cause significant delays or unanticipated costs, or that such development problems can be solved. We may also experience delays in developing a sustainable, reproducible, and scalable manufacturing process or transferring that process to commercial partners. Any of these factors may prevent us from completing our preclinical studies or any clinical trials that we may initiate or commercializing any product candidates we may develop on a timely or profitable basis, if at all.

Because gene therapy and gene editing are novel and the regulatory landscape that governs any product candidates we may develop is uncertain and continues to change, we cannot predict the time and cost of obtaining regulatory approval, if we receive it at all, for any product candidates we may develop.

Regulatory requirements governing products created with genome editing technology or involving gene therapy treatment have changed frequently and will likely continue to change in the future. Approvals by one regulatory agency may not be indicative of what any other regulatory agency may require for approval, and there is substantial, and sometimes uncoordinated, overlap in those responsible for regulation of gene therapy products, cell therapy products and other products created with genome editing technology. For example, the FDA established the Office of Tissues and Advanced Therapies within its Center for Biologics Evaluation and Research, or CBER, with responsibility for the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. These and other regulatory review agencies, committees and advisory groups and any requirements and guidelines they promulgate may lengthen the regulatory review process, require us to perform additional preclinical studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates or lead to significant post-approval limitations or restrictions.

Additionally, under the National Institutes of Health, or NIH, Guidelines for Research Involving Recombinant DNA Molecules, or NIH Guidelines, supervision of human gene transfer trials includes evaluation and assessment by an institutional biosafety committee, or IBC, a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment, and such review may result in some delay before initiation of a clinical trial. While the NIH Guidelines are not mandatory unless the research in question is being conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them.

In the European Union, the European Medicines Agency, or the EMA, has a Committee for Advanced Therapies, or CAT, that is responsible for assessing the quality, safety and efficacy of advanced therapy medicinal products. Advanced-therapy medical products include gene therapy medicine, somatic-cell therapy medicines and tissue-engineered medicines. The role of the CAT is to prepare a draft opinion on an application for marketing authorization for a gene therapy medicinal candidate that is submitted to the EMA. In the European Union, the development and evaluation of a gene therapy medicinal product must be considered in the context of the relevant European Union guidelines. The EMA may issue new guidelines concerning the development and marketing authorization for gene therapy medicinal products and require that we comply with these new guidelines. Similarly complex regulatory environments exist in other jurisdictions in which we might consider seeking regulatory approvals for our product candidates, further complicating the regulatory landscape. As a result, the procedures and standards applied to gene therapy products and cell therapy products may be applied to any of our gene therapy or genome editing product candidates, but that remains uncertain at this point.

The clinical trial requirements of the FDA, the EMA and other regulatory authorities and the criteria these regulators use to evaluate 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 product candidates created with novel genome editing technology such as ours can be more lengthy, rigorous and expensive than the process for other better known or more extensively studied product candidates and technologies. Since we are developing novel treatments for diseases in which there is little clinical experience with new endpoints and methodologies, there is heightened risk that the FDA, the EMA or comparable regulatory bodies may not consider the clinical trial endpoints to provide clinically meaningful results, and the resulting clinical data and results may be more difficult to analyze. This may be a particularly significant risk for many of the genetically defined diseases for which we may develop product candidates alone or with collaborators due to small patient populations for those diseases, and designing and executing a rigorous clinical trial with appropriate statistical power is more difficult than with diseases that have larger patient populations. Regulatory agencies administering existing or future regulations or legislation may not allow production and marketing

of products utilizing genome editing technology in a timely manner or under technically or commercially feasible conditions. Even if our product candidates obtain required regulatory approvals, such approvals may later be withdrawn as a result of changes in statute or regulations or the interpretation of new available data by applicable regulatory agencies.

Changes in applicable regulatory guidelines may lengthen the regulatory review process for our product candidates, require additional studies or trials, increase development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of such product candidates, or lead to significant post-approval limitations or restrictions. Additionally, adverse developments in clinical trials conducted by others of gene therapy products or products created using genome editing technology, or adverse public perception of the field of genome editing, may cause the FDA, the EMA and other regulatory bodies to revise the requirements for approval of any product candidates we may develop or limit the use of products utilizing genome editing technologies, either of which could materially harm our business. Furthermore, regulatory action or private litigation could result in expenses, delays or other impediments to our research programs or the development or commercialization of current or future product candidates.

As we advance product candidates, we will be required to consult with these regulatory and advisory groups and comply with all applicable guidelines, rules and regulations. If we fail to do so, we may be required to delay or terminate development of such product candidates. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a product candidate to market could decrease our ability to generate sufficient product revenue to maintain our business.

Clinical trials are expensive, time-consuming, difficult to design and implement, and involve an uncertain outcome.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. A number of companies in the biotechnology and genetic medicine industries have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Even if our future clinical trials are completed as planned, we cannot be certain that their results will support the safety and effectiveness of HMI-102 for PKU or any other potential indication. Our future clinical trial results may not be successful.

To date, we have not completed any clinical trials required for the approval of HMI-102 or any of our product candidates. Although we have initiated our Phase 1/2 pheNIX trial for HMI-102, we may experience delays in conducting any clinical trials and we do not know whether planned clinical trials will begin on time, need to be redesigned, recruit and enroll patients on time or be completed on schedule, or at all. Clinical trials can be delayed or terminated for a variety of reasons, including delays or failures related to:

- the FDA or comparable foreign regulatory authorities disagreeing as to the design or implementation of our clinical studies;
- obtaining regulatory approval to commence a trial;
- reaching an agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining institutional review board, or IRB, approval at each site;
- recruiting suitable patients to participate in a trial;
- developing and validating the companion diagnostic to be used in a clinical trial, if applicable;
- having patients complete a trial or return for post-treatment follow-up;
- clinical sites deviating from trial protocol or dropping out of a trial;
- addressing patient safety concerns that arise during the course of a trial;
- adding a sufficient number of clinical trial sites; or
- manufacturing sufficient quantities of product candidate for use in clinical trials.

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 or significantly increase the cost of such trials, including:

- we may receive feedback from regulatory authorities that requires us to modify the design of our clinical trials;
- clinical trials of our product candidates may produce negative safety and/or efficacy data or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon 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;
- we or our investigators might have to suspend or terminate clinical trials of our product candidates for various reasons, including non-compliance with regulatory requirements, a finding that our product candidates have undesirable side effects or other unexpected characteristics, or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate and we may not have funds to cover the costs;
- 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;
- regulators may revise the requirements for approving our product candidates, or such requirements may not be as we anticipate; and
- any future collaborators that conduct clinical trials may face any of the above issues, and may conduct clinical trials in ways they view as advantageous to them but that are suboptimal for us.

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:

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

In addition, disruptions caused by the COVID-19 pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials. 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 being conducted, by the Data Safety Monitoring Board, or DSMB, for such trial or by the FDA or other regulatory authorities. Such authorities may impose such a suspension or termination 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 or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. Furthermore, we may rely on CROs and clinical trial sites to ensure the proper and timely conduct of clinical trials and while we would have agreements governing their committed activities, we would have limited influence over their actual performance, as described in "—Risks Related to Our Dependence on Third Parties."

Our most advanced product candidate, HMI-102, will require extensive clinical testing before we are prepared to submit a BLA for regulatory approval. We cannot predict with any certainty if or when we might complete the development of HMI-102 and submit a BLA for regulatory approval of HMI-102 or whether any such BLA will be approved by the FDA. We may seek feedback from the FDA or other regulatory authorities on our clinical development program, and the FDA or such regulatory authorities may not provide such feedback on a timely basis, or such feedback may not be favorable, which could further delay our development programs.

If we experience delays in the commencement or completion of our clinical trials, or if we terminate a clinical trial prior to completion, the commercial prospects of HMI-102 could be harmed, and our ability to generate revenues from HMI-102 may be delayed. In addition, any delays in our clinical trials could increase our costs, slow down the development and approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may harm our business, financial condition and results of operations. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

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

Some of our potential therapeutic products involve editing the human genome. The clinical and commercial success of our potential products will depend in part on public acceptance of the use of gene editing and gene therapy for the prevention or treatment of human diseases. Public attitudes may be influenced by claims that gene therapy and gene editing 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.

In addition, gene editing technology is subject to public debate and heightened regulatory scrutiny due to ethical concerns relating to the application of gene editing technology to human embryos or the human germline. For example, in April 2015, Chinese scientists reported on their attempts to edit the genome of human embryos to modify the gene for hemoglobin beta. This is the gene in which a mutation occurs in patients with the inherited blood disorder beta thalassemia. Although this research was purposefully conducted in embryos that were not viable, the work prompted calls for a moratorium or other types of restrictions on gene editing of human eggs, sperm, and embryos. The Alliance for Regenerative Medicine in Washington, D.C. has called for a voluntary moratorium on the use of gene editing technologies in research that involved altering human embryos or human germline cells. Similarly, the NIH has announced that it would not fund any use of gene editing technologies in human embryos, noting that there are multiple existing legislative and regulatory prohibitions against such work, including the Dickey-Wicker Amendment, which prohibits the use of appropriated funds for the creation of human embryos for research purposes or for research in which human embryos are destroyed. Laws in the United Kingdom prohibit genetically modified embryos from being implanted into women, but embryos can be altered in research labs under license from the Human Fertilisation and Embryology Authority. Research on embryos is more tightly controlled in many other European countries.

Although we do not use our technologies to edit human embryos or the human germline, such public debate about the use of gene editing technologies in human embryos and heightened regulatory scrutiny could prevent or delay our development of product candidates. 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 products we may develop. Adverse events in our preclinical studies or clinical trials or those of our competitors or of academic researchers utilizing gene therapy or gene editing technologies, even if not ultimately attributable to product candidates we may discover 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, a decrease in demand for any such product candidates and a suspension or withdrawal of approval by regulatory authorities of our product candidates.

A Breakthrough Therapy Designation by the FDA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process and it does not increase the likelihood that our product candidates will receive marketing approval.

We may seek a Breakthrough Therapy Designation for our product candidates if the clinical data support such a designation for one or more product candidates. A breakthrough therapy is defined as a drug or biologic that is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug, or biologic in our case, 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 product candidates 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. Biologics designated as breakthrough therapies by the FDA may also be eligible for priority review.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy Designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under non-expedited FDA review procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

A Fast Track Designation by the FDA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive marketing approval.

On May 1, 2019, we received Fast Track Designation for HMI-102 for the prevention or treatment of neurocognitive defects due to phenylalanine hydroxylase deficiency through normalization of circulating phenylalanine levels, and we intend to seek such designation for some or all of our other product candidates. If a drug or biologic, in our case, is intended for the treatment of a serious or life-threatening condition and the biologic demonstrates the potential to address unmet medical needs for this condition, the biologic sponsor may apply for FDA Fast Track Designation. The FDA has broad discretion whether or not to grant this designation. Even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive Fast Track Designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program. Many biologics that have received Fast Track Designation have failed to obtain approval.

We may also seek accelerated approval for products that have obtained Fast Track Designation. Under the FDA's accelerated approval program, the FDA may approve a biologic for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. For biologics granted accelerated approval, post-marketing confirmatory trials are required to describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. These confirmatory trials must be completed with due diligence and, in some cases, the FDA may require that the trial be designed and/or initiated prior to approval. Moreover, the FDA may withdraw approval of any product candidate or indication approved under the accelerated approval pathway if, for example:

- the trial or trials required to verify the predicted clinical benefit of the product candidate fail to verify such benefit or do not demonstrate sufficient clinical benefit to justify the risks associated with the biologic;
- other evidence demonstrates that the product candidate is not shown to be safe or effective under the conditions of use;
- we fail to conduct any required post-approval trial of the product candidate with due diligence; or
- we disseminate false or misleading promotional materials relating to the product candidate.

We have received orphan drug designation for HMI-102, and we intend to seek orphan drug designation for our product candidates, but any orphan drug designations we receive may not confer marketing exclusivity or other expected benefits.

We have received orphan drug designation for HMI-102 in the United States and Europe for the use of AAVHSC15 expressing *PAH* for the treatment of PAH deficiency. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusivity. Orphan drug exclusivity in the United States provides that the FDA may not approve any other applications, including a full NDA, to market the same drug for the same indication for seven years, except in limited circumstances. The applicable exclusivity period is ten years in Europe. The European exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified.

Even if we, or any future collaborators, obtain orphan drug designation for a product candidate, we, or they, may not be able to obtain or maintain orphan drug exclusivity for that product candidate. We may not be the first to obtain marketing approval of any product candidate for which we have obtained orphan drug designation for the orphan-designated indication due to the uncertainties associated with developing pharmaceutical products. In addition, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan-designated indication or may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Further, even if we, or any future collaborators, obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties may be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug with the same active moiety for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care or the manufacturer of the product with orphan exclusivity is unable to maintain sufficient product quantity. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process, nor does it prevent competitors from obtaining approval of the same product candidate as ours for indications other than those in which we have been granted orphan drug designation.

We may seek a rare pediatric disease designation for our product candidates, however, there is no guarantee that we will obtain such designation, and even if we do, there is no guarantee that FDA approval will result in a priority review voucher.

In 2012, Congress authorized the FDA to award priority review vouchers to sponsors of certain rare pediatric disease product applications. This program is designed to encourage development of new drug and biological products for prevention and treatment of certain rare pediatric diseases. Specifically, under this program, a sponsor who receives an approval for a drug or biologic for a “rare pediatric disease” that meets certain criteria may qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product. The sponsor of a rare pediatric disease drug product receiving a priority review voucher may transfer (including by sale) the voucher to another sponsor. The voucher may be further transferred any number of times before the voucher is used, as long as the sponsor making the transfer has not yet submitted the application. The FDA may also revoke any priority review voucher if the rare pediatric disease drug for which the voucher was awarded is not marketed in the U.S. within one year following the date of approval.

We may seek a rare pediatric disease designation for HMI-102 or one of other product candidates; however, we may not be able to obtain such designation. If we are able to obtain rare pediatric disease designation, there is no guarantee that we will be able to obtain a priority review voucher, even if the designated product candidate is approved by the FDA. Moreover, Congress included a sunset provision in the statute authorizing the rare pediatric disease priority review voucher program. Specifically, FDA may not award the voucher to sponsors of marketing applications approved after September 30, 2020 unless either (i) the drug has received rare pediatric disease designation as of September 30, 2020, and is then approved by the FDA no later than September 30, 2022; or (ii) Congress reauthorizes the program, for which legislation has been proposed in the current Congress. If Congress does not reauthorize the rare pediatric disease priority review program in its current form, and if we do not receive rare pediatric disease designation before September 30, 2020, we will not be issued a voucher upon any approval that we receive. Moreover, even if we receive rare pediatric disease designation by the current statutory deadline of September 30, 2020, we may not receive the voucher if we do not obtain approval by September 30, 2022.

A Regenerative Medicine Advanced Therapy designation by the FDA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process and does not increase the likelihood that our product candidates will receive marketing approval.

We may seek a Regenerative Medicine Advanced Therapy, or RMAT, designation for HMI-102 or our other product candidates. In 2017, the FDA established the RMAT designation as part of its implementation of the 21st Century Cures Act. An investigational drug is eligible for RMAT designation if: (1) it meets the definition of a regenerative medicine therapy, which is defined as a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, with limited exceptions; (2) it is intended to treat, modify, reverse, or cure a serious disease or condition; and (3) preliminary clinical evidence indicates that the investigational drug has the potential to address unmet medical needs for such disease or condition. In a February 2019 final guidance, the FDA also stated that certain gene therapies that lead to a sustained effect on cells or tissues may meet the definition of a regenerative medicine therapy. RMAT designation provides potential benefits that include more frequent meetings with FDA to discuss the development plan for the product candidate, and eligibility for rolling review of BLAs and priority review. Product candidates granted RMAT designation may also be eligible for accelerated approval on the basis of a surrogate or intermediate endpoint reasonably likely to predict long-term clinical benefit, or reliance upon data obtained from a meaningful number of sites, including through expansion to additional sites, as appropriate. RMAT-designated product candidates that receive accelerated approval may, as appropriate, fulfill their post-approval requirements through the submission of clinical evidence, clinical studies, patient registries, or other sources of real world evidence (such as electronic health records); through the collection of larger confirmatory data sets; or via post-approval monitoring of all patients treated with such therapy prior to approval of the therapy.

RMAT designation does not change the standards for product approval, and there is no assurance that such designation or eligibility for such designation will result in expedited review or approval or that the approved indication will not be narrower than the indication covered by the RMAT designation. Additionally, RMAT designation can be revoked if the criteria for eligibility cease to be met as clinical data emerges.

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

We currently have relationships with a limited number of suppliers for the manufacturing of our viral vectors and product candidates. We recently completed the build-out of a GMP manufacturing facility to support our clinical development programs in both gene therapy and gene editing and commenced manufacturing activities in April 2019. However, if we experience delays or are unable to scale our internal manufacturing capabilities, we will need to contract with manufacturers that can produce the preclinical, clinical and commercial supply of our products. Each supplier may require licenses to manufacture such components if such processes are not owned by the supplier or in the public domain and we may be unable to transfer or sublicense the intellectual property rights we may have with respect to such activities.

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

The regulatory authorities also may, at any time following approval of a product for sale, audit our manufacturing facilities or those of our third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time-consuming for us or a third party to implement and that may include the temporary or permanent suspension of a clinical study or commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business.

If we or any of our third-party manufacturers fail to maintain regulatory compliance, the FDA can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new drug product or biologic product, or revocation of a pre-existing approval. As a result, our business, financial condition and results of operations may be materially harmed.

Additionally, if supply from one approved manufacturer is interrupted, there could be a significant disruption in commercial supply. An alternative manufacturer would need to be qualified through a BLA supplement which could result in further delay. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

These factors could cause the delay of clinical studies, regulatory submissions, required approvals or commercialization of our product candidates, cause us to incur higher costs and prevent us from commercializing our products successfully. Furthermore, if our suppliers fail to meet contractual requirements, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical studies may be delayed or we could lose potential revenue.

If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the study until its conclusion. We may encounter delays in enrolling, or be unable to enroll, a sufficient number of patients to complete any of our clinical trials, and even once enrolled we may be unable to retain a sufficient number of patients to complete any of our trials. The enrollment of patients depends on many factors, including:

- the patient eligibility criteria defined in the protocol;
- the size of the patient population required for analysis of the trial's primary endpoints;
- the proximity of patients to study sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new products that may be approved for the indications we are investigating;
- our ability to obtain and maintain patient consents; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion.

In addition, our clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials in such clinical trial site.

Delays or failures in planned patient enrollment or retention may result in increased costs, program delays or both, which could have a harmful effect on our ability to develop HMI-102, HMI-103, HMI-202 or any other product candidates, or could render further development impossible.

Our product candidates may cause serious adverse events or undesirable side effects or have other properties which may delay or prevent their regulatory approval, limit the commercial profile of an approved label, or, result in significant negative consequences following marketing approval, if any.

Serious adverse events or undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects, toxicities or unexpected characteristics, including death. A significant risk in any gene editing product is that the edit will be "off-target" (or "on-target," but unwanted) and cause serious adverse events, undesirable side effects, toxicities or unexpected characteristics. For example, off-target cuts could lead to disruption of a gene or a genetic regulatory sequence at an unintended site in the DNA, or, in those instances where we also provide a segment of DNA to serve as a repair template, it is possible that following off-target cut events, DNA from such repair template could be integrated into the genome at an unintended site, potentially disrupting another important gene or genomic element. We cannot be certain that off-target editing will not occur in any of our planned or future clinical studies. There is also the potential risk of delayed adverse events following exposure to gene editing therapy, due to the potential for persistent biological activity of the genetic material or other product components used to carry the genetic material.

If unacceptable side effects arise in the development of our product candidates, we, the FDA, the IRBs at the institutions in which our studies are conducted or DSMB, could suspend or terminate our clinical trials or the FDA or comparable foreign regulatory authorities could order us to cease clinical trials or deny approval of our product candidates for any or all targeted indications. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. We expect to have to train medical personnel using our product candidates to understand the side effect profiles for our clinical trials and upon any commercialization of any of our product candidates. Inadequate training in recognizing or managing the potential side effects of our product candidates could result in patient injury or death. Any of these occurrences may harm our business, financial condition and prospects significantly.

If any of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by any such product, including during any long-term follow-up observation period recommended or required for patients who receive treatment using our products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such product;
- we may be required to recall a product or change the way such product is administered to patients;
- additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product;
- regulatory authorities may require additional warnings on the label, such as a "black box" warning or contraindication;
- we may be required to implement a Risk Evaluation and Mitigation Strategy, or REMS, or create a medication guide outlining the risks of such side effects for distribution to patients;
- the product could become less competitive;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

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

The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.

The time required to obtain approval by the FDA and comparable foreign authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate and it is possible that neither HMI-102, HMI-103, HMI-202, nor any other product candidates we may seek to develop in the future will ever obtain regulatory approval. Neither we nor any future collaborator is

permitted to market any of our product candidates in the United States until we receive regulatory approval of a BLA from the FDA. It is possible that the FDA may refuse to accept for substantive review any biologic license applications, or BLAs, that we submit for our product candidates or may conclude after review of our data that our application is insufficient to obtain marketing approval of our product candidates.

Prior to obtaining approval to commercialize a product candidate in the United States or abroad, we or our collaborators must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA or foreign regulatory agencies, that such product candidates are safe and effective, or in the case of biologics, safe, pure, and potent, for their intended uses. Results from nonclinical studies and clinical trials can be interpreted in different ways. Even if we believe the nonclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. The FDA may also require us to conduct additional preclinical studies or clinical trials for our product candidates either prior to or post-approval, or it may object to elements of our clinical development program. Depending on the extent of these or any other FDA-required studies, approval of any BLA or application that we submit may be delayed by several years, or may require us to expend significantly more resources than we have available.

Of the large number of potential products in development, only a small percentage successfully complete the FDA or foreign regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, results of operations and prospects.

In addition, 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 not approve the price we intend to charge for our products, may grant approval contingent on the performance of costly post-marketing clinical trials, including Phase 4 clinical trials, and/or the implementation of a REMS, which may be required to ensure safe use of the drug after approval. The FDA or the applicable foreign regulatory agency also may approve a product candidate for a more limited indication or patient population than we originally requested, 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. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, which could negatively impact our business.

The ability of the FDA to review and or approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow the time necessary for new drugs and biologics to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including for 35 days beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

Separately, in response to the global pandemic of COVID-19, on March 10, 2020 the FDA announced its intention to postpone most foreign inspections of manufacturing facilities and products through April 2020, and subsequently, on March 18, 2020, the FDA announced its intention to temporarily postpone routine surveillance inspections of domestic manufacturing facilities. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Even if we obtain FDA approval for HMI-102, HMI-103, HMI-202 or any other product candidates in the United States, we may never obtain approval for or commercialize it in any other jurisdiction, which would limit our ability to realize its full market potential.

In order to market any products in any particular jurisdiction, we must establish and comply with numerous and varying regulatory requirements on a country-by-country basis regarding safety and efficacy. Approval by the FDA in the United States does not ensure approval by regulatory authorities in other countries or jurisdictions. However, the failure to obtain approval in one jurisdiction may negatively impact our ability to obtain approval elsewhere. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country.

Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approval could result in difficulties and increased costs for us and require additional preclinical studies or clinical trials which could be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. We do not have any product candidates approved for sale in any jurisdiction, including in international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of any product we develop will be unrealized.

Even if we receive regulatory approval of our product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our product candidates.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, packaging, distribution, adverse event reporting, storage, recordkeeping, export, import, advertising and promotional activities for such product, among other things, will be subject to extensive and ongoing requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, establishment registration and drug listing requirements, continued compliance with GMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping and GCP requirements for any clinical trials that we conduct post-approval.

The FDA closely regulates the post-approval marketing and promotion of genetic medicines to ensure they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we market our products for uses beyond their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the U.S. federal Food, Drug, and Cosmetic Act, or FDCA, relating to the promotion of prescription drugs may lead to FDA enforcement actions and investigations alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on manufacturing such products;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or holds on clinical trials;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;

- refusal to permit the import or export of our products;
- product seizure or detention; or
- injunctions or the imposition of civil or criminal penalties.

The FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of HMI-102, HMI-103, HMI-202 or any other product candidate. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained which would adversely affect our business, prospects and ability to achieve or sustain profitability.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the Trump administration may impact our business and industry. Namely, the Trump administration has taken several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. It is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

Potential product liability lawsuits against us could cause us to incur substantial liabilities and limit commercialization of any products that we may develop.

The use of our product candidates, including HMI-102, HMI-103, HMI-202 or any other product candidate, in clinical trials and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, health care providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. On occasion, large judgments have been awarded in class action lawsuits based on products that had unanticipated adverse effects. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- impairment of our business reputation and significant negative media attention;
- withdrawal of participants from our clinical trials;
- significant costs to defend the related litigation and related litigation;
- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- inability to commercialize HMI-102, HMI-103, HMI-202 or any other product candidate;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- decreased demand for HMI-102, HMI-103, HMI-202 or any other product candidate, if approved for commercial sale; and
- loss of revenue.

Our insurance policies are expensive and protect us only from some business risks, which leaves us exposed to significant uninsured liabilities.

We do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include general liability, employment practices liability, property, auto, workers' compensation, umbrella, and directors' and officers' insurance.

Any additional product liability insurance coverage we acquire in the future, may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and in the future we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If we obtain marketing approval for HMI-102, HMI-103, HMI-202 or any other product candidate, we intend to acquire insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. A successful product liability claim or series of claims brought against us could cause our share price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business, including preventing or limiting the commercialization of any product candidates we develop. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended.

We also expect that operating as a public company will continue to make it more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. As a result, it may be more difficult for us to attract and retain qualified people to serve on our board of directors, our board committees or as executive officers. We do not know if we will be able to maintain existing insurance with adequate levels of coverage. Any significant uninsured liability may require us to pay substantial amounts, which would adversely affect our cash position and results of operations.

Our employees and independent contractors, including principal investigators, CROs, consultants, vendors, and any third parties we may engage in connection with development and commercialization may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.

Misconduct by our employees and independent contractors, including principal investigators, CROs, consultants, vendors, and any third parties we may engage in connection with development and commercialization, could include intentional, reckless or negligent conduct or unauthorized activities that violate: (i) the laws and regulations of the FDA, EMA rules and regulations and other similar regulatory requirements, including those laws that require the reporting of true, complete and accurate information to such authorities; (ii) manufacturing standards; (iii) data privacy, security, fraud and abuse and other healthcare laws and regulations; or (iv) laws that require the reporting of true, complete and accurate financial information and data. Specifically, 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 may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws could also involve the improper use or misrepresentation of information obtained in the course of clinical trials, creation of fraudulent data in preclinical studies or clinical trials or illegal misappropriation of drug product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, 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 governmental investigations or other actions or lawsuits stemming from a failure to comply with such laws or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. 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 and results of operations, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgements, possible exclusion from participation in Medicare, Medicaid, other U.S. federal healthcare programs or healthcare programs in other jurisdictions, individual imprisonment, other sanctions, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations.

Our business and operations would suffer in the event of system failures.

Our computer systems, as well as those of our CROs and other contractors and consultants, are vulnerable to damage from computer viruses, unauthorized access, natural disasters (including hurricanes), terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our product candidate development programs. For example, the loss of preclinical or clinical trial data from completed, ongoing or planned 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 personal, confidential or proprietary information, we could incur liability and the further development of HMI-102, HMI-103, HMI-202 or any other product candidate could be delayed.

In the ordinary course of our business, we collect and store sensitive data, including intellectual property, clinical trial data, proprietary business information, personal data and personally identifiable information of our clinical trial subjects and employees, in our data centers and on our networks. The secure processing, maintenance and transmission of this information is critical to our operations. Despite our security measures, our information technology and infrastructure may be vulnerable to attacks by hackers or internal bad actors, or breached due to employee error, a technical vulnerability, malfeasance or other disruptions. Although, to our knowledge, we have not experienced any such material security breach to date, any such breach could compromise our networks and the information stored there could be accessed, publicly disclosed, lost or stolen. Any such access, disclosure or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, significant regulatory penalties, and such an event could disrupt our operations, damage our reputation, and cause a loss of confidence in us and our ability to conduct clinical trials, which could adversely affect our reputation and delay our clinical development of our product candidates.

Initial, "top-line" and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose initial, top-line or preliminary data from our clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. 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 and carefully evaluate all data. As a result, the initial, top-line or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Initial, top-line or preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the initial, top-line or preliminary data we previously published. As a result, initial, top-line and preliminary data should be viewed with caution until the final data are available.

From time to time, we may also disclose data from our preclinical studies and clinical trials. Initial or preliminary data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between initial or preliminary data and final data could significantly harm our business prospects. Further, disclosure of initial or preliminary data by us or by our competitors could result in volatility in the price of our common stock.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure.

If the top-line or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

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 focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to timely 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.

Risks Related to Healthcare Laws and Other Legal Compliance Matters

Enacted and future healthcare legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and may affect the prices we may set.

In the United States, the EU and other jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA, was enacted, which substantially changed the way healthcare is financed by both governmental and private insurers. Among the provisions of the ACA, those of greatest importance to the pharmaceutical and biotechnology industries include the following:

- an annual, non-deductible fee payable by any entity that manufactures or imports certain branded prescription drugs and biologic agents (other than those designated as orphan drugs), which is apportioned among these entities according to their market share in certain government healthcare programs;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and generic drugs, respectively;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- extension of a manufacturer's Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- establishment of a Center for Medicare Innovation at the Centers for Medicare & Medicaid Services, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. For example, on December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, or Texas District Court Judge, ruled that the entire ACA is invalid based primarily on the fact that the Tax Cuts and Jobs Act of 2017 repealed the tax-based shared responsibility payment imposed by the ACA, on certain individuals who fail to maintain qualifying health coverage for all or part of a year, which is commonly referred to as the "individual mandate". On December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the district court's decision that the individual mandate was unconstitutional but remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. It is unclear how these decisions, subsequent appeals, if any, and other efforts to challenge, repeal or replace the ACA or our business or financial condition.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, the Budget Control Act of 2011 resulted in aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2029 unless additional action is taken by Congress. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws or any other similar laws introduced in the future may result in additional reductions in Medicare and other health care funding, which could negatively affect our customers and accordingly, our financial operations.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as bundled payment models. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Individual states in the United States have also become increasingly active 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. Legally-mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates or put pressure on our product pricing.

In the EU, similar political, economic and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to commercialize our product candidates, if approved.

In markets outside of the United States and EU, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States, the EU or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

Our business operations and current and future relationships with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties.

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers, may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our product candidates, if approved. Such laws include:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under U.S. federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the U.S. federal false claims and civil monetary penalties laws, including the civil False Claims Act, which, among other things, impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the U.S. federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. In addition, the government may assert that a claim including

items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;

- the U.S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services; similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 and its implementing regulations, which also imposes certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without appropriate authorization by covered entities subject to the rule, such as health plans, healthcare clearinghouses and healthcare providers as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information;
- the FDCA, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices;
- the U.S. Public Health Service Act, which prohibits, among other things, the introduction into interstate commerce of a biological product unless a biologics license is in effect for that product;
- the U.S. federal legislation commonly referred to as the Physician Payments Sunshine Act, enacted as part of the ACA, and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program to report annually to the government information related to certain payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain health care professionals beginning in 2022, and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members;
- analogous U.S. state laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. For example, California recently enacted legislation, the California Consumer Privacy Act, or CCPA, which went into effect January 1, 2020. The CCPA, among other things, creates new data privacy obligations for covered companies and provides new privacy rights to California residents, including the right to opt out of certain disclosures of their information. The CCPA also creates a private right of action with statutory damages for certain data breaches, thereby potentially increasing risks associated with a data breach. Although the law includes limited exceptions, including for "protected health information" maintained by a covered entity or business associate, it may regulate or impact our processing of personal information depending on the context; and
- similar healthcare laws and regulations in the EU and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers and laws governing the privacy and security of certain protected information, such as the General Data Protection Regulation ("GDPR"), which imposes obligations and restrictions on the collection and use of personal data relating to individuals located in the European Union (including health data). In addition, the United Kingdom leaving the EU could also lead to further legislative and regulatory changes. It remains unclear how the United Kingdom data protection laws or regulations will develop in the medium to longer term and how data transfer to the United Kingdom from the EU will be regulated, especially following the United Kingdom's departure from the EU on January 31, 2020 without a deal. However, the United Kingdom has transposed the GDPR into domestic law with the Data Protection Act 2018, which remains in force following the United Kingdom's departure from the EU.

Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance 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 the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment, which could affect our ability to operate our business. Further, defending against any such actions can be costly, time-consuming and may require significant 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.

We are subject to environmental, health and safety laws and regulations, and we may become exposed to liability and substantial expenses in connection with environmental compliance or remediation activities.

Our operations, including our development, testing and manufacturing activities, are subject to numerous environmental, health and safety laws and regulations. These laws and regulations govern, among other things, the controlled use, handling, release and disposal of and the maintenance of a registry for, hazardous materials and biological materials, such as chemical solvents, human cells, carcinogenic compounds, mutagenic compounds and compounds that have a toxic effect on reproduction, laboratory procedures and exposure to blood-borne pathogens. If we fail to comply with such laws and regulations, we could be subject to fines or other sanctions.

As with other companies engaged in activities similar to ours, we face a risk of environmental liability inherent in our current and historical activities, including liability relating to releases of or exposure to hazardous or biological materials. Environmental, health and safety laws and regulations are becoming more stringent. We may be required to incur substantial expenses in connection with future environmental compliance or remediation activities, in which case, the production efforts of our third-party manufacturers or our development efforts may be interrupted or delayed.

Risks Related to Commercialization

We face significant competition in an environment of rapid technological change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer or more advanced or effective than ours, which may harm our financial condition and our ability to successfully market or commercialize any product candidates we may develop.

The development and commercialization of new genetic medicine products is highly competitive. Moreover, the gene editing field is characterized by rapidly changing technologies, significant competition, and a strong emphasis on intellectual property. We 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. 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 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 the disease indications for which we have research programs, including PKU, metachromatic leukodystrophy, hemoglobinopathies and ophthalmological diseases. 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.

Our platform and product focus is the development of genetic medicines using our proprietary AAVHSCs *in vivo* either through the gene therapy or nuclease-free gene editing modality. If our current programs are approved for the indications for which we are currently planning clinical trials, they may compete with other products currently under development, including gene editing and gene therapy products or other types of therapies, such as small molecule, antibody or protein therapies. If our PKU treatments are approved, they may compete with therapies from American Gene Technologies, BioMarin, Censa Pharmaceuticals, Generation Bio, Nestlé Health Science, Sangamo Therapeutics and Synlogic. However, we believe that only gene therapy or gene editing approaches have the potential to restore the normal Phe biochemical pathway with a single administration. If our MLD treatment is approved, it may compete with therapies from Orchard Therapeutics and/or Shire. *In vivo* gene therapy approaches provide potential advantages over *ex vivo* approaches. There are a number of companies developing nuclease-based gene editing technologies using CRISPR/Cas9, TALENs, meganucleases, Mega-TALs and ZFNs, including but not limited to Beam Therapeutics, bluebird bio, Caribou Biosciences, Cellectis, CRISPR Therapeutics, Editas Medicine, Intellia Therapeutics, Precision BioSciences, Prime Therapeutics and Sangamo Therapeutics and non-nuclease-based technology, including LogicBio Therapeutics.

Many of our current or potential competitors, either alone or with their collaboration partners, 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, biotechnology, and gene therapy industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. 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 or that would render any products that we may develop obsolete or non-competitive. 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. Additionally, technologies developed by our competitors may render our potential product candidates uneconomic or obsolete, and we may not be successful in marketing any product candidates we may develop against competitors.

In addition, as a result of the expiration or successful challenge of our patent rights, we could face more litigation with respect to the validity and/or scope of patents relating to our competitors' products. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize.

The successful commercialization of our product candidates will depend in part on the extent to which governmental authorities and health insurers establish adequate coverage, reimbursement levels and pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.

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 prescription medications such as our product candidates, assuming FDA approval. Our ability to achieve acceptable levels of coverage and reimbursement for products 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 our product candidates by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Moreover, for drugs and biologics administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such products. We cannot be sure that coverage and reimbursement in the United States, the EU or elsewhere will be available for our product candidates or any product that we may develop, and any reimbursement that may become available may be decreased or eliminated in the future.

Third-party payors increasingly are challenging prices charged for pharmaceutical products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs or biologics when an equivalent generic drug, biosimilar or a less expensive therapy is available. It is possible that a third-party payor may consider our product candidates as substitutable and only offer to reimburse patients for the less expensive product. Even if we show improved efficacy or improved convenience of administration with our product candidates, pricing of existing third-party therapeutics may limit the amount we will be able to charge for our product candidates. These payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in our product candidates. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates, and may not be able to obtain a satisfactory financial return on our product candidates.

There is significant uncertainty related to the insurance coverage and reimbursement of newly-approved products. In the United States, third-party payors, including private and governmental payors, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered. The Medicare and Medicaid programs increasingly are used as models in the United States for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs and biologics. Some third-party payors may require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers who use such therapies. We cannot predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

No uniform policy for coverage and reimbursement for products exists among third-party payors in the United States. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases on short notice, and we believe that changes in these rules and regulations are likely.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe and other countries have and will continue to put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our product candidates may be reduced compared with the United States and may be insufficient to generate commercially-reasonable revenue and profits.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of our product candidates due to the trend toward managed health care, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and biologics and surgical procedures and other treatments, has become intense. As a result, increasingly high barriers are being erected to the entry of new products.

Even if HMI-102, HMI-103, HMI-202 or any other product candidate receives marketing approval, it may fail to achieve market acceptance by physicians, patients, third-party payors or others in the medical community necessary for commercial success.

If HMI-102, HMI-103, HMI-202 or any other product candidate receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. If it does not achieve an adequate level of acceptance, we may not generate significant product revenues or become profitable. The degree of market acceptance of HMI-102, HMI-103, HMI-202 or any other product candidate, if approved for commercial sale, will depend on a number of factors, including but not limited to:

- the safety, efficacy and potential advantages compared to alternative treatments;
- effectiveness of sales and marketing efforts;
- the cost of treatment in relation to alternative treatments, including any similar generic treatments;
- our ability to offer our products for sale at competitive prices;
- 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;
- product labeling or product insert requirements of the FDA, EMA or other regulatory authorities, including any limitations or warnings contained in a product’s approved labeling;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our product together with other medications.

Because we expect sales of HMI-102, HMI-103, HMI-202 or any other product candidate, if approved, to generate substantially all of our product revenues for a substantial period, the failure of this product to find market acceptance would harm our business and could require us to seek additional financing.

If we are unable to establish sales, marketing and distribution capabilities either on our own or in collaboration with third parties, we may not be successful in commercializing HMI-102, HMI-103, HMI-202 or any other product candidate, if approved.

We do not have any infrastructure for the sales, marketing or distribution of our products, and the cost of establishing and maintaining such an organization may exceed the cost-effectiveness of doing so.

We expect to build a focused sales, distribution and marketing infrastructure to market HMI-102, HMI-103, HMI-202 or any other product candidate in the United States and European Union, if approved. There are significant expenses and risks involved with establishing our own sales, marketing and distribution capabilities, including our ability to hire, retain and appropriately incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel, and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution capabilities could delay any product launch, which would adversely impact the commercialization of HMI-102, HMI-103, HMI-202 or any other product candidate. Additionally, if the commercial launch of HMI-102, HMI-103, HMI-202 or any other 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. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

We do not anticipate having the resources in the foreseeable future to allocate to the sales and marketing of HMI-102, HMI-103, HMI-202 or any other product candidates in certain markets overseas. Therefore, our future sales in these markets will largely depend on our ability to enter into and maintain collaborative relationships for such capabilities, the collaborator's strategic interest in the product and such collaborator's ability to successfully market and sell the product. We intend to pursue collaborative arrangements regarding the sale and marketing of HMI-102, HMI-103, HMI-202 or any other product candidate, if approved, for certain markets overseas; however, we cannot assure that we will be able to establish or maintain such collaborative arrangements, or if able to do so, that they will have effective sales forces.

If we are unable to build our own sales force or negotiate a collaborative relationship for the commercialization of HMI-102, HMI-103, HMI-202 or any other product candidate, we may be forced to delay the potential commercialization of HMI-102, HMI-103, HMI-202 or any other product candidate or reduce the scope of our sales or marketing activities for HMI-102, HMI-103, HMI-202 or any other product candidate. If we elect to increase our expenditures to fund commercialization activities ourselves, we will need to obtain additional capital, which may not be available to us on acceptable terms, or at all. We could enter into arrangements with collaborative partners at an earlier stage than otherwise would be ideal and we may be required to relinquish rights to HMI-102, HMI-103, HMI-202 or any other product candidate or otherwise agree to terms unfavorable to us, any of which may have an adverse effect on our business, operating results and prospects.

If we are unable to establish adequate sales, marketing and distribution capabilities, either on our own or in collaboration with third parties, we will not be successful in commercializing HMI-102, HMI-103, HMI-202 or any other product candidate, and may not become profitable and may incur significant additional losses. We will be competing with many companies that currently have extensive and well-funded marketing and sales operations. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

If we obtain approval to commercialize any products outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

If HMI-102, HMI-103, HMI-202 or any other product candidate is approved for commercialization, we intend to enter into agreements with third parties to market it in certain jurisdictions outside the United States. We expect that we will be subject to additional risks related to international pharmaceutical operations, including:

- different regulatory requirements for drug and biologic approvals and rules governing drug and biologic commercialization and country-specific regulations of gene therapies in foreign countries;
- complex and restrictive import/export regulations;
- reduced protection for intellectual property rights;
- foreign reimbursement, pricing and insurance regimes;
- potential noncompliance with the U.S. Foreign Corrupt Practices Act, the U.K. Bribery Act 2010 and similar anti-bribery and anticorruption laws in other jurisdictions; and
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad.

We have no prior experience in these areas. In addition, there are complex regulatory, tax, labor and other legal requirements imposed by both the European Union and many of the individual countries in Europe with which we will need to comply. Many U.S.-based biotechnology companies have found the process of marketing their own products in Europe to be very challenging.

Any product candidates for which we intend to seek approval as biologic products may face competition sooner than anticipated.

The Patient Protection and Affordable Care Act, signed into law on March 23, 2010, 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-licensed 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 licensed 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 licensed. 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 their 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. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our biological products.

There is a risk that any of our product candidates approved as a biological product under a BLA would not qualify for the 12-year period of exclusivity or 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 generic 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.

Risks Related to Our Dependence on Third Parties

We currently contract with third parties for the manufacture of certain materials for our research programs, preclinical and clinical studies. This reliance on third parties increases the risk that we will not have sufficient quantities of such materials, product candidates, or any medicines that we may develop and commercialize, or that such supply will not be available to us at an acceptable cost or in compliance with regulatory requirements, which could delay, prevent, or impair our development or commercialization efforts.

We currently rely on third-party manufacturers for the manufacture of certain materials for research programs, preclinical and clinical studies. We do not have long-term supply agreements with all of the third-party manufacturers, and we purchase our required supply on a purchase order basis. We recently completed the build-out of a GMP manufacturing facility to support our clinical development programs in both gene therapy and gene editing and commenced manufacturing activities in 2019. However, if we experience delays or are unable to scale our internal manufacturing capabilities, we will need to contract with manufacturers that can produce the clinical and commercial supply of our product candidates.

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:

- the possible breach of the manufacturing agreement by the third party;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us; and
- reliance on the third party for regulatory compliance, quality assurance, safety, and pharmacovigilance and related reporting.

Third-party manufacturers may not be able to comply with GMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocations, seizures or recalls of product candidates or medicines, operating restrictions, and criminal prosecutions, any of which could significantly and adversely affect supplies of our medicines and harm our business, financial condition, results of operations, and prospects. Moreover, as a result of the COVID-19 pandemic, third-party manufacturers may be affected, which could disrupt their activities and as a result we could face difficulty sourcing key components necessary to produce supply of our product candidates, which may negatively affect our preclinical and clinical development activities.

Any medicines that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under GMP 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.

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

We intend to continue to rely on third parties to conduct, supervise and monitor our clinical trials. If those third parties do not successfully carry out their contractual duties, or if they perform in an unsatisfactory manner, it may harm our business.

We intend to continue to rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials, and we expect to have limited influence over their actual performance.

We intend to continue to rely upon CROs to monitor and manage data for our clinical programs, as well as the execution of future nonclinical studies. Our reliance on CROs for clinical development activities limits our control over these activities, but we will remain responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on the CROs does not relieve us of our regulatory responsibilities.

We and our CROs will be required to comply with GLP and GCP, which are regulations and guidelines enforced by the FDA and are also required by the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities in the form of International Conference on Harmonization guidelines for any of our product candidates that are in preclinical and clinical development. The Regulatory authorities enforce GCP through periodic inspections of trial sponsors, principal investigators and clinical trial sites. If we or our CROs fail to comply with GCP, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP requirements. In addition, our clinical trials must be conducted with product produced under GMP regulations. Accordingly, if our CROs fail to comply with these regulations or fail to recruit a sufficient number of subjects, we may be required to repeat clinical trials, which would delay the regulatory approval process.

Our CROs will not be our employees, and we will not control whether or not they devote sufficient time and resources to our future clinical and nonclinical programs. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials, or other product development activities which could harm our competitive position. We face the risk of potential unauthorized disclosure or misappropriation of our intellectual property by CROs, which may reduce our trade secret protection and allow our potential competitors to access and exploit our proprietary technology. If our CROs do not successfully carry out their contractual duties or obligations or fail to meet expected deadlines, including as a result of the impact of the COVID-19 pandemic, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for any other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize any product candidate that we develop. As a result, our financial results and the commercial prospects for any product candidate that we develop would be harmed, our costs could increase, and our ability to generate revenues could be delayed.

If our relationship with any CROs terminate, we may not be able to enter into arrangements with alternative CROs or do so on commercially reasonable terms. Switching or adding additional CROs involves substantial cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we intend to carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have an adverse impact on our business, financial condition and prospects.

We may collaborate with third parties for the development and commercialization of HMI-102, HMI-103, HMI-202 or any other product candidate. We may not succeed in establishing and maintaining collaborative relationships, which may significantly limit our ability to develop and commercialize HMI-102, HMI-103, HMI-202 or any other product candidate successfully, if at all.

We may seek collaborative relationships for the development and commercialization of HMI-102, HMI-103, HMI-202 or any other product candidate. Failure to obtain a collaborative relationship for HMI-102, HMI-103, HMI-202 or any other product candidate may significantly impair the potential for the product candidate. We also will need to enter into collaborative relationships to provide funding to support our other research and development programs. The process of establishing and maintaining collaborative relationships is difficult, time-consuming and involves significant uncertainty, such as:

- a collaboration partner may shift its priorities and resources away from our product candidates due to a change in business strategies, or a merger, acquisition, sale or downsizing;
- a collaboration partner may seek to renegotiate or terminate their relationships with us due to unsatisfactory clinical results, manufacturing issues, a change in business strategy, a change of control or other reasons;
- a collaboration partner may cease development in therapeutic areas which are the subject of our strategic collaboration;
- a collaboration partner may not devote sufficient capital or resources towards our product candidates;
- a collaboration partner may change the success criteria for a product candidate thereby delaying or ceasing development of such candidate;
- a significant delay in initiation of certain development activities by a collaboration partner will also delay payment of milestones tied to such activities, thereby impacting our ability to fund our own activities;
- a collaboration partner could develop a product that competes, either directly or indirectly, with our product candidate;
- a collaboration partner with commercialization obligations may not commit sufficient financial or human resources to the marketing, distribution or sale of a product;
- a collaboration partner with manufacturing responsibilities may encounter regulatory, resource or quality issues and be unable to meet demand requirements;
- a collaboration partner may terminate a strategic alliance;
- a dispute may arise between us and a partner concerning the research, development or commercialization of a product candidate resulting in a delay in milestones, royalty payments or termination of an alliance and possibly resulting in costly litigation or arbitration which may divert management attention and resources; and
- a partner may use our products or technology in such a way as to invite litigation from a third party.

If any collaborator fails to fulfill its responsibilities in a timely manner, or at all, our research, clinical development, manufacturing or commercialization efforts related to that collaboration could be delayed or terminated, or it may be necessary for us to assume responsibility for expenses or activities that would otherwise have been the responsibility of our collaborator. If we are unable to establish and maintain collaborative relationships on acceptable terms or to successfully transition terminated collaborative agreements, we may have to delay or discontinue further development of one or more of our product candidates, undertake development and commercialization activities at our own expense or find alternative sources of capital. Moreover, any collaborative partners we enter into agreements with in the future may shift their priorities and resources away from our product candidates or seek to renegotiate or terminate their relationships with us. For example, Novartis can terminate our collaboration agreement for convenience on a target-by-target basis and, in February 2019, Novartis elected to discontinue the sickle cell disease program under our collaboration agreement effective in August 2019.

We do not have multiple sources of supply for all of the components used in HMI-102 and our other product candidates. If we were to lose a supplier, it could have a material adverse effect on our ability to complete the development of HMI-102. If we obtain regulatory approval for HMI-102, we would need to expand the supply of its components in order to commercialize them.

We do not have multiple sources of supply for all of the components used in the manufacturing of HMI-102. We also do not have long-term supply agreements with any of our component suppliers. We are currently evaluating manufacturers that will commercially manufacture HMI-102. It is our expectation that we will only qualify one initial supplier that will need to be approved by the FDA. If for any reason we are unable to obtain product from the manufacturer we select, we would have to qualify new manufacturers. We may not be able to establish additional sources of supply for our product candidates, or may be unable to do so on acceptable terms. Manufacturing suppliers are subject to GMP quality and regulatory requirements, covering manufacturing, testing, quality control and record keeping relating to our product candidates and subject to ongoing inspections by the regulatory agencies. Failure by any of our suppliers to comply with applicable regulations may result in long delays and interruptions in supply. Manufacturing suppliers are also subject to local, state and federal regulations and licensing requirements. Failure by any of our suppliers to comply with all applicable regulations and requirements may result in long delays and interruptions in supply.

The number of suppliers of the raw material components of our product candidates is limited. In the event it is necessary or desirable to acquire supplies from alternative suppliers, we might not be able to obtain them on commercially reasonable terms, if at all. It could also require significant time and expense to redesign our manufacturing processes to work with another company.

As part of any marketing approval, a manufacturer of HMI-102 is required to be licensed by the FDA prior to commercialization. This licensing process normally includes inspections by regulatory authorities that must be successful prior to them being licensed. Failure of manufacturing suppliers to successfully complete these regulatory inspections will result in delays. If supply from the approved supplier is interrupted, there could be a significant disruption in commercial supply. An alternative vendor would need to be qualified through a BLA amendment or supplement which could result in further delay. The FDA or other regulatory agencies outside of the United States may also require additional studies if a new supplier is relied upon for commercial production. Switching vendors may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

If we are unable to obtain the supplies we need at a reasonable price or on a timely basis, it could have a material adverse effect on our ability to complete the development of HMI-102 and our other product candidates or, if we obtain regulatory approval for HMI-102 or our other product candidates, to commercialize them.

If we fail to comply with our obligations in the agreements under which we in-license or acquire development or commercialization rights to products, technology or data from third parties, including those for HMI-102, we could lose such rights that are important to our business.

We are a party to agreements with Caltech for certain AAV vector-related patents owned by Caltech for human therapeutic applications, or the Caltech License, and City of Hope for certain AAV vector-related patents and know-how, and we may enter into additional agreements, including license agreements, with other parties in the future that impose diligence, development and commercialization timelines, milestone payments, royalties, insurance and other obligations on us.

For example, in exchange for the rights granted to us under the Caltech License, we are obligated to pay Caltech up to a total of $7.2 million in milestone payments for the first licensed product, royalties, in the low single-digit percentages, on net sales of licensed products subject to a certain annual minimum royalty, and mid single- to high single-digit percentages of sublicensing revenues. If we fail to comply with our obligations under the Caltech License, or any of our other collaborators, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market any product candidate that is covered by these agreements, which 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 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.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent protection for our technology and products or if the scope of the patent protection obtained is not sufficiently broad, we may not be able to compete effectively in our markets.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our proprietary technologies, product candidate development programs and product candidates. Our success depends in large part on our ability to secure and maintain patent protection in the United States and other countries with respect to HMI-102, HMI-103, HMI-202 and any future product candidates. We seek to protect our proprietary position by filing or collaborating with our licensors to file patent applications in the United States and abroad related to our proprietary technologies, development programs and product candidates. The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner.

It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our proprietary products and technology, including HMI-102, HMI-103, HMI-202 or any other product candidate in the United States or in other foreign countries, in whole or in part. Alternately, our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from using our technology or from developing competing products and technologies. There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found, which can prevent a patent from issuing from a pending patent application or later invalidate or narrow the scope of an issued patent. Even if patents do successfully issue and even if such patents cover HMI-102, HMI-103, HMI-202 or any future product candidate, third parties may challenge their validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated, or held unenforceable. Any successful challenge to these patents or any other patents owned by or licensed to us could deprive us of rights necessary for the successful commercialization of any product candidates or companion diagnostic that we may develop. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate and companion diagnostic under patent protection could be reduced.

If the patent applications we hold or have in-licensed with respect to our development programs and product candidates fail to issue, if their validity, breadth or strength of protection is threatened, or if they fail to provide meaningful exclusivity for HMI-102, HMI-103, HMI-202 or any future product candidate, it could dissuade companies from collaborating with us to develop product candidates, encourage competitors to develop competing products or technologies and threaten our ability to commercialize future product candidates. Any such outcome could have a materially adverse effect on our business.

The patent position of biotechnology and pharmaceutical companies is highly uncertain, involves complex legal and factual questions, and is characterized by the existence of large numbers of patents and frequent litigation based on allegations of patent or other intellectual property infringement or violation. In addition, the laws of jurisdictions outside the United States may not protect our rights to the same extent as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. Since patent applications in the United States and other jurisdictions are confidential for a period of time after filing, we cannot be certain that we were the first to file for patents covering our inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in the issuance of patents, or may result in the issuance of patents which fail to protect our technology or products, in whole or in part, or which fail to effectively prevent others from commercializing competitive technologies and products.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of 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 products. Thus, even if our patent applications issue as patents, they may not issue in a form that will provide us with meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Moreover, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. Without patent protection for our current or future product candidates, we may be open to competition from generic versions of such products. 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.

Third parties may assert claims against us alleging infringement of their patents and proprietary rights, or we may need to become involved in lawsuits to defend or enforce our patents, either of which could result in substantial costs or loss of productivity, delay or prevent the development and commercialization of our product candidates, prohibit our use of proprietary technology or sale of products or put our patents and other proprietary rights at risk.

Our commercial success depends, in part, upon our ability to develop, manufacture, market and sell our product candidates without alleged or actual infringement, misappropriation or other violation of the patents and proprietary rights of third parties. Litigation relating to infringement or misappropriation of patent and other intellectual property rights in the pharmaceutical and biotechnology industries is common, including patent infringement lawsuits, interferences, oppositions and reexamination proceedings before the U.S. Patent and Trademark Office, or USPTO, and corresponding foreign patent offices. The various markets in which we plan to operate are subject to frequent and extensive litigation regarding patents and other intellectual property rights. In addition, many companies in intellectual property-dependent industries, including the biotechnology and pharmaceutical industries, have employed intellectual property litigation as a means to gain an advantage over their competitors. Numerous United States, EU and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing product candidates, and as the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the intellectual property rights of third parties. Some claimants may have substantially greater resources than we do and may be able to sustain the costs of complex intellectual property litigation to a greater degree and for longer periods of time than we could. In addition, patent holding companies that focus solely on extracting royalties and settlements by enforcing patent rights may target us.

We may be subject to third-party claims including infringement, interference or derivation proceedings, post-grant review and inter partes review before the USPTO or similar adversarial proceedings or litigation in other jurisdictions. Even if such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, and the holders of any such patents may be able to block our ability to commercialize the applicable product candidate unless we obtained a license under the applicable patents, or until such patents expire or are finally determined to be invalid or unenforceable. Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our compositions, formulations, or methods of treatment, prevention or use, the holders of any such patents may be able to prohibit our use of those compositions, formulations, methods of treatment, prevention or use or other technologies, effectively blocking our ability to develop and commercialize the applicable product candidate until such patent expires or is finally determined to be invalid or unenforceable or unless we obtained a license.

In addition, defending such claims would cause us to incur substantial expenses and, if successful, could cause us to pay substantial damages if we are found to be infringing a third party's patent rights. These damages potentially include increased damages and attorneys' fees if we are found to have infringed such rights willfully. Further, if a patent infringement suit is brought against us or our third-party service providers, our development, manufacturing or sales activities relating to the product or product candidate that is the subject of the suit may be delayed or terminated. As a result of patent infringement claims, or in order to avoid potential infringement claims, we may choose to seek, or be required to seek, a license from the third party, which may require payment of substantial royalties or fees, or require us to grant a cross-license under our intellectual property rights. These licenses may not be available on reasonable terms or at all. Even if a license can be obtained on reasonable terms, the rights may be nonexclusive, which would give our competitors access to the same intellectual property rights. If we are unable to enter into a license on acceptable terms, we could be prevented from commercializing one or more of our product candidates, or forced to modify such product candidates, or to cease some aspect of our business operations, which could harm our business significantly. We might also be forced to redesign or modify our product candidates so that we no longer infringe the third-party intellectual property rights, which may result in significant cost or delay to us, or which redesign or modification could be impossible or technically infeasible. Even if we were ultimately to prevail, any of these events could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business. In addition, if the breadth or strength of protection provided the patents and patent applications we own or in-license is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

If we or one of our licensors were to initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that our patent is invalid or unenforceable. In patent litigation in the United States and in Europe, 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, for example, lack of novelty, obviousness or non-enablement. Third parties might allege unenforceability of our patents because during prosecution of the patent an individual connected with such prosecution withheld relevant information, or made a misleading statement. The outcome of proceedings involving assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity of patents, for example, we cannot be certain that there is no invalidating prior art of which we and the patent examiner were unaware during prosecution, but that an adverse third party may identify and submit in support of such assertions of invalidity. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Our patents and other intellectual property rights also will not protect our technology if competitors design around our protected technology without infringing our patents or other intellectual property rights.

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, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments, and if securities analysts or investors view these announcements in a negative light, the price of our common stock could be adversely affected. Such litigation or proceedings could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have an adverse effect on our ability to compete in the marketplace.

We may not identify relevant third-party patents or may incorrectly interpret the relevance, scope or expiration of a third-party patent which might adversely affect our ability to develop, manufacture and market our product candidates.

We cannot guarantee that any of our or our licensors' patent searches or analyses, including but not limited to the identification of relevant patents, analysis of the scope of relevant patent claims or determination of the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending application in the United States, Europe and elsewhere that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction. For example, in the United States, applications filed before November 29, 2000 and certain applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Patent applications in the United States, EU and elsewhere are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our product candidates could be filed by others without our knowledge. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our product candidates or the use of our product candidates. After issuance, the scope of patent claims remains subject to construction as determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our product candidates. We may incorrectly determine that our product candidates are not covered by a third-party patent or may incorrectly predict whether a third party's pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States, the EU or elsewhere that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our product candidates. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our product candidates.

If we fail to correctly identify or interpret relevant patents, we may be subject to infringement claims. We cannot guarantee that we will be able to successfully settle or otherwise resolve such infringement claims. If we fail in any such dispute, in addition to being forced to pay monetary damages, we may be temporarily or permanently prohibited from commercializing our product candidates. We might, if possible, also be forced to redesign our product candidates in a manner that no longer infringes third-party intellectual property rights. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business.

Changes in patent laws or patent jurisprudence could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

As is the case with other biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology and genetic medicine industries involve both technological complexity and legal complexity. Therefore, obtaining and enforcing biotechnology and genetic medicine patents is costly, time-consuming and inherently uncertain. In addition, the America Invents Act, or the AIA, which was passed in September 2011, resulted in significant changes to the U.S. patent system.

An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned from a "first-to-invent" to a "first-to-file" system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. Under a "first-to-file" system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on the invention regardless of whether another inventor had made the invention earlier. A third party that files a patent application in the USPTO after that date but before us could therefore be awarded a patent covering an invention of ours even if we made the invention before it was made by the third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application and diligent in filing patent applications, but circumstances could prevent us from promptly filing patent applications on our inventions.

Among some of the other changes introduced by the AIA are changes that limit where a patentee may file a patent infringement suit and providing opportunities for third parties to challenge any issued patent in the USPTO. This applies to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. 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. It is not clear what, if any, impact the AIA will have on the operation of our business. However, the AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our or our licensors' patent applications and the enforcement or defense of our or our licensors' issued patents.

We may become involved in opposition, interference, derivation, inter partes review or other proceedings challenging our or our licensors' patent rights, and the outcome of any proceedings are highly uncertain. An adverse determination in any such proceeding could reduce the scope of, or invalidate, our owned or in-licensed patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights.

Additionally, the U.S. Supreme Court has ruled on several patent cases in recent years either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations, and there are other open questions under patent law that courts have yet to decisively address. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways and could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. In addition, the European patent system is relatively stringent in the type of amendments that are allowed during prosecution, but, the complexity and uncertainty of European patent laws has also increased in recent years. Complying with these laws and regulations could limit our ability to obtain new patents in the future that may be important for our business.

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

The USPTO and European and other patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In addition, periodic maintenance and annuity fees on any issued patent are due to be paid to the USPTO and European and other patent agencies over the lifetime of a patent. While an inadvertent failure to make payment of such fees or to comply with such provisions can in many cases be cured by additional payment of a late fee or by other means in accordance with the applicable rules, there are situations in which non-compliance with such provisions will result in the abandonment or lapse of the patent or patent application, and the 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 within prescribed time limits. If we or our licensors fail to maintain the patents and patent applications covering our product candidates or if we or our licensors otherwise allow our patents or patent applications to be abandoned or lapse, it can create opportunities for competitors to enter the market, which would hurt our competitive position and could impair our ability to successfully commercialize our product candidates in any indication for which they are approved.

We enjoy only limited geographical protection with respect to certain patents and we may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents covering our product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In-licensing patents covering our product candidates in all countries throughout the world may similarly be prohibitively expensive, if such opportunities are available at all. And in-licensing or filing, prosecuting and defending patents even in only those jurisdictions in which we develop or commercialize our product candidates may be prohibitively expensive or impractical. Competitors may use our and our licensors' technologies in jurisdictions where we have not obtained patent protection or licensed patents to develop their own products and, further, may export otherwise infringing products to territories where we and our licensors have patent protection, but enforcement is not as strong as that in the United States or the EU. These products may compete with our product candidates, and our or our licensors' patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

In addition, we may decide to abandon national and regional patent applications while they are still pending. The grant proceeding of each national or regional patent is an independent proceeding which may lead to situations in which applications may be rejected by the relevant patent office, while substantively similar applications are granted by others. For example, relative to other countries, China has a heightened requirement for patentability and specifically requires a detailed description of medical uses of a claimed drug. Furthermore, generic drug manufacturers or other competitors may challenge the scope, validity or enforceability of our or our licensors' patents, requiring us or our licensors to engage in complex, lengthy and costly litigation or other proceedings. Generic drug manufacturers may develop, seek approval for and launch generic versions of our products. It is also quite common that depending on the country, the scope of patent protection may vary for the same product candidate or technology.

The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws or regulations in the United States and the EU, and many companies have encountered significant difficulties in protecting and defending proprietary rights in such jurisdictions. Moreover, the legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets or other forms of intellectual property, which could make it difficult for us to prevent competitors in some jurisdictions from marketing competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, are likely to result in substantial costs and divert our efforts and attention from other aspects of our business, and additionally could put at risk our or our licensors' patents of being invalidated or interpreted narrowly, could increase the risk of our or our licensors' patent applications not issuing, or could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, while damages or other remedies may be awarded to the adverse party, which may be commercially significant. If we prevail, damages or other remedies awarded to us, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. Furthermore, while we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our product candidates. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate, which may have an adverse effect on our ability to successfully commercialize our product candidates in all of our expected significant foreign markets. If we or our licensors encounter difficulties in protecting, or are otherwise precluded from effectively protecting, the intellectual property rights important for our business in such jurisdictions, the value of these rights may be diminished and we may face additional competition in those jurisdictions.

In some jurisdictions, compulsory licensing laws compel patent owners to grant licenses to third parties. In addition, some 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 under patents relevant to our business, or if we or our licensors are prevented from enforcing patent rights against third parties, our competitive position may be substantially impaired in such jurisdictions.

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 marketing exclusivity for our product candidates, our business may be materially harmed.

The term of any individual patent depends on applicable law in the country where the patent is granted. In the United States, provided all maintenance fees are timely paid, a patent generally has a term of 20 years from its application filing date or earliest claimed non-provisional filing date. Extensions may be available under certain circumstances, but the life of a patent and, correspondingly, the protection it affords is limited. Even if we or our licensors obtain patents covering our product candidates, when the terms of all patents covering a product expire, our business may become subject to competition from competitive medications, including generic medications. Given the amount of time required for the development, testing and regulatory review and approval of new product candidates, patents protecting such candidates may 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.

In the United States, a patent that covers an FDA- approved drug or biologic may be eligible for a term extension designed to restore the period of the patent term that is lost during the premarket regulatory review process conducted by the FDA. Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act , which permits a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. In the EU, our product candidates may be eligible for term extensions based on similar legislation. In either jurisdiction, however, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Even if we are granted such extension, the duration of such extension may be less than our request. If we are unable to obtain a patent term extension, or if the term of any such extension is less than our request, the period during which we can enforce our patent rights for that product will be in effect shortened and our competitors may obtain approval to market competing products sooner. The resulting reduction of years of revenue from applicable products could be substantial.

Our proprietary rights may not adequately protect our technologies and product candidates, and do not necessarily address all potential threats to our competitive advantage.

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. The following examples are illustrative:

- others may be able to make products that are the same as or similar to our product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed;
- others, including inventors or developers of our owned or in-licensed patented technologies who may become involved with competitors, may independently develop similar technologies that function as alternatives or replacements for any of our technologies without infringing our intellectual property rights;
- we or our licensors or our other collaboration partners might not have been the first to conceive and reduce to practice the inventions covered by the patents or patent applications that we own, license or will own or license;
- we or our licensors or our other collaboration partners might not have been the first to file patent applications covering certain of the patents or patent applications that we or they own or have obtained a license, or will own or will have obtained a license;
- we or our licensors may fail to meet obligations to the U.S. government with respect to in-licensed patents and patent applications funded by U.S. government grants, leading to the loss of patent rights;
- it is possible that our pending patent applications will not result in issued patents;
- it is possible that there are prior public disclosures that could invalidate our or our licensors' patents;
- issued patents that we own or exclusively license may not provide us with any competitive advantage, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights, or in countries where research and development safe harbor laws exist, and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- ownership, validity or enforceability of our or our licensors' patents or patent applications may be challenged by third parties; and
- the patents of third parties or pending or future applications of third parties, if issued, may have an adverse effect on our business.

We depend on proprietary technology licensed from others. If we lose our existing licenses or are unable to acquire or license additional proprietary rights from third parties, we may not be able to continue developing our products.

We currently in-license certain intellectual property from COH and Caltech, and we have entered into a collaboration and license agreement with Novartis. In the future we may in-license intellectual property from other licensors. We rely on certain of these licensors to file and prosecute patent applications and maintain patents and otherwise protect the intellectual property we license from them. We have limited control over these activities or any other intellectual property that may be related to our in-licensed intellectual property. For example, we cannot be certain that such activities by these licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents and other intellectual property rights. We have limited control over the manner in which our licensors initiate an infringement proceeding against a third-party infringer of the intellectual property rights, or defend certain of the intellectual property that is licensed to us. It is possible that the licensors' infringement proceeding or defense activities may be less vigorous than had we conducted them ourselves. The licensing and acquisition of third-party intellectual property rights is a competitive practice, and companies that may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their larger size and cash resources or greater clinical development and commercialization capabilities. There can be no assurance that we will be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to acquire.

If we fail to comply with our obligations under our patent licenses with third parties, we could lose license rights that are important to our business.

We are a party to license agreements with COH and Caltech, pursuant to which we in-license patents and technology for our product candidates. These existing licenses impose various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with these obligations or otherwise materially breach a license agreement, our licensors may have the right to terminate the license, in which event we would not be able to develop or market the products covered by such licensed intellectual property. In addition, any claims asserted against us by our licensors may be costly and time-consuming, divert the attention of key personnel from business operations or otherwise have a material adverse effect on our business.

Our reliance on third parties may require us to share our trade secrets, which increases the possibility that our trade secrets will be misappropriated or disclosed, and confidentiality agreements with employees and third parties may not adequately prevent disclosure of trade secrets and protect other proprietary information.

We consider proprietary trade secrets, confidential know-how and unpatented know-how to be important to our business. We may rely on trade secrets and confidential know-how to protect our technology, especially where patent protection is believed by us to be of limited value. However, trade secrets and confidential know-how are difficult to protect, and we have limited control over the protection of trade secrets and confidential know-how used by our licensors, collaborators and suppliers. Because we expect to rely on third parties to manufacture HMI-102, HMI-103, HMI-202 and any future product candidates, and we expect to collaborate with third parties on the development of HMI-102, HMI-103, HMI-202 and any future product candidates, we may, at times, share trade secrets with them. We also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development partnerships or similar agreements. Under such circumstances, trade secrets and confidential know-how can be difficult to maintain as confidential.

To protect this type of information against disclosure or appropriation by competitors, our policy is to require our employees, consultants, contractors and advisors to enter into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with us prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. However, current or former employees, consultants, contractors and advisers may unintentionally or willfully disclose our confidential information to competitors, and confidentiality agreements may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. The need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our competitive position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have an adverse effect on our business and results of operations. Enforcing a claim that a third party obtained illegally and is using trade secrets and/or confidential know-how is expensive, time consuming and unpredictable, and the enforceability of confidentiality agreements may vary from jurisdiction to jurisdiction.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our trade secrets, although our agreements may contain certain limited publication rights. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third-party collaborators. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

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.

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. We currently own one registered trademark and two pending trademark applications in the United States, as well as 20 registered trademarks and 12 pending trademark applications in other countries around the world. 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 unregistered trademarks or trade names. Over the long term, if we are unable to successfully register our trademarks and trade names and 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.

We may need to license additional intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms.

The growth of our business may depend in part on our ability to acquire or in-license additional proprietary rights. For example, our programs may involve product candidates that may require the use of additional proprietary rights held by third parties. Our product candidates may also require specific formulations to work effectively and efficiently. These formulations may be covered by intellectual property rights held by others. We may develop products containing our compositions and pre-existing pharmaceutical compositions. These pharmaceutical products may be covered by intellectual property rights held by others. We may be required by the FDA or comparable foreign regulatory authorities to provide a companion diagnostic test or tests with our product candidates. These diagnostic test or tests may be covered by intellectual property rights held by others. We may be unable to acquire or in-license any relevant third-party intellectual property rights that we identify as necessary or important to our business operations. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all, which would harm our business. We may need to cease use of the compositions or methods covered by such third-party intellectual property rights, and may need to seek to develop alternative approaches that do not infringe on such intellectual property rights which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license under such intellectual property rights, any such license may be non-exclusive, which may allow our competitors access to the same technologies licensed to us.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of their former employers or other third parties.

We employ individuals who were previously employed at other biotechnology or pharmaceutical companies. Although we seek to protect our ownership of intellectual property rights by ensuring that our agreements with our employees, collaborators and other third parties with whom we do business include provisions requiring such parties to assign rights in inventions to us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information of our employees' former employers or other third parties. We may also be subject to claims that former employers or other third parties have an ownership interest in our patents. Litigation may be necessary to defend against these claims. There is no guarantee of success in defending these claims, and if we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Even if we are successful, litigation could result in substantial cost and reputational loss and be a distraction to our management and other employees.

Risks Related to Employee Matters and Managing Growth and Other Risks Related to Our Business

The COVID-19 pandemic caused by the novel strain of coronavirus could adversely impact our business, including our preclinical studies and clinical trials.

In December 2019, a novel strain of coronavirus causing the COVID-19 disease was reported to have surfaced in Wuhan, China. Since then, COVID-19 has spread to multiple countries, including the United States, where we have planned or ongoing preclinical studies and clinical trials. On March 11, 2020, the World Health Organization declared the outbreak of COVID-19 to be a global pandemic. On March 23, 2020, the governor of Massachusetts ordered the closure of all non-essential businesses effective March 24, 2020 through April 7, 2020, which order has been subsequently extended through May 18, 2020. Because of the nature of our operations, we are currently considered to be an essential business so, to date, our operations have only been partially affected by this order. 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, and facilities and production have been suspended.

In response to the spread of COVID-19, we have instructed all office-based employees to work from home, and have limited the number of staff in our research and development laboratories and in our manufacturing facility. While we are currently continuing our pheNIX clinical trial, disruptions caused by the COVID-19 pandemic may result in difficulties or delays in enrolling, conducting or completing this trial and any other planned clinical trials, and the incurrence of unforeseen costs as a result of preclinical study or clinical trial delays. Many of our clinical sites are not currently accepting new patients for enrollment in clinical trials and have placed limitations on patients already enrolled in clinical trials from visiting the clinical sites for follow-up monitoring visits. While we have entered into arrangements with third parties to provide remote patient visits and monitoring, we may still experience delays with the pheNIX trial. All of our ongoing and planned preclinical studies at external CROs are progressing and we have accelerated shipments of reagents and supplies to avoid any disruption of activities. However, it is possible that the COVID-19 pandemic may have an impact in the future on our CROs' ability to complete critical studies required for the progression of these programs. Moreover, while we currently do not anticipate any interruptions in our manufacturing process, it is possible that the COVID-19 pandemic and response efforts may have an impact in the future on our and/or our third-party suppliers and CMOs' ability to manufacture our product candidates or materials needed for our preclinical studies and clinical trials. If the COVID-19 pandemic continues to spread in the United States and elsewhere, we may experience disruptions that could severely impact our business, preclinical studies and clinical trials, including:

- delays in receiving approval from local regulatory authorities to initiate our planned clinical trials;
- delays or difficulties in enrolling patients in our clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- delays in clinical sites receiving the supplies and materials needed to conduct our clinical trials, including interruption in global shipping that may affect the transport of clinical trial materials;
- changes in local regulations as part of a response to the COVID-19 pandemic which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue the clinical trials altogether;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others, or interruption of clinical trial subject visits and study procedures, the occurrence of which could affect the integrity of clinical trial data;
- risk that participants enrolled in our clinical trials will acquire COVID-19 while the clinical trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed adverse events;
- interruptions or delays in preclinical studies due to restricted or limited operations at our research and development laboratory facility;
- delays in necessary interactions with local regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees;
- limitations in employee resources that would otherwise be focused on the conduct of our clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people;
- refusal of the FDA to accept data from clinical trials in affected geographies; and
- impacts from prolonged remote work arrangements, such as increased cybersecurity risks and strains on our business continuity plans.

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

While the potential economic impact brought by and the duration of the COVID-19 pandemic may be difficult to assess or predict, the widespread pandemic has resulted in, and may continue to result in, significant disruption of global financial markets, which could reduce our ability to access capital and negatively affect our liquidity. In addition, the recession or market correction resulting from the spread of COVID-19 could materially affect our business.

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

Our industry has experienced a high rate of turnover of management personnel in recent years. We are highly dependent on the development, regulatory, commercialization and business development expertise of Arthur Tzianabos, Ph.D., our President and Chief Executive Officer, and Albert Seymour, Ph.D., our Chief Scientific Officer, as well as the other principal members of our management, scientific and clinical teams. Although we have formal employment agreements with our executive officers, these agreements do not prevent them from terminating their employment with us at any time.

If we lose one or more of our executive officers or key employees, our ability to implement our business strategy successfully could be seriously harmed. 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 develop, gain regulatory approval of and commercialize product candidates successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional 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 engaged by entities other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to develop and commercialize product candidates will be limited.

We may engage in acquisitions that could disrupt our business, cause dilution to our stockholders or reduce our financial resources.

In the future, we may enter into transactions to acquire other businesses, products or technologies. If we do identify suitable candidates, we may not be able to make such acquisitions on favorable terms, or at all. Any acquisitions we make may not strengthen our competitive position, and these transactions may be viewed negatively by customers or investors. We may decide to incur debt in connection with an acquisition or issue our common stock or other equity securities to the stockholders of the acquired company, which would reduce the percentage ownership of our existing stockholders. We could incur losses resulting from undiscovered liabilities of the acquired business that are not covered by the indemnification we may obtain from the seller. In addition, we may not be able to successfully integrate the acquired personnel, technologies and operations into our existing business in an effective, timely and nondisruptive manner. Acquisitions may also divert management attention from day-to-day responsibilities, increase our expenses and reduce our cash available for operations and other uses. We cannot predict the number, timing or size of future acquisitions or the effect that any such transactions might have on our operating results.

We or the third parties upon whom we depend may be adversely affected by natural disasters public health emergencies and other natural catastrophic events, and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Natural disasters could severely disrupt our operations and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, public health emergency, such as the COVID-19 pandemic, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as our manufacturing facilities, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business. For example, following Hurricane Maria, shortages in production and delays in a number of medical supplies produced in Puerto Rico resulted, and any similar interruption due to a natural disaster affecting us or any of our third-party manufacturers could materially delay our operations.

Risks Related to Our Common Stock

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

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, you may not be able to sell your shares of common stock at or above the price at which you purchased them. The market price for our common stock may be influenced by many factors, including:

- the success of competitive products or technologies;
- actual or expected changes in our growth rate relative to our competitors;
- results of clinical trials of our product candidates or those of our competitors;
- developments related to our existing or any future collaborations;
- regulatory actions with respect to our product candidates or our competitors' products and product candidates;
- regulatory or legal developments in the United States and other countries;
- development of new product candidates that may address our markets and make our product candidates less attractive;
- changes in physician, hospital or healthcare provider practices that may make our product candidates less useful;

- announcements by us, our collaborators or our competitors of significant acquisitions, strategic collaborations, joint ventures or capital commitments;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- failure to meet or exceed financial estimates and projections of the investment community or that we provide to the public;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- actual or expected changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this "Risk Factors" section.

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

Our executive officers and directors and their respective affiliates, in the aggregate, hold shares representing approximately 26% of our outstanding voting stock as of March 31, 2020. As a result, if these stockholders choose to act together, they would be able to control or 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 control or significantly influence the election of directors, the composition of our management and approval of any merger, consolidation or sale of all or substantially all of our assets.

A significant portion of our total outstanding shares are eligible, or will soon become eligible, to be sold into the market, 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. Based on filings with the SEC, as of September 1, 2018, holders of an aggregate of approximately 24.3 million shares of our common stock have rights, subject to specified conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders, until the rights terminate pursuant to the terms of the investors' rights agreement between us and such holders. We have also registered all shares of common stock that we may issue under our equity compensation plans, which can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and the lock-up agreements, if applicable.

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

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company until the last day of the fiscal year following the fifth anniversary of the closing of the initial public offering of our common stock. However, if certain events occur prior to the end of such five-year period, including if we become a "large accelerated filer," our annual gross revenues exceed $1.07 billion or we issue more than $1.0 billion of non-convertible debt in any three-year period, we will cease to be an emerging growth company prior to the end of such five-year period. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. 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 shareholder approval of any golden parachute payments not previously approved.

We cannot predict whether investors will find our common stock less attractive if we rely on 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 reduced or more volatile. In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of these accounting standards until they would otherwise apply to private companies. We have elected to take advantage of this extended transition period.

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

As a public company, we have incurred and expect to continue to incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and have made some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified members of our board of directors.

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 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company, 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 have engaged in a process to document and evaluate our internal control over financial reporting, which has been both costly and challenging. We will need to continue to dedicate internal resources, engage outside consultants, 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 whether such 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 that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could cause us to need to restate our previously issued financial statements and result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

If securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our stock, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that industry or securities analysts publish about us or our business. If any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our target animal studies and operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts ceases coverage of us or fails to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Provisions in our restated certificate of incorporation and amended and restated bylaws 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 management.

Provisions in our restated certificate of incorporation and our amended and restated 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 you might otherwise receive a premium for your 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 include those establishing:

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from filling vacancies on our board of directors;
- the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquirer;
- the ability of our board of directors to alter our bylaws without obtaining stockholder approval;
- the required approval of the holders of at least two-thirds of the shares entitled to vote at an election of directors to adopt, amend or repeal our bylaws or repeal the provisions of our restated certificate of incorporation regarding the election and removal of directors;
- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- the requirement that a special meeting of stockholders may be called only by the chairman of the board of directors, the chief executive officer, the president or the board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and
- advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of us.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, 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. Furthermore, our restated certificate of incorporation specifies that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for most legal actions involving claims brought against us by stockholders. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our restated certificate of incorporation described above.

We believe this provision benefits us by providing increased consistency in the application of Delaware law by chancellors particularly experienced in resolving corporate disputes, efficient administration of cases on a more expedited schedule relative to other forums and protection against the burdens of multi-forum litigation. However, the provision may have the effect of discouraging lawsuits against our directors, officers, employees and agents as it may limit any stockholder's ability to bring a claim in a judicial forum that such stockholder finds favorable for disputes with us or our directors, officers, employees or agents. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with any applicable action brought against us, a court could find the choice of forum provisions contained in our restated certificate of incorporation to be inapplicable or unenforceable in such action. If a court were to find the choice of forum provision contained in our restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business, financial condition or results of operations.

Because we do not anticipate paying any cash dividends on our common shares in the foreseeable future, capital appreciation, if any, would be your sole source of gain.

We have never declared or paid any cash dividends on our common shares. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. As a result, capital appreciation, if any, of our common shares would be your sole source of gain on an investment in our common shares for the foreseeable future.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biopharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

Recent U.S. tax legislation may materially adversely affect our financial condition, results of operations and cash flows.

The Tax Cuts and Jobs Act of 2017, or the TCJA, has significantly changed the U.S. federal income taxation of U.S. corporations. The TCJA remains unclear in many respects and has been, and may continue to be, the subject of amendments and technical corrections, as well as interpretations and implementing regulations by the Treasury and Internal Revenue Service, which lessened or increased certain adverse impacts of the TCJA and may do so in the future. We continue to work with our tax advisors to determine the full impact that the TCJA will have on us. We urge our investors to consult with their legal and tax advisors with respect to the TCJA.

Our ability to use net operating losses and research and development credits to offset future taxable income may be subject to certain limitations.

As of December 31, 2019, we had federal and state net operating loss carryforwards, or NOLs, of approximately $150.7 million and $157.3 million, respectively. Our NOLs arising before January 1, 2018 are subject to expiration and will expire at various dates through 2039. As of December 31, 2019, we also had federal and state research and development and other tax credit carryforwards, or credits, including the orphan drug credit, of approximately $21.2 million and $5.2 million, respectively, available to reduce future tax liabilities. The federal and state credits expire at various dates through 2039. These NOLs and credits could expire unused and be unavailable to offset future taxable income or income tax liabilities. In addition, in general, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change NOLs or credits to offset future taxable income or income tax liabilities. For these purposes, an ownership change generally occurs where the aggregate change in stock ownership of one or more stockholders or groups of stockholders owning at least 5% of a corporation's stock exceeds 50 percentage points over a three-year period. Our existing NOLs or credits may be subject to limitations arising from previous ownership changes, if any. In addition, future changes in our stock ownership, many of which are outside of our control, could result in an ownership change. Our NOLs or credits may also be impaired under state law. Accordingly, even if we attain profitability, we may not be able to utilize a material portion of our NOLs or credits. Furthermore, under the TCJA, although the treatment of NOLs arising on or before December 31, 2017 has generally not changed, NOLs arising on or after January 1, 2018 and beyond may only be used to offset 80% of taxable income. This change may require us to pay federal income taxes in future years despite generating a loss for federal income tax purposes in prior years.

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

Not applicable.

Item 3. Defaults Upon Senior Securities.

Not applicable.

Item 4. Mine Safety Disclosures.

Not applicable.

Item 5. Other Information.

Not applicable.

Item 6. Exhibits.

Exhibit Number	Description	Form	File No.	Exhibit	Filing Date	Filed/Furnished Herewith
3.1	Restated Certificate of Incorporation of Homology Medicines, Inc.	8-K	001-38433	3.1	4/3/2018	
3.2	Amended and Restated Bylaws of Homology Medicines, Inc.	8-K	001-38433	3.2	4/3/2018	
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					*
31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					*
32.1	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.,					**
32.2	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					**
101.INS	XBRL Instance Document					*
101.SCH	XBRL Taxonomy Extension Schema Document					*
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document					*
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document					*
101.LAB	XBRL Taxonomy Extension Label Linkbase Document					*
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document					*

* Filed herewith.

** 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.

HOMOLOGY MEDICINES, INC.

Date: May 7, 2020

By: /s/ Arthur O. Tzianabos, Ph.D.

Arthur O. Tzianabos, Ph.D.
President, Chief Executive Officer and Director
(principal executive officer)

Date: May 7, 2020

By: /s/ Bradford Smith

Bradford Smith
Chief Financial Officer, Treasurer and Secretary
(principal financial officer and principal accounting officer)

Exhibit 31.1

CERTIFICATION

I, Arthur O. Tzianabos, Ph.D., certify that:

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

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

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

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

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

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

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

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

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

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

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

Date: May 7, 2020

By: /s/ Arthur O. Tzianabos, Ph.D.

Arthur O. Tzianabos, Ph.D.
President, Chief Executive Officer and Director
(principal executive officer)

Exhibit 31.2

CERTIFICATION

I, Bradford Smith, certify that:

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

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

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

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

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

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

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

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

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

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

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

Date: May 7, 2020

By: /s/ Bradford Smith

Bradford Smith
Chief Financial Officer, Treasurer and Secretary
(principal financial officer and principal accounting officer)

Exhibit 32.1

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

I, Arthur O. Tzianabos, Ph.D., President and Chief Executive Officer of Homology Medicines, Inc. (the "Company"), hereby certify, pursuant to 18 U.S.C. §1350, as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002, that, to the best of my knowledge:

(1) The Quarterly Report on Form 10-Q of the Company for the period ended March 31, 2020 (the "Report") fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

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

May 7, 2020

By: /s/ Arthur O. Tzianabos, Ph.D.

Arthur O. Tzianabos, Ph.D.
President, Chief Executive Officer and Director
(principal executive officer)

Exhibit 32.2

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

I, Bradford Smith, Chief Financial Officer of Homology Medicines, Inc. (the "Company"), hereby certify, pursuant to 18 U.S.C. §1350, as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002, that, to the best of my knowledge:

(1) The Quarterly Report on Form 10-Q of the Company for the period ended March 31, 2020 (the "Report") fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

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

May 7, 2020

By: /s/ Bradford Smith

Bradford Smith
Chief Financial Officer, Treasurer and Secretary
(principal financial officer and principal accounting officer)