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

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**FORM 10-Q**

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(Mark One)

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

**For the quarterly period ended June 30, 2018**

**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**

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**Homology Medicines, Inc.**

(Exact Name of Registrant as Specified in its Charter)

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**Delaware**

(State or other jurisdiction of  
incorporation or organization)

**45 Wiggins Avenue  
Bedford, MA**

(Address of principal executive offices)

**47-3468154**

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

**01730**

(Zip Code)

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

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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 and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted 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 and post such files). Yes ☒ No ☐

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

Large accelerated filer ☐

Non-accelerated filer ☒ (Do not check if a small reporting company)

Accelerated filer ☐

Smaller reporting company ☐

Emerging growth company ☒

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

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

As of August 10, 2018, the registrant had 37,474,649 shares of common stock, \$0.0001 par value per share, outstanding.

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## 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 and Section 21E of the Securities Exchange Act of 1934. All statements other than statements of historical facts contained in this Quarterly Report, including statements regarding our future results of operations and financial position, 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.

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**PART I—FINANCIAL INFORMATION**

**Item 1. Financial Statements.**

**HOMOLOGY MEDICINES, INC.  
CONDENSED CONSOLIDATED BALANCE SHEETS  
(UNAUDITED)**

	<b>As of</b>	
	<b>June 30, 2018</b>	<b>December 31, 2017</b>
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 94,960,535	\$ 51,574,932
Short-term investments	160,547,550	78,083,604
Prepaid expenses and other current assets	6,074,268	1,944,751
Total current assets	261,582,353	131,603,287
Property and equipment, net	6,942,457	3,154,205
Deferred offering costs	—	1,000,262
Restricted cash	1,789,962	1,772,587
Total assets	\$ 270,314,772	\$ 137,530,341
<b>Liabilities, convertible preferred stock and stockholders' equity (deficit)</b>		
Current liabilities:		
Accounts payable	\$ 5,017,426	\$ 2,538,057
Accrued expenses and other liabilities	2,358,433	2,860,025
Deferred rent	—	122,601
Deferred revenue	3,499,700	3,341,063
Total current liabilities	10,875,559	8,861,746
Non-current liabilities:		
Deferred rent, net of current portion	2,893,331	290,923
Deferred revenue, net of current portion	29,747,451	30,069,563
Total liabilities	43,516,341	39,222,232
Commitments and contingencies (Note 6)		
Convertible preferred stock:		
Series A convertible preferred stock, \$0.0001 par value; 11,838,182 shares authorized; 11,831,489 shares issued and outstanding and aggregate liquidation preference of \$44,211,092 as of December 31, 2017	—	42,994,550
Series B convertible preferred stock, \$0.0001 par value; 12,337,176 shares authorized, issued and outstanding and aggregate liquidation preference of \$93,500,008 as of December 31, 2017	—	94,767,610
Total convertible preferred stock	—	137,762,160
Stockholders' equity (deficit):		
Preferred stock, \$0.0001 par value, 10,000,000 shares authorized as of June 30, 2018 and no shares authorized as of December 31, 2017; no shares issued and outstanding at June 30, 2018 and December 31, 2017	—	—
Common stock, \$0.0001 par value; 200,000,000 and 170,000,000 shares authorized as of June 30, 2018 and December 31, 2017, respectively; 37,474,649 and 2,902,109 shares issued as of June 30, 2018 and December 31, 2017, respectively; and 37,254,902 and 2,637,011 shares outstanding as of June 30, 2018 and December 31, 2017, respectively	3,726	264
Additional paid-in capital	290,442,015	799,859
Accumulated other comprehensive loss	(48,646)	(73,308)
Accumulated deficit	(63,598,664)	(40,180,866)
Total stockholders' equity (deficit)	226,798,431	(39,454,051)
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	\$ 270,314,772	\$ 137,530,341

*See notes to condensed consolidated financial statements.*

HOMOLOGY MEDICINES, INC.

CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS  
(UNAUDITED)

	Three months ended June 30,		Six months ended June 30,	
	2018	2017	2018	2017
Collaboration revenue	\$ 926,477	\$ —	\$ 1,749,849	\$ —
Operating expenses:				
Research and development	10,289,871	4,056,289	18,288,266	6,855,261
General and administrative	4,527,335	1,982,231	8,355,357	3,874,778
Total operating expenses	14,817,206	6,038,520	26,643,623	10,730,039
Loss from operations	(13,890,729)	(6,038,520)	(24,893,774)	(10,730,039)
Other income (expense):				
Change in fair value of convertible preferred stock tranche liability	—	—	—	(876,000)
Interest income	996,493	35,766	1,475,976	48,492
Total other income (expense)	996,493	35,766	1,475,976	(827,508)
Net loss and net loss attributable to common stockholders-basic and diluted	\$ (12,894,236)	\$ (6,002,754)	\$ (23,417,798)	\$ (11,557,547)
Net loss per share attributable to common stockholders-basic and diluted	\$ (0.35)	\$ (2.61)	\$ (1.19)	\$ (4.89)
Weighted-average common shares outstanding-basic and diluted	36,860,619	2,296,118	19,606,543	2,365,021

See notes to condensed consolidated financial statements.

HOMOLOGY MEDICINES, INC.

CONDENSED CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS  
(UNAUDITED)

	Three months ended June 30,		Six months ended June 30,	
	2018	2017	2018	2017
Net loss	\$ (12,894,236)	\$ (6,002,754)	\$ (23,417,798)	\$ (11,557,547)
Other comprehensive gain:				
Change in unrealized gain on available for sale securities, net	37,519	—	24,662	—
Total other comprehensive gain	37,519	—	24,662	—
Comprehensive loss	<u>\$ (12,856,717)</u>	<u>\$ (6,002,754)</u>	<u>\$ (23,393,136)</u>	<u>\$ (11,557,547)</u>

*See notes to condensed consolidated financial statements.*

HOMOLOGY MEDICINES, INC.

CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS  
(UNAUDITED)

	Six months ended June 30,	
	2018	2017
Cash flows from operating activities:		
Net loss	\$ (23,417,798)	\$ (11,557,547)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	457,799	293,667
Stock-based compensation expense	949,192	58,258
Accretion on short-term investments	110,794	—
Change in fair value associated with convertible preferred stock tranche liability	—	876,000
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(4,129,517)	(490,997)
Accounts payable	2,566,699	148,586
Accrued expenses and other liabilities	355,175	409,415
Deferred revenue	(163,475)	—
Deferred rent	2,479,807	142,505
Net cash used in operating activities	(20,791,324)	(10,120,113)
Cash flows from investing activities:		
Purchases of short-term investments	(143,770,078)	—
Maturities of short-term investments	61,220,000	—
Purchases of property and equipment	(4,184,136)	(1,321,727)
Changes in restricted cash	(17,375)	—
Net cash used in investing activities	(86,751,589)	(1,321,727)
Cash flows from financing activities:		
Proceeds from issuance of common stock in initial public offering, net of discounts and issuance costs	150,843,215	—
Proceeds from issuance of common stock from option exercises	85,301	—
Proceeds from issuance of Series A convertible preferred stock, net of issuance costs	—	20,479,488
Net cash provided by financing activities	150,928,516	20,479,488
Increase in cash and cash equivalents	43,385,603	9,037,648
Cash and cash equivalents, beginning of period	51,574,932	11,392,207
Cash and cash equivalents, end of period	\$ 94,960,535	\$ 20,429,855
Supplemental disclosures of noncash investing and financing activities:		
Conversion of Series A convertible preferred stock into common stock upon initial public offering	\$ 42,994,550	\$ —
Conversion of Series B convertible preferred stock into common stock upon initial public offering	\$ 94,767,610	\$ —
Reclassification of liability for common stock vested	\$ 5,750	\$ 20,605
Property and equipment additions included in accounts payable	\$ 229,509	\$ 146,735
Reclassification of tranche liability upon issuance of convertible preferred stock	\$ —	\$ 5,123,000

See notes to condensed consolidated financial statements.

NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS  
(UNAUDITED)

## 1. NATURE OF BUSINESS AND BASIS OF PRESENTATION

**Nature of Business**—Homology Medicines, Inc. (the “Company”) is a pre-clinical stage biopharmaceutical company dedicated to translating proprietary gene editing and gene therapy technology into novel treatments for patients with rare genetic diseases. 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 manufacturing processes 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 dependent on key individuals and intellectual property, competition from other products and companies, and the technical risks associated with the successful research, development and clinical 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.

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 June 30, 2018, the Company has financed its operations primarily through the public offering of its common stock, the issuance of convertible preferred stock, and with proceeds from its collaboration and license agreement with Novartis (see Note 10).

On April 2, 2018, the Company completed an initial public offering (“IPO”) in which the Company issued and sold 10,350,000 shares of its common stock at a public offering price of \$16.00 per share, for aggregate gross proceeds of \$165.6 million before fees and expenses. The Company expects to incur additional operating losses and negative operating cash flows for the foreseeable future.

In connection with the IPO, the Company effected a one-for-5.263 reverse stock split of its issued and outstanding shares of common stock and a proportional adjustment to the existing conversion ratios for the Company’s Series A and Series B preferred stock. Accordingly, all share and per share amounts for all periods presented in the accompanying financial statements and notes thereto have been retroactively adjusted, where applicable, to reflect this reverse stock split and adjustment of the preferred stock conversion ratios. The reverse stock split became effective on March 16, 2018.

Upon the closing of the IPO, all of the outstanding shares of convertible preferred stock automatically converted into 24,168,656 shares of common stock at the applicable conversion ratio then in effect. Subsequent to the closing of the IPO, there were no shares of preferred stock outstanding.

Management believes that existing cash, cash equivalents and short-term investments will allow the Company to continue its operations for at least the next two years. 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 Securities and Exchange Commission (“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, 2017, included in the Company’s final prospectus that forms a part of the Company’s Registration Statement on Form S-1 (Reg. No. 333-223409), filed with the SEC pursuant to Rule 424(b)(4) on March 29, 2018.

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 June 30, 2018, and consolidated results of operations and cash flows for the three and six months ended June 30, 2018 and 2017, respectively. Such adjustments are of a normal and recurring nature. The results of operations for the three and six months ended June 30, 2018 are not necessarily indicative of the results of operations that may be expected for the year ending December 31, 2018.



## 2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

**Principles of Consolidation**—The Company’s condensed consolidated financial statements include the accounts of the Company and 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, useful lives assigned to property and equipment, as well as the fair values of common stock, convertible preferred stock and convertible preferred stock tranche liability. The Company assesses estimates on an ongoing basis; however, actual results could materially differ from those estimates.

**Cash and Cash Equivalents**—Cash and cash equivalents consist of standard checking accounts, money market accounts and certain investments. The Company considers all highly liquid investments with original maturities of 90 days or less at the time of purchase to be cash equivalents.

**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’ deficit 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 (expense).

**Revenue Recognition**— The Company recognizes revenue when all of the following criteria are met: persuasive evidence of an arrangement exists; delivery has occurred or services have been rendered; the Company’s price to the buyer is fixed or determinable; and collectability is reasonably assured. The Company records as deferred revenue any amounts received or billed prior to satisfying the revenue recognition criteria. Deferred revenue not expected to be recognized within the next twelve months is reported as non-current deferred revenue.

In November 2017, the Company entered into a collaboration and license agreement for research, development, manufacturing and commercialization of products using the Company’s gene editing technology for the treatment of certain diseases (see Note 10). Consideration the Company may receive under the collaboration and license agreement include upfront nonrefundable payments, payments for research and manufacturing activities, payments based upon the achievement of certain milestones and royalties on any resulting net product sales.

### *Multiple Element Arrangements*

The terms of the collaboration and license agreement contain multiple deliverables, including licenses, research and development activities, participation on steering committees and manufacturing activities. The Company evaluates the activities in its collaboration agreements to determine if the activities are consistent with a typical vendor-customer relationship, and if so, accounts for them in accordance with Accounting Standards Codification (“ASC”) Topic 605-25, *Revenue Recognition – Multiple Element Arrangements*. If not, the Company evaluates other applicable guidance.

The Company evaluates multiple element arrangements to determine the deliverables included in the arrangement and whether the individual deliverables represent separate units of accounting, or whether they must be accounted for as a combined unit of accounting. When deliverables are separable, consideration received is allocated to the separate units of accounting based on the relative selling price method and the appropriate revenue recognition principles are applied to each unit. This evaluation requires the Company to make judgments about the individual deliverables and whether such deliverables (1) have value to the customer on a standalone basis and (2) if the arrangement includes a general right of return with respect to the delivered item, delivery or performance of the undelivered item is considered probable and substantially in the Company’s control. In assessing whether an item has standalone value, the Company considers factors such as the research, development, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, the Company considers whether the collaboration partner can use any other deliverable for its intended purpose without the receipt of the remaining deliverables, whether the value of the deliverable is dependent on any undelivered item, and whether there are other vendors that can provide the undelivered items.

The consideration received under the arrangement that is fixed or determinable is then allocated among the separate units of accounting based on the relative selling prices of the separate units of accounting. For arrangements identified with multiple units of accounting, an allocation of the consideration is performed. The Company determines the estimated selling price for units of accounting within each arrangement using vendor-specific objective evidence (“VSOE”), if available; third-party evidence (“TPE”) of selling price if VSOE is not available; or best estimate of selling price (“BESP”), if neither VSOE nor TPE is available. The Company typically uses BESP to estimate the selling price as it generally does not have VSOE or TPE of selling price for its units of accounting. Determining the BESP for a unit of accounting requires significant judgment. In developing the BESP for a unit of accounting, the Company considers applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs.

The Company recognizes arrangement consideration allocated to each unit of accounting when all of the revenue recognition criteria are satisfied for that particular unit of accounting. The Company recognizes revenue from a combined unit of accounting over the contractual or estimated performance period for the undelivered items. If there is no discernible pattern of performance or objectively measurable performance measures do not exist for a unit of accounting, then the Company recognizes revenue on a straight-line basis over the period the Company is expected to complete its performance obligations. Conversely, if the pattern of performance over which the service is provided to the customer can be determined and objectively measurable performance measures exist, then the Company recognizes revenue under the arrangement using the proportional performance method. Amounts received prior to satisfying the associated revenue recognition criteria are recorded as deferred revenue on the consolidated balance sheets. Amounts not expected to be recognized within one year following the balance sheet date are classified as non-current deferred revenue.

Significant management judgment is required in determining the level of effort required under an arrangement and the period over which the Company expects to complete its performance obligations under an arrangement. Steering committee services that are not inconsequential or perfunctory and that are determined to be performance obligations are combined with other research services or performance obligations required under an arrangement, if any, in determining the level of effort required in an arrangement and the period over which the Company expects to complete its aggregate performance obligations.

Consideration for development and sales milestones are generally not considered fixed or determinable until the milestone is achieved. Consideration due to or received by the Company for the achievement of milestones are allocated to the units of accounting, if applicable, and recognized as revenue for the portion of the performance obligation that is complete at the time the milestone is achieved. The Company will defer the remaining portion of the milestone payment and recognize it as revenue over the remaining term of the performance obligation. If no such performance obligation exists, milestone payments are recognized as revenue upon achievement, assuming all other revenue recognition criteria are met.

Royalties earned on product sales, if any, are recognized based on contractual terms of the agreement when reported sales are reliably measurable and collectibility is reasonably assured, provided that there are no performance obligations then remaining. To date, none of the Company’s product candidates have been approved and, therefore, the Company has not earned any royalty revenue from product sales.

In the event that the agreement was to be terminated and the Company had no further performance obligations at that time, the Company would recognize as revenue any portion of the upfront payment and other payments that had not previously been recorded as revenue and were classified as deferred revenue at the date of such termination.

**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. Net loss per share attributable to common stockholders is calculated using the two-class method, which is an earnings allocation formula that determines net loss per share for the holders of the Company’s common shares and participating securities. The Company’s convertible preferred stock contains participation rights in any dividend paid by the Company and is deemed to be a participating security. Net loss attributable to common stockholders and participating preferred shares are allocated to each share on an as-converted basis as if all of the earnings for the period had been distributed. The participating securities do not include a contractual obligation to share in losses of the Company and are not included in the calculation of net loss per share in the periods in which a net loss is recorded.

Diluted net loss per share is computed using the more dilutive of (a) the two-class method or (b) the if converted method. The Company allocates earnings first to preferred stockholders based on dividend rights and then to common and preferred stockholders based on ownership interests. 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, unvested shares of common stock and convertible preferred 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. The Company reported a net loss attributable to common stockholders for the three and six months ended June 30, 2018 and 2017.

**Subsequent Events**—The Company considers events or transactions that occur after the balance sheet date but prior to the issuance of the financial statements to provide additional evidence relative to certain estimates or to identify matters that require additional disclosure. The Company has completed an evaluation of all subsequent events through the date the financial statements were issued.

**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 May 2014, the Financial Accounting Standards Board (“FASB”) issued Accounting Standards Update (“ASU”) No. 2014-09, *Revenue (Topic 606): Revenue from Contracts with Customers* (“ASU 2014-09”), which will replace existing revenue recognition standards and significantly expand the disclosure requirements for revenue arrangements. The new standard and the subsequent amendments will be effective for the Company beginning on January 1, 2019. The Company is in the process of evaluating the impact of the adoption of ASU No. 2014-09 on its condensed consolidated financial statements. The Company will continue to assess the potential impact that Topic 606 may have on its financial position and results of operations as it relates to the collaboration and license agreement with Novartis (see Note 10). The Company expects that certain accounting conclusions will require further judgment, including, but not limited to, the evaluation of variable consideration, and in particular, milestone payments due from Novartis as the inclusion of milestone payments in the transaction price could accelerate revenue recognized under ASC 606 compared to ASC 605.

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*, which eliminates the current tests for lease classification under U.S. GAAP and requires lessees to recognize the right-to-use assets and related lease liabilities in the balance sheet. ASU No. 2016-02 is effective for the Company beginning January 1, 2020 with early application permitted. The new standard provides for a modified retrospective application. The Company is in the process of evaluating the impact of the adoption of ASU No. 2016-02 on its condensed consolidated financial statements.

In March 2016, the FASB issued ASU No. 2016-09, *Compensation—Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting*, which changes certain aspects of the accounting for share-based payments granted to employees. Certain changes will be applied prospectively and other changes will be applied using a modified retrospective approach with the recognition of the cumulative effect of the application of the new standard as of the beginning of the period of initial application. ASU No. 2016-09 was adopted by the Company on January 1, 2018 and the adoption did not have a material impact on its condensed consolidated financial statements.

In December 2016, the FASB issued ASU No. 2016-18, *Statement of Cash Flows (Topic 230): Restricted Cash (a consensus of the FASB Emerging Issues Task Force)*, which requires that amounts described as restricted cash or cash equivalents must be included with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the statement of cash flows. ASU 2016-18 is effective for the Company beginning January 1, 2019, with early application permitted. The new standard must be applied retrospectively to all periods presented. The Company does not expect the adoption of this standard will have a material impact 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*, which changes certain aspects of the accounting for share-based payments granted to nonemployees. Under the ASU, most of the guidance on such payments to nonemployees would be aligned with the requirements for share-based payments granted to employees. ASU 2018-07 is effective for the Company beginning January 1, 2020. Early application of this standard is permitted however companies may not apply this standard earlier than it applies ASU 2014-09. The Company is evaluating the impact adoption of this standard will have on its condensed consolidated financial statements.

### 3. 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 (deficit), 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 June 30, 2018 and December 31, 2017:

<b>As of June 30, 2018</b>	<b>Amortized Cost</b>	<b>Unrealized Gains</b>	<b>Unrealized Losses</b>	<b>Fair Value</b>
Money market mutual funds	\$ 35,781,822	\$ —	\$ —	\$ 35,781,822
Asset-backed securities	20,160,567	1,279	(2,074)	20,159,772
Commercial paper	85,895,613	—	—	85,895,613
Corporate debt securities	64,147,033	813	(35,971)	64,111,875
U.S. Treasury securities	49,008,349	55	(12,748)	48,995,656
Total	<u>\$ 254,993,384</u>	<u>\$ 2,147</u>	<u>\$ (50,793)</u>	<u>\$ 254,944,738</u>
<b>As of December 31, 2017</b>	<b>Amortized Cost</b>	<b>Unrealized Gains</b>	<b>Unrealized Losses</b>	<b>Fair Value</b>
Money market mutual funds	\$ 44,181,756	\$ —	\$ —	\$ 44,181,756
Asset-backed securities	7,428,021	—	(6,318)	7,421,703
Commercial paper	34,882,298	—	—	34,882,298
Corporate debt securities	26,905,815	—	(49,532)	26,856,283
U.S. Treasury securities	8,940,778	—	(17,458)	8,923,320
Total	<u>\$ 122,338,668</u>	<u>\$ —</u>	<u>\$ (73,308)</u>	<u>\$ 122,265,360</u>

As of June 30, 2018, the Company does not consider those securities that are in an unrealized loss position to be other-than-temporarily impaired, as it has the ability to hold such investments until recovery of the fair value. 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 and six months ended June 30, 2018 and 2017. 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	As of June 30, 2018	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
<b>Cash equivalents:</b>				
Money market mutual funds	\$ 35,781,822	\$ 35,781,822	\$ —	\$ —
Commercial paper	32,876,471	—	32,876,471	—
Corporate debt securities	5,643,984	—	5,643,984	—
U.S. Treasury securities	20,094,911	—	20,094,911	—
Total cash equivalents	\$ 94,397,188	\$ 35,781,822	\$ 58,615,366	\$ —
<b>Short-term investments:</b>				
Asset-backed securities	\$ 20,159,772	\$ —	\$ 20,159,772	\$ —
Commercial paper	53,019,143	—	53,019,143	—
Corporate debt securities	58,467,890	—	58,467,890	—
U.S. Treasury securities	28,900,745	—	28,900,745	—
Total short-term investments	\$ 160,547,550	\$ —	\$ 160,547,550	\$ —
Total financial assets	\$ 254,944,738	\$ 35,781,822	\$ 219,162,916	\$ —

Description	As of December 31, 2017	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
<b>Cash equivalents:</b>				
Money market mutual funds	\$ 44,181,756	\$ 44,181,756	\$ —	\$ —
Total cash equivalents	\$ 44,181,756	\$ 44,181,756	\$ —	\$ —
<b>Short-term investments:</b>				
Asset-backed securities	\$ 7,421,703	\$ —	\$ 7,421,703	\$ —
Commercial paper	34,882,298	—	34,882,298	—
Corporate debt securities	26,856,283	—	26,856,283	—
U.S. Treasury securities	8,923,320	—	8,923,320	—
Total short-term investments	\$ 78,083,604	\$ —	\$ 78,083,604	\$ —
Total financial assets	\$ 122,265,360	\$ 44,181,756	\$ 78,083,604	\$ —

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.

The convertible preferred stock tranche liability was stated at fair value and was measured using a Level 3 input because the fair value measurement was based, in part, on significant inputs not observed in the market.

The reconciliation of changes in the fair value of financial instruments based on Level 3 inputs for the six months ended June 30, 2017, consisted of:

<b>Fair value as of January 1, 2017</b>	<b>\$ 4,247,000</b>
Change in fair value of convertible preferred stock tranche liability	876,000
Reduction in tranche liability due to preferred stock issuance	(5,123,000)
<b>Fair value as of June 30, 2017</b>	<b>\$ —</b>

There were no transfers between fair value measure levels during the three and six months ended June 30, 2018 and 2017.

## 5. ACCRUED EXPENSES AND OTHER LIABILITIES

Accrued expenses and other liabilities at June 30, 2018 and December 31, 2017 consist of the following:

	As of	
	June 30, 2018	December 31, 2017
Accrued compensation and benefits	\$ 1,526,964	\$ 1,435,015
Accrued professional fees	388,267	1,119,959
Accrued research and development expenses	326,401	182,500
Accrued unvested common stock subject to repurchase	116,801	122,551
	<u>\$ 2,358,433</u>	<u>\$ 2,860,025</u>

## 6. 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. In addition to the leased space, the Company has certain rights to expand the lease to include certain adjacent property. As of June 30, 2018, no expansion rights had been exercised.

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 will be due under the lease in two phases with rent on the first 46,000 square feet starting in September 2018 and with rent on the remaining 21,000 square feet starting 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.

Future minimum lease payments as of June 30, 2018 are as follows:

Years Ending December 31,	Amount
2018	\$ 1,038,918
2019	3,424,313
2020	3,669,236
2021	3,619,333
2022	2,928,014
Thereafter	13,177,338
Total future minimum lease payments	<u>\$ 27,857,152</u>

The lease agreement entered into in December 2017 allows for a tenant improvement allowance not to exceed \$10.9 million to be applied to the total cost of tenant improvements to the leased premises. The tenant improvement allowance must be used on or before August 31, 2019 or it will be deemed forfeited with no further obligation by the landlord. Tenant improvement allowances due or received are recorded as deferred rent incentives on the Company's condensed consolidated balance sheets, which are amortized to rent expense over the term of the lease. As of June 30, 2018, deferred rent incentives totaled \$1.1 million.

The Company recorded rent expense of \$0.9 million and \$1.8 million for the three and six months ended June 30, 2018, respectively, and \$0.2 million and \$0.4 million for the three and six months ended June 30, 2017, respectively. The Company maintains letters of credit, secured by restricted cash, for security deposits totaling \$1.8 million as of June 30, 2018 and December 31, 2017, respectively, in conjunction with its current leases.

## 7. STOCK INCENTIVE PLANS

### *2015 Stock Incentive Plan*

In December 2015, the 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. In February 2017 and July 2017, the Board of Directors amended the 2015 Plan to increase the number of shares available for issuance under the 2015 Plan to 2,446,323 and 3,225,346, respectively.

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 June 30, 2018, 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 upon the effectiveness of the registration statement on Form S-1 for the Company’s initial public offering. 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, nonstatutory stock options, restricted stock awards, restricted stock units, stock appreciation rights and other stock-based awards. 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. At June 30, 2018, there were 2,493,415 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 “ESPP”). The ESPP allows employees to buy Company stock through after-tax payroll deductions at a discount from market value. The number of shares of common stock initially available for issuance under the 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 ESPP. As of June 30, 2018, there were no purchase rights outstanding under the ESPP.

Total stock-based compensation expense for employees, directors and non-employees for the three and six months ended June 30, 2018 and 2017 is as follows:

	Three months ended June 30,		Six months ended June 30,	
	2018	2017	2018	2017
Research and development	\$ 167,306	\$ 11,262	\$ 300,347	\$ 22,123
General and administrative	401,766	19,316	648,845	36,135
	<u>\$ 569,072</u>	<u>\$ 30,578</u>	<u>\$ 949,192</u>	<u>\$ 58,258</u>

As of June 30, 2018, there was \$9.3 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 3.4 years at June 30, 2018.

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 option was used for the expected life of nonemployees. The assumed dividend yield is based upon the Company's expectation of not paying dividends in the foreseeable future. The risk-free rate for periods within the expected life of the option is based upon the U.S. Treasury yield curve in effect at the time of grant.

In determining the exercise prices for options granted, the Company's Board of Directors considered the fair value of the common stock as of the measurement date. For the awards that were granted prior to the Company's IPO, the Board of Directors determined the fair value of the common stock at each award grant date based upon a variety of factors, including the results obtained from an independent third-party valuation, the Company's financial position and historical financial performance, the status of technological developments within the Company's proposed products, an evaluation or benchmark of the Company's competition, the current business climate in the marketplace, the illiquid nature of the common stock, arm's length sales of the Company's capital stock, including convertible preferred stock, the effect of the rights and preferences of the preferred shareholders, and the prospects of a liquidity event, among others.

The assumptions used in Black-Scholes option pricing model for the three and six months ended June 30, 2018 and 2017 are as follows:

	Three months ended June 30,		Six months ended June 30,	
	2018	2017	2018	2017
Expected volatility	56.36%	53.52%	52.80% - 60.12%	53.52% - 53.53%
Weighted-average risk-free interest rate	2.84%	2.00%	2.33% - 2.84%	2.00% - 2.28%
Expected dividend yield	— %	— %	— %	— %
Expected term (in years)	6.25	6.25	5.5 - 7.6	6.25
Underlying common stock fair value	\$20.98	\$0.63	\$6.63 - \$20.98	\$0.63

A summary of option activity under the Plans for the six months ended June 30, 2018 is as follows:

	Number of Options	Weighted-Average Exercise Price per Share	Weighted-Average Remaining Contractual Term (in Years)	Aggregate Intrinsic Value
Outstanding at January 1, 2018	1,971,711	\$ 3.61	9.3	\$ 5,977,162
Granted	793,287	\$ 15.96		
Exercised	(53,884)	\$ 1.58		
Cancelled/Forfeited	(69,314)	\$ 2.82		
Outstanding at June 30, 2018	2,641,800	\$ 7.37	9.1	\$ 34,438,555
Exercisable at June 30, 2018	454,799	\$ 2.45	8.4	\$ 8,163,075
Expected to vest at June 30, 2018	2,187,001	\$ 8.97	9.3	\$ 26,008,045

The total intrinsic value of options exercised during the six months ended June 30, 2018 was \$1.0 million. The weighted-average grant date fair value per share for options granted during the six months ended June 30, 2018 and 2017 was \$8.38 and \$0.33, 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, 2018	265,098
Vested	(61,501)
Exercised	16,150
Repurchased	—
Unvested shares - June 30, 2018	219,747

As of June 30, 2018 and December 31, 2017, 219,747 and 265,098 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 \$0.1 million as of each date .

## 8. CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY

On April 2, 2018, the Company closed its initial public offering with the sale of 10,350,000 shares of 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.

The following table provides a rollforward of the changes in convertible preferred stock and stockholders' equity (deficit) for the six months ended June 30, 2018:

	Convertible Preferred Stock \$0.0001 Par Value		Common Stock \$0.0001 Par Value		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount				
Balance, January 1, 2018	127,199,705	\$ 137,762,160	2,637,011	\$ 264	\$ 799,859	\$ (73,308)	\$ (40,180,866)	\$ (39,454,051)
Conversion of convertible preferred stock into common stock upon initial public offering	(127,199,705)	(137,762,160)	24,168,656	2,417	137,759,743	—	—	137,762,160
Issuance of common stock in initial public offering, net of discounts and issuance costs	—	—	10,350,000	1,035	150,842,180	—	—	150,843,215
Vesting of common stock from option exercise	—	—	61,501	6	5,744	—	—	5,750
Issuance of common stock from option exercise	—	—	37,734	4	85,297	—	—	85,301
Stock-based compensation	—	—	—	—	949,192	—	—	949,192
Comprehensive gain	—	—	—	—	—	24,662	—	24,662
Net loss	—	—	—	—	—	—	(23,417,798)	(23,417,798)
Balance, June 30, 2018	—	\$ —	37,254,902	\$ 3,726	\$ 290,442,015	\$ (48,646)	\$ (63,598,664)	\$ 226,798,431

## 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 June 30, 2018 and 2017, 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 June 30,	
	2018	2017
Convertible preferred shares (as converted to common stock)	—	11,831,489
Unvested common stock from early exercise of options	219,747	360,335
Stock options to purchase common stock	2,641,800	897,622
Total	2,861,547	13,089,446

## 10. COLLABORATION AND LICENSE 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. Under the terms of the Collaboration Agreement, 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, the *ex vivo* applications of the sickle cell disease program and the *in vivo* applications of the sickle cell disease target outside of the U.S. The Company retained U.S. commercialization rights to the *in vivo* applications of the sickle cell disease program. 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 Collaboration Agreement consists of a research term, where the Company and Novartis will collaborate to perform research and conduct preclinical development to identify candidates that modulate the ophthalmic targets and sickle cell disease targets. Novartis may select up to four targets, with limited substitution rights. The Company will be 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 will be reimbursed at a full-time equivalent rate ("FTE") and manufacturing activities will be reimbursed at cost, 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 four 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 four candidates or products arising from the research activities, with the exception of the right to commercialize in the U.S. the *in vivo* applications of sickle cell disease products, for which the Company maintains the exclusive right. Novartis will fund all development and commercialization costs, with the exception of the *in vivo* applications of the sickle cell disease candidate, for which the Company will fund less than half of the global development costs and fund all U.S. commercialization costs. The Company will also share U.S. commercialization profits with Novartis from the *in vivo* applications of sickle cell disease products. 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, the Company is also eligible to receive up to a total of \$960.0 million in milestone payments, including up to \$335.0 million in development milestone payments, up to \$275.0 million in regulatory milestone payments and up to \$350.0 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, which royalties are potentially subject to various reductions and offsets.

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. There are no performance, cancellation, termination or refund provisions in the arrangement that contain material financial consequences to the Company.

### **Revenue Recognition**

The Company evaluated the terms of the Collaboration Agreement and determined the development and commercialization activities related to the *in vivo* application of the sickle cell disease program represent active involvement and the sharing of risks and rewards between the Company and Novartis. The Company will segregate these activities and the related cost sharing, and record payments made to Novartis for such activities as expense. The Company evaluated the remaining terms of the Collaboration Agreement pursuant to ASC Topic 605, *Revenue Recognition*.

The Company has identified the following deliverables in the Collaboration Agreement in accordance with the provisions of ASC Topic 605-25, *Revenue Recognition—Multiple Element Arrangements*: (1) the research license, (2) the development and commercialization license, (3) the manufacturing license, (4) research activities performed by the Company, (5) service on the joint committees, (6) manufacturing during the research and development terms, and (7) manufacturing during the commercialization term. Except for manufacturing during the commercialization term, none of the other deliverables have standalone value to the customer. Since separability criteria have not been met for these deliverables, the deliverables are being accounted for as a single combined unit of accounting at the outset of the Collaboration Agreement (the “combined unit of accounting”). The manufacturing services during the commercialization term are being accounted for a separate unit of accounting.

Upon entering into the Collaboration Agreement, the Company received a nonrefundable upfront payment of \$35.0 million and a \$10.0 million investment in its Series B preferred stock by Novartis. The Company recorded the Series B preferred stock at its estimated fair value of \$11.7 million, and allocated the remaining \$33.3 million to the Collaboration Agreement. The Company believes the consideration it will receive for the manufacturing services during the commercialization term, when and if it provides such services, is representative of the best estimate of selling price of the services. Therefore, the entire \$33.3 million of upfront nonrefundable consideration was allocated to the combined unit of accounting.

At the inception of the Collaboration Agreement, the Company could not reasonably estimate the level of effort required to fulfill its obligations for the combined unit of accounting. Therefore, revenue is being recognized on a straight-line basis over the estimated period of performance for the combined unit of accounting, which the Company estimates to be approximately ten years from the inception of the Collaboration Agreement. The Company commenced revenue recognition upon delivery of the final deliverable included in the combined unit of accounting which occurred in January 2018. Accordingly, no amounts of revenue were recognized for the year ended December 31, 2017. All payments due or received from Novartis as of December 31, 2017, including amounts due for research activities performed, were recorded as deferred revenue as of December 31, 2017.

The Company recognized revenue of \$1.7 million for the six months ended June 30, 2018, based on a straight-line basis over the estimated period of performance taking into consideration all upfront payments and research funding payments together as a single unit. The amount recorded as deferred revenue under this agreement totaled \$33.2 million as of June 30, 2018.

\* \* \* \* \*

## 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 genetic medicines *in vivo* either through a gene therapy or nuclease-free gene editing modality across a broad range of genetic disorders. The unique properties of our proprietary suite of 15 novel AAVHSCs enable us to focus on a method of gene editing called gene correction, either through the replacement of an entire diseased gene in the genome with a whole functional copy or the precise repair of individual mutated nucleotides, 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 correction 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. Our diverse set of AAVHSCs allows us to precisely target, via a single intravenous injection, a wide range of disease-relevant tissues, including the liver, central nervous system, or CNS, bone marrow, lung, muscle and eye, across both modalities—gene editing and gene therapy. We believe these advantages will allow us to safely provide transformative cures using either modality.

We have generated compelling preclinical data for our first and lead product candidate, HMI-102, a gene therapy for the treatment of phenylketonuria, or PKU, and are advancing HMI-102 into a Phase 1/2 clinical trial. We expect to initiate the Phase 1/2 trial in adult patients with PKU and to receive initial clinical data in 2019. We continue to advance our gene editing modality and have generated *in vivo* preclinical data demonstrating achievement of gene correction editing efficiencies that are significantly greater than both nuclease-based and other AAV-based approaches. We expect to nominate a lead gene editing product candidate for the treatment of pediatric patients with PKU in 2018. In addition, we are advancing a pipeline of other gene therapy and gene editing research initiatives in the liver, CNS, bone marrow, lung and eye.

We are a preclinical company and have not yet initiated human clinical trials for HMI-102 or any other product candidate. We will require additional capital in order to advance HMI-102 beyond our planned Phase 1/2 clinical trial.

Our management team has a successful track record of discovering, developing and commercializing therapeutics with a particular focus on rare diseases. Our genetic medicines platform is based on gene editing and gene therapy technologies resulting from the pioneering work conducted on AAVHSCs in the laboratory of one of our founders, Saswati Chatterjee, Ph.D., of the City of Hope Medical Center, or COH. 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 efforts to discover new AAVHSCs. We have internal process development and pilot manufacturing capabilities and are in the process of building out a cGMP manufacturing facility to support our clinical development programs. We entered into a collaboration with Novartis in November 2017 to develop new genetic medicines using our HR-based gene correction editing approach in ophthalmology, which leverages our platform technology into a new therapeutic area, and sickle cell disease. Since our inception in 2015, we have raised approximately \$288.0 million in aggregate net proceeds through our initial public offering, or IPO, and preferred stock financings. We have 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 believe that our compelling preclinical data, 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, researching and identifying additional product candidates, developing manufacturing processes, building 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 in our IPO, through the sales of preferred stock, and through funding from our collaboration partner.

We are a development stage company and our lead product candidate and our research initiatives are all at a preclinical stage of development. 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 \$1.7 million in collaboration revenue for the six months ended June 30, 2018. We did not recognize any collaboration revenue for the same period in 2017. Since inception, we have incurred significant operating losses. Our net losses for the six months ended June 30, 2018 and 2017 were \$23.4 million and \$11.6 million, respectively. As of June 30, 2018, we had an accumulated deficit of \$63.6 million.

Our total operating expenses were \$26.6 million and \$10.7 million for the six months ended June 30, 2018 and 2017, respectively. We expect our operating expenses to increase substantially in connection with our ongoing development activities related to our product candidates. We anticipate that our expenses will increase substantially due to costs associated with our preclinical activities for our lead gene therapy program for the treatment of PKU and the advancement of this product candidate into a Phase 1/2 clinical trial in the U.S., which we expect to commence and have initial clinical data in 2019, development activities associated with our other gene editing and gene therapy product candidates, 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 preclinical and clinical studies, as well as the further development of internal manufacturing capabilities and capacity 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.

As a result of these anticipated expenditures, we will need additional financing to support our continuing operations. We expect to continue to finance our operations through a combination of public or private equity or debt financings or other sources, which may include collaborations with third parties. Adequate additional financing may not be available to us on acceptable terms, or at all. Our inability to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy. We will need to generate significant revenue to achieve profitability, and we may never do so.

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 for at least the next two years. 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.” Because of the numerous risks and uncertainties associated with the development of our current and any future product candidates and our platform 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 on our lead gene therapy program, HMI-102 for the treatment of PKU;
- the costs, timing, and results of our research and development efforts on future product candidates in our gene editing and gene therapy pipeline;
- the costs and timing of process development and manufacturing scale-up activities, supplies of our product candidates for preclinical studies and clinical trials through CMOs and internal manufacturing;
- the costs and timing of capital expenditures for the build-out of research and development labs, office space and manufacturing suites in a new facility 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.

Adequate additional funds may not be available to us on acceptable terms, or at all. 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 the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate 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.

## **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 \$1.7 million in collaboration revenue for the six months ended June 30, 2018 (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 CROs and other third parties that conduct research, preclinical activities and clinical trials on our behalf as well as CMOs that manufacture our product candidates for use in our preclinical and potential future clinical trials;
- costs of outside consultants, including their fees, stock-based compensation 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 June 30,		Six months ended June 30,	
	2018	2017	2018	2017
HMI-102 external development costs	\$ 3,824,280	\$ 1,185,851	\$ 6,397,707	\$ 1,664,531
Employee-related costs	3,077,032	1,285,342	6,028,130	2,407,636
Other research and development costs	3,388,559	1,585,096	5,862,429	2,783,094
Total research and development expenses	<u>\$ 10,289,871</u>	<u>\$ 4,056,289</u>	<u>\$ 18,288,266</u>	<u>\$ 6,855,261</u>

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 initiate clinical trials of HMI-102 for the treatment of PKU, including our Phase 1/2 clinical trial, 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 or any other 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 and any other our 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, 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;
- the actual probability of success for our product candidates, including 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 and allocated expenses for rent and 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 our HMI-102 product development candidate and any other product candidate we may develop. We also expect to incur increased expenses associated with being a public company, including costs of accounting, audit, legal, regulatory and tax-related services associated with maintaining compliance with Nasdaq and SEC requirements; director and officer insurance costs; and investor and public relations costs.

### **Interest Income**

Interest income consists of amounts earned on our cash, cash equivalents and short-term investments. Our interest income has increased due to higher investment balances in 2018.

### **Change in Fair Value of Convertible Preferred Stock Tranche Liability**

We have determined that our obligation to issue, and our investors' obligation to purchase, additional shares of Series A preferred stock in the second of two tranches represent a freestanding financial instrument. The freestanding tranche liability was initially recorded at fair value, with gains and losses arising from changes in fair value recognized in other income in the statements of operations at each period end such instruments are outstanding. The liability was valued using an income approach, specifically the discounted cash flow method. On February 10, 2017, we issued 28,873,237 shares of our Series A preferred stock at \$0.71 per share upon the achievement of certain development milestones, resulting in net proceeds of approximately \$20.5 million. We adjusted the carrying value of the convertible preferred stock tranche liability to its estimated fair value at each reporting date and upon issuance of the second tranche of Series A preferred stock on February 10, 2017, recognizing the changes in fair value in other income (expense) in the consolidated statement of operations. We recognized total other expense of \$0.9 million for the six months ended June 30, 2017 related to changes in the fair value of the convertible preferred stock tranche liability. We had no liability related to the convertible preferred stock as of June 30, 2018.

### **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 we have prepared in accordance with United States generally accepted accounting principles. The preparation of our financial statements and related disclosures requires us to make estimates, assumptions and judgments that affect the reported amount of assets, liabilities, revenue, costs and expenses, and related disclosures. 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 final prospectus for our IPO filed pursuant to Rule 424(b)(4) under the Securities Act of 1933, as amended (the "Securities Act") with the SEC on March 29, 2018 and the notes to the consolidated financial statements appearing elsewhere in this Quarterly Report on Form 10-Q. There were no material changes to our critical accounting policies through June 30, 2018 from those discussed in our final prospectus filed on March 29, 2018. For information regarding our recent accounting pronouncements, see Note 1 to our condensed consolidated financial statements included elsewhere in this Quarterly Report on Form 10-Q.

### **Results of Operations**

#### **Comparison of Three Months Ended June 30, 2018 and 2017**

The following table summarizes our results of operations:

	<b>Three months ended June 30,</b>		
	<b>2018</b>	<b>2017</b>	<b>Change</b>
Collaboration revenue	\$ 926,477	\$ —	\$ 926,477
Operating expenses:			
Research and development	10,289,871	4,056,289	6,233,582
General and administrative	4,527,335	1,982,231	2,545,104
Total operating expenses	14,817,206	6,038,520	8,778,686
Loss from operations	\$ (13,890,729)	\$ (6,038,520)	\$ (7,852,209)
Other income:			
Interest income	996,493	35,766	960,727
Net loss	\$ (12,894,236)	\$ (6,002,754)	\$ (6,891,482)



## Revenues

Revenues for the three months ended June 30, 2018 were \$0.9 million, and consisted solely of collaboration revenue under our Collaboration Agreement with Novartis that we entered into in November 2017, representing the portion of the \$35.0 million upfront payment and research funding payments that were recognized in the three months ended June 30, 2018. We recognize revenues based on a straight-line basis over the estimated period of performance taking into consideration all upfront payments and research funding payments, under this arrangement, together as a single unit. We did not recognize any revenue in the three months ended June 30, 2017.

## Research and Development Expenses

	Three months ended June 30,		Change
	2018	2017	
HMI-102 external development costs	\$ 3,824,280	\$ 1,185,851	\$ 2,638,429
Employee-related costs	3,077,032	1,285,342	1,791,690
Other research and development costs	3,388,559	1,585,096	1,803,463
Total research and development expenses	<u>\$ 10,289,871</u>	<u>\$ 4,056,289</u>	<u>\$ 6,233,582</u>

Research and development expenses for the three months ended June 30, 2018 were \$10.3 million, compared to \$4.1 million for the three months ended June 30, 2017. The increase of \$6.2 million was primarily due to an increase of \$2.6 million in direct research expenses, primarily CMO costs, related to our HMI-102 program, a \$1.8 million increase due to an increase in employee headcount to support our ongoing development programs, research initiatives, technology platform and manufacturing capabilities and a \$1.8 million increase in non-employee-related pre-clinical activities.

## General and Administrative Expenses

General and administrative expenses were \$4.5 million for the three months ended June 30, 2018, compared to \$2.0 million for the three months ended June 30, 2017. The increase of \$2.5 million was primarily due to \$1.1 million in increased employee-related costs, \$0.8 million in increased facility costs, \$0.3 million in increased consulting costs and \$0.2 million in increased insurance and other public company related expenses.

## Interest Income

Interest income was \$1.0 million for the three months ended June 30, 2018, compared to less than \$0.1 million for the three months ended June 30, 2017. The increase was the result of interest income generated on our higher average cash, cash equivalents and short-term investment balances for the three months ended June 30, 2018 compared to the three months ended June 30, 2017, due to the receipt of \$83.5 million in proceeds from our Series B preferred stock financing in July 2017, Novartis' up-front payment of \$35.0 million and additional proceeds of \$10.0 million from the issuance of Series B preferred stock to Novartis in November 2017 and the receipt of \$150.8 million in net proceeds from the issuance of common stock in our initial public offering in April 2018.

## Comparison of Six Months Ended June 30, 2018 and 2017

The following table summarizes our results of operations:

	Six months ended June 30,		Change
	2018	2017	
Collaboration revenue	\$ 1,749,849	\$ —	\$ 1,749,849
Operating expenses:			
Research and development	18,288,266	6,855,261	11,433,005
General and administrative	8,355,357	3,874,778	4,480,579
Total operating expenses	<u>26,643,623</u>	<u>10,730,039</u>	<u>15,913,584</u>
Loss from operations	<u>\$ (24,893,774)</u>	<u>\$ (10,730,039)</u>	<u>\$ (14,163,735)</u>
Other income (expense):			
Change in fair value of convertible preferred stock tranche liability	—	(876,000)	876,000
Interest income	1,475,976	48,492	1,427,484
Net loss	<u>\$ (23,417,798)</u>	<u>\$ (11,557,547)</u>	<u>\$ (11,860,251)</u>

## Revenues

Revenues for the six months ended June 30, 2018 were \$1.7 million, and consisted solely of collaboration revenue under our Collaboration Agreement with Novartis, representing the portion of the \$35.0 million upfront payment and the research funding payments that were recognized in the six months ended June 30, 2018. We recognize revenues based on a straight-line basis over the estimated period of performance taking into consideration all upfront payments and research funding payments, under this arrangement, together as a single unit. We did not recognize any revenue in the six months ended June 30, 2017.

## Research and Development Expenses

	Six months ended June 30,		Change
	2018	2017	
HMI-102 external development costs	\$ 6,397,707	\$ 1,664,531	\$ 4,733,176
Employee-related costs	6,028,130	2,407,636	3,620,494
Other research and development costs	5,862,429	2,783,094	3,079,335
Total research and development expenses	<u>\$ 18,288,266</u>	<u>\$ 6,855,261</u>	<u>\$ 11,433,005</u>

Research and development expenses for the six months ended June 30, 2018 were \$18.3 million, compared to \$6.9 million for the six months ended June 30, 2017. The increase of \$11.4 million was primarily due to an increase of \$4.7 million in direct research expenses, primarily CMO costs, related to our HMI-102 program, a \$3.6 million increase due to an increase in employee headcount to support our ongoing development programs, research initiatives, technology platform and manufacturing capabilities and a \$3.1 million increase in non-employee-related pre-clinical activities.

## General and Administrative Expenses

General and administrative expenses were \$8.4 million for the six months ended June 30, 2018, compared to \$3.9 million for the six months ended June 30, 2017. The increase of \$4.5 million was primarily due to \$2.1 million in increased employee-related costs and \$1.6 million in increased facility costs, \$0.3 million in increased consulting costs and \$0.3 million in increased insurance and other public company related expenses.

## Change in Fair Value of Tranche Liability

For the six months ended June 30, 2017, there was a \$0.9 million loss due to the re-measurement and subsequent de-recognition of the tranche liability upon achievement of a development milestone in February 2017 and the issuance of shares of our Series A preferred stock. There was no impact during the six months ended June 30, 2018, due to the de-recognition of the tranche liability in February 2017.

## Interest Income

Interest income was \$1.5 million for the six months ended June 30, 2018, compared to less than \$0.1 million for the six months ended June 30, 2017. The increase was the result of interest income generated on our higher average cash, cash equivalents and short-term investment balances for the six months ended June 30, 2018 compared to the six months ended June 30, 2017, due to the receipt of \$83.5 million in proceeds from our Series B preferred stock financing in July 2017, Novartis' up-front payment of \$35.0 million and additional proceeds of \$10.0 million from the issuance of Series B preferred stock to Novartis in November 2017 and the receipt of \$150.8 million in net proceeds from the issuance of common stock in our initial public offering in April 2018.

## Liquidity and Capital Resources

Since our inception, we have incurred significant operating losses. We expect to incur significant operating expenses, capital expenditures 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 building out internal capacity to have product manufactured 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 in our IPO and the sale of preferred stock and through an up-front payment from a collaboration partner. Since we were incorporated, we have raised a total of \$288.0 million in combined net proceeds from our IPO and sales of preferred stock, as well as an up-front payment of \$50.0 million from a collaboration partner, including \$35.0 million in cash and a \$15.0 million equity investment.

## Cash Flows

Our cash, cash equivalents and short-term investments totaled \$255.5 million and \$129.7 million as of June 30, 2018 and December 31, 2017, respectively. We had no indebtedness as of June 30, 2018 and December 31, 2017.

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

	Six months ended June 30,	
	2018	2017
Net cash used in operating activities	\$ (20,791,324)	\$ (10,120,113)
Net cash used in investing activities	(86,751,589)	(1,321,727)
Net cash provided by financing activities	150,928,516	20,479,488
Increase in cash and cash equivalents	\$ 43,385,603	\$ 9,037,648

## Cash Flows for the Six Months ended June 30, 2018

### Operating Activities

Net cash used in operating activities for the six months ended June 30, 2018 of \$20.8 million was primarily due to our net loss of \$23.4 million as we incurred expenses associated with research activities on our lead gene therapy program for PKU and research activities on other applications for our technology, changes in working capital of \$1.2 million and changes in deferred revenues of \$0.2 million, partially offset by changes in long-term deferred rent of \$2.5 million and non-cash charges related to stock-based compensation expense of \$0.9 million, depreciation expense of \$0.5 million and accretion on short-term investments of \$0.1 million.

### Investing Activities

Net cash used in investing activities for the six months ended June 30, 2018 was \$86.8 million, attributable to \$143.8 million in purchases of short-term investments and \$4.2 million in purchases of property and equipment, partially offset by maturities of short-term investments of \$61.2 million.

### Financing Activities

Net cash provided by financing activities for the six months ended June 30, 2018 was \$150.9 million, primarily due to proceeds from the issuance of common stock in our initial public offering, net of discounts and issuance costs, of \$150.8 million.

## Cash Flows for the Six Months ended June 30, 2017

### Operating Activities

Net cash used in operating activities for the six months ended June 30, 2017 was \$10.1 million, consisting of our net loss of \$11.6 million as we incurred expenses associated with research activities on our lead gene therapy program for PKU and research activities on other applications for our technology, partially offset by the change in fair value associated with our convertible preferred stock tranche liability of \$0.9 million, depreciation expense of \$0.3 million, changes in long-term deferred rent of \$0.1 million, and stock-based compensation expense of \$0.1 million.

### Investing Activities

Net cash used in investing activities for the six months ended June 30, 2017 was \$1.3 million, attributable to purchases of property and equipment.

## *Financing Activities*

Net cash provided by financing activities for the six months ended June 30, 2017 was \$20.5 million in proceeds from the issuance of Series A convertible preferred stock, net of issuance costs.

## **Funding Requirements**

Our operating expenses increased substantially in the second quarter of 2018 and are expected to increase substantially in the future in connection with our ongoing activities, particularly as we advance our preclinical activities including pre-IND enabling studies, scale-up of manufacturing processes and engagement with CMOs and initiation of human clinical trials. In addition, we have incurred, and expect to continue to incur additional costs associated with operating as a public company. In addition, we 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 our lead product candidate in gene therapy, HMI-102, for the treatment of PKU;
- pursue the preclinical and clinical development of other product candidates based on our gene editing and gene therapy technology;
- further scale up our internal manufacturing processes and capabilities and contract with CMOs to support our preclinical studies and clinical trials of our product candidates;
- occupy a substantially larger facility with expanded research and development labs and manufacturing suites and purchase additional equipment for our operations. We expect the total capital expenditures for the buildout of research and development labs, office space and manufacturing suites and the procurement of equipment in a new facility we have recently leased to be approximately \$22.0 million to \$24.0 million in 2018 and the first half of 2019, net of approximately \$10.8 million in reimbursement from our landlord through a tenant improvement allowance;
- 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, including the net proceeds from our IPO, will enable us to fund our operating expenses and capital expenditure requirements for at least the next two years. 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 our lead gene therapy program, HMI-102, for the treatment of PKU;
- the progress, costs and results of our additional research and preclinical development programs in gene editing and gene therapy;
- the costs and timing of internal process development and manufacturing scale-up activities and outsourcing activities with CMOs associated with our PKU program 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.

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.

### **Contractual Obligations**

There have been no material changes to our contractual obligations from those described in our final prospectus for our initial public offering filed pursuant to Rule 424(b)(4) under the Securities Act with the SEC on March 29, 2018.

### **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 \$255.5 million, or 94.5% of our total assets at June 30, 2018, and \$129.7 million, or 94.3% of our total assets at December 31, 2017. Interest income earned on these assets was \$1.5 million and less than \$0.1 million for the six months ended June 30, 2018 and 2017, respectively. Our interest income is sensitive to changes in the general level of interest rates, primarily U.S. interest rates. At June 30, 2018, 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 June 30, 2018.

### **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 Securities Exchange Act of 1934, as amended (the “Exchange Act”)). Based on that 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 June 30, 2018.

**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 June 30, 2018 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

**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 preclinical-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 \$23.4 million for the six months ended June 30, 2018. As of June 30, 2018, we had an accumulated deficit of approximately \$63.6 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 transition to 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;
- validate and build-out a commercial-scale current Good Manufacturing Practices, or cGMP, manufacturing facility; and
- operate as a public company.

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 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 and our 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 resources will enable us to fund our operating expenses and capital expenditure requirements for at least the next two years, including the top-line data readout for our planned Phase 1/2 clinical trial for HMI-102, the nomination and advancement of a lead gene editing product candidate, the scale-up of our manufacturing processes, the build-out of our internal manufacturing capacity 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 and our 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 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 in regions where we choose to commercialize our products; and
- the initiation, progress, timing and results of our commercialization of HMI-102, if approved for commercial sale.

We cannot be certain that additional funding will be available on acceptable terms, or at all. 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 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, 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, which is still under preclinical development, 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 preclinical and clinical development, management of clinical, preclinical, 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 June 30, 2018, we had 84 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. 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 pre-clinical 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 may 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.***

The regulatory requirements that will govern any novel gene therapy or gene editing product candidates we develop are not entirely clear and may change. Within the broader genetic medicine field, few have received marketing authorization from the European Commission, and only three gene therapy products have received marketing approval in the United States. Even with respect to more established products that fit into the categories of gene therapies or cell therapies, the regulatory landscape is still developing. Regulatory requirements governing gene therapy products and cell therapy products have changed frequently and will likely continue to change in the future. Moreover, there is substantial, and sometimes uncoordinated, overlap in those responsible for regulation of existing gene therapy products and cell therapy products. For example, in the United States, the FDA has established the Office of Tissues and Advanced Therapies within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. Gene therapy clinical trials are also subject to review and oversight by an institutional biosafety committee, or IBC, a local institutional committee that reviews and oversees basic and clinical research conducted at the institution participating in the clinical trial. Gene therapy clinical trials conducted at institutions that receive funding for recombinant DNA research from the United States National Institutes of Health, or the NIH, are also subject to review by the NIH Office of Biotechnology Activities' Recombinant DNA Advisory Committee. Although the FDA decides whether individual gene therapy protocols may proceed, the review process and determinations of other reviewing bodies can impede or delay the initiation of a clinical trial, even if the FDA has reviewed the trial and approved its initiation. The same applies in the European Union. The EMA's Committee for Advanced Therapies, or CAT, is responsible for assessing the quality, safety, and efficacy of advanced-therapy medicinal products. The role of the CAT is to prepare a draft opinion on an application for marketing authorization for a gene therapy medicinal candidate that is submitted to the 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. As a result, the procedures and standards applied to gene therapy products and cell therapy products may be applied to any gene therapy or gene editing product candidates we may develop, but that remains uncertain at this point.

Adverse developments in pre-clinical or clinical trials conducted by others in the field of gene therapy products, cell therapy products, or products developed through the application of gene editing technology 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 gene editing technologies, either of which could materially harm our business. In addition, the clinical trial requirements of the FDA, the EMA, and other regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty, and intended use and market of the potential products. The regulatory approval process for product candidates such as ours can be more expensive and take longer than for other, better known, or more extensively studied pharmaceutical or other product candidates. Further, as we are developing novel 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 foreign 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. Regulatory agencies administering existing or future regulations or legislation may not allow production and marketing of products utilizing gene editing technology in a timely manner or under technically or commercially feasible conditions. In addition, regulatory action or private litigation could result in expenses, delays, or other impediments to our research programs or the commercialization of resulting products.

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

***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. Although we plan to initiate a Phase 1/2 clinical trial in 2019, 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 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 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.

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, is still in preclinical development and 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 plan to submit an IND for HMI-102 in PKU, and we cannot provide any assurance that the FDA will authorize us to initiate any of our planned clinical trials on a timely basis, or at all, or that the FDA will agree with the design of our protocol. We may also 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.***

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 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.***

We do not currently have Fast Track Designation for any of our product candidates but intend to seek such designation for some or all of our 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 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.***

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 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 are building a cGMP manufacturing facility and expect it to be available for use in 2019. However, if we experience delays or are unable to establish and 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 cGMP 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 or our 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 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 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.

***Even if we obtain FDA approval for HMI-102 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 cGMP 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 or any other product candidate. For example, in December 2016, the 21st Century Cures Act, or Cures Act, was signed into law. The Cures Act, among other things, is intended to modernize the regulation of drugs and biologics and spur innovation and contains provisions applicable to the development of gene therapies, but its ultimate implementation is unclear. 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, 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 or any other product candidate;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- decreased demand for HMI-102 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, 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 make it more difficult and 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, however, 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, contract research organizations, or 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 pre-clinical 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 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.

***Interim “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 publish interim “top-line” or preliminary data from our clinical studies. Interim 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. Preliminary or “top-line” data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects.

***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 50% 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;
- new requirements to report certain financial arrangements with physicians and teaching hospitals, including reporting "transfers of value" made or distributed to prescribers and other healthcare providers and reporting investment interests held by physicians and their immediate family members;
- 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;
- creation of the Independent Payment Advisory Board, which, once empaneled, will have the authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription drugs and those recommendations could have the effect of law unless overruled by a supermajority vote of Congress; 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. The current presidential administration and Congress will likely continue to seek to modify, repeal, or otherwise invalidate all, or certain provisions of, the ACA. It is uncertain the extent to which any such changes may impact our business or financial condition.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2025 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 aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. 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 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; and
- similar healthcare laws and regulations in the EU and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers.

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, lung disease, 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. There are a number of companies developing nuclease-based gene editing technologies using CRISPR/Cas9, TALENs, meganucleases, Mega-TALs and ZFNs, including bluebird bio, Caribou Biosciences, Cellectis, CRISPR Therapeutics, Editas Medicine, Intellia Therapeutics, Poseida Therapeutics, Precision BioSciences and Sangamo Therapeutics. Additional companies developing gene therapy products include Abeona Therapeutics, Adverum Biotechnologies, Applied Genetic Technologies, Audentes Therapeutics, AveXis, an indirect wholly-owned subsidiary of Novartis, BioMarin, bluebird bio, Nightstar Therapeutics, REGENXBIO, Spark Therapeutics, Ultragenyx Pharmaceutical, uniQure and Voyager Therapeutics. In addition to competition from other gene editing therapies or gene therapies, any products we may develop may also face competition from other types of therapies, such as small molecule, antibody, protein or other therapies.

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. 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. 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 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 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, if approved for commercial sale, will depend on a number of factors, including but not limited to:

- the 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, 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, 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 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. Additionally, if the commercial launch of HMI-102 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 or our 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, 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, we may be forced to delay the potential commercialization of HMI-102 or reduce the scope of our sales or marketing activities for HMI-102. 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 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 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 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 in foreign countries;
- 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 pre-clinical 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 materials for our research programs and preclinical 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, which could delay, prevent, or impair our development or commercialization efforts.***

We currently rely on third-party manufacturers for the manufacture of our materials for preclinical studies. We do not have a long-term supply agreement with any of the third-party manufacturers, and we purchase our required supply on a purchase order basis. We are currently building a cGMP manufacturing facility that will have capability to process both gene therapy and gene editing products, which is expected to be available for cGMP manufacturing in 2019. However, if we experience delays or are unable to establish and 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 cGMP 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.

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 cGMP regulations and that might be capable of manufacturing for us. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval.

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 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 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 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 the GLPs and GCPs, 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 GCPs through periodic inspections of trial sponsors, principal investigators and clinical trial sites. If we or our CROs fail to comply with GCPs, 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 regulations. In addition, our clinical trials must be conducted with product produced under cGMP 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, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for any other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize 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. We may not succeed in establishing and maintaining collaborative relationships, which may significantly limit our ability to develop and commercialize HMI-102 successfully, if at all.***

We may seek collaborative relationships for the development and commercialization of HMI-102. Failure to obtain a collaborative relationship for HMI-102 may significantly impair the potential for this 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 its agreement with us for convenience on a target-by-target basis.

***We do not have multiple sources of supply for 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 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 cGMP 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 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 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 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 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 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 government 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 City of Hope Medical Center, or COH, and the California Institute of Technology, or Caltech, and we have entered into a collaboration and license agreement with Novartis Institutes for Biomedical Research, Inc., or 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 and any future product candidates, and we expect to collaborate with third parties on the development of HMI-102 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 three pending trademark applications in the United States, as well as 13 registered trademarks and 17 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**

***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 expect to grow our organization, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.***

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of product candidate development, regulatory affairs and sales, marketing and distribution. Our management may need to divert a disproportionate amount of its attention away from our day-to-day activities to devote time to managing these growth activities. To manage these growth activities, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. Our inability to effectively manage the expansion of our operations 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 additional product candidates. If our management is unable to effectively manage our expected growth, our expenses may increase more than expected, our potential ability to generate revenue could be reduced and we may not be able to implement our business strategy.

***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 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, 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 partners or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations 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, directors and stockholders who own more than 5% of our outstanding common stock and their respective affiliates, in the aggregate, hold shares representing approximately 66.1% of our outstanding voting stock as of June 30, 2018. 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 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. As of June 30, 2018, approximately 27.1 million shares of our common stock are restricted as a result of securities laws or lock-up agreements but will become eligible to be sold at various times beginning 180 days after the date of the initial public offering of our common stock, unless held by one of our affiliates, in which case the resale of those securities will be subject to volume limitations under Rule 144 of the Securities Act of 1933, as amended, or Rule 144. Moreover, 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 such shares can otherwise be sold without restriction under Rule 144 or 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.

***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 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 will be 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 are engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, 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, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

***If 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, which became effective upon the closing of the initial public offering of our common stock 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.***

Recently-enacted U.S. tax legislation has significantly changed the U.S. federal income taxation of U.S. corporations, including by reducing the U.S. corporate income tax rate, limiting interest deductions, and revising the rules governing net operating losses. Many of these changes are effective immediately, without any transition periods or grandfathering for existing transactions. The legislation is unclear in many respects and could be subject to potential amendments and technical corrections, as well as interpretations and implementing regulations by the Treasury and Internal Revenue Service, any of which could lessen or increase certain adverse impacts of the legislation. In addition, it is unclear how these U.S. federal income tax changes will affect state and local taxation, which often uses federal taxable income as a starting point for computing state and local tax liabilities.

The reduction of the corporate tax rate under the legislation may cause a reduction in the economic benefit of our net operating loss carryforwards and other deferred tax assets available to us. Furthermore, under the legislation, although the treatment of tax losses generated before December 31, 2017 has generally not changed, tax losses generated in calendar year 2018 and beyond will only be able 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.

While some of the changes made by the tax legislation may adversely affect the Company in one or more reporting periods and prospectively, other changes may be beneficial on a going forward basis. We continue to work with our tax advisors to determine the full impact that the recent tax legislation as a whole will have on us. We urge our investors to consult with their legal and tax advisors with respect to such legislation.

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

### **Use of Proceeds**

On April 2, 2018, we completed the initial public offering of our common stock and issued and sold 10,350,000 shares of our common stock at a price to the public of \$16.00 per share.

The offer and sale of all of the shares in the offering was registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333-223409), which was declared effective by the SEC on March 27, 2018. The offering terminated after the sale of all securities registered pursuant to the Registration Statement. The net proceeds of approximately \$150.8 million from our IPO have been invested in short-term, investment-grade, interest-bearing instruments and U.S. government securities. There has been no material change in the expected use of the net proceeds from our IPO as described in our final prospectus, dated March 27, 2018, filed with the SEC pursuant to Rule 424(b) relating to our Registration Statement on Form S-1.

## **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	<a href="#">Restated Certificate of Incorporation of Homology Medicines, Inc.</a>	8-K	001-38433	3.1	4/3/2018	
3.2	<a href="#">Amended and Restated Bylaws of Homology Medicines, Inc.</a>	8-K	001-38433	3.2	4/3/2018	
31.1	<a href="#">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.</a>					*
31.2	<a href="#">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.</a>					*
32.1	<a href="#">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.</a>					**
32.2	<a href="#">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.</a>					**
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: August 13, 2018

By: /s/ Arthur O. Tzianabos, Ph.D.  
**Arthur O. Tzianabos, Ph.D.**  
**President, Chief Executive Officer and Director**  
***(principal executive officer)***

Date: August 13, 2018

By: /s/ Bradford Smith  
**Bradford Smith**  
**Chief Financial Officer, Treasurer and Secretary**  
***(principal financial officer and principal accounting officer)***

# 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)) 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) [omitted];
  - (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: August 13, 2018

By: /s/ Arthur O. Tzianabos, Ph.D.  
**Arthur O. Tzianabos, Ph.D.**  
**President, Chief Executive Officer and Director**  
*(principal executive officer)*

# 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)) 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) [omitted];
  - (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: August 13, 2018

By: /s/ Bradford Smith  
**Bradford Smith**  
**Chief Financial Officer, Treasurer and Secretary**  
*(principal financial officer and principal accounting officer)*

**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 June 30, 2018 (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.

August 13, 2018

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

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

- (1) The Quarterly Report on Form 10-Q of the Company for the period ended June 30, 2018 (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.

By: /s/ Bradford Smith  
**Bradford Smith**  
**Chief Financial Officer, Treasurer and Secretary**  
*(principal financial officer and principal accounting officer)*