As filed with the Securities and Exchange Commission on March 23, 2018

Registration No. 333-223409

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

AMENDMENT NO. 2
TO
FORM S-1
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

Homology Medicines, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**2834**	**47-3468154**
(State or other jurisdiction of incorporation or organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification No.)

45 Wiggins Avenue
Bedford, MA 01730
(781) 301-7277
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Arthur O. Tzianabos, Ph.D.
President and Chief Executive Officer
Homology Medicines, Inc.
45 Wiggins Avenue
Bedford, MA 01730
(781) 301-7277
(Name, address, including zip code, and telephone number, including area code, of agent for service)

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Approximate date of commencement of proposed sale to the public:
As soon as practicable after this Registration Statement is declared effective.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box. ☐

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

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

Large accelerated filer	☐	**Accelerated filer**	☐
Non-accelerated filer	☒	**Smaller reporting company**	☐
(Do not check if a smaller reporting company)		**Emerging growth company**	☒

If an emerging growth company, indicate by checkmark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided to Section 7(a)(2)(B) of the Securities Act. ☐

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

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The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

Subject to Completion
Preliminary Prospectus dated March 23, 2018.

PROSPECTUS

6,667,000 Shares

Common Stock

This is Homology Medicines, Inc.'s initial public offering. We are selling 6,667,000 shares of our common stock.

We expect the public offering price to be between $14.00 and $16.00 per share. Currently, no public market exists for the shares. After pricing of the offering, we expect that the shares will trade on the Nasdaq Global Select Market under the symbol "FIXX."

We are an "emerging growth company" under the federal securities laws and are subject to reduced public company disclosure standards. See "Prospectus Summary—Implications of Being an Emerging Growth Company."

Investing in the common stock involves risks that are described in the "Risk Factors" section beginning on page 12 of this prospectus.

	Per Share	Total
Public offering price	$	$
Underwriting discount(1)	$	$
Proceeds, before expenses, to us	$	$

(1) We refer you to "Underwriting" beginning on page 166 for additional information regarding underwriting compensation.

The underwriters may also exercise their option to purchase up to an additional 1,000,050 shares from us, at the public offering price, less the underwriting discount, for 30 days after the date of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Certain of our existing stockholders, including entities affiliated with certain of our directors, have indicated an interest in purchasing an aggregate of approximately $50.0 million in shares of our common stock in this offering at the initial public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, fewer or no shares in this offering to any or all of these stockholders, or any or all of these stockholders may determine to purchase more, fewer or no shares in this offering. The underwriters will receive the same underwriting discount on any shares purchased by these stockholders as they will on any other shares sold to the public in this offering.

The shares will be ready for delivery on or about , 2018.

Joint Book-Running Managers

BofA Merrill Lynch **Cowen** **Evercore ISI**

Lead Manager

BTIG

The date of this prospectus is , 2018.

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Neither we nor the underwriters have authorized anyone to provide any information or to make any representations other than those contained in this prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus is an offer to sell only the shares offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus or in any applicable free writing prospectus is current only as of its date, regardless of its time of delivery or any sale of shares of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date.

Through and including , 2018 (25 days after the commencement of this offering), all dealers effecting transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to the obligation of dealers to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

We have proprietary rights to trademarks, trade names and service marks appearing in this prospectus that are important to our business. Solely for convenience, the trademarks, trade names and service marks may appear in this prospectus without the ® and TM symbols, but any such references are not intended to indicate, in any way, that we forgo or will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensors to these trademarks, trade names and service marks. All trademarks, trade names and service marks appearing in this prospectus are the property of their respective owners.

For investors outside the United States: Neither we nor the underwriters have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus outside the United States.

PROSPECTUS SUMMARY

This summary highlights, and is qualified in its entirety by, the more detailed information and financial statements included elsewhere in this prospectus. This summary does not contain all of the information that may be important to you in making your investment decision. You should read this entire prospectus carefully, especially the "Risk Factors" section beginning on page 12 and our consolidated financial statements and the related notes appearing at the end of this prospectus, before deciding to invest in our common stock.

As used in this prospectus, unless the context otherwise requires, references to "we," "us," "our" and "Homology" refer to the consolidated operations of Homology Medicines, Inc. and its consolidated subsidiaries.

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 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 a 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, which 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 potentially 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 PKU patients and to receive initial clinical data in 2019. We continue to advance our gene editing modality and have generated *in vivo* preclinical data showing gene correction efficiencies that are significantly greater than both nuclease-based and other adeno-associated virus, or AAV, based approaches. We expect to nominate a lead gene editing product candidate for the treatment of PKU in 2018. We are a preclinical company and have not yet submitted an investigational new drug application, or IND, 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 in California, 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 planning stage of building a current Good Manufacturing

Practices, or cGMP, manufacturing facility to support our clinical development programs. We recently entered into a collaboration with Novartis Institutes for Biomedical Research, Inc., or Novartis, to develop new genetic medicines using our HR-based gene correction 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 $137 million through preferred stock financings, including investments from 5AM Ventures, ARCH Venture Partners, Deerfield, Temasek, Fidelity Management & Research, or FMR, Novartis, Rock Springs Capital, VIVO, HBM Partners, Maverick and Vida, or affiliates thereof, in addition to others. 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.

Our Opportunity in Genetic Medicines

We are currently focused on monogenic diseases where the genetic abnormality is known to occur in a single diseased gene. The majority of monogenic diseases harbor thousands of individual mutations within the diseased gene, each resulting in a loss of function. Replacing an entire diseased gene with a whole functional gene is the optimal therapeutic approach for addressing these monogenic disorders. This can be accomplished either through a method of gene therapy called gene transfer in slowly or non-dividing cells, or through a method of gene editing called gene correction in rapidly dividing cells. Gene transfer seeks to introduce a functional copy of a defective gene or gene sequence into a patient's own cells, but not incorporate such copy into the patient's genome. This method results in the expression of the therapeutic protein of interest without changing the genome. Gene editing, on the other hand, seeks to change the course of genetic disease by physically correcting aberrant genes through the replacement, deletion or repair of defective DNA in its native location.

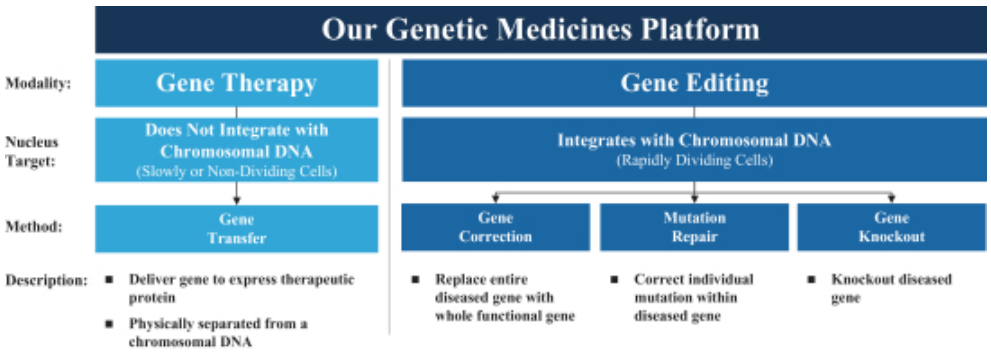
Gene editing technologies to date primarily leverage two independent pathways to modify DNA: homologous recombination, or HR, and non-homologous end joining, or NHEJ. HR is a process in which cells repair DNA through highly precise incorporation of correct DNA sequences complementary to the site of damage. HR has evolved to repair DNA with high fidelity and avoids the introduction of unwanted mutations at the site of correction. NHEJ is a less selective, error-prone process that rapidly joins the ends of broken DNA resulting in a high frequency of insertions or deletions at the break site. Despite high potential for error, the majority of nuclease-based gene editing companies primarily utilize the NHEJ pathway.

The current focus of most nuclease-based gene editing methods is gene knockout, or knocking out a diseased gene to prevent the expression of an undesired protein. Since gene knockout does not result in a fully-corrected gene, this method can only potentially address the minority of monogenic diseases where a diseased protein is overexpressed. In addition to our knockout capabilities, our HR-driven gene correction method allows us to potentially address the significant majority of monogenic diseases by replacing an entire diseased gene with a whole functional gene or by repairing a single mutation to fully correct the defect. Furthermore, while other AAV vectors have been known to deliver homologous DNA to specific regions in the genome and induce the HR pathway, their limited gene correction efficiency of approximately 1% has limited their use as a viable option for *in vivo* therapeutics. In contrast, preclinical studies have provided evidence that our HR-driven gene correction method has achieved *in vivo* therapeutically-relevant efficiencies averaging 19.5%.

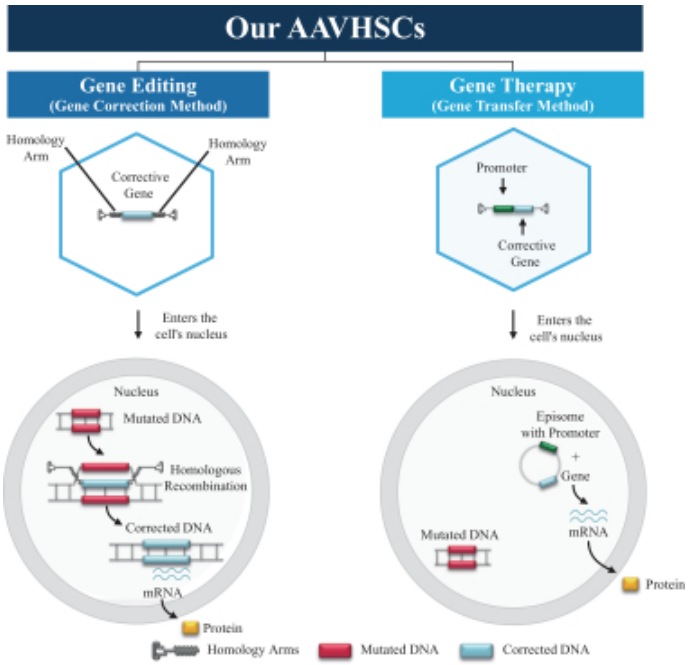
We believe the unique characteristics of our genetic medicines platform will allow us to focus on the HR pathway, enabling precise nuclease-free gene correction and a broader set of disease targets with improved efficiency.

Our Approach

Our unique genetic medicines platform is designed to provide us the flexibility to choose the best suited method from either gene correction or gene transfer for each disease we pursue, based on such factors as the targeted disease biology, the biodistribution of our AAVHSCs to key tissues and the rate of cell division the tissues exhibit. The figure below depicts our platform.



Our novel AAVHSCs are packaged with either a gene editing or traditional gene therapy construct. The gene editing construct includes lengthy guide sequences, or homology arms, which enable the specific alignment to the desired genomic location and then, through the natural process of HR, correct the diseased gene in the genome by replacement with a whole functional copy. Our gene therapy construct includes a functional copy of the gene and a promotor sequence that is designed to enable the gene to be turned on in the cell and ultimately transcribed to express the therapeutic protein of interest without integrating into the genome. The figure below depicts how our AAVHSCs enable each therapeutic modality.



We believe our approach has several key advantages that include:

- our proprietary platform AAVHSCs enable both gene therapy and gene editing modalities;
- ability to perform nuclease-free gene editing mediated by HR with high gene correction efficiency;
- ability to introduce an entire gene into the genome or the precise repair of individual mutated nucleotides in addition to gene knockout;
- high precision and lack of unwanted off-target or on-target DNA modifications;
- ability to target multiple tissues;
- *in vivo* administration with a single component delivery system; and
- ability to target a broad range of patients given the low frequency of preexisting neutralizing antibodies.

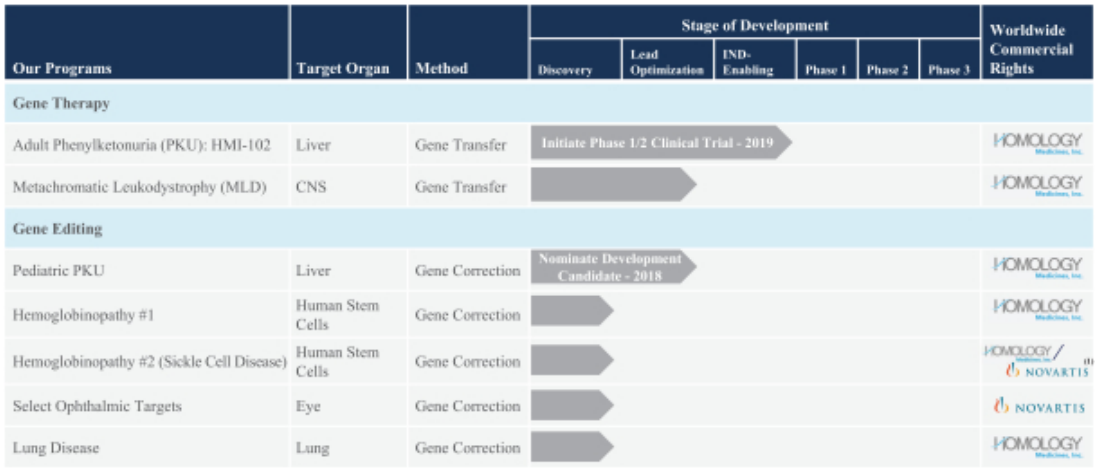
Our Pipeline Strategy

We believe our genetic medicines platform can be applied broadly to treat and potentially cure a wide range of genetic diseases, and we have carefully designed and prioritized our pipeline strategy to maximize this opportunity. We are initially pursuing monogenic diseases where we know exactly what we are seeking to correct and exactly what gene to insert into patients' cells, thus mitigating the uncertainty of the disease biology. We are prioritizing monogenic diseases with significant unmet medical needs, validated regulatory pathways and significant commercial opportunities. We are currently focused on developing product candidates to treat monogenic diseases in the liver, CNS, bone marrow, lung and the eye, given that our AAVHSCs naturally show a high degree of tropism, or ability to preferentially target cells in these organs and organ systems.

We are purposefully deploying our proprietary AAVHSCs in certain indications first with a gene therapy approach followed by a gene editing approach, in order to maximize the likelihood of translating our platform into clinical and commercial success. We are building a deep pipeline across a wide range of diseases and tissue types to leverage the broad potential of our platform. We also intend to selectively partner to expand the indications and accelerate development of programs where collaborators can contribute further disease-specific expertise to our platform.

We are advancing into a Phase 1/2 trial with our lead product candidate, HMI-102, a gene therapy for the treatment of PKU, a rare, inherited metabolic disorder that causes a toxic buildup of the amino acid phenylalanine, or Phe, in the brain. To date, no treatment addresses the core genetic defect in PKU. Our PKU program is initially focused on adults using the gene therapy approach. This strategy is designed to help us further characterize the delivery, safety and manufacturing of our AAVHSCs, and to apply our experiences to our gene editing approach in the pediatric PKU population and to our broader platform. In initial preclinical studies, mice treated with HMI-102 showed a reduction in serum Phe to normal levels within one week and the reduction in serum Phe persisted for more than 16 weeks following a single intravenous administration. In our initial gene correction preclinical studies, we introduced our gene editing construct containing human phenylalanine hydroxylase, or PAH, intravenously targeting the endogenous PAH locus through HR. In treated mice we have observed greater than 50% reduction in serum Phe sustained for at least five months.

The current status of our programs is summarized in the table below:



(1) Homology retains U.S. rights and has licensed the Ex-U.S. rights to Novartis.

Our Strategy

The critical components of our strategy include:

- transform the treatment paradigm for rare genetically-defined diseases with the delivery of single-administration curative therapies;
- advance our pipeline programs through clinical proof of concept and commercialization;
- continue to expand our pipeline in existing and new therapeutic areas;
- strengthen our platform by leveraging our internal discovery and development capabilities and selectively collaborating;
- control manufacturing through our in-house capabilities; and
- continue to strengthen and expand our intellectual property portfolio.

Risk Factors

Our business is subject to a number of risks of which you should be aware before making an investment decision. These risks are discussed more fully in the “Risk Factors” section of this prospectus immediately following this prospectus summary. These risks include the following:

- we are a development-stage company, have incurred significant losses since our inception, expect to incur losses for the foreseeable future and may never achieve or maintain profitability;

- even if this offering is successful, we will need additional funding in order to complete development of our product candidates and commercialize our products, if approved, and if we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts;

- we are very early in our development efforts, with all of our programs in the research or preclinical stage, and may not be successful in our efforts to use our novel genetic medicines platform to identify additional product candidates and develop marketable products;

- our lead product candidate is based on our novel genetic medicines platform, which uses both nuclease-free gene editing and gene therapy technologies, and to date, 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, none of which utilize our novel gene correction technology;

- our product candidates may cause serious adverse events, side effects, toxicities 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;

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

- the clinical trial and regulatory approval processes are lengthy, time consuming and inherently unpredictable, and we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates;

- we currently contract with third parties for the manufacture of our research programs and preclinical studies and we intend to establish and scale our internal manufacturing capabilities, both of which increase the risk that we will not have sufficient quantities of our product candidates or that such quantities may not be available at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts;

- our existing collaborations are important to our business and future licenses may also be important to us, and if we are unable to maintain any of these collaborations, or if these arrangements are not successful, our business could be adversely affected; and

- if we are unable to adequately protect our proprietary technology, or obtain and maintain issued patents which are sufficient to protect our product candidates, others could compete against us more directly, which would negatively impact our business.

Implications of Being an Emerging Growth Company

As a company with less than $1.07 billion in revenue during our last fiscal year, we qualify as an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012, as amended, or JOBS Act. An “emerging growth company” may take advantage of reduced reporting requirements that are otherwise applicable to public companies. These provisions include, but are not limited to:

- being permitted to present only two years of audited financial statements and only two years of related Management’s Discussion and Analysis of Financial Condition and Results of Operations in this prospectus;

- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended;
- reduced disclosure obligations regarding executive compensation in our periodic reports, proxy statements and registration statements; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We may remain an emerging growth company until the earlier of (i) the last day of the fiscal year following the fifth anniversary of the completion of this offering, (ii) the last day of the fiscal year in which we have more than $1.07 billion in annual gross revenue, (iii) the last day of the fiscal year in which we are deemed to be a "large accelerated filer," as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended, or the Exchange Act, which would occur if the market value of our common stock held by non-affiliates exceeded $700.0 million as of the last business day of the second fiscal quarter of such fiscal year, or (iv) the date on which we issue more than $1 billion of non-convertible debt securities during the prior three-year period.

We have elected to take advantage of certain of the reduced disclosure obligations in the registration statement of which this prospectus is a part and may elect to take advantage of other reduced reporting requirements in future filings. As a result, the information that we provide to our stockholders may be different than you might receive from other public reporting companies in which you hold equity interests.

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. We have elected to take advantage of this extended transition period.

Corporate Information

We were incorporated under the laws of the state of Delaware in 2015. Our principal executive offices are located at 45 Wiggins Avenue, Bedford, MA 01730 and our telephone number is (781) 301-7277. Our website address is *www.homologymedicines.com*. The information contained in, or accessible through, our website does not constitute a part of this prospectus.

The Offering

Common stock offered by us	6,667,000 shares
Common stock to be outstanding after this offering	33,747,819 shares (or 34,747,869 shares if the underwriters exercise their option to purchase additional shares in full).
Option to purchase additional shares	The underwriters have a 30-day option to purchase up to 1,000,050 additional shares of our common stock at the public offering price less estimated underwriting discounts and commissions.
Use of proceeds	We estimate that the net proceeds from this offering will be approximately $90.2 million (or approximately $104.1 million if the underwriters exercise in full their option to purchase additional shares of common stock), at an assumed public offering price of $15.00 per share, after deducting the estimated underwriting discounts and commissions and the estimated offering expenses payable by us. We anticipate that we will use the net proceeds of this offering to advance our lead and other product candidates, scale-up our manufacturing processes, build-out our internal manufacturing capacity, expand our intellectual property portfolio and pursue additional research and development efforts as set forth under "Use of Proceeds" beginning on page 66 for additional information.
Risk factors	You should carefully read the "Risk Factors" beginning on page 12 and the other information included in this prospectus for a discussion of factors you should consider carefully before deciding to invest in our common stock.
Nasdaq Global Select Market symbol	"FIXX"

Certain of our existing stockholders, including entities affiliated with certain of our directors, have indicated an interest in purchasing an aggregate of approximately $50.0 million in shares of our common stock in this offering at the initial public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, fewer or no shares in this offering to any or all of these stockholders, or any or all of these stockholders may determine to purchase more, fewer or no shares in this offering. The underwriters will receive the same underwriting discount on any shares purchased by these stockholders as they will on any other shares sold to the public in this offering.

The number of shares of our common stock to be outstanding after this offering is based on 2,912,163 shares of our common stock legally outstanding as of February 28, 2018, which included 242,342 shares of unvested restricted stock subject to repurchase and excludes:

- 1,972,027 shares of common stock issuable upon exercise of stock options outstanding under our 2015 Stock Incentive Plan, referred to as our 2015 Plan, as of February 28, 2018, at a weighted-average exercise price of $3.68 per share;

- 731,757 shares of common stock issuable upon the exercise of stock options to be granted in connection with this offering under our 2018 Incentive Award Plan, or the 2018 Plan, which will become effective in connection with this offering, to certain of our executive officers, directors and employees, at an exercise price per share equal to the initial public offering price in this offering;

- 2,454,448 additional shares of our common stock reserved for future issuance under our 2018 Plan, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under our 2018 Plan; and

- 353,980 shares of our common stock reserved for future issuance under our 2018 Employee Stock Purchase Plan, referred to as our 2018 ESPP, which will become effective in connection with this offering, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under our 2018 ESPP.

Unless otherwise indicated, this prospectus reflects and assumes the following:

- a 1-for-5.263 stock split of our common stock, which will become effective prior to the effectiveness of the registration statement of which this prospectus forms a part;

- the automatic conversion of all outstanding shares of our Series A and Series B preferred stock into an aggregate of 24,168,656 shares of our common stock upon the closing of this offering;

- no exercise of outstanding options after February 28, 2018;

- the filing of our restated certificate of incorporation, which will occur upon the closing of this offering; and

- no exercise by the underwriters of their option to purchase additional shares of our common stock.

Summary Consolidated Financial Data

The following tables set forth our summary consolidated financial data for the period indicated. We have derived the consolidated statements of operations data for the years ended December 31, 2017 and 2016 and the consolidated balance sheet data as of December 31, 2017 from our audited consolidated financial statements included elsewhere in this prospectus. Our historical results are not necessarily indicative of the results that should be expected for any future period. You should read the following summary consolidated financial data together with the more detailed information contained in "Selected Consolidated Financial Data," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and the related notes included elsewhere in this prospectus.

(in thousands, except share and per share data)	Year Ended December 31, 2017	2016
Consolidated Statements of Operations Data:		
Operating expenses:		
Research and development	$ 21,378	$ 5,695
General and administrative	8,279	4,305
Total operating expenses	29,657	10,000
Loss from operations	(29,657)	(10,000)
Other income (expense):		
Change in fair market value of convertible preferred stock tranche liability	(876)	1,929
Interest income	542	24
Total other income (expense)	(334)	1,953
Net loss and net loss attributable to common stockholders—basic and diluted	$ (29,991)	$ (8,047)
Net loss per share attributable to common stockholders—basic and diluted	$ (12.10)	$ (4.23)
Weighted average common shares outstanding—basic and diluted(1)	2,479,432	1,900,531
Pro forma net loss per share attributable to common stockholders—basic and diluted (unaudited)(1)	$ (1.57)	
Pro forma weighted average common shares of common stock outstanding—basic and diluted (unaudited)(1)	18,602,429	

(1) See Note 14 to our consolidated financial statements included elsewhere in this prospectus for an explanation of the method used to calculate the historical and pro forma basic and diluted net loss per common share and the weighted average number of shares used in the computation of the per share amounts.

	As of December 31, 2017		
	Actual	Pro Forma(1)	Pro Forma As Adjusted(2)(3)
		(in thousands)	
Consolidated Balance Sheet Data:			
Cash, cash equivalents and short-term investments	$129,659	$ 129,659	$ 219,810
Total assets	137,530	137,530	226,681
Accumulated deficit	(40,181)	(40,181)	(40,181)
Total stockholders' (deficit) equity	(39,454)	98,308	188,459

(1) The pro forma consolidated balance sheet data gives effect to the automatic conversion of all outstanding shares of our Series A and Series B preferred stock into an aggregate of 24,168,656 shares of common stock, which will occur upon the closing of this offering.

(2) Reflects the pro forma adjustments described in footnote (1) and to the issuance and sale of shares of common stock in this offering at an assumed initial public offering price of $15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

(3) Each $1.00 increase (decrease) in the assumed initial public offering price of $15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash, cash equivalents and short-term investments, total assets and total stockholders' equity (deficit) by $6.2 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, each increase (decrease) of 1.0 million shares in the number of shares offered by us at the assumed initial public offering price would increase (decrease) each of cash, cash equivalents and short-term investments, total assets and total stockholders' equity (deficit) by $14.0 million. The pro forma information discussed above is illustrative only and will be adjusted based on the actual initial public offering price and other terms of our initial public offering determined at pricing.

RISK FACTORS

You should carefully consider the risks and uncertainties described below and the other information in this prospectus before making an investment in our common stock. Our business, financial condition, results of operations or prospects could be materially and adversely affected if any of these risks occurs, and as a result, the market price of our common stock could decline and you could lose all or part of your investment. This prospectus also contains forward-looking statements that involve risks and uncertainties. See "Cautionary Statement Regarding Forward-Looking Statements." Our actual results could differ materially and adversely from those anticipated in these forward-looking statements as a result of certain factors, including those set forth below.

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 $30.0 million for the year ended December 31, 2017. As of December 31, 2017, we had an accumulated deficit of approximately $40.2 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 beyond the proceeds of this offering, 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 the net proceeds from this offering 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, including purchasers of common stock in this offering, 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, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, 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 March 1, 2018, we had 67 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 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 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, metachromic 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, 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 governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The USPTO and European and other patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In addition, periodic maintenance and annuity fees on any issued patent are due to be paid to the USPTO and European and other patent agencies over the lifetime of a patent. While an inadvertent failure to make payment of such fees or

to comply with such provisions can in many cases be cured by additional payment of a late fee or by other means in accordance with the applicable rules, there are situations in which non-compliance with such provisions will result in the abandonment or lapse of the patent or patent application, and the partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents within prescribed time limits. If we or our licensors fail to maintain the patents and patent applications covering our product candidates or if we or our licensors otherwise allow our patents or patent applications to be abandoned or lapse, it can create opportunities for competitors to enter the market, which would hurt our competitive position and could impair our ability to successfully commercialize our product candidates in any indication for which they are approved.

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

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

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

The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws or regulations in the United States and the EU, and many companies have encountered significant difficulties in protecting and defending proprietary rights in such jurisdictions. Moreover, the legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets or other forms of intellectual property, which could make it difficult for us to prevent competitors in some jurisdictions from marketing competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, are likely to result in substantial costs and divert our efforts and attention from other aspects of our business, and additionally could put at risk our or our licensors' patents of being invalidated or interpreted narrowly, could increase the risk of our or our licensors' patent applications not issuing, or could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, while damages or other remedies may be awarded to the adverse party, which may be commercially significant. If we prevail, damages or other remedies awarded to us, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or

license. Furthermore, while we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our product candidates. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate, which may have an adverse effect on our ability to successfully commercialize our product candidates in all of our expected significant foreign markets. If we or our licensors encounter difficulties in protecting, or are otherwise precluded from effectively protecting, the intellectual property rights important for our business in such jurisdictions, the value of these rights may be diminished and we may face additional competition in those jurisdictions.

In some jurisdictions, compulsory licensing laws compel patent owners to grant licenses to third parties. In addition, some countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors are forced to grant a license to third parties under patents relevant to our business, or if we or our licensors are prevented from enforcing patent rights against third parties, our competitive position may be substantially impaired in such jurisdictions.

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

The term of any individual patent depends on applicable law in the country where the patent is granted. In the United States, provided all maintenance fees are timely paid, a patent generally has a term of 20 years from its application filing date or earliest claimed non-provisional filing date. Extensions may be available under certain circumstances, but the life of a patent and, correspondingly, the protection it affords is limited. Even if we or our licensors obtain patents covering our product candidates, when the terms of all patents covering a product expire, our business may become subject to competition from competitive medications, including generic medications. Given the amount of time required for the development, testing and regulatory review and approval of new product candidates, patents protecting such candidates may expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

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

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

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

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

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

We currently in-license certain intellectual property from 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 11 registered trademarks and 19 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 and this Offering

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

Prior to this offering, there has been no public market for our common stock. The initial public offering price for our common stock will be determined through negotiations with the underwriters. Although we have been approved to list our common stock on The Nasdaq Global Select Market, an active trading market for our shares may never develop or be sustained following this offering. If an active market for our common stock does not develop, it may be difficult for you to sell shares you purchase in this offering without depressing the market price for the shares, or at all.

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 in this offering.

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 common stock at or above the initial public offering price. 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 and elsewhere in this prospectus.

After this offering, 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.

Upon the closing of this offering, based on the number of shares of common stock outstanding as of February 28, 2018, our executive officers, directors and stockholders who owned more than 5% of our outstanding common stock before this offering and their respective affiliates will, in the aggregate, hold shares representing approximately 68.2% of our outstanding voting stock. 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. Certain of our existing stockholders, including certain affiliates of our directors, have indicated an interest in purchasing shares of our common stock in this offering at the initial public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, fewer or no shares in this offering to any of these stockholders, or any of these stockholders may determine to purchase more, fewer or no shares in this offering. The foregoing discussion does not give effect to any potential purchases by these stockholders in this offering.

If you purchase shares of common stock in this offering, you will suffer immediate dilution of your investment.

The initial public offering price of our common stock will be substantially higher than the net tangible book value per share of our common stock. Therefore, if you purchase shares of our common stock in this offering, you will pay a price per share that substantially exceeds our net tangible book value per share after this offering. To the extent shares subsequently are issued under outstanding options or warrants, you will incur further dilution. Based on an assumed initial public offering price of $15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, you will experience immediate dilution of $9.41 per share as of December 31, 2017, representing the difference between our pro forma as adjusted net tangible book value per share, after giving effect to this offering, and the assumed initial public offering price. In addition, purchasers of common stock in this offering will have contributed approximately 42.1% of the aggregate price paid by all purchasers of our stock but will own only approximately 19.9% of our common stock outstanding after this offering.

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. We expect that we will use the net proceeds of this offering to advance our lead and other product candidates, scale-up our manufacturing processes, build-out our internal manufacturing capacity, expand our intellectual property portfolio and pursue additional research and development activities as set forth under “Use of Proceeds.” However, our use of these proceeds may differ substantially from our current plans. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

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

Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our

common stock. After this offering, we will have outstanding 33,747,819 shares of common stock based on the number of shares outstanding as of February 28, 2018. This includes the shares that we are selling in this offering, which may be resold in the public market immediately without restriction, unless purchased by our affiliates or existing stockholders. The remaining 27,080,819 shares are currently restricted as a result of securities laws or lock-up agreements (which may be waived, with or without notice, by Merrill Lynch, Pierce, Fenner & Smith Incorporated and Cowen and Company, LLC) but will become eligible to be sold at various times beginning 180 days after this offering, 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, after this offering, holders of an aggregate of 24,270,061 shares of our common stock will have rights, subject to specified conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders, 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 also intend to register all shares of common stock that we may issue under our equity compensation plans. Once we register these shares, they can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and the lock-up agreements described in the "Underwriting" section of this prospectus.

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 this offering. 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:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure in this prospectus;
- 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 have taken advantage of reduced reporting burdens in this prospectus. In particular, in this prospectus, we have provided only two years of audited financial statements and have not included all of the executive compensation related information that would be required if we were not an emerging growth company. 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 will 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, and particularly after we are no longer an emerging growth company, we will 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 will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. 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 will be 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, potentially 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. We do not currently have, and may never obtain, research coverage by securities and industry analysts. If no or few securities or industry analysts commence coverage of us, the trading price for our stock would be negatively impacted. In the event we obtain securities or industry analyst coverage, 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 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 restated bylaws, which will become effective upon the closing of this offering 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, which will become effective upon the closing of this offering, 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. See the "Dividend Policy" section of this prospectus for additional information.

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.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements that can involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this prospectus, including statements regarding our future results of operations and financial position, business strategy, prospective products, product approvals, research and development costs, future revenue, timing and likelihood of success, plans and objectives of management for future operations, future results of anticipated products and prospects, plans and objectives of management 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,” “would” or “continue” or the negative of these terms or other similar expressions. The forward-looking statements in this prospectus 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 prospectus and are subject to a number of risks, uncertainties and assumptions described under the sections in this prospectus entitled “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and elsewhere in this prospectus. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. 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. 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.

INDUSTRY AND OTHER DATA

We obtained the industry, market and competitive position data in this prospectus from our own internal estimates and research as well as from industry and general publications and research, surveys and studies conducted by third parties. Industry publications, studies and surveys generally state that they have been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. While we believe that each of these studies and publications is reliable, we have not independently verified market and industry data from third-party sources. While we believe our internal company research as to such matters is reliable and the market definitions are appropriate, neither such research nor these definitions have been verified by any independent source.

USE OF PROCEEDS

We estimate that the net proceeds to us from our issuance and sale of shares of our common stock in this offering will be approximately $90.2 million, assuming an initial public offering price of $15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters' option to purchase additional shares from us is exercised in full, we estimate that our net proceeds will be approximately $104.1 million. Each $1.00 increase (decrease) in the assumed initial public offering price of $15.00 per share would increase (decrease) the net proceeds to us from this offering by approximately $6.2 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. Each increase (decrease) of 1.0 million in the number of shares we are offering would increase (decrease) the net proceeds to us from this offering, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, by $14.0 million, assuming the assumed initial public offering price stays the same.

We anticipate that we will use the net proceeds of this offering for the following purposes:

- approximately $18.0 million to 20.0 million to advance our lead gene therapy product candidate, HMI-102, through preclinical studies and through topline results in a Phase 1/2 clinical trial;
- approximately $8.0 million to 10.0 million to nominate our lead gene editing product candidate and advance this program through preclinical studies;
- approximately $15.0 million to 20.0 million to build-out internal cGMP manufacturing capacity sufficient for clinical supply of product;
- approximately $2.0 million to 3.0 million to expand our intellectual property portfolio to further protect our proprietary AAVHSCs and other aspects of our technology platform; and
- the remainder to fund new and ongoing research and development activities in our CNS, hemoglobinopathy and other programs and for working capital and other general corporate purposes.

This expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. We may also use a portion of the net proceeds to in-license, acquire or invest in additional businesses, technologies, products or assets, although currently we have no specific agreements, commitments or understandings in this regard. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the net proceeds to be received upon the closing of this offering or the amounts that we will actually spend on the uses set forth above. Predicting the cost necessary to develop product candidates can be difficult and we anticipate that we will need additional funds to complete the development of any product candidates we identify. The amounts and timing of our actual expenditures and the extent of clinical development may vary significantly depending on numerous factors, including the progress of our development efforts, the status of and results from pre-clinical studies and any ongoing clinical trials or clinical trials we may commence in the future, as well as any collaborations that we may enter into with third parties for our product candidates and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering.

Based on our planned use of the net proceeds of this offering and our current cash and cash equivalents, we estimate that such funds will be sufficient to enable us to fund our operating expenses and capital expenditure requirements through at least the next two years. We have based this estimate on assumptions that may prove to be incorrect, and we could use our available capital resources sooner than we currently expect. We may satisfy our future cash needs through the sale of equity securities, debt financings, working capital lines of credit, corporate collaborations or license agreements, grant funding, interest income earned on invested cash balances or a combination of one or more of these sources.

Pending our use of the net proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation investments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our capital stock. We intend to retain future earnings, if any, to finance the operation and expansion of our business and do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors after considering our financial condition, results of operations, capital requirements, business prospects and other factors the board of directors deems relevant, and subject to the restrictions contained in any future financing instruments.

CAPITALIZATION

The following table sets forth our cash and cash equivalents and capitalization as of December 31, 2017, as follows:

- on an actual basis;
- on a pro forma basis to reflect:
  - the automatic conversion of all outstanding shares of our preferred stock into 24,168,656 shares of common stock upon the closing of this offering; and
  - the filing and effectiveness of our restated certificate of incorporation which will occur upon the closing of this offering.
- on a pro forma as adjusted basis to give further effect to our issuance and sale of 6,667,000 shares of common stock in this offering at an assumed initial public offering price of $15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

Our capitalization following the closing of this offering will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing. You should read this information in conjunction with our consolidated financial statements and the related notes appearing at the end of this prospectus and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section and other financial information contained in this prospectus.

	As of December 31, 2017 (in thousands, except share data)		
	Actual	Pro Forma	Pro Forma As Adjusted(1)
Cash, cash equivalents and short-term investments	$129,659	$129,659	$ 219,810
Convertible preferred stock (Series A and B), par value $0.0001 per share; 127,234,915 shares authorized, 127,199,705 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	137,762	—	—
Stockholders' (deficit) equity:			
Preferred stock, $0.0001 par value; no shares authorized, issued or outstanding, actual; 10,000,000 shares authorized and no shares issued or outstanding, pro forma and pro forma as adjusted	—	—	—
Common stock, par value $0.0001 per share; 170,000,000 shares authorized, 2,902,109 shares issued and 2,637,011 shares outstanding, actual; 200,000,000 shares authorized, pro forma and pro forma as adjusted; 27,070,765 shares issued and 26,805,667 shares outstanding, pro forma; 33,737,765 shares issued and 33,472,667 shares outstanding, pro forma as adjusted	1	3	3
Additional paid-in capital	799	138,560	228,710
Accumulated other comprehensive loss	(73)	(73)	(73)
Accumulated deficit	(40,181)	(40,181)	(40,181)
Total stockholders' (deficit) equity	(39,454)	98,308	188,459
Total capitalization	$ 98,308	$ 98,308	$ 188,459

(1) Each $1.00 increase (decrease) in the assumed initial public offering price of $15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the pro

forma as adjusted amount of each of cash, cash equivalents and short-term investments, additional paid-in capital, total stockholders' equity (deficit) and total capitalization by $6.2 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, each increase (decrease) of 1.0 million shares in the number of shares offered by us at the assumed initial public offering price per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash, cash equivalents and short-term investments, additional paid-in capital, total stockholders' equity (deficit) and total capitalization by approximately $14.0 million.

The number of shares in the table above includes 265,098 shares of unvested restricted stock subject to repurchase and does not include:

- 1,971,711 shares of common stock issuable upon exercise of stock options outstanding under our 2015 Plan as of December 31, 2017, at a weighted-average exercise price of $3.61 per share; and
- 731,757 shares of common stock issuable upon the exercise of stock options to be granted in connection with this offering under our 2018 Incentive Award Plan, or the 2018 Plan, which will become effective in connection with this offering, to certain of our executive officers, directors and employees, at an exercise price per share equal to the initial public offering price in this offering;
- 2,454,448 additional shares of our common stock reserved for future issuance under our 2018 Plan, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under our 2018 Plan; and
- 353,980 shares of our common stock reserved for future issuance under our 2018 ESPP, which will become effective in connection with this offering, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under the 2018 ESPP.

DILUTION

If you invest in our common stock in this offering, your ownership interest will be immediately diluted to the extent of the difference between the initial public offering price per share of our common stock and the pro forma as adjusted net tangible book value per share of our common stock after this offering.

As of December 31, 2017, we had a historical net tangible book value of $(40.5) million, or $(13.94) per share of common stock. Our historical net tangible book value per share represents total tangible assets less total liabilities and less convertible preferred stock, divided by the number of shares of our common stock outstanding as of December 31, 2017.

Our pro forma net tangible book value as of December 31, 2017 was $97.3 million, or $3.59 per share. Pro forma net tangible book value represents the amount of our total tangible assets less total liabilities, after giving effect to the automatic conversion of all shares of our preferred stock outstanding as of December 31, 2017 into an aggregate of 24,168,656 shares of our common stock in connection with this offering. Pro forma net tangible book value per share represents our pro forma net tangible book value divided by the total number of shares outstanding as of December 31, 2017, after giving effect to the pro forma adjustment described above.

After giving further effect to receipt of the net proceeds from our issuance and the sale of 6,667,000 shares of common stock in this offering at an assumed initial public offering price of $15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of December 31, 2017 would have been approximately $188.5 million, or approximately $5.59 per share. This amount represents an immediate increase in pro forma net tangible book value of $1.99 per share to our existing stockholders and an immediate dilution of approximately $9.41 per share to new investors participating in this offering. We determine dilution by subtracting the pro forma as adjusted net tangible book value per share after this offering from the amount of cash that a new investor paid for a share of common stock. The following table illustrates this dilution:

Assumed initial public offering price per share		$15.00
Historical net tangible book value per share as of December 31, 2017	$(13.94)	
Increase per share attributable to the conversion of our preferred stock	17.53	
Pro forma net tangible book value per share as of December 31, 2017	3.59	
Increase per share attributable to this offering	1.99	
Pro forma as adjusted net tangible book value per share after this offering		5.59
Dilution per share to new investors in this offering		$ 9.41

Each $1.00 increase (decrease) in the assumed initial public offering price of $15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted net tangible book value per share after this offering by $0.18, and dilution in pro forma net tangible book value per share to new investors by $0.82, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Each increase (decrease) of 1.0 million shares in the number of shares offered by us would increase (decrease) our pro forma as adjusted net tangible book value per share after this offering by $0.24 per share and decrease (increase) the dilution to new investors by $0.24 per share, assuming that the assumed initial public offering price remains the same, and after deducting the estimated underwriting discounts and commissions and the estimated offering expenses payable by us.

If the underwriters exercise their option to purchase additional shares of our common stock in full, the pro forma as adjusted net tangible book value after this offering would be $5.83 per share, the increase in pro

forma net tangible book value per share would be $2.23 and the dilution per share to new investors would be $9.17 per share, in each case assuming an initial public offering price of $15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, and after deducting the estimated underwriting discounts and commissions and the estimated offering expenses payable by us.

The following table summarizes the pro forma as adjusted basis described above, as of December 31, 2017, the differences between the number of shares purchased from us, the total consideration paid to us in cash and the average price per share that existing stockholders and new investors paid. The calculation below is based on an assumed initial public offering price of $15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, before deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

	Shares Purchased		Total Consideration		Average Price Per Share
	Number	Percent	Amount	Percent	
Existing stockholders(1)	26,805,667	80.1%	$137,361,824	57.9%	$ 5.12
New investors	6,667,000	19.9	100,005,000	42.1	$ 15.00
Total	33,472,667	100.0%	$237,366,824	100.0%	

(1) Certain of our existing stockholders, including entities affiliated with certain of our directors and director nominee, have indicated an interest in purchasing an aggregate of approximately $50.0 million in shares of our common stock in this offering at the initial public offering price. The presentation in this table regarding ownership by existing stockholders does not give effect to any purchases in this offering by such stockholders.

A $1.00 increase or decrease in the assumed initial public offering price of $15.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase or decrease the total consideration paid by new investors by $6.7 million and, in the case of an increase, would increase the percentage of total consideration paid by new investors by 1.6 percentage points and, in the case of a decrease, would decrease the percentage of total consideration paid by new investors by 1.7 percentage points, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same. An increase or decrease of 1.0 million shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase or decrease the total consideration paid by new investors by $15.0 million and, in the case of an increase, would increase the percentage of total consideration paid by new investors by 3.4 percentage points and, in the case of a decrease, would decrease the percentage of total consideration paid by new investors by 3.9 percentage points, assuming no change in the assumed initial public offering price.

The foregoing tables and calculations are based on the number of shares of our common stock legally outstanding as of December 31, 2017 (which included 265,098 shares of unvested restricted stock subject to repurchase), after giving effect to the automatic conversion of all outstanding shares of our preferred stock into common stock in connection with this offering, and exclude:

- 1,971,711 shares of common stock issuable upon exercise of stock options outstanding under our 2015 Plan as of December 31, 2017, at a weighted-average exercise price of $3.61 per share;
- 731,757 shares of common stock issuable upon the exercise of stock options to be granted in connection with this offering under our 2018 Incentive Award Plan, or the 2018 Plan, which will become effective in connection with this offering, to certain of our executive officers, directors and employees, at an exercise price per share equal to the initial public offering price in this offering;
- 2,454,448 additional shares of our common stock reserved for future issuance under our 2018 Plan, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under our 2018 Plan; and

- 353,980 shares of our common stock reserved for future issuance under our 2018 ESPP, which will become effective in connection with this offering, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under the 2018 ESPP.

To the extent any of these outstanding options is exercised, there will be further dilution to new investors. If all of such outstanding options had been exercised as of December 31, 2017, the pro forma as adjusted net tangible book value per share after this offering would be $5.88, and total dilution per share to new investors would be $9.12.

If the underwriters exercise their option to purchase additional shares of our common stock in full:

- the percentage of shares of common stock held by existing stockholders will decrease to approximately 77.8% of the total number of shares of our common stock outstanding after this offering; and

- the number of shares held by new investors will increase to 7,667,050, or approximately 22.2% of the total number of shares of our common stock outstanding after this offering.

SELECTED CONSOLIDATED FINANCIAL DATA

You should read the following selected consolidated financial data together with our consolidated financial statements and the related notes appearing at the end of this prospectus and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this prospectus. We have derived the consolidated statement of operations data for the years ended December 31, 2017 and 2016 and the consolidated balance sheet data as of December 31, 2017 and 2016 from our audited consolidated financial statements appearing at the end of this prospectus. Our historical results are not necessarily indicative of the results that should be expected in any future period.

(in thousands, except per share data)	Year Ended December 31, 2017	2016
Consolidated Statements of Operations Data:		
Operating expenses:		
Research and development	$ 21,378	$ 5,695
General and administrative	8,279	4,305
Total operating expenses	29,657	10,000
Loss from operations	(29,657)	(10,000)
Other income (expense):		
Change in fair market value of convertible preferred stock tranche liability	(876)	1,929
Interest income	542	24
Total other income (expense)	(334)	1,953
Net loss and net loss attributable to common stockholders-basic and diluted	$ (29,991)	$ (8,047)
Net loss per share attributable to common stockholders- basic and diluted	$ (12.10)	$ (4.23)
Weighted average common shares outstanding-basic and diluted(1)	2,479,432	1,900,531
Pro forma net loss per share attributable to common stockholders-basic and diluted (unaudited)(1)	$ (1.57)	
Pro forma weighted average common shares of common stock outstanding-basic and diluted (unaudited)(1)	18,602,429	

(1) See Note 14 to our consolidated financial statements included elsewhere in this prospectus for an explanation of the method used to calculate the historical and pro forma basic and diluted net loss per common share and the weighted average number of shares used in the computation of the per share amounts.

(in thousands)	As of December 31, 2017	As of December 31, 2016
Consolidated Balance Sheet Data:		
Cash, cash equivalents and short-term investments	$ 129,659	$ 11,392
Total assets	137,530	14,219
Total liabilities	39,222	6,719
Total stockholders' (deficit) equity	(39,454)	(9,892)
Total liabilities, convertible preferred stock and stockholders' deficit	137,530	14,219

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of financial condition and operating results together with the section captioned "Selected Consolidated Financial Data" and our financial statements and the related notes appearing at the end of this prospectus. This discussion contains forward-looking statements that involve risks and uncertainties. As a result of many factors, such as those set forth in the section of the prospectus captioned "Risk Factors" and elsewhere in this prospectus, our actual results may differ materially from those anticipated in these forward-looking statements. For convenience of presentation some of the numbers have been rounded in the text below.

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 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, 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 PKU patients 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 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 PKU in 2018. We are a preclinical company and have not yet submitted an investigational new drug application 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 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 recently entered into a collaboration with Novartis to develop new genetic medicines using our HR-based gene correction 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 $137.0 million through preferred stock financings, including investments from 5AM Ventures, ARCH Venture Partners, Deerfield, Temasek, FMR, Novartis, Rock Springs Capital, VIVO, HBM Partners, Maverick and Vida, or affiliates thereof, in addition to others. 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, 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 with proceeds from the sales of our preferred stock. Through December 31, 2017, we raised approximately $137 million in gross proceeds from the sale of Series A and Series B convertible preferred stock, and we received an up-front payment of $35 million from Novartis, 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. Since inception, we have incurred significant operating losses. Our net losses for the years ended December 31, 2017 and 2016 were $30.0 million and $8.0 million, respectively. As of December 31, 2017, we had an accumulated deficit of $40.2 million. We do not expect to generate revenue from sales of any products for years, if at all.

Our total operating expenses were $29.7 million and $10.0 million for the years ended December 31, 2017 and 2016, 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 initiate 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 trials, 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 associated costs including the management of our intellectual property portfolio. In addition, upon the closing of this offering, 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 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 resources, not including the proceeds from this offering, will enable us to fund our projected operating expenses and capital expenditures for at least the next 12 months. We expect that these cash resources, together with anticipated net proceeds from the offering, will enable us to fund our current and planned 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 product candidates and any future product candidates, our platform and technology and because the extent to which we may enter into collaborations with third parties for development of any of our product candidates is unknown, we are unable to estimate the amounts of increased capital outlays and operating expenses 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 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 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, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your 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 your ownership interests.

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 did not recognize any revenue from our collaboration with Novartis in 2017. We recorded the amounts received from Novartis as deferred revenue (see Note 16 to our Financial Statements 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:

	Year Ended December 31,		
(in thousands)	2017	2016	Decrease (Increase)
HMI-102 external development costs	$ 3,964	$ 849	$ (3,115)
Employee-related costs	5,518	2,299	(3,219)
Other research and development costs	11,896	2,547	(9,349)
Total research and development expenses	$21,378	$5,695	$(15,683)

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 additional clinical trials of HMI-102, 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 the safety and efficacy, 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, 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 interest income earned on our cash, cash equivalents and short-term investments. Our interest income has increased due to higher investment balances in 2017.

Income Taxes

Since our inception in 2015, we have not recorded any U.S. federal or state income tax benefits for the net losses we have incurred in any year or for our earned research and development tax credits, due to our uncertainty of realizing a benefit from those items. As of December 31, 2017, we had federal and state net

operating loss carryforwards of $33.4 million and $34.2 million, respectively, each of which begin to expire in 2036. As of December 31, 2017, we also had federal and state research and development tax credit carryforwards of $1.1 million and $0.8 million, respectively, each of which begin to expire in 2036.

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. During the years ended December 31, 2017 and 2016, we recognized total other income (expense) of $(876,000) and $1,929,000, respectively, related to changes in the fair value of the convertible preferred stock tranche liability.

Critical Accounting Policies and Use of Estimates

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

While our significant accounting policies are described in more detail in the notes to our financial statements appearing at the end of this prospectus, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our financial statements.

Revenue Recognition—We recognize revenue when all of the following criteria are met: persuasive evidence of an arrangement exists; delivery has occurred or services have been rendered; our price to the buyer is fixed or determinable; and collectability is reasonably assured. We record 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, we entered into a collaboration and license agreement for research, development, manufacturing and commercialization of products using our gene editing technology for the treatment of certain diseases (see Note 16 to our consolidated financial statements included elsewhere in this prospectus). Consideration we 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 Agreement contain multiple deliverables, including licenses, research and development activities, participation on steering committees and manufacturing activities. We evaluate the

activities in our collaboration agreements to determine if the activities are consistent with a typical vendor-customer relationship, and if so, account for them in accordance with Accounting Standards Codification, or ASC, Topic 605-25, *Revenue Recognition—Multiple Element Arrangements*. If not, we evaluate other applicable guidance.

We evaluate 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 us 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 our control. In assessing whether an item has standalone value, we consider 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, we consider 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. We determine the estimated selling price for units of accounting within each arrangement using vendor-specific objective evidence, or VSOE, if available; third-party evidence, or TPE, of selling price if VSOE is not available; or best estimate of selling price, or BESP, if neither VSOE nor TPE is available. We typically use 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, we consider applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs.

We recognize arrangement consideration allocated to each unit of accounting when all of the revenue recognition criteria are satisfied for that particular unit of accounting. We recognize 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 we recognize revenue on a straight-line basis over the period we are expected to complete our 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 we recognize 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 we expect to complete our 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 we expect to complete our 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 us 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. We 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 our product candidates have been approved and, therefore, we have not earned any royalty revenue from product sales.

In the event that the agreement were to be terminated and we had no further performance obligations at that time, we 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.

Accrued Research and Development Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing open contract and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated costs incurred for the services when we have not yet been invoiced or otherwise notified of the actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advanced payments. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. Examples of estimated accrued research and development expenses include fees paid to:

- CROs and other third parties in connection with performing research activities on our behalf and conducting preclinical studies on our behalf and CMOs in connection with producing product for our preclinical studies;
- vendors in connection with preclinical development activities; and
- vendors related to product manufacturing and development and distribution of preclinical supplies.

We base our expenses related to preclinical studies on our estimates of the services received and efforts expended pursuant to quotes and contracts with CROs that conduct and manage preclinical studies and clinical trials and CMOs that manufacture product for our research and development activities on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. In accruing fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or amount of prepaid expense accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in us reporting amounts that are too high or too low in any particular period. To date, we have not made any material adjustments to our prior estimates of accrued research and development expenses.

Fair Value Measurements

Tranche Rights

The Series A preferred stock purchase agreement that we entered into provided the investors with the right, upon achievement of certain milestones, to participate in subsequent offerings of Series A preferred stock, which we refer to as convertible preferred stock tranche rights. The tranche rights meet the definition of a freestanding financial instrument, as the tranche rights are legally detachable and separately exercisable from the Series A preferred stock. Since the Series A preferred stock is redeemable upon certain change in control events that are outside of our control, the tranche rights are classified as an asset or liability and were initially recorded at fair value and then marked to market at each subsequent reporting period, through the settlement of the tranche rights.

We determine fair value utilizing the concept of "Fair Value" from ASC Topic 820, *Fair Value Measurement*, or ASC 820, that states that any fair value measurement requires that the reporting entity to determine the valuation technique(s) appropriate for the measurement, considering the availability of data with which to develop inputs that represent the assumptions that market participants would use in pricing the asset or liability and the level in the fair value hierarchy within which the inputs are categorized.

The estimated fair value of the tranche rights was determined using an income approach, specifically the discounted cash flow method, that considered the probability and timing of closing a tranche, the estimated future value of the Series A preferred stock to be issued at each closing, and the amount of the investment required at each closing. Future values were converted to present value using a discount rate appropriate for probability-adjusted cash flows. Upon the settlement of each tranche, the fair value of the tranche rights associated with that tranche was reclassified to Series A preferred stock at its then fair value and thereafter was no longer re-measured.

Stock-Based Compensation

We measure stock options and other stock-based awards granted to employees, directors, consultants or advisors of the company or its affiliates based on their fair value on the date of the grant and recognize compensation expense of those awards, net of estimated forfeitures, over the requisite service period, which is generally the vesting period of the respective award. We apply the straight-line method of expense recognition to all awards with only service-based vesting conditions and apply the graded-vesting method to all awards with performance-based vesting conditions or to awards with both service-based and performance-based vesting conditions.

For stock-based awards granted to non-employees, compensation expense is recognized over the period during which services are rendered by such non-employees until completed. At the end of each financial reporting period prior to the completion of the service, the fair value of these awards is re-measured using the then-current fair value of our common stock and updated assumption inputs in the Black-Scholes option-pricing model.

We estimate the fair value of each stock option grant on the date of grant using the Black-Scholes option-pricing model, which uses as inputs the fair value of our common stock and assumptions we make for the volatility of our common stock, the expected term of our stock options, the risk-free interest rate for a period that approximates the expected term of our stock options and our expected dividend yield.

Determination of Fair Value of Common Stock

As there has been no public market for our common stock to date, the estimated fair value of our common stock has been determined by our board of directors as of the date of each option grant, with input from

management, considering our most recently available third-party valuations of common stock and our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant. Third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. Our common stock valuations were prepared using a market approach, specifically the guideline transaction method. To derive the total equity value under the guideline transaction method, recent mergers and acquisitions within the biotechnology and pharmaceutical industries were compared for similar stage companies. An option pricing allocation method, or OPM, was selected to allocate the total equity value. The OPM treats common stock and preferred stock as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, the common stock has value only if the funds available for distribution to stockholders exceeded the value of the preferred stock liquidation preference at the time of the liquidity event, such as a strategic sale or a merger. These third-party valuations resulted in a valuation of our common stock of $6.63 and $0.63 per share as of December 31, 2017 and 2016, respectively.

In addition to considering the results of these third-party valuations, our board of directors considered various objective and subjective factors to determine the fair value of our common stock as of each grant date, including:

- the prices at which we sold shares of preferred stock and the superior rights and preferences of the preferred stock relative to our common stock at the time of each grant;
- the progress of our research and development programs, including the status and results of preclinical studies for our product candidates;
- our stage of development and commercialization and our business strategy;
- external market conditions affecting the biopharmaceutical industry and trends within the biopharmaceutical industry;
- our financial position, including cash on hand, and our historical and forecasted performance and operating results;
- the lack of an active public market for our common stock and our preferred stock;
- the likelihood of achieving a liquidity event, such as an initial public offering, or IPO, or sale of our company in light of prevailing market conditions; and
- the analysis of IPOs and the market performance of similar companies in the biopharmaceutical industry.

The assumptions underlying these valuations represented management's best estimate, which involved inherent uncertainties and the application of management's judgment. As a result, if we had used different assumptions or estimates, the fair value of our common stock and our stock-based compensation expense could have been materially different.

Emerging Growth Company Status

The Jumpstart Our Business Startups Act of 2012, or the JOBS Act, permits an "emerging growth company," which we are, to take advantage of an extended transition period to comply with new or revised

accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have elected to take advantage of this extended transition period.

Recent Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, No. 2014-09, *Revenue (Topic 606): Revenue from Contracts with Customers, or 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 us beginning on January 1, 2019. We are in the process of evaluating the impact of the adoption of ASU No. 2014-09 on our consolidated financial statements. We will continue to assess the potential impact that Topic 606 may have on our financial position and results of operations as it relates to our collaboration with Novartis (see Note 16 to our consolidated financial statements included elsewhere in this prospectus). We expect 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 us beginning January 1, 2020 with early application permitted. The new standard provides for a modified retrospective application. We are in the process of evaluating the impact of the adoption of ASU No. 2016-02 on our 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 to employees. ASU No. 2016-09 is effective for us beginning January 1, 2018, with early application permitted. 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. We are in the process of evaluating the impact of the adoption of ASU No. 2016-09 on our 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 us beginning January 1, 2019 , with early application permitted. The new standard must be applied retrospectively to all periods presented. We are in the process of evaluating the impact that this standard will have on our consolidated financial statements.

Results of Operations

Comparison of Years Ended December 31, 2017 and 2016

The following table summarizes our results of operations for the years ended December 31, 2017 and 2016, respectively:

(in thousands)	Year Ended December 31, 2017	2016	Decrease (Increase)
Operating expenses:			
Research and development	$ 21,378	$ 5,695	$(15,683)
General and administrative	8,279	4,305	(3,974)
Total operating expenses	29,657	10,000	(19,657)
Loss from operations	(29,657)	(10,000)	(19,657)
Other income (expense):			
Change in fair value of convertible preferred stock tranche liability	(876)	1,929	(2,805)
Interest income	542	24	518
Total other income (expense)	(334)	1,953	(2,287)
Net loss	$(29,991)	$ (8,047)	$(21,944)

Research and Development Expenses

(in thousands)	Year Ended December 31, 2017	2016	Decrease (Increase)
HMI-102 external development costs	$ 3,964	$ 849	$ (3,115)
Employee-related costs	5,518	2,299	(3,219)
Other research and development costs	11,896	2,547	(9,349)
Total research and development expenses	$21,378	$5,695	$(15,683)

Research and development expenses for the year ended December 31, 2017 were $21.4 million, compared to $5.7 million for the year ended December 31, 2016. The increase of $15.7 million was primarily due to an increase of $3.1 million in direct research expenses related to our HMI-102 program, a $4.5 million payment to COH for sublicensing fees which was expensed to research and development and the majority of the remaining increase was due to an increase in employee headcount to support technology platform and manufacturing capabilities.

General and Administrative Expenses

General and administrative expenses were $8.3 million for the year ended December 31, 2017, compared to $4.3 million for the year ended December 31, 2016. The increase of $4.0 million was primarily due to $1.9 million in increased employee headcount, $0.9 million in occupancy costs and professional fees of $0.6 million as a result of ongoing business activities.

Interest Income

Interest income was $0.5 million for the year ended December 31, 2017 compared to less than $0.1 million for the year ended December 31, 2016. The increase was the result of interest income generated on our higher average cash, cash equivalent and short-term investment balances for the year ended December 31, 2017 compared to the year ended December 31, 2016, due to the receipt of $20.5 million in proceeds from our Series A preferred stock financing in February 2017, receipt of $83.5 million in proceeds from our Series B preferred stock financing in July 2017 and 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.

Change in Fair Value of Tranche Liability

For the year ended December 31, 2017, the changes in fair value of our preferred stock tranche liability resulted in a $0.9 million loss compared to a $1.9 million gain for the year ended December 31, 2016. The derivative loss in 2017 was due to the re-measurement and subsequent de-recognition of the tranche liability upon achievement of the development milestone in February 2017 and the issuance of shares of our Series A preferred stock. For the year ended December 31, 2016, the gain was due to the increase in the fair value of the underlying preferred shares on a period-over-period basis.

Liquidity and Capital Resources

Since our inception, we have incurred significant operating losses. We expect to incur significant expenses and operating losses for the foreseeable future as we advance the preclinical and clinical development of our product candidates. We expect that our research and development and general and administrative costs 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 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 preferred stock and through an up-front payment from a collaboration partner. Since we were incorporated, we have raised a total of $137.0 million in gross proceeds from the sale of shares of our Series A and Series B convertible preferred stock and a one-time up-front payment of $35.0 million from a collaboration partner.

Cash Flows

Our cash, cash equivalents and short-term investments totaled $129.7 million and $11.4 million as of December 31, 2017 and 2016, respectively. We had no indebtedness as of December 31, 2017 and 2016.

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

	Year Ended December 31,	
(in thousands)	**2017**	**2016**
Net cash provided by (used in) operating activities	$ 6,479	$ (8,484)
Net cash used in investing activities	(81,526)	(2,265)
Net cash provided by financing activities	115,230	378
Increase (decrease) in cash and cash equivalents	$ 40,183	$(10,371)

Cash Flows for the year ended December 31, 2017

Operating Activities

Net cash provided by operating activities for the year ended December 31, 2017 was $6.5 million, consisting of a $35.0 million up-front payment received from a collaboration partner and recorded as deferred revenue, net of $1.7 million allocated to convertible preferred stock and changes in our operating assets and liabilities of $1.3 million. This was partially offset by our net losses of $30.0 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 and incurred general and administrative expenses. In addition, we had non-cash charges totaling $1.8 million including the change in fair value of a convertible preferred stock tranche liability, depreciation and stock-based compensation expense offset by accretion on short-term investments. Net cash provided by changes in our operating assets and liabilities was due to increases of $33.4 million in deferred revenue, $1.7 million in accounts payable and $0.9 million in accrued expenses and other liabilities, partially offset by a decrease of $1.5 million in prepaid expenses and other current assets.

Investing Activities

Net cash used in investing activities for the year ended December 31, 2017 was $81.5 million, attributable to the purchases of short-term investments of $78.1 million, the purchases of property and equipment of $2.0 million, and the change in restricted cash of $1.5 million related to a new facility lease.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2017 was $115.2 million, consisting of the net proceeds from the second tranche of the Series A convertible preferred stock financing of $20.5 million and the net proceeds from the issuance of Series B convertible preferred stock of $94.8 million, net of issuance costs.

Cash Flows for the year ended December 31, 2016

Operating Activities

Net cash used in operating activities for the year ended December 31, 2016 was $8.5 million, consisting of our net loss of $8.0 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 and incurred general and administrative expenses. In addition, we had a gain of $1.9 million on the change in fair value of a convertible preferred stock tranche liability, offset by non-cash charges of $0.4 million for depreciation and stock-based compensation expense. Net cash used in operating activities were also impacted by $0.9 million in changes in operating assets and liabilities including $0.5 million in accounts payable, $0.7 million in accrued expenses and other liabilities and $0.2 million in deferred rent, partially offset by a change of $0.5 million in prepaid expenses and other current assets.

Investing Activities

Net cash used in investing activities for the year ended December 31, 2016 was $2.3 million, attributable to purchases of property and equipment of $2.0 million and the change in restricted cash of $0.3 million.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2016 was $0.4 million in proceeds from the issuance of restricted common stock relating to the exercise of stock options by employees.

Funding Requirements

Our operating expenses have increased substantially in 2017 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, upon the closing of this offering, we expect to incur additional costs associated with operating as a public company.

Specifically, our expenses 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;
- 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 the anticipated net proceeds from this offering, together with our existing cash on hand 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 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 contract 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, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity

financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, 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

The following is a summary of our significant contractual obligations as of December 31, 2017:

		Payments Due by Period			
Contractual Obligation (in thousands)	**Total**	**Less Than 1 Year**	**More Than 1 Year and Less Than 3**	**More Than 3 years and Less Than 5**	**More Than 5 years**
Operating lease obligation (1)	$28,604	$ 1,546	$ 7,255	$ 6,625	$ 13,178
License obligations (2)	$ 790	$ 45	$ 90	$ 90	$ 565
Sponsored research agreement (3)	$ 791	$ 672	$ 119	$ —	$ —

(1) Represents future minimum lease payments under our operating leases for office and lab space in Bedford, Massachusetts that expire in October 2021 and February 2027.

(2) Represents minimum annual license fees under our license agreements with Caltech and COH. These amounts do not include any potential contingent payments upon the achievement by us of specified clinical, regulatory and commercial events, as applicable, or patent prosecution or royalty payments we may be required to make under license agreements we have entered into with various universities or collaboration partners pursuant to which we have in-licensed certain intellectual property, including our license agreements with Caltech and COH. We have excluded these potential payments in the contractual obligations table because the timing and likelihood of these contingent payments are not currently known and would be difficult to predict or estimate. See “Business—Strategic Collaborations” for additional information about these license agreements, including with respect to potential payments thereunder.

(3) Represents future minimum payments under our sponsored research agreement with COH.

Off-Balance Sheet Arrangements

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

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 $129.7 million, or 94.3% of our total assets at December 31, 2017, and $11.4 million, or 80.1% of our total assets at December 31, 2016. Interest income earned on these assets was $543,000 in 2017 and $24,000 in 2016. Our interest income is sensitive to changes in the general level of interest rates, primarily U.S. interest rates. At December 31, 2017, 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 December 31, 2017 and 2016.

BUSINESS

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 DNA repair process of homologous recombination, or HR. We believe our HR-driven gene editing approach will allow us to efficiently perform gene correction 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 PKU patients 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 efficiencies that are significantly greater than both nuclease-based and other adeno-associated virus, or AAV, based approaches. We expect to nominate a lead gene editing product candidate for the treatment of PKU in 2018. We are a preclinical company and have not yet submitted an investigational new drug application, or IND, 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 in California, 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 Current Good Manufacturing Practices, or cGMP, manufacturing facility to support our clinical development programs. We recently entered into a collaboration with Novartis Institutes for Biomedical Research, Inc., or Novartis, to develop new genetic medicines using our HR-based gene correction 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 $137 million through preferred stock financings, including investments from 5AM Ventures, ARCH Venture Partners, Deerfield, Temasek, Fidelity Management & Research, or FMR, Novartis, Rock Springs Capital, VIVO HBM Partners, Maverick and Vida, or affiliates thereof, in addition to others. 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.

Our Opportunity in Genetic Medicines

We are currently focused on monogenic diseases where the genetic abnormality is known to occur in a single diseased gene. The majority of monogenic diseases harbor thousands of individual mutations within the

diseased gene, each resulting in a loss of function. Replacing an entire diseased gene with a whole functional gene is the optimal therapeutic approach for addressing these monogenic disorders. This can be accomplished either through a method of gene therapy called gene transfer in slowly or non-dividing cells, or through a method of gene editing called gene correction in rapidly dividing cells.

The current focus of most nuclease-based gene editing methods is gene knockout, or knocking out a diseased gene to prevent the expression of an undesired protein. Since gene knockout does not result in a fully-corrected gene, this method can only potentially address the minority of monogenic diseases where a diseased protein is overexpressed. In addition to our knockout capabilities, our HR-driven gene correction method allows us to potentially address the significant majority of monogenic diseases by replacing an entire diseased gene with a whole functional gene or repairing a single mutation to fully correct the defect. Gene therapy, on the other hand, seeks to introduce a functional copy of a defective gene or gene sequence into a patient's own cells, but not incorporate such copy into the patient's genome. This method, called gene transfer, results in the expression of the therapeutic protein of interest without changing the genome.

DNA Repair Pathways

Human cells harbor two primary independent pathways to maintain the integrity of DNA: homologous recombination, or HR, and non-homologous end joining, or NHEJ, which are described below:

- ***HR*** is a process in which cells repair DNA through highly precise incorporation of correct DNA sequences that are homologous, or matching, to the site of damage. HR has evolved to repair DNA with high fidelity and avoids the introduction of unwanted mutations at the site of correction. In the late 1990's, researchers discovered that certain adeno-associated virus, or AAV, vectors deliver gene sequences into the genome specifically through the HR process. These AAV vectors delivered long single strands of homologous DNA to specific regions in the genome and induced the HR pathway, but their low efficiency of approximately 1% limited their use as a viable option for *in vivo* therapeutics.

- ***NHEJ*** is a less selective, error-prone process that rapidly joins the ends of broken DNA resulting in a high frequency of insertions or deletions at the break site. The discovery of nuclease-based gene editing technologies provided researchers with novel tools to specifically introduce DNA breaks into the genome. The most common repair pathway following a DNA break is NHEJ. Despite high potential for error, the majority of nuclease-based gene editing companies primarily utilize the NHEJ pathway.

While the introduction of nuclease-based gene editing technologies provides the capability to initiate DNA repair pathways in the cell and further increase the frequency of targeted gene modification, we believe its major limitation is the preferential utilization of the error prone NHEJ pathway instead of the HR pathway. Because of this preference, the greatest utility of nuclease-based gene editing technologies may lie in their ability to knockout genes rather than the replacement of an entire diseased gene in the genome with a whole functional copy. Furthermore, the use of nuclease-based gene editing technologies for insertion of a corrective sequence requires the separate delivery of both nuclease and homologous DNA template, and carries the risk of unwanted mutations from NHEJ including insertions and deletions or opposite orientation insertion of the template DNA.

We believe the unique characteristics of our genetic medicines platform will allow us to focus on the HR pathway, enabling precise nuclease-free gene correction and a broader set of disease targets with improved efficiency.

Our Approach

Our unique genetic medicines platform is designed to provide us the flexibility to choose the best suited method from either gene correction or gene transfer for each disease we pursue, based on such factors as the

targeted disease biology, the biodistribution of our AAVHSCs to key tissues, and the rate of cell division the tissues exhibit. Our product development strategy is to continue to develop in parallel both gene therapy and gene editing modalities, while initially leveraging the experience from our gene transfer modality to further advance our gene correction modality. Refer to Figure 1 below for a graphical depiction of our platform.

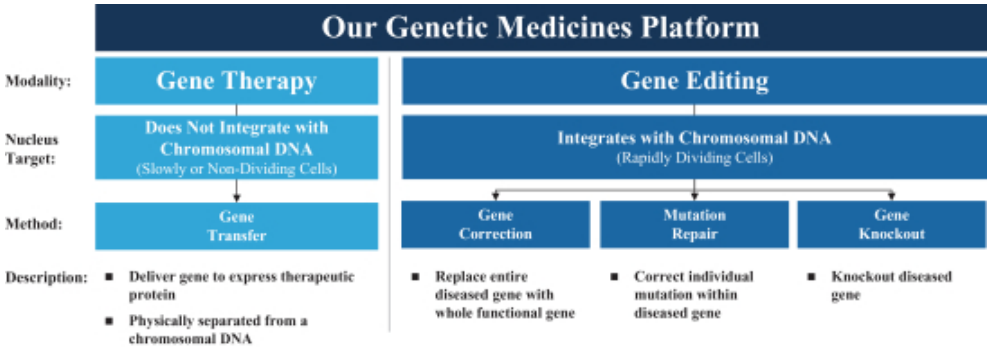


Figure 1. Our Genetic Medicines Platform.

While others are working on identifying and testing ways to mitigate the inherent risk in working with nucleases, our approach avoids the use of nucleases entirely. By targeting the HR pathway, our proprietary AAVHSCs mitigate the risks of nuclease-based technologies and have the potential to overcome other AAV vector limitations by combining the precision and high fidelity of HR with highly efficient *in vivo* gene correction, which we believe is capable of providing potential cures for a wide range of rare genetic diseases.

Our novel AAVHSCs are packaged with either a gene editing or traditional gene therapy construct. The gene editing construct includes lengthy guide sequences, or homology arms, which are designed to enable the specific alignment to the desired genomic location and then, through the natural process of HR, correction of the diseased gene in the genome by replacement with a whole functional copy. Our gene therapy construct includes a functional copy of the gene and a promotor sequence that is designed to enable the gene to be turned on in the cell and ultimately transcribed to express the therapeutic protein of interest without integrating into the genome. Refer to Figure 2 below for a graphical depiction of how our AAVHSCs enable each therapeutic modality.

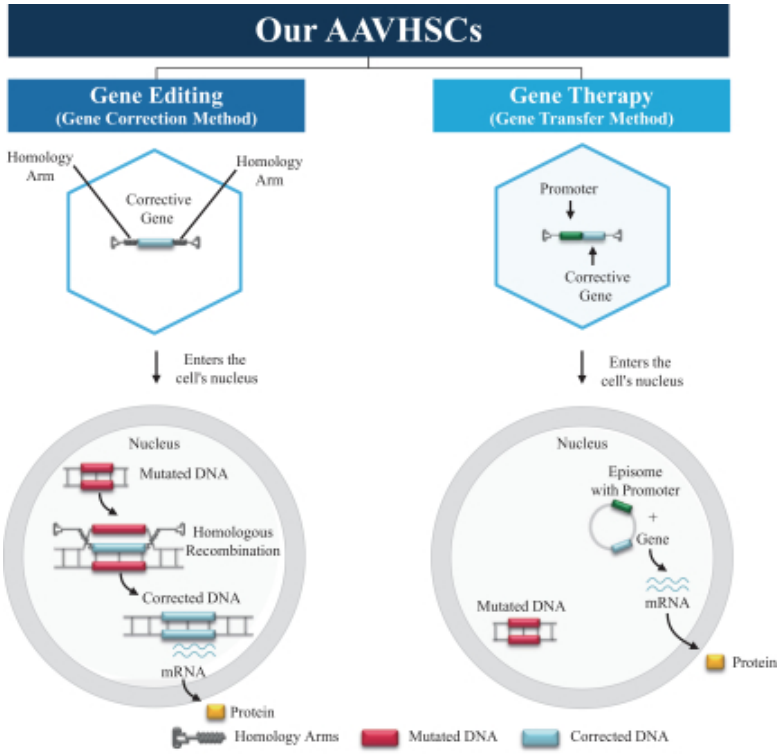


Figure 2. How Our AAVHSCs Enable Each Therapeutic Modality.

We believe our approach has several key advantages that include:

- ***Our proprietary platform AAVHSCs enable both gene therapy and gene editing modalities.*** Our platform provides us the flexibility to deliver genetic medicines through the best suited modality from either gene therapy or gene editing for each disease we pursue, based on such factors as the targeted disease biology, the biodistribution of our AAVHSCs to key tissues, and the rate of cell division the tissues exhibit.

- ***Ability to perform nuclease-free gene editing mediated by HR with high gene correction efficiency.*** Our suite of 15 novel AAVHSCs are designed to enable us to take advantage of the precise and high fidelity process of HR-directed gene insertion for nuclease-free gene editing while achieving gene correction efficiencies that are in therapeutic ranges and significantly higher than both nuclease-based and other AAV-based approaches. While nuclease-based gene editing technologies have achieved high gene knockout efficiencies in preclinical studies, they have shown limited published evidence of gene correction efficiencies to date.

- ***Ability to introduce an entire gene into the genome or the precise repair of individual mutated nucleotides in addition to gene knockout.*** Our HR-based gene editing approach provides the flexibility to introduce an entire copy of a functional gene into the genome in addition to repairing single mutations or knocking out entire genes, thus allowing us to potentially address the significant majority of monogenic diseases.

- ***High precision and lack of unwanted off-target or on-target DNA modifications.*** Our gene editing approach leverages HR, which makes DNA repairs with high fidelity, and enables us to precisely

perform gene correction without unwanted off- and on-target modifications. Furthermore, we are able to directly measure and confirm those modifications throughout the entire genome to ensure only the intended changes are made.

- ***Ability to target multiple tissues.*** In preclinical studies, intravenous administration of our suite of AAVHSCs have demonstrated ability to target a wide variety of tissues including the liver, CNS, bone marrow, eye, lung, and muscle, enabling us to potentially address a broad range of monogenic diseases.

- **In vivo *administration with a single component delivery system.*** Our platform is designed to perform gene editing at high efficiency without the use of a nuclease, enabling us to deliver genetic medicines *in vivo* using a single vector system that contains everything required to edit DNA. These characteristics simplify the manufacturing and delivery of our therapeutics relative to existing nuclease-based gene editing approaches.

- ***Ability to target a broad range of patients given low frequency of preexisting neutralizing antibodies.*** We believe our AAVHSCs can target a broad range of patient populations given the low prevalence of preexisting neutralizing antibodies relative to other AAV vectors.

Our Pipeline Strategy

We believe our genetic medicines platform can be applied broadly to treat and potentially cure a wide range of genetic diseases, and we have carefully designed and prioritized our pipeline strategy to maximize this opportunity. We are initially pursuing monogenic diseases where we know exactly what we are seeking to correct and exactly what gene to insert into patients' cells, thus mitigating the uncertainty of the disease biology. We are prioritizing monogenic diseases with significant unmet medical needs, validated regulatory pathways and significant commercial opportunities. We are currently focused on developing product candidates to treat monogenic diseases in the liver, CNS, bone marrow, lung and the eye, given that our AAVHSCs naturally show a high degree of tropism or ability to preferentially target cells in these organs and organ systems. These tissues are affected in many rare genetic diseases.

Our initial focus areas include developing product candidates for intracellular, inborn errors of metabolism and other genetic conditions that are especially well suited to correction by our gene editing or gene therapy methods. In slow- or non-dividing cells (*e.g.*, CNS and adult liver cells), gene therapy can potentially be curative, while rapidly dividing cells (*e.g.*, hematopoietic CD34+ cells and pediatric liver cells) require a gene editing approach to provide a permanent correction in the genome that can be replicated with each cell division. We are purposefully deploying our proprietary AAVHSCs in certain indications first with a gene therapy approach followed by a gene editing approach, in order to maximize the likelihood of translating our platform into widespread clinical and commercial success.

We are advancing into the clinic with our first and lead product candidate, HMI-102, for the treatment of PKU, a rare, inherited metabolic disorder that causes a buildup of the amino acid phenylalanine, or Phe, in the brain. Elevated Phe levels in children lead to impaired brain development, severe intellectual disability and behavior problems with a high frequency of seizures. To date, no treatment addresses the core genetic defect in PKU. The current standard of care consists of a highly restrictive diet, which is not always effective in normalizing the levels of serum Phe and its important metabolite, tyrosine. Low adherence to the diet leads to significant cognitive and behavioral problems, such as impairments in executive function, including planning, problem solving, information processing, and ability to focus. Kuvan, the only FDA approved therapy for PKU in conjunction with dietary supplementation, provides limited or no benefit to approximately 90% of patients with PKU. PKU has an easily measurable and translatable biomarker (blood Phe), facilitating both a rapid path to the clinic and characterization of therapeutic response. Our PKU program is initially focused on adults using the gene therapy approach. This strategy is designed to help us to further characterize the delivery, safety, and

manufacturing of our AAVHSCs, and to apply these learnings to our gene editing approach in the pediatric PKU population and to our broader platform. In initial preclinical studies, mice treated with HMI-102 showed a reduction in serum Phe to normal levels within one week and the reduction in serum Phe persisted for more than 16 weeks following a single intravenous administration. We anticipate entering into a Phase 1/2 clinical trial for HMI-102 in adult PKU patients in 2019. We have also received orphan drug designation for the use of AAVHSCs expressing human phenylalanine hydroxylase, or PAH, for the treatment of PKU from the U.S. Food and Drug Administration, or FDA.

Beyond PKU, we are building a deep pipeline across a wide range of diseases and tissue types to leverage the broad potential of our platform. We also intend to selectively partner to expand indications and accelerate development of programs where collaborators can contribute further disease-specific expertise to our platform.

Our Product Pipeline

The current status of our programs is summarized in the table below:

Our Programs	Target Organ	Method	Stage of Development						Worldwide Commercial Rights
			Discovery	Lead Optimization	IND-Enabling	Phase 1	Phase 2	Phase 3	
Gene Therapy									
Adult Phenylketonuria (PKU): HMI-102	Liver	Gene Transfer	Initiate Phase 1/2 Clinical Trial - 2019						HOMOLOGY
Metachromatic Leukodystrophy (MLD)	CNS	Gene Transfer							HOMOLOGY
Gene Editing									
Pediatric PKU	Liver	Gene Correction	Nominate Development Candidate - 2018						HOMOLOGY
Hemoglobinopathy #1	Human Stem Cells	Gene Correction							HOMOLOGY
Hemoglobinopathy #2 (Sickle Cell Disease)	Human Stem Cells	Gene Correction							HOMOLOGY / NOVARTIS (1)
Select Ophthalmic Targets	Eye	Gene Correction							NOVARTIS
Lung Disease	Lung	Gene Correction							HOMOLOGY

(1) Homology retains U.S. rights and has licensed the Ex-U.S. rights to Novartis.

Our Strategy

Our goal is to transform the lives of patients suffering from severe genetic diseases by using gene editing and gene therapy to cure the underlying cause of the disease. The critical components of our strategy to achieve this goal include:

- ***Transform the treatment paradigm for rare genetically-defined diseases with the delivery of single-administration curative therapies.*** Utilizing our proprietary AAVHSCs, we intend to deliver genetic medicines *in vivo* via a single intravenous administration to address the underlying genetic problem in a given disease. For each of the programs in our pipeline, we have identified the mutations of a specific gene that we believe can potentially be addressed by replacing an aberrant gene with a healthy one via HR-driven gene correction or by introducing a functional copy of a defective gene via gene therapy. Our genetic medicines platform allows us to choose the best suited modality for each disease we pursue and we believe our nuclease-free editing approach will provide life-long clinical benefits for patients.

- ***Advance our pipeline programs through clinical proof of concept and commercialization.*** We intend to advance our lead product candidate, HMI-102, into a Phase 1/2 clinical trial in adult

PKU patients in 2019. We believe that our approach of initially utilizing our AAVHSCs for gene therapy in adult PKU patients while, in parallel, advancing gene editing for pediatric PKU patients will maximize the efficiency of our pipeline development while providing potential solutions for the unique needs of each particular PKU patient population. Given the well-defined nature of PKU, we intend to bring HMI-102, if approved, to patients through a small, targeted internal commercial organization.

- ***Continue to expand our pipeline within existing therapeutic areas and expand into other therapeutic areas.*** We are focused on applying the transformative potential of our genetic medicines platform to developing medicines for patients with monogenic diseases. Initially, we are targeting diseases occurring in the liver, hematopoietic system and the CNS. Given the ability of our AAVHSCs to deliver to a wide range of disease-relevant tissues, we believe there are many additional indications for which our technology may be applicable, including a number of inborn genetic deficiencies in metabolism, lysosomal storage diseases, hematological diseases, and CNS diseases. Our research and development collaboration with Novartis for select ophthalmic targets and sickle cell disease illustrates the broad potential of our platform. In addition to our Novartis collaboration, we may also choose to selectively collaborate to expand the indications we can pursue and accelerate development of programs where collaborators can contribute further disease-specific expertise to our platform.

- ***Strengthen our platform by leveraging our discovery and development capabilities and selectively collaborating.*** We are committed to investing in our research and development activities to expand the capabilities of our platform, specifically our AAVHSCs as well as HR gene editing technology. We are optimizing our AAVHSC genetic medicines platform with focused efforts on AAVHSC characterization, gene therapy and editing construct design and screening, and genomic assays to characterize and quantitate our editing efficiencies. To augment our own efforts, we intend to continue to work with our scientific founders at COH who discovered our proprietary AAVHSCs as well as partner with other academic institutions to pursue new scientific and therapeutic insights and strengthen our position as a leader in gene correction.

- ***Control manufacturing through our in-house capabilities.*** We have developed internal process development and pilot manufacturing capabilities and are in the planning stages of building a cGMP manufacturing facility to support our clinical development programs. We believe the quality, reliability and scalability of our gene editing and gene therapy manufacturing approach will be a core competitive advantage crucial to our long-term success, and internal manufacturing capabilities will further safeguard our intellectual property.

- ***Continue to strengthen and expand our intellectual property portfolio.*** We have exclusive worldwide rights to our technologies including issued composition of matter patents in the United States for 15 of our novel AAVHSCs for both gene editing and gene therapy. We exclusively acquired rights to this foundational intellectual property for the AAVHSCs from COH for developing and commercializing therapeutics based on these vectors. We continue to strengthen our intellectual property estate through the continued discovery of new AAVHSCs further characterization around our existing AAVHSCs as well as the technology involved in delivering our product candidates to patients. To further advance our leadership in nuclease-free gene editing and gene therapy, we actively explore opportunities to partner with other leading scientific institutions in the field, as illustrated by our co-exclusive licensing agreement with the California Institute of Technology, or Caltech.

Genetically Defined Disease and Genetic Medicine

Each person’s genetic material, or genome, is encoded by DNA in sequences of genetic code called genes. Genes, in turn, through a process called gene expression, produce proteins that perform a vast array of

functions within all living organisms. The human genome consists of roughly three billion base pairs of nucleotides, which are the basic structural unit of nucleic acids like DNA, and small changes, or mutations, routinely occur in the base pairs of our DNA. A mutation in the gene or in sequences that control the expression of that gene can cause proteins to be produced aberrantly in the cell—for example, too little or too much protein can be produced in the cell—which can cause disease.

Significant investments in the human genome project, clinical data collection and analysis, and the development of affordable and efficient DNA sequencing and informatics tools have transformed the scientific community's understanding of genetically defined diseases and brought significant advancement to the field of genetic medicine. For example, many diseases previously thought to be genetically complex in nature have now been re-categorized as multiple distinct diseases that present with similar clinical dispositions, but are caused by different single-gene defects. Currently, there are approximately 3,600 diseases that are understood to be caused by single-gene mutations, which vary dramatically in their pathologies, their sites of manifestation, and the specific natures of their root causes.

According to the Online Mendelian Inheritance in Man database, a majority of genetically defined diseases are autosomal recessive in nature (meaning two copies of an abnormal gene must be present in order for the disease or trait to develop) resulting in a loss of function, whereas the remaining diseases are autosomal dominant (meaning you need only one copy of the mutated gene to be affected) with a gain of function. In loss of function based diseases, the mutation results in a protein that is not adequately produced; conversely, in the case of gain of function diseases the mutated gene product is inappropriately or excessively active. The majority of genetic diseases harbor thousands of individual mutations within a single gene, each resulting in a loss of function, thus treatment requires replacing or supplementing the diseased gene with the whole correct gene. Two approaches are currently used to restore function—gene therapy and gene editing.

Current Treatment Modalities and their Limitations

Traditional genetic medicines have focused on the addition of new genes to human cells, or gene therapy. Recent advances in the field, however, have led to the development of gene editing technologies that enable the introduction of DNA breaks to potentially achieve a therapeutic effect. However, competing gene editing approaches have been limited due to high rates of unwanted on- and off-target modifications and low gene correction efficiency due to the cell trying to rapidly repair the introduced DNA break. Other therapeutic approaches to genetic disease do not address the underlying genetic cause of the disease and offer solutions that typically only treat symptoms and require chronic administration, and as a result most genetic diseases tend to have significant unmet need.

Gene Therapy Overview

Gene therapy, through the process of gene transfer, seeks to introduce a functional copy of a defective gene or gene sequence into a patient's own cells alongside the existing genome, without integration, as an episome, which is a non-essential portion of genetic material that can exist autonomously within a cell. The episome drives functional gene expression using engineered promoters that can be designed to limit expression to specific cell types or be expressed in all cell types. Gene therapy is a viable option for delivery of potential cures in diseases where the target cell type does not divide frequently (*e.g.*, neurons in the CNS and adult liver cells). However, since gene therapy works through an episome that does not integrate into the genome, each time a cell divides, the number of episomes per cell decreases by 50%. After a few rounds of cell division, the episomes will be lost, limiting therapeutic relevance in rapidly dividing cells (*e.g.*, blood, lung and pediatric liver cells).

Gene therapy has been studied for over 50 years, and the first therapeutic use of gene transfer in humans occurred in 1990. Since then, more than 2,300 gene therapy trials have been planned or completed, covering a broad range of disease targets. Recently, gene therapies have progressed beyond academic trials to regulatory approvals, resulting in a growing acceptance and de-risking of the modality. In 2012, UniQure's Glybera became

the first gene therapy to be approved by the European Medicines Agency, or EMA, and was followed by the EMA approval of GlaxoSmithKline's Strimvelis in 2016. Spark Therapeutics' Luxturna is the first directly administered gene therapy approved in the U.S. that targets a disease caused by mutations in a specific gene.

Gene Editing Overview

Gene editing is a powerful new approach that has been developed in the last few years to change the course of genetic disease by physically correcting aberrant genes in a variety of tissues in the body. Gene editing is the process of replacing, deleting, or repairing defective DNA in its native location. The current focus of gene editing is knocking out a diseased gene or correcting an individual mutation within a gene that is frequent within the disease population, neither of which can address the larger population of recessive genetic diseases that would require the insertion of a full corrective gene.

Unlike the gene therapy approach, in gene editing the repaired genetic region is replicated through normal cell division and allows the protein to be expressed using its natural regulators. There are two approaches to gene editing, the traditional nuclease-based approach and our nuclease-free HR-driven gene correction approach.

Gene editing technologies to date primarily leverage two independent pathways to modify DNA: HR and NHEJ. HR is a process in which cells repair DNA through highly precise incorporation of correct DNA sequences complementary to the site of damage. HR has evolved to repair DNA with high fidelity and avoids the introduction of unwanted mutations at the site of correction. NHEJ is a less selective, error-prone process that rapidly joins the ends of broken DNA resulting in a high frequency of insertions or deletions at the break site.

Nuclease-Based Gene Editing

Nuclease-based gene editing utilizes nucleases, which are enzymes that were initially identified in bacteria and evolved to act like "molecular scissors." Nuclease-based gene editing is fundamentally a two-step process. First, a nuclease, which is capable of cutting one or both strands in the double-stranded DNA, is directed to the desired site and makes a specific cut. After the desired cut or cuts are made, the cell's DNA repair machinery responds to complete the edit through one of two possible repair mechanisms—the more common NHEJ or the less common HR—that can be leveraged for therapeutic effect.

NHEJ occurs in the absence of a DNA template for the cell to copy as it repairs a DNA cut. This is the primary or default pathway that the cell uses to repair double-stranded breaks. The NHEJ mechanism can be used to introduce small insertions or deletions, or indels, resulting in the knocking out of the function of the gene. NHEJ creates indels due to its mode of repair and can also result in the introduction of off-target, unwanted mutations including chromosomal aberrations.

Nuclease-based HR occurs with the co-delivery of the nuclease and a DNA template that is similar to the DNA that has been cut. Consequently, the cell can use this template to construct reparative DNA, resulting in the replacement of defective genetic sequences with correct ones. The HR mechanism is the preferred repair pathway when using a nuclease-based approach to insert a corrective sequence due to its high fidelity. However, a majority of the repair to the genome after being cut with a nuclease continues to go through the NHEJ mechanism and the more frequent NHEJ repair in the presence of a DNA template has the potential to result in unwanted mutations at the cut site including:

- insertion of the template DNA in the wrong orientation;
- unwanted mutations added at the site of integration;
- integration of template DNA fragments; and
- insertion of inverted terminal repeat sequences if AAV is used as the delivery vehicle.

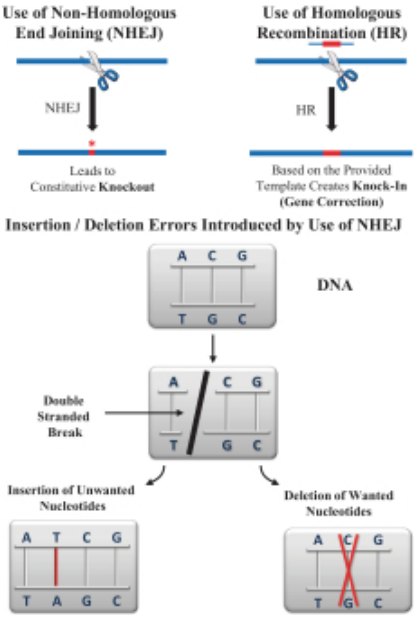


Figure 3. Non-Homologous End Joining and Homologous Recombination.

Much of the early recognition for gene editing's potential has come in response to these nuclease-based approaches, which include: Transcription activator-like effector nucleases, or TALENs; Clustered, Regularly Interspaced Short Palindromic Repeats (CRISPR) Associated protein-9, or CRISPR/Cas9; Zinc Finger Nucleases, or ZFN; and Transcription Activator-Like meganuclease, or megaTAL. While these approaches have already made and will likely continue to make an impact on biology research, we believe they face significant shortcomings.

Limitations of Nuclease-Based Gene Editing

- ***Unwanted on- and off-target DNA modifications.*** The use of exogenous nucleases results in DNA breakage which is predominantly repaired via NHEJ, an error-prone process involving the insertion or deletion of DNA residues as well as the possibility that DNA will be cut in the wrong place, resulting in unwanted mutations driven through NHEJ instead of a therapeutic correction at the precise location. This process coupled with the ability of these nucleases to break the DNA at off-target sites comprises one of the major safety concerns about these gene editing methods.
- ***Inability to efficiently and precisely introduce entire gene to the genome.*** Current gene editing approaches are unable to achieve high efficiencies of targeted gene correction *in vivo*.
- ***Complexity of vector delivery and manufacturing to achieve gene insertion.*** In order to deliver an entire functional gene, existing nuclease-based gene editing approaches require co-delivery of multiple constructs of editing machinery into the same cell. The need to use multiple vectors increases the complexity and cost of manufacturing.

Our Nuclease-Free Gene Editing Opportunity

Gene editing through the precise HR pathway can also be conducted without the use of nucleases. Although such approaches were pioneered in the 1990's before the advent of the nuclease-based gene editing

platforms, their use and progression to clinical trials since has been held back by issues including gene correction efficiencies that are typically well below those needed to achieve potential therapeutic effect. Nevertheless, early work in the field of nuclease-free gene editing elucidated some of the key characteristics of various platforms that are now providing higher editing frequencies. However, the published efficiency of this technology for gene correction is approximately 1%, significantly below levels that are typical for generating a therapeutic effect. This underscores a clear need for novel nuclease-free gene editing technologies capable of achieving higher gene correction efficiencies.

Our Genetic Medicines Platform

The unique characteristics of our platform enable nuclease-free gene editing, specifically gene correction, and broad, systemic tissue distribution. Our proprietary genetic medicines platform is built on our novel AAVHSCs, which allow us to choose the best suited modality from either gene correction or gene therapy for each disease we pursue, based on such factors as the targeted disease biology, the biodistribution of our AAVHSCs to key tissues, and the rate of cell division the target tissues exhibit. Our AAVHSCs are designed to directly integrate corrective DNA through HR with therapeutically relevant efficiencies. Our HR-based gene editing approach utilizes a single component AAV system that contains everything required to selectively edit DNA with no need for exogenous nucleases or editing machinery. This single-component approach simplifies the manufacturing and delivery of our therapeutics. Our AAVHSCs are naturally occurring and have been modified to be non-replicating to minimize potential safety issues. We believe our platform's combined attributes will allow us to develop more efficient and safer therapeutics for a wide range of genetic diseases.

Homologous Recombination—A Powerful Basis for Gene Editing

Unlike other gene editing approaches, our technology is based on the natural DNA repair process of HR, and is designed to enable precise and efficient correction or replacement of gene mutations without an exogenous nuclease. HR is a process that is used by cells to repair DNA through the incorporation of a template of homologous DNA. This pathway is not prone to the nucleotide insertions and/or deletions that occur frequently in the NHEJ process.

By pursuing one-time correction of underlying genomic defects using a nuclease-free, naturally occurring DNA repair process that addresses the underlying genetic problem in a given disease, we believe our approach has the potential to simplify production and delivery of therapeutics, minimize the risk of unwanted mutations and provide life-long clinical benefits for patients. Our gene editing approach has the potential to be curative in both dividing and non-dividing cells as it provides a permanent correction in the genome that is then replicated with each cell division so that new generations of cells will carry the corrected gene.

Our genetic medicines platform induces the endogenous HR cellular process using our AAVHSCs to insert replacement or corrective genes into cells that contain mutated or deleterious genes. We engineer our AAVHSCs to contain long, single-stranded DNA corrective sequences highly specific to the target region in the genome. These single-stranded DNA molecules are then delivered to cells in our AAVHSC vectors, which we believe results in precise and efficient gene correction via the HR pathway. The design of our long and specific sequences, up to the 4.7 kilobase packaging limit of our AAVHSCs, is intended to significantly reduce the risk of off-target integration. The engagement of the HR pathway to drive gene correction results in a highly precise and efficient on-target integration, with no detectable introduction of unwanted mutations at the corrective site. These guide sequences can be engineered to be as long as necessary to deliver highly efficient HR-based on-target correction while significantly minimizing off-target effects. We typically use homology arms as long as 1,600 base pairs of DNA to target corrective gene sequences into precise regions of the genome, in contrast to the guide sequences used in CRISPR/Cas 9-based gene editing, which are typically less than 100 base pairs in length. We also benefit from the ability of our platform to utilize HR to precisely insert gene sequences into the DNA of cells, similar to how mammalian cells repair their own DNA. This is a key distinction from approaches that rely on exogenous nucleases that were initially identified in organisms, such as bacteria, and evolved just to cut DNA. In order to bring about the excision and subsequent replacement that some forms of gene editing require, those other approaches must combine multiple additional techniques and deliver into the cell the requisite cellular

machinery, increasing the complexity of the task, introducing the possibility of integrating the wrong DNA due to non-HR-based repair mechanisms, and reducing the likelihood of success.

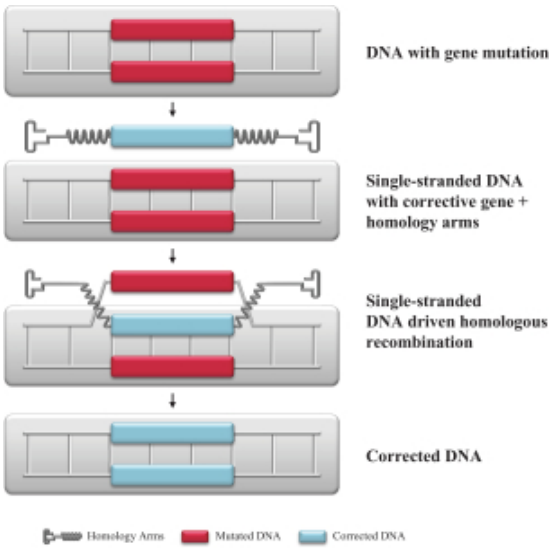


Figure 4. Schematic of Homologous Recombination.

Our Proprietary AAVHSCs

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. Our AAVHSCs were isolated from human stem cells and we believe they can direct nuclease-free gene correction with higher efficiency and precision relative to that indicated in published data for other AAV-based gene editing approaches. 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 COH. Our AAVHSCs display the following advantages:

Single AAVHSC Platform for Both Gene Therapy and Gene Editing Modalities

Our platform provides us the flexibility to deliver genetic medicines through the best suited modality from either gene therapy or gene editing for each disease we pursue, based on such factors as the targeted disease biology, the biodistribution of our AAVHSCs to key tissues, and the rate of cell division the tissues exhibit.

Ability to Perform Nuclease-free Gene Editing Mediated by HR with Higher Efficiency

A 2016 study conducted by COH assessed the ability of AAVHSCs to carry out gene editing *in vivo* using a luciferase gene that lacked a promoter sequence. A vector with homology arms was designed to introduce D-luciferin, or luciferase, into the Rosa26 locus in the mouse genome. Rosa26 is a locus in the mouse genome that is known to have a strong promoter capable of driving constitutive expression of genes in all cell types. AAVHSC15 constructs with (N=3) and without (N=2) homology arms and an AAV8 construct with homology arms (N=3), were injected into mice intravenously at a dose of 1e13 vector genomes per kilogram, or vg/kg. High levels of luciferase expression were detected throughout the mouse up to 63 days after injection of the AAVHSC15 construct with homology arms. Luciferase expression was not seen if the homology arms were not present and was barely detectable when AAV8 was used instead of AAVHSC15. We presented these data at the 2017 American Society of Gene and Cell Therapy annual meeting.

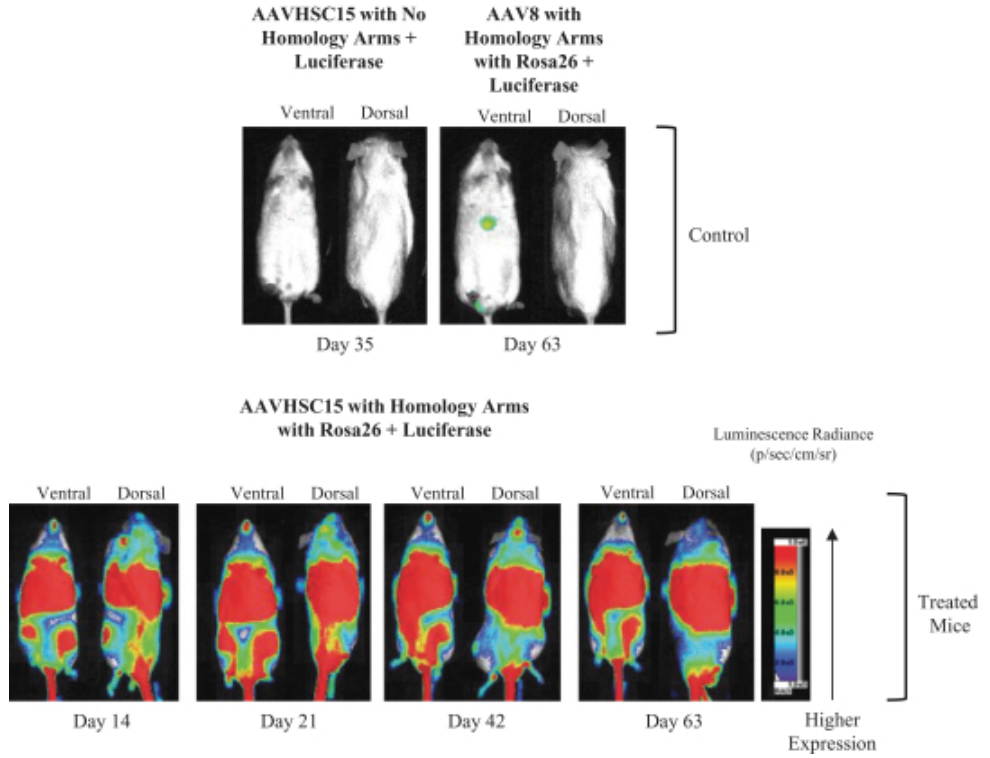


Figure 5. *In vivo* Gene Editing. Mice treated with our AAVHSC15 construct with homology arms specific to Rosa26 showed high expression of luciferase up to 63 days. Control mice injected without homology arms or with AAV8 constructs had none or limited luciferase expression.

Factor 8, or F8, is a locus in the mouse genome that is known to have a strong promoter but is expressed only in the liver. In a study we conducted in 2017 at our headquarters, AAVHSC15 and AAVHSC17 constructs, at a dose of 5e12vg/kg (N=3), containing homology arms specific to the murine F8 locus were injected into mice intravenously. Live luciferase imaging was conducted pre-dosing and weekly thereafter through week nine, with the exception of week four. Murine biodistribution data with AAVHSC15 and AAVHSC17 both show tropism to multiple tissues beyond the liver. However, in this study only liver-specific expression of luciferase was observed as early as 24 hours and sustained through 60 days post-injection, suggesting significant editing in the murine F8 locus. To assess the evidence of F8 gene correction, genomic DNA from the livers were extracted at 60 days post-injection and integration was assessed molecularly confirming editing of the promoterless luciferase into 6% to 12% of the F8 alleles, which we believe to be therapeutically relevant, as depicted in Figure 6 below.

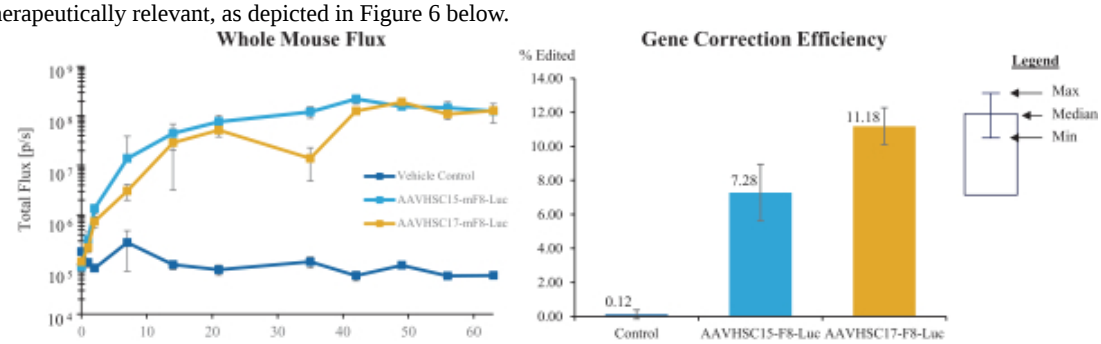


Figure 6. *In vivo* Gene Editing. In the active groups, liver specific expression of luciferase were observed up to 60 days and gene correction efficiencies were observed in a range of 6% to 12%.

In a subsequent study we conducted in 2017 using our internal manufacturing process, an AAVHSC15 construct, at a dose of 1.5e14vg/kg, containing homology arms specific to the murine F8 locus was injected into mice (N=3) intravenously. Genomic DNA from the livers were extracted at seven days post-injection in this study and editing efficiency was determined molecularly. As depicted in Figure 7 below, F8 gene correction editing efficiencies averaging 19.5% were observed when dosed at 1.5e14vg/kg.

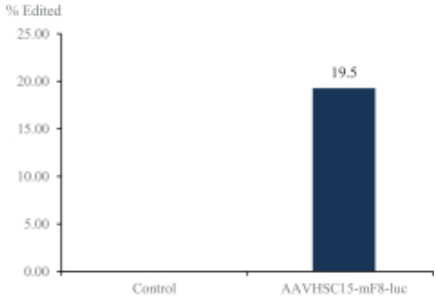


Figure 7. *In vivo* Gene Editing. In the dosed group, liver specific expression of luciferase was observed up to seven days post-injection and gene correction efficiencies were observed averaging 19.5%.

Ability to Introduce Entire Gene into the Genome Mediated via HR

In order to generate evidence regarding this gene editing capability, we carried out cellular assays with the widely used reporter protein green fluorescent protein, or GFP, which glows visibly green when it is expressed in a cell. In this study, which was conducted in 2016 at Charles River Labs in the Netherlands in collaboration with Charles River Labs and COH, a series of AAV vectors using sequences from widely used strains such as AAV2, AAV6, and AAV8, as well as our AAVHSC strains was constructed such that a promoterless copy of the gene for GFP was surrounded by 1,600 base pairs of an endogenous human gene, PPP1R12C. Previous work demonstrated that these surrounding sequences or homology arms can direct the process of HR into the genomic DNA at the desired site. Genes require promoters to signal the cell machinery to copy the gene instructions into messenger RNA or mRNA, which is then turned into protein. The artificial GFP construct alone is unable to direct the synthesis of mRNA and therefore no GFP protein can be synthesized from the episomal vector. The PPP1R12C gene sequences are homologous to a specific region in the human genome and are meant to direct the incorporation of GFP into the genome of the human near a particular, known endogenous promoter. The synthesis of GFP protein, as detected by its fluorescence, can be used as a surrogate for the successful integration of the GFP gene downstream of this promoter.

These GFP constructs were introduced into a broad panel of human cell lines and primary cells and recombination frequencies were determined using bioluminescence from expression of GFP. All cells were treated with a multiplicity of infection of 150,000. AAVHSCs resulted in much higher GFP positive cells and thus HR events than other AAV strains. This high level of HR has been observed with multiple genomic targets and independently confirmed in multiple laboratories. We presented these data at the 2017 American Society of Gene and Cell Therapy annual meeting.

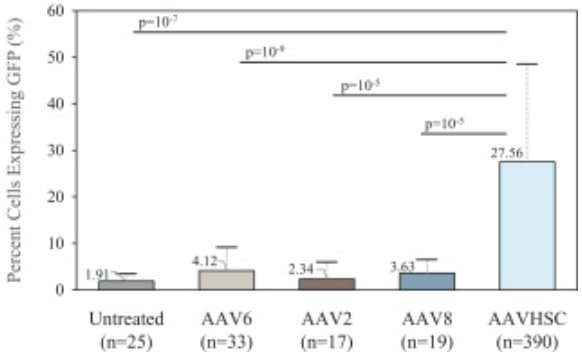


Figure 8. Targeted gene correction of AAVHSCs vs. other AAV strains was measured by assaying for the expression of GFP. Our AAVHSCs resulted in significantly higher GFP expression compared to other AAV strains, indicating higher levels of HR.

Direct confirmation of HR was observed using a DNA-based assay that can detect the insertion of the GFP gene at the desired location in the genome. The level of GFP expression was found to directly correlate to the recombination frequency. Furthermore, studies in cell lines with various mutations in DNA repair and recombination genes identified BRCA2 as a critical gene in AAVHSC-directed gene editing. Mutations in BRCA2, a gene that encodes a protein known to be essential for HR, completely eliminate gene editing but have no effect on transduction efficiencies, thereby providing evidence that the gene editing is accomplished through HR.

In initial preclinical experiments conducted at our headquarters in 2017, we introduced our initial gene editing construct containing human PAH intravenously targeting the endogenous PAH locus in the mouse through HR. Mice were dosed at 1e14 vg/kg and serum PHE was measured weekly through 21 weeks post-dosing, at which time livers were harvested to test for allele quantitation. Treated mice (N=3) had a greater than 50% reduction in serum Phe as compared to control mice (N=2) and these reduced levels persisted for at least five months. This represents a statistically significant reduction in Phe at every time point post treatment ($p<0.001$). We continue to optimize the gene editing and transfection rates through testing of various AAVHSC strains and alterations to the gene construct.

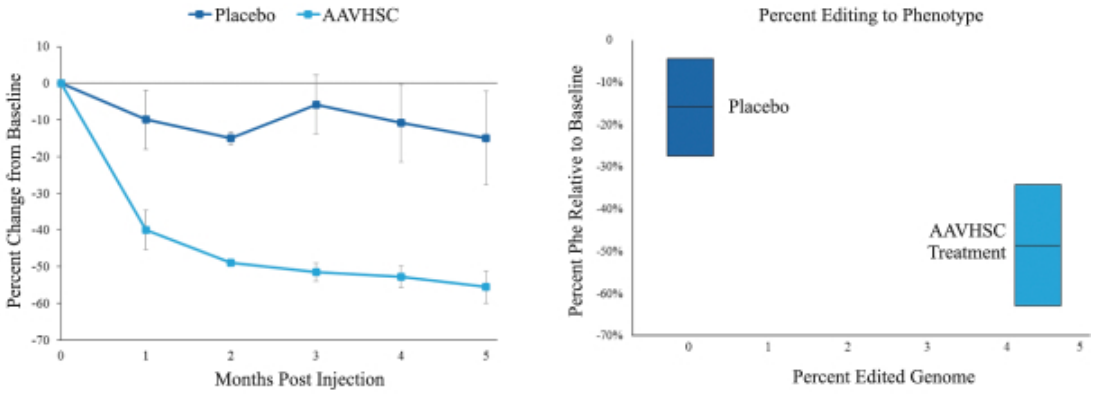


Figure 9. PAH gene editing meaningfully reduced serum Phe levels. A single injection of our AAVHSC15 construct delivering a functional copy of PAH through homology arms targeting the murine PAH resulted in rapid and sustained reduction in serum Phe levels in PAH deficient mice. The Phe level reduction was achieved within a week of administration and was observed out to 21 weeks, with an average gene correction efficiency of approximately 5%. Change in serum PHE from baseline is plotted as the average change from baseline each month.

We believe our approach, when compared to published third party data, can result in significantly higher and therapeutically meaningful *in vivo* gene correction efficiencies than those provided by existing methods, although we have not conducted any head-to-head studies comparing our AAVHSCs with existing products or treatment methods. In a 2015 study described in Nature and depicted in the second bar from the right in figure below for illustrative purposes, third-party researchers injected a gene editing construct, packaged in AAV8, targeting the murine albumin gene with a cDNA encoding human Factor 9, a gene responsible for encoding the production of a protein called coagulation factor IX, into a C57BL6 mouse at a dosage of 5e13vg/kg (N=7). Genomic DNA was harvested from the livers at 14 weeks post-dosing and a two-step nested qPCR assay was used to quantify the percentage of alleles with the integration of human Factor 9. The efficiency was determined to be approximately 0.5%. A qPCR assay was then used to measure the percentage of mRNA transcripts with the integration of human Factor 9. This assay was based on primers specific for the wild type albumin transcript and another set specific to the albumin transcript with the integration of human Factor 9. In this assay, the estimated proportion of transcripts from the edited allele was determined to be approximately 0.1%.

In an unrelated 2017 study described in EMBO Molecular Medicine and depicted in the far right bar in the figure below for illustrative purposes, third-party researchers injected a gene editing construct, packaged in AAV8, targeting the murine albumin gene with a cDNA encoding human UGT1A1, a gene belonging to a family of genes responsible for encoding the production of certain enzymes, into a mouse model at a dosage of 1e12 total vg (N=6). In this study, the estimated editing efficiency was determined through immunohistochemical assessment of hepatocytes staining positive for human UGT1A1. Using this method, the estimated efficiency was determined to range from 0.033% at one month post-dosing to 0.015% at one year post-dosing.

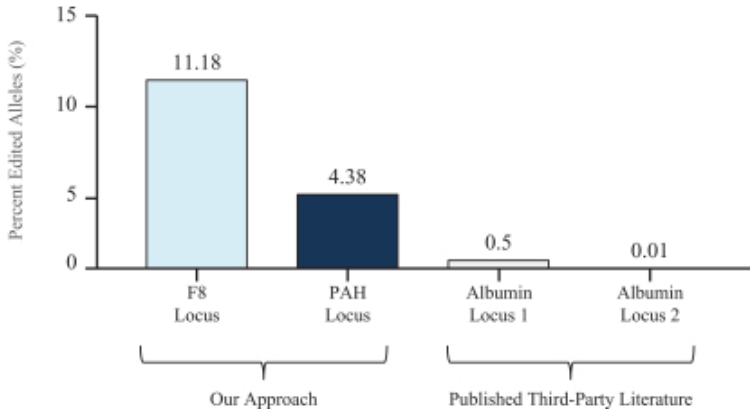


Figure 10. Significantly higher and therapeutically meaningful *in vivo* gene correction efficiencies observed in the livers of mice using our approach compared to published third party data.

We have successfully inserted full-length cDNA encoding luciferase and PAH into two separate genomic regions *in vivo* reaching levels of efficiency required for therapeutic efficacy. The ability to introduce entire genes specifically into the genome at these efficiencies provides an opportunity to target multiple monogenic diseases where the correction of a defective gene would result in therapeutic benefit. Given that a majority of monogenic diseases harbor mutations that render the gene inactive, we believe our gene correction modality can be expanded well beyond our initial focus on liver-based inborn errors of metabolism.

High Precision and Lack of Unwanted Off-target or On-target DNA Modifications

Using next-generation sequencing, we have developed methodologies to test for on-target mutations at the site of integration. Using these methods, we observed that HR using our AAVHSCs is very precise at the site of correction. We have amplified the corrected region in the genome and sequenced more than 2 million reads and were not able to detect any indels or traces of viral sequence at the detection limit of this sequencing.

We developed a method to enable whole genome unbiased next-generation sequencing for the detection and mapping of off-target integration sites. By leveraging the potential ability of our AAVHSCs to drive HR-based targeted integration we can utilize next-generation sequencing technologies to identify and quantify where the inserted sequence maps. Using this method, and based on over 2.2 million sequence reads, we estimate that 99.967% of insertions are at the targeted site.

Ability to Target Multiple Tissues

Through intravenous administration of our AAVHSCs into rodents and non-human primates, we have generated evidence of their ability to target a number of tissues including:

- crossing the blood-brain barrier to neurons throughout the brain, spinal cord, and dorsal root ganglion;
- retinal ganglion cells and neurons of the retinal outer nuclear layer; we have also demonstrated the ability to target retinal tissue via intravenous injection as well as multiple layers of target cells through sub-retinal injection;
- skeletal muscle myocytes in all skeletal muscle tissues examined, including gastrocnemius, soleus, diaphragm, esophagus, and biceps;
- cardiomyocytes throughout the heart; and
- extensive liver tropism.

In addition to our proprietary AAVHSCs, we have also co-exclusively licensed a set of modified AAV vectors and peptide sequences from Caltech that were designed to further increase the ability of our AAVHSCs to selectively cross the blood-brain barrier to target the central nervous system, including the brain and spinal cord. We are using these vectors to support our discovery efforts for central nervous system disorders, with an initial focus on monogenic indications.

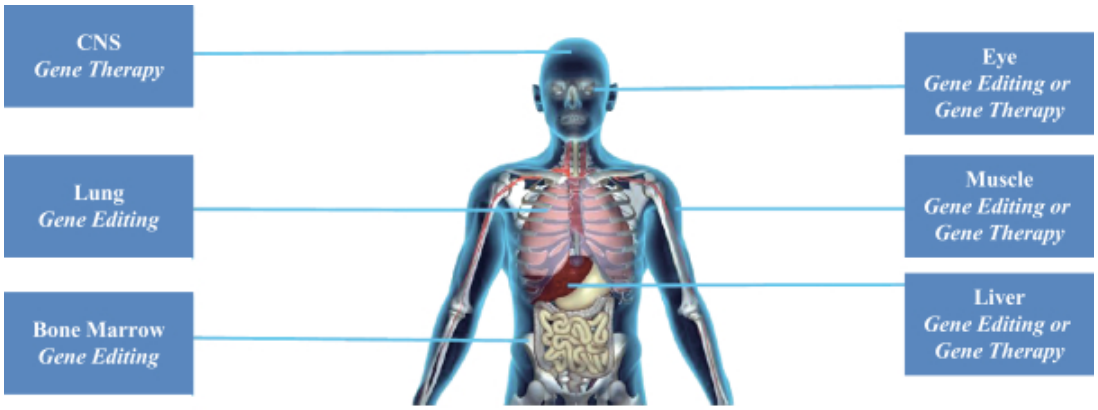


Figure 11. Our AAVHSCs show significant biodistribution to key tissues for treating genetic diseases.

In vivo *Administration With a Single Component Delivery System*

Our platform is designed to perform gene editing at higher efficiency without the use of a nuclease, enabling us to deliver genetic medicines *in vivo* using a single vector system. Existing nuclease-based gene editing technologies, when replacing a defective gene with a functional gene through gene editing, require the use of two or more different vector constructs in combination to perform their gene editing functions. One or more vector constructs house the nuclease, and the other vector construct houses the DNA template, and all vectors must reach and penetrate the specific target cell at the same time to edit the DNA. In contrast to these nuclease-based gene editing technologies, our AAVHSC technology is a single component system that contains everything required to selectively edit DNA across all gene editing methods with no need for additional exogenous nucleases, template DNA or editing machinery.

We believe our ability to perform gene editing at efficiencies that are significantly greater than both nuclease-based and other AAV-based approaches, coupled with our single component delivery system, enable us to administer genetic medicines *in vivo.* We believe the advantages of *in vivo* administration of therapeutics via a single component delivery system include the following:

- simpler and faster manufacturing relative to *ex vivo* resulting in reduced manufacturing costs;
- improved delivery of therapeutic as only a single vector is required to reach a cell instead of multiple vectors;
- ease of use for the patient, eliminating the need for bone marrow extraction, a common requirement for many *ex vivo* gene editing therapies; and
- improved safety profile, eliminating the risk of rejection or other unwanted immune response that can result from the administration of an *ex vivo* therapy.

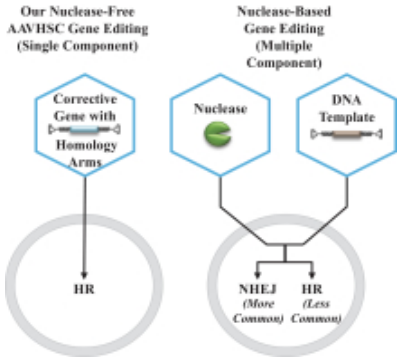


Figure 12. Our nuclease-free AAVHSC single component gene editing construct vs. nuclease-based multiple component gene editing construct for gene correction applications.

Ability to Target a Broad Range of Patients Given Low Frequency of Preexisting Neutralizing Antibodies

A potential concern for all AAV vectors is the presence of preexisting neutralizing antibodies that have the potential to reduce their effectiveness. We conducted a study across 100 human serum donors representing different ethnic segments of the U.S. population. Based on the initial results, we believe the findings suggest that approximately 80% of individuals lack antibodies that recognize AAVHSCs, which is comparable to AAV9, a commonly used vector for development of other gene therapies.

Our Product Candidates

We believe our genetic medicines platform can be applied broadly to treat and cure a wide range of genetic diseases, and have carefully designed and prioritized our pipeline strategy to maximize this opportunity. We are initially pursuing diseases where the genetic abnormality is known and is found in a single gene. These are also known as monogenic diseases. We therefore know exactly what we are correcting and exactly what gene to insert into the patient's cells, thus mitigating against the uncertainty of the disease biology. We are prioritizing monogenic diseases with significant unmet medical needs, validated regulatory pathways and significant commercial opportunities. We are currently focused on developing product candidates to treat monogenic diseases in the liver, bone marrow and the CNS, given that our AAVHSCs naturally show a high degree of tropism or ability to preferentially target cells in these organs and organ systems. These tissues are affected in many rare genetic diseases.

HMI-102 for Treatment of PKU

Our lead program, HMI-102, is an AAVHSC vector gene therapy candidate designed to treat the underlying genetic cause of PKU. We have received orphan drug designation from the FDA for the use of AAVHSCs expressing PAH for the treatment of PKU. We expect to initiate a Phase 1/2 clinical trial in PKU patients and to receive initial clinical data in 2019. HMI-102 is intended to treat adult patients with deficiencies in PAH regardless of the specific underlying PAH mutation.

PKU Disease Overview

PKU is an inborn error of metabolism that results from a mutation in the PAH gene. PAH is an enzyme that is normally expressed in the liver and is necessary to metabolize dietary phenylalanine, or Phe, to the amino acid and neurotransmitter tyrosine. PKU results from mutations in PAH that render its enzymatic activity deficient. If it is not metabolized by PAH, Phe builds up in the blood and the nervous system. Approximately 75% of all dietary Phe is typically metabolized by PAH so the absence of PAH leads directly to the pathological excess of Phe as well as a deficiency of tyrosine. Excessive blood Phe and low levels of tyrosine result in intellectual disability, which is possibly caused by a variety of mechanisms including effects on neuronal development, myelination, and neurotransmitter synthesis. Blood Phe is an easily measurable and translatable biomarker. It is also a surrogate clinical endpoint in clinical trials for PKU, facilitating both a rapid path to the clinic and characterization of therapeutic response.

Newborns in all 50 states are screened for PKU. It has been estimated that the incidence of PKU in the United States is one in 12,707 which translates to approximately 300 cases per year with an overall prevalence of 15,000. It has also been estimated that the prevalence of PKU in the European Union is 25,000. Worldwide, the estimated prevalence is 50,000.

The majority of patients are identified soon after birth and are primarily treated by dietary restriction of Phe. While Phe-restricted diets have dramatically reduced the intellectual deficiencies associated with this disease, they fail to address the cognitive and behavioral problems that continue throughout a patient's life. Lifetime adherence to a Phe-restricted diet is challenging and blood Phe is not achievable within the recommended range for the vast majority of patients. The inability to achieve recommended levels of Phe results in neurological as well as metabolic problems. Long-term studies in adults identify neurocognitive, psychosocial, quality of life, growth, nutrition, bone pathology and maternal PKU outcomes that are suboptimal despite early and continuous treatment. In a retrospective study of PKU patients, young children were adherent to Phe-restricted diet, whereas most adolescents (79%) did not achieve recommended Phe levels, and 88% of adults were no longer on a diet. Relaxing of dietary restrictions beyond preschool years, or failure to adhere to physician-assigned diets, which is the current guideline for most adolescents and adults, results in loss of metabolic control and wide fluctuations in Phe levels that are both directly associated with progressive neurological damage.

Current Treatments

There are currently no available treatments that address the core genetic biochemical defect in PKU, the deficiency of PAH.

Saproterin dihydrochloride, or Kuvan, is an FDA approved therapy to reduce elevations in serum Phe. Saproterin is a synthetic version of BH4, a cofactor that is required for PAH activity. The addition of saproterin helps deficient PAH to metabolize some Phe. However, clinical data suggests that saproterin is not fully effective in lowering high serum levels of Phe back to normal levels and must be used in conjunction with a low Phe diet. Kuvan reported worldwide sales of $348 million in 2016.

Pegvaliase is a pegylated plant-derived enzyme called phenylalanine ammonia lyase that has completed Phase 3 trials in PKU patients. This approach does not correct the underlying genetic disorder (PAH deficiency) and will not reconstitute the natural pathway that is needed to address the neurocognitive defects associated with PKU. Patients will still need to follow a Phe-restricted diet and supplement it with tyrosine. If approved, we believe pegvaliase will entail certain limitations. For example, pegvaliase must be administered via multiple daily injections and 8% of patients in the Phase 3 trials had an anaphylactic reaction. In 2016, BioMarin reported that patients in their Phase 3 trials did not experience cognitive benefit from pegvaliase.

Our Gene Therapy and Gene Editing Approaches to PKU

We are taking two approaches towards developing a potential therapy for PKU. The first is a proposed gene therapy in which a gene construct encoding human PAH is delivered to liver cells where it directs production of normal PAH via episomal expression driven off an exogenous promoter. The second proposed therapy involves true gene correction of the defect found in the chromosomes of affected patients. We believe that the gene therapy approach offers an expedited clinical development path towards delivery of a therapeutic to adult patients where the majority of target cells are non-dividing in the liver. We believe the gene correction approach would be more efficient in newborn and pediatric patients due to the higher rate of dividing cells as the child grows. The goal of both approaches is to enable production of functional PAH, thus restoring the normal biochemical pathway of Phe metabolism. This can reduce the abnormally high levels of Phe in the blood, while also increasing tyrosine levels, the product of PAH-driven Phe metabolism. Using gene editing to correct the defective PAH gene in young patients has the potential to provide long-term benefit as the corrected gene will persist as cells replicate. Correcting the gene while it remains under the control of its natural promoter early in disease progression has the potential to normalize not only Phe levels, but also tyrosine levels, the product of the PAH enzyme and a precursor to neurotransmitter synthesis. This may allow affected children to avoid many of the serious neurological consequences associated with PKU.

We believe that an effective gene therapy or gene correction for PKU has the potential to eliminate the need for Phe restricted diet and may lead to significant improvements in the morbidity and quality of life for patients. Published estimates suggest that restoration of PAH activity to 10% or more of normal levels would lead to significant improvements in serum Phe levels.

Our Gene Therapy Solution–HMI-102

We identified HMI-102 as our lead product candidate after screening multiple vector constructs. HMI-102 consists of an AAVHSC15 vector containing the coding sequence of human PAH under control of a promoter designed to continuously express PAH, specifically in the liver. We chose AAVHSC15 as the basis of this product candidate because of its observed propensity to target liver cells, the normal site for PAH protein expression.

The potential of an AAVHSC15-delivered PAH gene was assessed in a well-established mouse model of PKU called the ENU2 mouse. This model contains a mutation in the murine PAH gene that results in abolished activity and results in elevated serum Phe levels. Baseline levels of serum Phe in these mice are approximately 1,500 micromoles per liter compared to normal levels of 80 micromoles per liter, levels that are similar to those seen in patients and normal controls. Single intravenous injections of HMI-102 into these deficient mice resulted in reductions of serum to levels that are within the range for normal mice. The reduction in serum Phe levels persisted for greater than 16 weeks in treated mice on a normal protein diet. In addition to a reduction in serum Phe, the administration of our gene therapy candidate also resulted in elevations of serum tyrosine due to the restoration of the normal biochemical pathway.

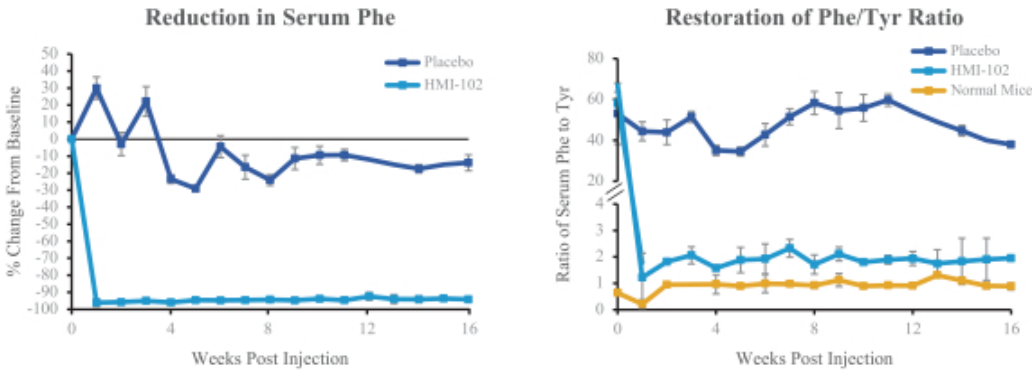


Figure 13. A single injection of HMI-102 resulted in rapid and sustained reductions in serum Phe and increased tyrosine levels in PAH deficient mice that are on a regular diet.

Our Gene Editing Approach for PKU

In order to address the pediatric PKU population, we are developing a gene editing therapy for PKU that is designed to replace the defective PAH gene with a normal copy. This therapy is designed to correct the defect in treated liver cells, such that they would be indistinguishable from those from an unaffected individual. These cells would direct the synthesis of PAH from its natural promoter, and therefore would be capable of normal regulation of its expression. The corrected copy of the PAH gene would be retained as these cells divide into daughter cells as the liver grows. Screening for PKU of all newborns in the United States allows the identification of affected individuals before serious neurological complications develop. We believe our AAVHSC vector HR approach possesses the efficacy and safety characteristics that would be appropriate to treat PKU in newly identified patients. As we further develop our expertise in treating PKU by correcting the defective PAH gene in the liver, we intend to develop treatments for other inborn errors of metabolism in the liver.

Our clinical product candidate for gene editing in PKU will be based on the optimized constructs used in the mouse experiments, but with the incorporation of human PAH gene sequences.

Additional Product Opportunities

CNS Diseases

Our CNS programs, which are initially focused on MLD, are designed to take advantage of our AAVHSCs' observed ability to cross the blood-brain barrier in non-human primates. We are also applying Caltech's technology that has shown significantly higher transduction in murine neuronal cells such as astrocytes, glial cells and neurons in the CNS, across multiple regions of the brain. We intend to apply this technology in a gene therapy setting in which genes for therapeutic proteins are delivered intravenously to

non-dividing cells in the brain. We initially expect to apply this technology to monogenic diseases in which defective genes in cells in the brain contribute to serious neurological complications. Specific disorders that we are evaluating at the preclinical stage include metachromatic leukodystrophy or MLD, a lysosomal storage disease caused by mutation of a gene called arylsulfatase A, or ASA. ASA is required for the breakdown of cellular components that in MLD accumulate in myelin, leading to progressive serious neurological deterioration. The prevalence of subtypes of MLD range between 1:40,000 and 1:150,000. Another CNS disease we are evaluating is Friedreich's ataxia or FA. In FA, mutations in a gene called frataxin, or FXN, lead to progressive deterioration of the spinal cord leading to difficulty walking and eventual complete incapacitation and shortened life-span. FA is the most common form of inherited ataxia with a prevalence of 1:40,000. Other diseases in this area include a subset of Parkinson's disease which is associated with Gaucher disease. Gaucher disease patients have a defect in the gene for glucocerebrosidase which is important for various processes in the body and in certain patients these mutations also lead to the development of Parkinson's disease. We believe our gene therapy technology has the potential to address directly the deficiency in glucocerebrosidase in the brain in a manner that is not possible with other Gaucher disease treatments that do not cross the blood-brain barrier.

Hemoglobinopathies

We are also pursuing treatment of diseases that affect blood cells such as sickle cell disease and beta thalassemia using our AAVHSC vector HR technology. We believe that our potential ability to correct the defective beta globin gene in blood precursor cells may lead to long-term functional cures for affected patients. Sickle cell disease affects over 100,000 individuals and beta thalassemia over 1,000 individuals in the United States. We are actively pursuing multiple programs in hemoglobinopathies including in sickle cell disease in collaboration with Novartis.

Ophthalmological Diseases

A number of serious, but rare diseases of the eye such as Leber's congenital amaurosis and Choroideremia, as well as more common diseases such as macular degeneration have been targeted using gene therapy approaches by academic groups as well as the pharmaceutical industry. Certain of our AAVHSCs have shown the unique ability to deliver genes to the eye when administered intravenously. Furthermore, in preclinical studies we conducted at our headquarters in 2017 in a minipig model, we evaluated the ability of our AAVHSCs, containing a vector that expresses a GFP transgene, to transduce retinal cells following localized delivery via subretinal injection to the eye at a dose of 1.3e12vg/kg (N=2). Expression of GFP was seen in all layers of the retina including the retinal pigment epithelium, photoreceptors and the outer nuclear layer out to day 28 and the AAVHSC subretinal treatment was well tolerated. We believe these studies suggest that our AAVHSCs have the potential to be useful as therapeutic vectors for treating retinal diseases in humans based on significant tropism to these target cells. We believe that these vectors have the potential to deliver long-lasting therapeutic benefit to patients that may eliminate the need for the regular and burdensome intravitreal injections that are required for many current treatments. We are collaborating with Novartis, experts in developing and marketing ophthalmic drugs, for select ophthalmology programs.

Lung Diseases

Biodistribution of our AAVHSCs in primate experiments showed that intravenous administration results in expression in a variety of lung cells. We believe this finding may provide a novel path to gene editing of serious genetic diseases such as cystic fibrosis, or CF. According to the Cystic Fibrosis Foundation Patient Registry there are more than 30,000 patients in the United States living with CF and more than 70,000 worldwide. Defects in the gene for an ion channel called cystic fibrosis transmembrane conductance regulator, or CFTR, result in a thick layer of mucus surrounding lung epithelial cells that obstructs airways and provides sites that can harbor life-threatening infections. This layer of mucus also limits the ability of therapeutics, including gene therapies, to be delivered by inhalation directly to the lungs. We intend to use our gene editing technology to develop therapies that can correct the underlying mutations in CF, focusing first on a specific mutation, delta 508, which is found in approximately 75% of patients. We believe that our technology can lead to significant correction of this mutation in the lung and in other tissues via intravenous administration.

Manufacturing

As a company committed to curing diseases, the ability to deliver our novel therapeutic vectors to patients is critical. Therefore, we are building strong internal scientific AAV process development and manufacturing capabilities and we are investing in a cGMP manufacturing facility to support our clinical development programs. We have established scalable manufacturing platforms for both gene editing and gene therapy. We view the development of internal manufacturing capacity and expertise as a key competitive advantage as it allows for better control over process development timelines, costs and intellectual property, and allows us to master our unique technology. Our process development and manufacturing teams are composed of industry veterans in the field of AAV and protein technologies, as well as experts in our novel AAVHSCs, with experience in both early development and commercialization of therapeutics.

Our process development and manufacturing strategy is to leverage technology platforms for both gene therapy and gene editing that are scalable and facilitate rapid development to the clinic. The gene therapy and gene editing platforms include development from vector design through to drug product manufacture. Expertise and learnings will be leveraged across both platform technologies.

Our gene therapy manufacturing strategy initially focuses on utilizing mammalian cells for our AAVHSC vector-based product candidates. Our current production process for the PKU program utilizes HEK293 cells in a serum free suspension bioreactor. The HEK293 is a well-characterized system and commonly used host cell for many clinical stage AAV vector products. Additionally, these cells are familiar to regulatory authorities and commercial raw materials and reagents are readily available. We have established a relationship with a contract manufacturing organization, or CMO, who specializes in the use of HEK293 gene therapy manufacturing. Our CMO partner will perform toxicology and cGMP manufacturing to supply our PKU program through Phase 1/2 clinical development.

Our gene editing manufacturing strategy is to internally control the process development and manufacturing to safeguard the proprietary nature of our technology, as well as to master all aspects of this technology. Furthermore, as part of our research and development collaboration with Novartis we have retained process development and manufacturing rights to the gene editing programs included within the collaboration.

We are in the planning stages of building a cGMP manufacturing facility that will have capability to process both gene therapy and gene editing batches in parallel. The initial scope will be for preclinical through Phase 1/2 manufacturing. Our manufacturing facility will leverage single use, disposable, closed system operations aligned to our technology platforms to ensure both flexibility and cost effectiveness. Our manufacturing facility is expected to be available for cGMP manufacturing of our product candidates in 2019.

Competition

The biotechnology and pharmaceutical industries, including in the gene therapy and gene editing fields, are characterized by rapidly advancing technologies, intense competition and a strong emphasis on intellectual property and proprietary products. While we believe that our technology, development experience and scientific knowledge provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies, and public and private research institutions that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization. Not only must we compete with other companies that are focused on gene therapy and/or gene editing technologies, any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

We compete in the segments of the pharmaceutical, biotechnology and other related markets that utilize technologies encompassing genomic medicines to create therapies, including gene therapy and gene editing. There are additional companies that are working to develop therapies in areas related to our research programs.

Our platform and product focus is the development of genetic medicines using our proprietary AAVHSCs *in vivo* either through the gene therapy or nuclease-free gene editing modality. If our current programs are approved for the indications for which we are currently planning clinical trials, they may compete with other products currently under development, including gene editing and gene therapy products. 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, 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, or protein therapies.

In addition, 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 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. 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. The key competitive factors affecting the success of all of our programs are likely to be their efficacy, safety, convenience and availability of reimbursement.

Furthermore, we rely upon a combination of patents and trade secret protection, as well as license 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. Moreover, our industry is characterized by the existence of large numbers of patents and frequent allegations of patent infringement. If, therefore, we are unable to obtain and maintain patent protection for our technology and products or if the scope of the patent protection obtained or in-licensed is not sufficiently broad or if the validity of such patent is threatened, we may not be able to compete effectively in our markets, as it could create opportunities for competitors to enter the market or dissuade other companies from collaborating with us to develop products and technology, any of 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. For more information regarding these competitive risks, see “Risk Factors—Risks Related to Our Intellectual Property.”

Intellectual Property

Our success depends in large part upon our ability to secure and maintain proprietary protection for our technologies and products and to operate without infringing the proprietary rights of others. Our policy is to protect our proprietary position by, among other methods, filing or collaboration with our licensors to file U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. We also use other forms of protection, such as confidential information and trademark protection, particularly where we do not believe patent protection is appropriate or obtainable.

Our patent portfolio consists of a combination of issued patents and pending patent applications that are licensed from third parties. As of March 1, 2018, we have an exclusive license or co-exclusive license under ten United States issued patents and 17 patent applications, pending in the United States and internationally.

For any individual patent, the term depends on the applicable law in the country in which the patent is granted. In most countries where we have filed patent applications or in-licensed patents and patent applications, patents have a term of 20 years from the application filing date or earliest claimed non-provisional priority date. In the United States, the patent term is 20 years but may be shortened if a patent is terminally disclaimed over another patent that expires earlier. The term of a U.S. patent may also be lengthened by a patent term adjustment, in order to address administrative delays by the United States Patent and Trademark Office in granting a patent.

In the United States, the term of a patent that covers an FDA-approved drug or biologic may be eligible for patent term extension in order to restore the period of a patent term lost during the premarket FDA regulatory review process. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the natural expiration of the patent. The patent term restoration period is generally equal to the regulatory review period for the approved product which period occurs after the date the patent issued, subject to certain exceptions. Only one patent may be extended for a regulatory review period for any product, and the application for the extension must be submitted prior to the expiration of the patent. In the future, we may decide to apply for restoration of patent term for one of our currently owned or licensed patents to extend its current expiration date, depending on the expected length of the clinical studies and other factors involved in the filing of the relevant BLA.

Licensed Intellectual Property

Certain of our issued patents and pending patent applications are exclusively licensed to us in all fields of use from COH. Certain of our issued patents and pending patent applications are co-exclusively licensed to us in all human therapeutic applications with and from Caltech.

The City of Hope Portfolio

In April 2016, we exclusively licensed two families of patents and patent applications directed to novel AAV capsids and their manufacture and methods of use, including their use in genome editing from COH.

These two families of patents and patent applications together include nine granted patents in the United States and 12 pending applications in the United States, Europe, Canada, Australia and other selected countries in Central America, South America, and Asia. The first family of issued patents and patent applications is material to HMI-102 and relates to our novel AAV capsids and vectors and their use in cellular transduction. The eight issued U.S. patents in this family are expected to expire in 2031, and may be extended by up to five years in certain countries via patent term extension depending on the regulatory pathway of the products covered by such patents. The second family includes one issued U.S. patent and patent applications directed to our AAV capsids, their methods of manufacture, and their use in genome editing. The issued patent in this family is expected to expire in 2035, and may be extended by up to five years in certain countries via patent term extension depending on the regulatory pathway of the products covered by such patents.

The Caltech Portfolio

In September 2016, we co-exclusively licensed, with another commercial third party, two families of patents and patent applications directed to novel AAV capsids and vectors that demonstrate enhanced blood-brain barrier penetration for the potential treatment of CNS diseases from Caltech.

These families of patents and patent applications include one granted patent in the United States and four pending applications in the United States and Europe and one international patent application under the Patent Cooperation Treaty. The issued U.S. patent relating to novel AAV capsids and vectors is expected to expire in 2034. Certain other patent applications directed to novel AAV capsids and vectors, if they were to issue, may have later expirations.

We also rely on trade secrets, technical know-how and continuing innovation to develop and maintain our competitive advantage. Our policy requires inventors who are identified on any company-owned patent applications to assign rights to us. We also rely on confidentiality agreements with our employees, consultants and other advisors to protect our proprietary information. Our policy is to require third parties that receive material confidential information to enter into confidentiality agreements with us.

Trademarks

Our trademarks Homology Medicines and HMI are pending or registered in the United States and certain international countries. We currently own three pending trademark applications in the United States, approximately 11 registered trademarks around the world, as well as 22 pending trademark applications. This includes our trademarks Homology Medicines, AMEnDR, and HMI, which are pending or registered in the United States and certain other countries.

Strategic Collaborations

Collaboration and License Agreement with the Novartis Institutes for BioMedical Research, Inc.

In November 2017, we entered into a collaboration and license agreement with Novartis, pursuant to which we agreed to collaborate on researching, developing, and commercializing novel genome editing products that modulate certain gene targets.

Under the terms of the agreement, we and Novartis agreed to collaborate to identify and synthesize gene editing vector candidates that modulate certain ophthalmic and sickle cell disease gene targets, against which Novartis agreed to develop licensed products. Our obligation to perform research for the targets will continue for five years from the effective date of the agreement.

We and Novartis agreed also to collaborate to explore the applicability of our technology with respect to other gene targets. Our obligation to perform such exploratory research concludes in November 2020.

We retain the right to commercialize products with *in vivo* applications related to sickle cell disease in the United States. Novartis will be responsible for commercializing products with *in vivo* applications related to sickle cell disease outside of the United States and globally for all other licensed products. We also retain the exclusive right to develop and commercialize products designed and optimized using our platform technology that modulates sickle cell disease gene targets.

Subject to certain limitations pursuant to the terms of the agreement, Novartis will be responsible for the internal and external costs incurred by us for the research activities as contemplated under the agreement. Novartis will also pay for the development of gene editing vector candidates and licensed products although we will reimburse Novartis for a certain percentage of the development costs for the *in vivo* applications related to sickle cell disease.

Subject to the terms of the agreement, we will generally be responsible for manufacturing gene editing vector candidates for certain ophthalmic and sickle cell disease gene targets for research, and gene editing vector candidates and licensed products for development and commercialization, and Novartis will bear all such manufacturing costs that we incur.

Subject to the terms of the agreement, we granted Novartis the following licenses: (i) a worldwide, non-exclusive, sublicensable license under certain of our intellectual property rights to perform Novartis' responsibilities under the applicable research plan; (ii) a worldwide, sublicensable license under certain of our intellectual property rights to conduct preclinical development activities, which license is co-exclusive (with us) during the research term, and exclusive for the remainder of the term of the agreement; (iii) a worldwide, non-exclusive, perpetual, irrevocable license, without the right to grant sublicenses, to use certain reagents generated as a result of our exploratory research activities under the agreement solely for Novartis' internal

research purposes; (iv) an exclusive, royalty-bearing, sublicensable license under certain of our intellectual property rights to develop and commercialize certain gene editing vector candidates and licensed products directed to certain ophthalmic and sickle cell disease gene targets, except for the rights to commercialize products with *in vivo* applications related to sickle cell disease in the United States; (v) as of the effective date, a co-exclusive (with us), royalty-bearing, sublicensable, worldwide license under certain of our intellectual property rights to manufacture certain gene editing vector candidates and/or licensed products directed to certain ophthalmic and sickle cell disease gene targets, which license will be exclusive as of a certain date on which Novartis is permitted to manufacture certain gene editing vector candidates and/or licensed products pursuant to the terms of the agreement; and (vi) a non-exclusive, royalty-free, fully paid, perpetual, irrevocable, worldwide license under certain of our intellectual property rights in connection with research, development, manufacturing, commercialization or other exploitation of products or services.

Subject to the terms of the agreement, Novartis granted to us the following licenses: (i) a worldwide, non-exclusive, sublicensable license under certain of Novartis' intellectual property rights to perform certain research activities during the research term; (ii) a worldwide, exclusive license, without the right to sublicense, under certain of Novartis' intellectual property rights to commercialize the *in vivo* products related to sickle cell disease developed pursuant to the agreement in the United States; and (iii) a non-exclusive, royalty-bearing, perpetual, irrevocable, worldwide, sublicensable license under certain of Novartis' intellectual property rights that may arise under the agreement that relate to our manufacturing know-how for our manufacture of gene editing vector candidates and products created using our platform technology.

Under the terms of the agreement, we received an upfront payment of $35.0 million. Novartis also purchased shares of our Series B preferred stock for an aggregate purchase price of $15.0 million. We are also eligible to receive up to a total of $20.0 million upon completion of certain development candidate selection activities. In addition, we are eligible to receive up to a total of $960.0 million in milestone payments, including up to $335 million in development milestone payments, up to $275 million in regulatory milestone payments and up to $350 million in commercial milestone payments, with respect to the licensed products. We are 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.

With respect to any products with *in vivo* applications related to the sickle cell disease program commercialized in the United States, we may book sales of such products and share net profits from such sales with Novartis (subject to certain circumstances in which Novartis obtains the right to book such sales, in which case Novartis will share such net profits with us) and we will reimburse Novartis for a percentage of the development costs incurred in connection with this program. The parties share such net profits equally.

The term of the agreement continues on a target-by-target basis until the expiration of all royalty payment obligations for the licensed products that modulate the applicable target on a country-by-country basis. Our royalty obligations under the agreement continue on a country-by-country and licensed product-by-licensed product basis until the later of (a) 10 years after the first commercial sale of such licensed product in a country, (b) the date on which such licensed product is no longer covered by certain intellectual property rights, and (c) the date on which certain regulatory exclusivity for such product expires. Either party may terminate the agreement on a target-by-target basis for the other party's material breach with respect to such target, or in the event of the other party's bankruptcy. Novartis may terminate the agreement for convenience on a target-by-target basis. We may terminate the agreement if Novartis files, or joins a third party in filing or maintaining, a patent challenge against certain of the patent rights we license to Novartis under the terms of the agreement.

License Agreement with the California Institute of Technology

In September 2016, we entered into a license agreement with Caltech, pursuant to which Caltech granted us a co-exclusive (subject to certain reserved non-commercial rights), sublicensable, and worldwide

license under certain AAV-related patents owned by Caltech for human therapeutic applications. Under this agreement, Caltech also granted us a non-exclusive, worldwide license under certain patents and other intellectual property controlled by Caltech to develop, manufacture, commercialize, and otherwise exploit products covered by such intellectual property rights for human therapeutic applications. We may grant sublicenses under the non-exclusive license to third parties to the extent necessary or useful for our, or our sublicensees', development, manufacturing, or sale of such products.

Under the Caltech agreement, we paid Caltech an initial licensing fee of $100,000. We are also required 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 to high single-digit percentages of sublicensing revenues. Subject to certain exceptions, our royalty obligations under the agreement continue on a country-by-country and licensed product-by-licensed product basis until the earliest of (a) the date on which such licensed product is no longer covered by certain intellectual property rights, (b) 10 years after the first commercial sale of such licensed product, or (c) 15 years after the effective date of the agreement. As partial consideration for the licenses granted under the agreement, we issued 101,405 shares of our common stock to Caltech.

The agreement will expire upon the expiration of the last-to-expire patent that is licensed to us or as long as royalties are due under the agreement, whichever is later. We agreed to use commercially reasonable efforts to introduce commercially, and reasonably fulfill market demand for, licensed products as soon as practicable. Either party may terminate the agreement in the event of the other party's uncured material breach and in the event of the other party's bankruptcy or insolvency. We may terminate the agreement for convenience.

City of Hope License Agreement

In April 2016, we entered into a license agreement with COH, pursuant to which COH granted us an exclusive, sublicensable, worldwide license to certain AAV vector-related patents and know-how owned by COH to develop, manufacture, use and commercialize products and services covered by such patents and know-how in any and all fields. COH also granted us a non-exclusive, sublicensable, worldwide license to certain background patents owned by COH to develop, manufacture, use and commercialize licensed products and licensed services in any and all fields.

Under the agreement, we paid COH an initial licensing fee of $75,000, and made a subsequent payment of $4.5 million representing a percentage of sublicensing revenue. We are also required to pay COH an annual license maintenance fee; up to a total of $3.2 million in potential milestone fees; a royalty in the low single-digit percentages on net sales of licensed products or services, subject to certain reductions in certain circumstances, with a certain annual minimum royalty; and low double-digit percentages of sublicensing revenues. As partial consideration for the licenses granted under the agreement, we issued 154,837 shares of our common stock to COH.

The COH agreement will expire on a country-by-country and on a licensed patent-by-licensed patent basis upon the expiration of the last-to-expire valid claim of such patent in such country. We agreed to use commercially reasonable efforts to develop and commercialize licensed products and licensed services. If we fail to achieve certain diligence milestones, COH may terminate the agreement or convert the exclusive rights under the agreement from exclusive to non-exclusive. Either party may terminate the agreement in the event of the other party's material breach, subject to an opportunity to cure, and in the event of the other party's bankruptcy or insolvency. We may terminate the agreement for convenience.

Government Regulation and Product Approval

Governmental authorities in the U.S., at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, labeling, packaging, promotion, storage, advertising, distribution, marketing, post-approval monitoring and reporting and export and import of

products such as those we are developing. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, are extensive and require the expenditure of substantial time and financial resources. For the purposes of this Section, the term "gene therapy" includes both traditional gene therapy products as well as gene editing and our gene correction product candidates.

FDA Approval Process

We expect our future product candidates to be regulated as biologics. Biological products, including gene therapy products, are subject to extensive regulation by the FDA under the Federal Food, Drug, and Cosmetic Act, or FD&C Act, and the Public Health Service Act, or PHS Act, and other federal, state, local and foreign statutes and regulations. Both the FD&C Act and the PHS Act and their corresponding regulations govern, among other things, the research, development, safety, testing, packaging, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of biological products. Before clinical testing of biological products in the United States may begin, we must submit an IND to the FDA, which reviews the clinical protocol, and the IND must become effective before clinical studies may begin. In some instances, we must also submit our protocols to the National Institutes of Health, or NIH, through its Recombinant DNA Advisory Committee, or RAC, for review before initiating clinical testing of gene therapy products.

Gene therapy products must be approved by the FDA before they may be legally marketed in the United States and by the appropriate foreign regulatory agencies before they may be legally marketed in foreign countries. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources and we may not be able to obtain the required regulatory approvals.

Within the FDA, the Center for Biologics Evaluation and Research, or CBER, regulates gene therapy products. The CBER works closely with the NIH and its RAC, which makes recommendations to the NIH on gene therapy issues and engages in a public discussion of scientific, safety, ethical and societal issues related to proposed and ongoing gene therapy protocols. The FDA has published guidance documents with respect to the development and submission of gene therapy protocols. The FDA also has published guidance documents related to, among other things, gene therapy products in general, their preclinical assessment, observing subjects involved in gene therapy clinical trials for delayed adverse events, potency testing, and chemistry, manufacturing and control information in gene therapy INDs.

To date, the FDA has approved three human gene therapy products for sale, including Kite Pharma's Yescarta, Novartis' Kymriah and Spark's Luxturna, and has provided general guidance regarding the development of gene therapy products. For example, the FDA has established the Office of Tissue and Advanced Therapies, or OTAT, within CBER, to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee, or CTGTAC, to advise CBER on its reviews. In addition, the FDA has issued a growing body of clinical guidelines, chemical, manufacturing and control, or CMC, guidelines and other guidelines, all of which are intended to facilitate industry's development of gene therapy products.

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

U.S. Biological Products Development Process

The FDA determined that more than minimally manipulated products must be approved by the FDA through the Biologics License Application, or BLA, process before they may be legally marketed in the United States. The process required by the FDA before a biologic may be marketed in the United States generally involves the following:

- completion of extensive nonclinical, sometimes referred to as pre-clinical laboratory tests, and pre-clinical animal trials and applicable requirements for the humane use of laboratory animals and formulation studies in accordance with applicable regulations, including good laboratory practices, or GLPs;
- submission to the FDA of an IND application, which must become effective before human clinical trials may begin;
- approval by an independent Institutional Review Board, or IRB, or ethics committee at each clinical site before the trial is commenced;
- performance of adequate and well-controlled human clinical trials according to the FDA's regulations commonly referred to as good clinical practices, or GCPs, and any additional requirements for the protection of human research subjects and their health information, to establish the safety and efficacy of the proposed biological product for its intended use;
- submission to the FDA of a BLA for marketing approval that includes substantive evidence of safety, purity, potency and efficacy from results of nonclinical testing and clinical trials;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the biological product is produced to assess compliance with cGMP to assure that the facilities, methods and controls are adequate to preserve the biological product's identity, strength, quality and purity;
- potential FDA audit of the nonclinical and clinical study sites that generated the data in support of the BLA; and
- FDA review and approval, or licensure, of the BLA.

Before testing any biological product candidate, including a gene therapy product, in humans, the product candidate enters the preclinical testing stage. Preclinical tests, also referred to as nonclinical studies, include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and activity of the product candidate. The conduct of the preclinical tests must comply with federal regulations and requirements, including GLPs.

The clinical study sponsor must submit the results of the preclinical tests, together with manufacturing and controls, information about product chemistry, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. Some preclinical testing, such as reproductive toxicity tests and carcinogenicity in animals, may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, after which human clinical trials may begin unless the FDA places the clinical study on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical study can begin. With gene therapy protocols, if the FDA allows the IND to proceed, but a RAC decides that full public review of the protocol is warranted, the FDA will request at the completion of its IND review that sponsors delay initiation of the protocol until after completion of the RAC review process. The FDA may also impose clinical holds on a biological product

candidate at any time before or during clinical trials due to safety concerns or non-compliance. If the FDA imposes a clinical hold, trials may not recommence without FDA authorization and then only under terms authorized by the FDA. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that suspend or terminate such trials. In addition to the IND submission process, sponsors of certain clinical studies of cells containing recombinant or synthetic nucleic acid molecules, including human gene transfer studies, must comply with the NIH's Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules, or NIH Guidelines. The NIH Guidelines set forth the principles and requirements for NIH and institutional oversight of research with recombinant or synthetic nucleic acid molecules, including the standards for investigators and institutions to follow to ensure the safe handling and containment of such molecules. In April 2016, modifications to the NIH Guidelines went into effect, pursuant to which only a subset of human gene transfer protocols are subject to review by the RAC. Specifically, under the modified NIH Guidelines, RAC review of the protocol will be required only in exceptional cases where an oversight body such as an Institutional Biosafety Committee, or IBC, which provides local review and oversight of research utilizing recombinant or synthetic nucleic acid molecules, or an IRB determines that the protocol would significantly benefit from RAC review, and the protocol (a) uses a new vector, genetic material, or delivery methodology that represents a first-in-human experience and thus presents an unknown risk, and/or (b) relies on preclinical safety data that were obtained using a new preclinical model system of unknown and unconfirmed value, and/or (c) involves a proposed vector, gene construct, or method of delivery associated with possible toxicities that are not widely known and that may render it difficult for oversight bodies to evaluate the protocol rigorously. The RAC review proceedings are public, and reports are posted publicly to the website for the NIH's Office of Biotechnology Activities. Although compliance with the NIH Guidelines is mandatory for research conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them. Independent of RAC review, the NIH Guidelines also require all human gene transfer protocols subject to the NIH Guidelines to be registered with NIH, with limited exemptions. A study subject to the NIH Guidelines may not begin until the IBC approves the protocol, and the IBC cannot approve the protocol until confirmation from the NIH that such registration is complete. In the event that RAC review is warranted, the protocol registration process cannot be completed until RAC review has taken place.

Clinical trials involve the administration of the biological product candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the study sponsor's control. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical study, dosing procedures, subject selection and exclusion criteria, the efficacy measurements to be evaluated and the parameters to be used to monitor subject safety, including stopping rules that assure a clinical study will be stopped if certain adverse events should occur. Each protocol and any amendments to the protocol must be submitted to the FDA as part of the IND. Clinical trials must be conducted and monitored in accordance with the FDA's regulations comprising the GCP requirements, including the requirement that all research subjects provide informed consent. Further, each clinical study must be reviewed and approved by an independent institutional review board, or IRB, at or servicing each institution at which the clinical study will be conducted. An IRB is charged with protecting the welfare and rights of study participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the form and content of the informed consent that must be signed by each clinical study subject or his or her legal representative and must monitor the clinical study until completed. Clinical trials also must be reviewed by an IBC, a local institutional committee that reviews and oversees basic and clinical research conducted at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- Phase I. The biological product candidate is initially introduced into healthy human subjects and tested for safety. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.

- Phase II. The biological product candidate is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule.

- Phase III. Clinical trials are undertaken to further evaluate dosage, clinical efficacy, potency, and safety in an expanded patient population at geographically dispersed clinical study sites. These clinical trials are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for product labeling.

In most cases, the FDA requires two adequate and well-controlled Phase 3 clinical trials to demonstrate the safety and efficacy of a biological product. In rare instances, a single Phase 3 trial, together with other confirmatory evidence may be sufficient to support a BLA submission. Post-approval clinical trials, sometimes referred to as Phase IV clinical trials, may be conducted after initial marketing approval. These clinical trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication, particularly for long-term safety follow-up. The FDA recommends that sponsors observe subjects for potential gene therapy-related delayed adverse events for a 15-year period, including a minimum of five years of annual examinations followed by ten years of annual queries, either in person or by questionnaire.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical study investigators. Annual progress reports detailing the results of the clinical trials must be submitted to the FDA. Written IND safety reports must be promptly submitted to the FDA, the NIH and the investigators for serious and unexpected adverse events, any findings from other trials, tests in laboratory animals or *in vitro* testing that suggest a significant risk for human subjects, or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information. Phase I, Phase II and Phase III clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor or its data safety monitoring board may suspend or permanently discontinue a clinical study at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk or the clinical study is not being conducted in accordance with FDA regulations. Similarly, an IRB can suspend or terminate approval of a clinical study at its institution if the clinical study is not being conducted in accordance with the IRB's requirements or if the biological product candidate has been associated with unexpected serious harm to patients. The FDA and the IRB may also halt, terminate or impose other conditions if either believes the patients are subject to unacceptable risk.

There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries. Sponsors of clinical trials of FDA-regulated products, including biologics, are required to register and disclose certain clinical trial information, which is publicly available at www.clinicaltrials.gov. Information related to the product, patient population, phase of investigation, study sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved.

Human gene therapy products based on gene-editing technology are a new category of therapeutics. Because this is a relatively new and expanding area of novel therapeutic interventions, there can be no assurance as to the length of the study period, the number of patients the FDA will require to be enrolled in the trials in order to establish the safety, efficacy, purity and potency of human gene therapy products, or that the data generated in these trials will be acceptable to the FDA to support marketing approval. The NIH and the FDA have a publicly accessible database, the Genetic Modification Clinical Research Information System, which includes information on gene transfer trials and serves as an electronic tool to facilitate the reporting and analysis of adverse events in these trials.

Concurrent with clinical trials, companies usually complete additional animal trials and must also develop additional information about the physical characteristics of the biological product candidate as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. To help reduce the risk of the introduction of adventitious agents with use of biological products, the PHS Act emphasizes the importance of manufacturing control for products whose attributes cannot be precisely defined. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the sponsor must develop methods for testing the identity, strength, quality, potency and purity of the final biological product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the biological product candidate does not undergo unacceptable deterioration over its shelf life.

U.S. Review and Approval Processes

After the completion of clinical trials of a biological product candidate, FDA approval of a BLA must be obtained before commercial marketing and distribution of the biological product. The BLA must include results of product development, laboratory and animal trials, human trials, information on the manufacture, pharmacology, chemistry and controls of the product, proposed labeling and other relevant information. In addition, under the Pediatric Research Equity Act, or PREA, a BLA or supplement to a BLA must contain data to assess the safety and effectiveness of the biological product candidate for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective.

The Food and Drug Administration Safety and Innovation Act, or FDASIA, requires that a sponsor who is planning to submit a marketing application for a drug or biological product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan, or PSP, within sixty days after an end-of-Phase 2 meeting or as may be agreed between the sponsor and FDA. The initial PSP must include, among other things, an outline of the pediatric study or studies that the sponsor plans to conduct, including to the extent practicable study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information, along with any other information specified in FDA regulations. The FDA and the sponsor must reach agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from nonclinical studies, early phase clinical trials, and/or other clinical development programs. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any biological product for an indication for which orphan designation has been granted. The testing and approval processes require substantial time and effort and there can be no assurance that the FDA will accept the BLA for filing and, even if filed, that any approval will be granted on a timely basis, if at all.

Under the Prescription Drug User Fee Act, or PDUFA, as amended, each BLA must be accompanied by a user fee. The FDA adjusts the PDUFA user fees on an annual basis. PDUFA also imposes an annual program fee for products. Fee waivers or reductions are available in certain circumstances, including a waiver of the

application fee for the first human drug application filed by a small business. Additionally, no user fees are assessed on BLAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

Within 60 days following submission of the application, the FDA reviews a BLA submitted to determine if it is substantially complete before the agency accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the BLA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the BLA. Under PDUFA, the FDA has agreed to certain performance goals to complete the review of BLAs. The FDA may give a priority review designation to biological products that offer major advances in treatment, or provide a treatment where no adequate therapy exists. A priority review means that the goal for the FDA to review an application is six months, rather than the standard review of ten months under current PDUFA guidelines. Under the current PDUFA agreement, these six and ten month review periods are measured from the “filing” date rather than the receipt date for original BLAs, which typically adds approximately two months to the timeline for review and decision from the date of submission.

The FDA reviews the BLA to determine, among other things, whether the proposed product is safe and potent, or effective, for its intended use, and has an acceptable purity profile, and whether the product is being manufactured in accordance with cGMP requirements to assure and preserve the product’s identity, safety, strength, quality, potency and purity. The FDA may refer applications for novel biological products or biological products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. During the biological product approval process, the FDA also will determine whether a Risk Evaluation and Mitigation Strategy, or REMS, is necessary to assure the safe use of the biological product candidate. If the FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS; the FDA will not approve the BLA without a REMS, if required.

Before approving a BLA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure that the clinical trials were conducted in compliance with IND study requirements and GCP requirements. To assure cGMP and GCP compliance, an applicant must incur significant expenditure of time, money and effort in the areas of training, record keeping, production, and quality control.

Notwithstanding the submission of relevant data and information, the FDA may ultimately decide that the BLA does not satisfy its regulatory criteria for approval and deny approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data. If the agency decides not to approve the BLA in its present form, the FDA will issue a complete response letter that usually describes all of the specific deficiencies in the BLA identified by the FDA. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, the applicant may either resubmit the BLA, addressing all of the deficiencies identified in the letter, or withdraw the application. If, or when, those deficiencies have been addressed to the FDA’s satisfaction in a resubmission of the BLA, the FDA will issue an approval letter. Under the current PDUFA guidelines, the FDA has committed to reviewing such resubmissions in two or six months of receipt depending on the type of information included.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the BLA with a Risk Evaluation and Mitigation Strategy, or REMS, to ensure the benefits of the product outweigh its potential risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a medicine and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. The requirement for a REMS can materially affect the potential market and profitability of the product.

Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. Changes to some of the conditions established in an approved BLA, including changes in indications, product labeling, manufacturing processes or facilities, require submission and FDA approval of a new BLA or BLA supplement before the change can be implemented. A BLA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing BLA supplements as it does in reviewing BLAs. The FDA may require one or more Phase IV post-market studies or surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies.

Additionally, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could impact the timeline for regulatory approval or otherwise impact ongoing development programs. For example, in December 2016, the 21st Century Cures Act was signed into law. The Act is intended, among other things, to modernize the regulation of drugs and biologics and to spur innovation, and contains provisions specific to the development of cell therapies.

One of the performance goals agreed to by the FDA under the PDUFA is to review 90% of standard BLAs in 10 months from the filing date and 90% of priority BLAs in six months from the filing date, whereupon a review decision is to be made. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs and its review goals are subject to change from time to time. The review process and the PDUFA goal date may be extended by three months if the FDA requests or the BLA sponsor otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

Orphan Drug Designation

The FDA may grant Orphan Drug Designation to drugs or biologics intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and marketing the drug or biologic for this type of disease or condition will be recovered from its sales in the United States. Orphan product designation must be requested before submitting a BLA. After the FDA grants orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

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 BLA user-fee waivers. In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application, including a full BLA, to market the same drug or biologic for the same indication for a period of seven years, except in limited

circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer with orphan exclusivity is unable to assure sufficient quantities of the approved orphan-designated product. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same biological product as defined by the FDA or if our product candidate is determined to be contained within the competitor's product for the same indication or disease. If a drug or biological product designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity. In addition, exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. We have received orphan drug designation for the use of AAVHSC expressing human PAH for the treatment of PKU. There can be no assurance that we will receive orphan drug designation for additional indications or for any additional product candidates.

Expedited Development and Review Programs

The FDA has a Fast Track program that is intended to expedite or facilitate the process for reviewing new biological products that meet certain criteria. Specifically, new biological products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a new biologic may request that the FDA designate the biologic as a Fast Track product at any time during the clinical development of the product. The FDA must determine if the biologic product candidate qualifies for Fast Track designation within 60 days of receipt of the sponsor's request. Unique to a Fast Track product, the FDA may consider for review sections of the marketing application on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the application, the FDA agrees to accept sections of the application and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the application.

Any product submitted to the FDA for marketing, including under a Fast Track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. Any product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or a significant improvement in the treatment, diagnosis or prevention of a disease compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new biological product designated for priority review in an effort to facilitate the review. Additionally, a product may be eligible for accelerated approval. Biological products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may be eligible for accelerated approval, which means that they may be approved on the basis of adequate and well-controlled clinical studies establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or 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. As a condition of approval, the FDA may require that a sponsor of a biological product subject to accelerated approval perform adequate and well-controlled post-marketing Phase IV clinical studies. Failure to conduct required post-approval trials, or to confirm a clinical benefit during post-marketing trials, will allow the FDA to withdraw the approved biologic product from the market on an expedited basis. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. Fast Track designation, priority review and accelerated approval do not change the standards for approval but may expedite the development or approval process.

In addition, under the provisions of FDASIA, enacted in 2012, the FDA established a Breakthrough Therapy Designation which is intended to expedite the development and review of products that treat serious or life-threatening diseases or conditions. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the features of Fast Track designation, as well as more intensive FDA interaction and guidance. The Breakthrough Therapy Designation is a distinct status from both accelerated approval and priority review, but these can also be granted to the same product candidate if the relevant criteria are met. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy. All requests for breakthrough therapy designation will be reviewed within 60 days of receipt, and FDA will either grant or deny the request.

Fast Track designation, priority review, accelerated approval and breakthrough therapy designation do not change the standards for approval but may expedite the development or approval process. Even if we receive one or both of these designations for our product candidates, the FDA may later decide that our product candidates no longer meets the conditions for qualification. In addition, receiving these designations may not provide us with a material commercial advantage.

Post-Approval Requirements

Maintaining substantial compliance with applicable federal, state, and local statutes and regulations requires the expenditure of substantial time and financial resources. Rigorous and extensive FDA regulation of biological products continues after approval, particularly with respect to cGMP requirements. We will rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of any products that we may commercialize. Manufacturers of our products are required to comply with applicable requirements in the cGMP regulations, including quality control and quality assurance and maintenance of records and documentation. Other post-approval requirements applicable to biological products, include reporting of cGMP deviations that may affect the identity, potency, purity and overall safety of a distributed product, record-keeping requirements, reporting of adverse effects, reporting updated safety and efficacy information, and complying with electronic record and signature requirements.

After a BLA is approved, the product also may be subject to official lot release. As part of the manufacturing process, the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release by the FDA, the manufacturer submits samples of each lot of product to the FDA together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot. The FDA also may perform certain confirmatory tests on lots of some products, such as viral vaccines, before releasing the lots for distribution by the manufacturer. In addition, the FDA conducts laboratory research related to the regulatory standards on the safety, purity, potency, and effectiveness of biological products.

To help reduce the increased risk of the introduction of adventitious agents, the PHS Act emphasizes the importance of manufacturing controls for products whose attributes cannot be precisely defined. The PHS Act also provides authority to the FDA to immediately suspend biologics licenses in situations where there exists a danger to public health, to prepare or procure products in the event of shortages and critical public health needs, and to authorize the creation and enforcement of regulations to prevent the introduction or spread of communicable diseases within the United States.

The FDA may require one or more Phase IV post-market studies or surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies. We also must comply with the FDA's advertising

and promotion requirements, such as those related to direct-to-consumer advertising, the prohibition on promoting products for uses or in patient populations that are not described in the product's approved labeling (known as "off-label use"), industry-sponsored scientific and educational activities, and promotional activities involving the internet. Biologics may be marketed only for the approved indications and in accordance with the provisions of the approved labeling.

Discovery of previously unknown problems or the failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product or withdrawal of the product from the market as well as possible civil or criminal sanctions. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant or manufacturer to administrative or judicial civil or criminal sanctions and adverse publicity. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, clinical hold, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, mandated corrective advertising or communications with doctors, debarment, restitution, disgorgement of profits, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Biological product manufacturers and other entities involved in the manufacture and distribution of approved biological products are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP requirements and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved BLA, including withdrawal of the product from the market. In addition, changes to the manufacturing process or facility generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

U.S. Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of the FDA approval of the use of our product candidates, some 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, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally equal to the regulatory review period for the approved product which period occurs after the date the patent issued, subject to certain exceptions. Only one patent may be extended for a regulatory review period for any product, and the application for the extension must be submitted prior to the expiration of the patent. The U.S. Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may intend to apply for restoration of patent term for one of our currently owned or licensed patents to extend its current expiration date, depending on the expected length of the clinical studies and other factors involved in the filing of the relevant BLA.

For patents that might expire during the BLA review phase, the patent owner may request an interim patent term extension. If eligible, an interim patent term extension may be granted for a period of not more than one year. The patent owner may apply for not more than four subsequent interim extensions. Any interim extension granted will not be longer than the maximum period of extension allowed post-approval.

Biosimilars and Exclusivity

The Patient Protection and Affordable Care Act, or 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. To date, fewer than 10 biosimilars have been licensed under the BPCIA, and numerous biosimilars have been approved in Europe. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars.

Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. However, complexities associated with the larger, and often more complex, structures of biological products, as well as the processes by which such products are manufactured, pose significant hurdles to implementation of the abbreviated approval pathway that are still being worked out by the FDA.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor’s own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed “interchangeable” by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

A biological product can also obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued “Written Request” for such a study.

The BPCIA is complex and continues to be interpreted and implemented by the FDA. In addition, recent government proposals have sought to reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate impact, implementation, and meaning of the BPCIA remains subject to significant uncertainty.

Other Healthcare Laws and Compliance Requirements

Pharmaceutical companies are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business. Such laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, privacy and security and physician sunshine laws and regulations. If their operations are found to be in violation of any of such laws or any other governmental regulations that apply, they may be subject to penalties, including, without limitation, civil and criminal penalties, damages, fines, the curtailment or restructuring of operations, exclusion from participation in federal and state healthcare programs and individual imprisonment.

Coverage and Reimbursement

Sales of any product depend, in part, on the extent to which such product will be covered by third-party payors, such as federal, state, and foreign government healthcare programs, commercial insurance and managed healthcare organizations, and the level of reimbursement for such product by third-party payors. Decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. These third-party payors are increasingly reducing reimbursements for medical products, drugs and services. In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product. Decreases in third-party reimbursement for any product or a decision by a third-party payor not to cover a product could reduce physician usage and patient demand for the product and also have a material adverse effect on sales.

Healthcare Reform

In March 2010, President Obama signed the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively known as the Affordable Care Act, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly affected the pharmaceutical industry. The Affordable Care Act contains a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement adjustments and fraud and abuse changes. Additionally, the Affordable Care Act:

- increases the minimum level of Medicaid rebates payable by manufacturers of brand name drugs from 15.1% to 23.1%;
- requires collection of rebates for drugs paid by Medicaid managed care organizations;
- requires manufacturers to participate in a coverage gap discount program, under which they must agree to offer 50 percent 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, beginning January 2011; and
- imposes a non-deductible annual fee on pharmaceutical manufacturers or importers who sell “branded prescription drugs” to specified federal government programs.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the Affordable Care Act, and we expect there will be additional challenges and amendments to the Affordable Care Act in the future. Other legislative changes have been proposed and adopted since the Affordable Care Act was enacted, including aggregate reductions of Medicare payments to providers of 2% per fiscal year and reduced payments to several types of Medicare providers. Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. Individual states in the United States have also become increasingly active in implementing regulations designed to control pharmaceutical 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.

Additional Regulation

In addition to the foregoing, state and federal laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservancy and Recovery Act and the Toxic Substances Control Act, affect our business. These and other laws govern our use, handling and disposal of various biological, chemical and radioactive substances used in, and wastes generated by, our operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. We believe that we are in material compliance with applicable environmental laws and that continued compliance therewith will not have a material adverse effect on our business. We cannot predict, however, how changes in these laws may affect our future operations.

Government Regulation Outside of the United States

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical studies and any commercial sales and distribution of our products. Because biologically sourced raw materials are subject to unique contamination risks, their use may be restricted in some countries.

Whether or not we obtain FDA approval of a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical studies or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical study application, or CTA, much like the IND prior to the commencement of human clinical studies. In the European Union, for example, a CTA must be submitted to each country's national health authority and an independent ethics committee, much like the FDA and the IRB, respectively. Once the CTA is approved in accordance with a country's requirements, clinical study development may proceed.

The requirements and process governing the conduct of clinical studies, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical studies are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

To obtain regulatory approval of an investigational biological product under European Union regulatory systems, we must submit a marketing authorization application. The application used to file the BLA in the United States is similar to that required in the European Union, with the exception of, among other things, country-specific document requirements. The European Union also provides opportunities for market exclusivity. For example, in the European Union, upon receiving marketing authorization, new chemical entities generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, data exclusivity prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic application. During the additional two-year period of market exclusivity, a generic marketing authorization can be submitted, and the innovator's data may be referenced, but no generic product can be marketed until the expiration of the market exclusivity. However, there is no guarantee that a product will be considered by the European Union's regulatory authorities to be a new chemical entity, and products may not qualify for data exclusivity. Products receiving orphan designation in the European Union can receive ten years of market exclusivity, during which time no similar medicinal product for the same indication may be placed on the market. An orphan product can also obtain an additional two years of market exclusivity in the European Union for pediatric studies. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications.

The criteria for designating an "orphan medicinal product" in the European Union are similar in principle to those in the United States. Under Article 3 of Regulation (EC) 141/2000, a medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or

chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the European Union when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the European Union to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the European Union, or if such a method exists, the product will be of significant benefit to those affected by the condition, as defined in Regulation (EC) 847/2000. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and are, upon grant of a marketing authorization, entitled to ten years of market exclusivity for the approved therapeutic indication. The application for orphan drug designation must be submitted before the application for marketing authorization. The applicant will receive a fee reduction for the marketing authorization application if the orphan drug designation has been granted, but not if the designation is still pending at the time the marketing authorization is submitted. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The 10-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, marketing authorization may be granted to a similar product for the same indication at any time if:

- the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior;
- the applicant consents to a second orphan medicinal product application; or
- the applicant cannot supply enough orphan medicinal product.

For other countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical studies, product licensing, pricing and reimbursement vary from country to country. In all cases, again, the clinical studies are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Employees

As of March 1, 2018, we had 67 full-time employees, including 26 employees with M.D. or Ph.D. degrees. Of these full-time employees, 41 employees are engaged in research and development activities. None of our employees is represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

Facilities

We currently occupy approximately 23,000 square feet of office and laboratory space in Bedford, Massachusetts, under a lease that expires in 2021. We have also signed a lease for an additional 67,000 square feet of office, laboratory and manufacturing space that expires in 2027, and we expect to occupy a portion of that space beginning in the second half of 2018. We believe that our facilities are sufficient to meet our current needs and that suitable additional space will be available as and when needed.

Legal Proceedings

We are not subject to any material legal proceedings.

MANAGEMENT

Executive Officers and Directors

The following table sets forth the name, age and position of each of our executive officers and directors as of March 18, 2018.

Name	Age	Position
Executive Officers		
Arthur O. Tzianabos, Ph.D.	54	President and Chief Executive Officer and Director
Bradford Smith	62	Chief Financial Officer, Treasurer and Secretary
Siyamak (Sam) Rasty, Ph.D.	54	Chief Operating Officer
Albert Seymour, Ph.D.	50	Chief Scientific Officer
Directors		
Steven Gillis, Ph.D.(1)	64	Director
Richard J. Gregory, Ph.D.(2)	60	Director
Kush M. Parmar, M.D., Ph.D.(2)	37	Director
Matthew R. Patterson(3)	46	Director
Mahendra G. Shah, Ph.D.(1)	73	Director
Mary Thistle(1)	58	Director
Cameron Wheeler, Ph.D.(3)	39	Director

(1) Member of the audit committee.
(2) Member of the compensation committee.
(3) Member of the nominating and corporate governance committee.

Executive Officers and Key Employees

Arthur O. Tzianabos, Ph.D. has served as our President, Chief Executive Officer and member of our board of directors since April of 2016. Dr. Tzianabos joined Homology from OvaScience where he served as President and Chief Scientific Officer from September of 2013 to March of 2016. Prior to OvaScience, Dr. Tzianabos spent nine years at Shire Pharmaceuticals where he served in positions of increasing responsibility, including Senior Director, Discovery Research, Vice President, Program Management and Senior Vice President and Head, Research and Early Development. From 1992 to 2005, Dr. Tzianabos was a faculty member at Harvard Medical School and maintained laboratories at the Channing Laboratory, Brigham and Women's Hospital and the Department of Microbiology and Molecular Genetics at Harvard Medical School. Dr. Tzianabos previously served as a director of BIND Therapeutics, Inc. Dr. Tzianabos holds a B.S. in Biology from Boston College and a Ph.D. in Microbiology from the University of New Hampshire. We believe Dr. Tzianabos' extensive academic and clinical experience, as well as his knowledge of the industry, qualifies him to serve on our board of directors.

Bradford Smith has served as our Chief Financial Officer and Treasurer since April of 2017 and our Secretary since July of 2017. From March 2014 to April 2017, Mr. Smith was Chief Financial Officer of Ocular Therapeutix, Inc. Prior to joining Ocular Therapeutix, Mr. Smith served as the Chief Financial Officer of OmniGuide, Inc., a medical device company, from July 2008 to March 2014. Mr. Smith holds a B.S. in Biology from Tufts University and an M.B.A. from the Whittemore School of Business and Economics at the University of New Hampshire.

Siyamak (Sam) Rasty, Ph.D. has served as our Chief Operating Officer since March 2016. Prior to joining Homology, Dr. Rasty was Vice President and Head of New Products at Shire Pharmaceuticals from August 2011 to January 2016. Dr. Rasty received a B.S. and Ph.D. in Biochemistry from Louisiana State University and holds an M.B.A. from Villanova University which he received in 2002.

Albert Seymour, Ph.D. has served as our Chief Scientific Officer since April of 2016. Prior to joining Homology, Dr. Seymour was Senior Vice President, Head of Global Research and Nonclinical Development at

Shire Pharmaceuticals from 2011 to 2016. Dr. Seymour received his B.A. in Biology from the University of Delaware, an M.S. from Johns Hopkins University School of Medicine and his Ph.D. in Human Genetics from the University of Pittsburgh.

Directors

Steven Gillis, Ph.D. has served as a member of our board of directors since 2016. Since 2005, Dr. Gillis has been a managing director at ARCH Venture Partners, a venture capital firm. From 1994 to 2005, Dr. Gillis served as chief executive officer and chairman of the board of directors of Corixa Corporation, which he co-founded in October 1994. Previously, Dr. Gillis served as a director, head of research and development, chief scientific officer and acting chief executive officer of Immunex Corporation, which he co-founded, from 1981 until his departure in 1994. As a former director and chairman of Trubion Pharmaceuticals, Inc., Dr. Gillis led its acquisition by Emergent BioSolutions in the fall of 2010. Dr. Gillis currently serves as a director of Shire plc, Oncofactor Corp., Pulmatrix, Inc. and serves as director and chairman of Accelerator Corporation, VBI Vaccines Inc., VentiRX Pharmaceuticals, Inc., Theraclone Sciences, Inc. and Lycera Corp. Dr. Gillis previously served as a director at PhaseRx, Inc. from 2008 to 2018 and at bluebird bio, Inc. from 2011 to 2015. Dr. Gillis received his B.A. in biology and English from Williams College and his Ph.D. in biological science from Dartmouth College. We believe that Dr. Gillis's knowledge in immunology and experience in the venture capital industry, particularly with biotechnology and pharmaceutical companies, qualifies him to serve as a member of our board of directors.

Richard J. Gregory, Ph.D. has served as a member of our board of directors since 2015. Dr. Gregory is Executive Vice President and Chief Scientific Officer of ImmunoGen, Inc., where he has been since 2015. Prior to joining ImmunoGen, he spent 25 years at Genzyme Corporation, a biotechnology company, in roles of increasing responsibility, including Senior Vice President and Head of Research from 2003 until Genzyme's acquisition by Sanofi in 2011, and Head of Research and Development for Genzyme from 2011 through 2014. Dr. Gregory serves as a director of ProMIS Neurosciences, Inc. Dr. Gregory holds a Ph.D. from the University of Massachusetts, Amherst, and completed his post-doctoral work at the Worcester Foundation for Experimental Biology. We believe that Dr. Gregory's knowledge of immunology qualifies him to serve as a member of our board of directors.

Kush M. Parmar, M.D., Ph.D. has served as a member of our board of directors since 2015. Dr. Parmar is a Managing Partner at 5AM Ventures, an early stage venture capital firm focused on the life sciences, where he has been since 2010. Before joining 5AM, from 2002 to 2010, he was at Harvard Medical School, where he was an NIH-sponsored M.D./Ph.D. physician scientist fellow in the joint Harvard-MIT Health Sciences and Technology Program. Dr. Parmar currently serves as a director on the boards of Arvinas, Audentes, scPharmaceuticals Inc. and CycloPorters. He previously served as board observer for Envoy (acquired by Takeda) and Achaogen. He is a member of the scientific advisory board of the Grace Wilsey Foundation and is a fellow of the Society of Kauffman Fellows. Before joining 5AM, Dr. Parmar completed clinical clerkships at the Massachusetts General & Brigham and Women's Hospitals, attended courses at Harvard Business School and consulted for an oncology startup. He also founded a non-profit international development organization, the Cruz Blanca Initiative. He holds an A.B. in Molecular Biology and Medieval Studies from Princeton University, a Ph.D. in Experimental Pathology from Harvard University, and an M.D. from Harvard Medical School. We believe that Dr. Parmar's experience in the life sciences industry, his experience as a venture capitalist and senior executive, as well as his service on the boards of directors of numerous companies provide him with the qualifications to serve as a director of our company.

Matthew R. Patterson has served as a member of our board of directors since 2018. Mr. Patterson is the co-founder of Audentes Therapeutics and has served as the President and Chief Executive Officer and a member of the board of directors since November 2012. Previously, Mr. Patterson was the Entrepreneur-In-Residence at OrbiMed Advisors LLC, an investment firm, from November 2011 to December 2012. Prior to OrbiMed, Mr. Patterson served in roles at Amicus Therapeutics, Inc., BioMarin Pharmaceutical Inc. and Genzyme Corporation. Mr. Patterson is a member of the board of directors of Gilda's Club of New York City, which provides social and

emotional support for people living with cancer. Mr. Patterson holds a B.A. from Bowdoin College. We believe that Mr. Patterson's experience in the biotechnology and biopharmaceutical industries, as well as his service on the board of directors of a public company provide him with the qualifications to serve as a director of our company.

Mahendra G. Shah, Ph.D. has served as a member of our board of directors since 2017. Dr. Shah has been with Vivo Capital, LLC, a healthcare focused investment firm, since March 2010, and is currently serving as its managing director. Dr. Shah is the founder and executive chairman of Semnur Pharmaceuticals. Dr. Shah previously served as chairman of the board of Essentialis, and currently serves as a board member of Soleno Therapeutics, Verona Pharma and several other privately held companies in the biopharmaceutical and biotechnology industries. Dr. Shaw is also a member of the board of trustees of St. John's University. From September 2005 to December 2009, he was the founder, chairman and CEO of NextWave Pharmaceuticals, a pediatric focused specialty pharmaceutical company, which was acquired by Pfizer. From 1993 to May 2003, he was the chairman and CEO of First Horizon Pharmaceuticals, a publicly traded specialty pharmaceutical company before it was sold to Shionogi Pharmaceuticals. From 1991 to October 1999, he was vice president of E. J. Financial Enterprises, Inc., a healthcare fund management company. He previously served on the boards of Biotie Therapies, Unimed Pharmaceuticals (UMED), Introgen Therapeutics, Inpharmakon, Protomed, Structural Bioinformatics and Zarix. From 1987 to 1991 he was the senior director of new business development with Fujisawa USA (now part of Astellas Pharma US, Inc.). Prior to that time he worked in various scientific and management positions with Schering-Plough and Bristol Myers-Squibb. Dr. Shah received his Ph.D. in industrial pharmacy from St. John's University and his Bachelor's and Master's Degree in Pharmacy from L.M. College of Pharmacy in Gujarat, India. We believe Dr. Shah is able to make a valuable contribution to our board of directors due to his vast experience as a finance professional in the biomedical and pharmaceutical industries.

Mary Thistle has served as a member of our board of directors since March 2018. Ms. Thistle has served as the Chief of Staff of the Bill & Melinda Gates Medical Research Institute since January 2018. Prior to that, she held senior leadership positions at Dimension Therapeutics, Inc., including Chief Operating Officer from 2016 to 2017 and Chief Business Officer from 2015 to 2016. Prior to joining Dimension, she spent six years at Cubist Pharmaceuticals, Inc., where she held various leadership positions, including Senior Vice President, Business Development from 2014 to 2015, Vice President, Business Development from 2012 to 2013 and Senior Director, Business Development from 2009 to 2012. Prior to that, she held various positions at ViaCell, Inc. and PerkinElmer. Ms. Thistle serves as a director of Enterome SA, a pharmaceutical and diagnostics company based in Paris, France. Ms. Thistle holds a B.S. in accounting from the University of Massachusetts, Boston. We believe that Ms. Thistle is qualified to serve on our board of directors due to her finance background and industry experience.

Cameron Wheeler, Ph.D. has served as a member of our board of directors since 2017. Dr. Wheeler serves as a Principal at Deerfield Management. Prior to joining Deerfield in 2014, Cameron was at Eleven Biotherapeutics, Inc., an oncology biotech company, for more than five years, where he was responsible for corporate development and commercial strategy. Prior to Eleven, Cameron was at Third Rock Ventures, a Boston-based venture capital firm focused on launching and building life science companies. While at Third Rock, Cameron gained business development and operating experience as a member of the founding team of Constellation Pharmaceuticals. Cameron holds a Ph.D. and S.M. in Biological Engineering and an S.B. in Mechanical Engineering from the Massachusetts Institute of Technology. We believe Dr. Wheeler's extensive business experience in the biotechnology and biopharmaceutical industries qualifies him to serve on our board of directors.

Board Composition and Election of Directors

Director Independence

Our board of directors currently consists of eight members. Our board of directors has determined that, of our eight directors, Steven Gillis, Richard Gregory, Kush Parmar, Mahendra Shaw, Mary Thistle, Cameron

Wheeler and Matthew Patterson do not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is "independent" as that term is defined under the rules of The Nasdaq Stock Market LLC, or Nasdaq. There are no family relationships among any of our directors or executive officers.

Classified Board of Directors

In accordance with our restated certificate of incorporation that will go into effect upon the closing of this offering, our board of directors will be divided into three classes with staggered, three-year terms. At each annual meeting of stockholders, the successors to directors whose terms then expire will be elected to serve from the time of election and qualification until the third annual meeting following election. Effective upon the closing of this offering, our directors will be divided among the three classes as follows:

- the Class I directors will be Mahendra Shah and Cameron Wheeler, and their terms will expire at our first annual meeting of stockholders following this offering;
- the Class II directors will be Steven Gillis, Richard Gregory and Kush Parmar, and their terms will expire at our second annual meeting of stockholders following this offering; and
- the Class III directors will be Matthew Patterson, Mary Thistle and Arthur Tzianabos, and their terms will expire at the third annual meeting of stockholders following this offering.

Our restated certificate of incorporation that will go into effect upon the closing of this offering will provide that the authorized number of directors may be changed only by resolution of the board of directors. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of the directors. The division of our board of directors into three classes with staggered three-year terms may delay or prevent a change of our management or a change in control of our company. Our directors may be removed only for cause by the affirmative vote of the holders of at least two-thirds of our outstanding voting stock entitled to vote in the election of directors.

Board Leadership Structure

Our board of directors is currently chaired by Kush Parmar. Our corporate governance guidelines provide that, if the chairman of the board is a member of management or does not otherwise qualify as independent, the independent directors of the board may elect a lead director. The lead director's responsibilities would include, but would not be limited to: presiding over all meetings of the board of directors at which the chairman is not present, including any executive sessions of the independent directors; approving board meeting schedules and agendas; and acting as the liaison between the independent directors and the chief executive officer and chairman of the board. Our corporate governance guidelines further provide the flexibility for our board of directors to modify our leadership structure in the future as it deems appropriate.

Role of the Board in Risk Oversight

One of the key functions of our board of directors is informed oversight of our risk management process. Our board of directors does not have a standing risk management committee, but rather administers this oversight function directly through our board of directors as a whole, as well as through various standing committees of our board of directors that address risks inherent in their respective areas of oversight. In particular, our board of directors is responsible for monitoring and assessing strategic risk exposure and our audit committee has the responsibility to consider and discuss our major financial risk exposures and the steps our management has taken to monitor and control these exposures, including guidelines and policies to govern the process by which risk assessment and management is undertaken. Our audit committee also monitors compliance with legal and regulatory requirements. Our nominating and corporate governance committee monitors the

effectiveness of our corporate governance practices, including whether they are successful in preventing illegal or improper liability-creating conduct. Our compensation committee assesses and monitors whether any of our compensation policies and programs has the potential to encourage excessive risk-taking. While each committee is responsible for evaluating certain risks and overseeing the management of such risks, our entire board of directors is regularly informed through committee reports about such risks.

Board Committees

Our board of directors has established three standing committees—audit, compensation and nominating and corporate governance—each of which operates under a charter that has been approved by our board of directors. Upon our listing on The Nasdaq Global Market, each committee's charter will be available under the Corporate Governance section of our website at *www.homologymedicines.com*. The reference to our website address does not constitute incorporation by reference of the information contained at or available through our website, and you should not consider it to be a part of this prospectus.

Audit Committee

The audit committee's responsibilities include:

- appointing, approving the compensation of, and assessing the independence of our registered public accounting firm;
- overseeing the work of our registered public accounting firm, including through the receipt and consideration of reports from such firm;
- reviewing and discussing with management and the registered public accounting firm our annual and quarterly financial statements and related disclosures;
- coordinating our board of directors' oversight of our internal control over financial reporting, disclosure controls and procedures and code of business conduct and ethics;
- discussing our risk management policies;
- meeting independently with our internal auditing staff, if any, registered public accounting firm and management;
- reviewing and approving or ratifying any related person transactions; and
- preparing the audit committee report required by Securities Exchange Commission, or SEC, rules.

The members of our audit committee are Steven Gillis, Mahendra Shah and Mary Thistle. Mary Thistle serves as the chairperson of the committee. All members of our audit committee meet the requirements for financial literacy under the applicable listing rules of Nasdaq (the "Nasdaq rules"). Our board of directors has determined that Mahendra Shah and Mary Thistle meet the independence requirements of Rule 10A-3 under the Exchange Act and the applicable Nasdaq rules. Since our board of directors has determined that Dr. Gillis does not currently meet the requirements of Rule 10A-3 under the Exchange Act, we are relying on the independence phase-in rules for newly listed companies and, if Dr. Gillis does not meet the requirements of Rule 10A-3 under the Exchange Act within one year of listing, we plan to add a third independent director to the audit committee within one year of listing. Our board of directors has determined that Mary Thistle is an "audit committee financial expert" as defined by applicable SEC rules and has the requisite financial sophistication as defined under the applicable Nasdaq rules.

Compensation Committee

The compensation committee's responsibilities include:

- reviewing and approving, or recommending for approval by the board of directors, the compensation of our Chief Executive Officer and our other executive officers;

- overseeing and administering our cash and equity incentive plans;
- reviewing and making recommendations to our board of directors with respect to director compensation;
- reviewing and discussing annually with management our "Compensation Discussion and Analysis," to the extent required; and
- preparing the annual compensation committee report required by SEC rules, to the extent required.

The members of our compensation committee are Richard Gregory and Kush Parmar. Kush Parmar serves as the chairperson of the committee. Our board of directors has determined that each of Richard Gregory and Kush Parmar is independent under the applicable Nasdaq rules, including the Nasdaq rules specific to membership on the compensation committee, and is a "non-employee director" as defined in Rule 16b-3 promulgated under the Exchange Act.

Nominating and Corporate Governance Committee

The nominating and corporate governance committee's responsibilities include:

- identifying individuals qualified to become board members;
- recommending to our board of directors the persons to be nominated for election as directors and to each board committee;
- developing and recommending to our board of directors corporate governance guidelines, and reviewing and recommending to our board of directors proposed changes to our corporate governance guidelines from time to time; and
- overseeing a periodic evaluation of our board of directors.

The members of our nominating and corporate governance committee are Matthew Patterson and Cameron Wheeler. Cameron Wheeler serves as the chairperson of the committee. Our board of directors has determined that Matthew Patterson and Cameron Wheeler are independent under the applicable Nasdaq rules.

Compensation Committee Interlocks and Insider Participation

No member of our compensation committee is or has been our current or former officer or employee. None of our executive officers served as a director or a member of a compensation committee (or other committee serving an equivalent function) of any other entity, one of whose executive officers served as a director or member of our compensation committee during the fiscal year ended December 31, 2017.

Code of Ethics and Code of Conduct

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. Upon our listing on The Nasdaq Global Select Market, our code of business conduct and ethics will be available under the Corporate Governance section of our website at *www.homologymedicines.com*. In addition, we intend to post on our website all disclosures that are required by law or the Nasdaq rules concerning any amendments to, or waivers from, any provision of the code. The reference to our website address does not constitute incorporation by reference of the information contained at or available through our website, and you should not consider it to be a part of this prospectus.

EXECUTIVE AND DIRECTOR COMPENSATION

Executive Compensation

This section discusses the material components of our 2017 compensation program for our principal executive officer and next two most highly compensated executive officers who are named in the 2017 Summary Compensation Table below. These "named executive officers" and their positions are:

- Arthur O. Tzianabos, Ph.D., President and Chief Executive Officer;
- Bradford Smith, Chief Financial Officer; and
- Albert Seymour, Ph.D., Chief Scientific Officer.

This discussion may contain forward-looking statements that are based on our current plans, considerations, expectations and determinations regarding future compensation programs. Actual compensation programs that we adopt following the completion of this offering may differ materially from the currently planned programs summarized in this discussion.

2017 Summary Compensation Table

The following table sets forth information concerning the compensation of our named executive officers for the year ended December 31, 2017:

Name and Principal Position	Year	Salary ($)	Bonus ($)	Option Awards ($)(3)	Non-Equity Incentive Plan Compensation ($)	Total
Arthur O. Tzianabos, Ph.D. President and Chief Executive Officer	2017	422,300	—	1,815,295	168,920	$ 2,406,515
Bradford Smith Chief Financial Officer	2017	262,500(1)	20,000(2)	278,387	122,500	$ 683,387
Albert Seymour, Ph.D. Chief Scientific Officer	2017	360,500	—	269,541	126,175	$ 756,216

(1) Mr. Smith joined the Company in April 2017. The amount reported represents the base salary that he earned for the portion of the year that he was employed. Mr. Smith's annual base salary for 2017 was $350,000.
(2) The amount reported represents a signing bonus paid to Mr. Smith in connection with his commencing employment in April, 2017.
(3) Amounts reflect the full grant date fair value of stock options granted during 2017 computed in accordance with ASC Topic 718, rather than the amounts paid to or realized by the named individual. We provide information regarding the assumptions used to calculate the value of the option awards in Note 13 to our consolidated financial statements included in this prospectus.

2017 Salaries

The named executive officers receive base salary to provide a fixed component of compensation reflecting the executive's skill set, experience, role and responsibilities. The following table shows the annual base salaries for 2017 and 2018 of our named executive officers:

Name	2017 Annual Base Salary ($)	2018 Annual Base Salary ($)
Arthur O. Tzianabos, Ph.D.	$ 422,300	$ 462,000(1)
Bradford Smith	$ 350,000	$ 364,000
Albert Seymour, Ph.D	$ 360,500	$ 374,920

(1) Effective on the closing of this offering, Dr. Tzianabos's annual 2018 annual base salary will increase to $500,000.

2017 Bonuses

We offer our named executive officers the opportunity to earn annual cash bonuses to compensate them for attaining short-term company and individual goals as approved by our board of directors. For 2017, bonuses were based on attaining corporate goals relating to product development, establishment of manufacturing processes and overall business development and individual goals related to each named executive officer's area of responsibility within the Company. The 2017 target bonus amounts, expressed as a percentage of annual base salary, of our named executive officers were 40% for Dr. Tzianabos, 35% for Mr. Smith, and 35% for Dr. Seymour.

In December, 2017 our board of directors met to review performance against the 2017 bonus goals and approved cash bonuses for the named executive officers in the amounts set forth in the Non-Equity Incentive Plan Compensation column of the 2017 "Summary Compensation Table" above.

Equity Compensation

We generally offer stock options to our employees, including our named executive officers, as the long-term incentive component of our compensation program. Stock options allow our employees to purchase shares of our common stock at a price equal to the fair market value of our common stock on the date of grant, as determined by the board of directors. Our stock options generally vest as to 25% of the underlying shares on either the first anniversary of the date of grant or a specified vesting commencement date and in equal monthly installments over the following 36 months, subject to the holder's continued service with us. Historically, our stock options have been intended to qualify as "incentive stock options" to the extent permitted under Internal Revenue Code of 1986, as amended, or the Code, and allowed "early exercise" of an unvested option in exchange for shares or restricted stock subject to the same vesting schedule as the underlying stock option.

We granted the following stock options to our named executive officers during 2017:

Named Executive Officer	2017 Stock Options Granted
Arthur O. Tzianabos, Ph.D.	514,653
Bradford Smith	63,497
Albert Seymour, Ph.D	76,417

These options were issued under our 2015 Stock Incentive Plan, which we refer to as the 2015 Plan, with exercise prices equal to the fair market value of our common stock on the date of grant, as determined by the board of directors, and subject to our standard vesting schedule described above.

In connection with this offering, we adopted a 2018 Incentive Award Plan, referred to below as the 2018 Plan, to facilitate the grant of cash and equity incentives to directors, employees (including our named executive officers) and consultants of our company and to enable our company to obtain and retain services of these individuals, which we believe is essential to our long-term success. Following the effective date of the 2018 Plan, we will not make any further grants under our 2015 Plan. However, the 2015 Plan will continue to govern the terms and conditions of the outstanding awards granted under it. For additional information about the 2018 Plan, please see the section titled "Incentive Plans" below.

Retirement Plans

We maintain a 401(k) retirement savings plan in which our named executive officers are eligible to participate on the same terms as other full-time employees. Currently, we do not match contributions made by participants in the 401(k) plan.

Employee Benefits and Perquisites

Our named executive officers are eligible to participate in our employee benefit plans and programs, which include medical, dental, and vision benefits, health spending accounts, and short- and long-term disability, accidental death and dismemberment, and life insurance, to the same extent as our other full-time employees generally, subject to the terms and eligibility requirements of those plans.

Outstanding Equity Awards at 2017 Fiscal Year-End

The following table summarizes the number of shares of common stock underlying outstanding equity incentive plan awards for each named executive officer as of December 31, 2017.

		Option Awards(1)				Stock Awards(1)	
Name	Vesting Commencement Date	Number of Securities Underlying Unexercised Options (#) Exercisable (2)	Number of Securities Underlying Unexercised Options (#) Unexercisable (2)	Option Exercise Price ($)	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (#)(3)	Market Value of Shares or Units of Stock That Have Not Vested ($)
Arthur O. Tzianabos, Ph.D.	3/31/2016	202,184	259,952	0.47	4/22/2026		
	1/1/2018		514,653	6.63	12/7/2027		
Bradford Smith	4/3/2017		163,405	0.63	4/5/2027		
	1/1/2018		63,497	6.63	12/7/2027		
Albert Seymour, Ph.D.	3/28/2016					128,391	851,410
	1/1/2018		76,417	6.63	12/7/2027		

(1) All awards vest as to 25% of the underlying shares on the first anniversary of the specified vesting commencement date and in equal monthly installments over the following 36 months, subject to the named executive officer's continued employment with the Company.

(2) All stock options held by our named executive officers permit early exercise in exchange for restricted stock and were, therefore, exercisable as of December 31, 2017. The number of shares for which each option is shown as being exercisable and unexercisable represent, respectively, the numbers shares for which each option was vested and unvested as of December 31, 2017.

(3) Represents shares of unvested restricted stock acquired by the named executive officer upon exercise of unvested stock option.

Executive Compensation Arrangements Effective on Closing of this Offering

In March 2018, in anticipation and subject to the consummation of this offering, our board of directors approved certain changes to our named executive officers' compensation arrangements. These included adjusting annual base salaries and target bonus opportunities, granting equity incentive awards and entering into new employment agreements, each as described in more detail below.

Annual Base Salaries

Our board of directors approved an increase to Dr. Tzianabos's annual base salary to $500,000, effective on the closing of this offering.

Target Bonuses

Our board of directors approved 2018 target bonus amounts for our named executive officers of 50% of his base salary for Dr. Tzianabos and 40% of his base salary for each of Dr. Seymour and Mr. Smith, effective on the closing of this offering.

Equity Incentive Awards

Effective on the date that the registration statement of which this prospectus forms a part becomes effective, our board of directors granted stock options under the 2018 Plan to our named executive officers in the following amounts: Dr. Tzianabos: 92,376 shares, Dr. Seymour: 66,501 shares and Mr. Smith: 49,711 shares. The stock options will have a per share exercise price equal to the initial public offering price of our common stock and will vest in 48 equal monthly installments on the first day of each calendar month following the effective date of grant.

Employment Agreements

We have entered into new employment agreements with each of our named executive officers that will supersede their prior employment agreements with us effective on consummation of this offering. The employment agreements are for unspecified terms and entitle Dr. Tzianabos to receive an annual base salary of $500,000, as stated above under the heading "—Annual Base Salaries," and Dr. Seymour and Mr. Smith to receive the annual base salaries that were in effect immediately prior to the consummation of this offering. In addition, the employment agreements entitle each of our named executive officers to receive the target bonuses stated above under the heading "Target Bonuses."

Under the new employment agreements, if we terminate Drs. Tzianabos or Seymour or Mr. Smith without "cause" or he resigns for "good reason" (each as defined below), subject to his timely executing a release of claims and continued compliance with a separate restrictive covenant agreement (described below), he is entitled to receive (i) base salary continuation for a period of 9 months (or, for Dr. Tzianabos, 12 months), (ii) payment of all bonuses earned but unpaid as of the date of termination and (iii) direct payment of or reimbursement for continued medical, dental or vision coverage pursuant to COBRA for up to 9 months (or, for Dr. Tzianabos, 12 months), less the amount each named executive officer would have had to pay to receive such coverage as an active employee based on the cost sharing levels in effect on the named executive officer's termination date.

If we terminate Drs. Tzianabos or Seymour or Mr. Smith without "cause" or he resigns for "good reason," in either case, on or within 12 months following a change in control, then, in lieu of the severance benefits described above, subject to his timely executing a release of claims, he is entitled to receive (i) an amount equal in cash equal to 1.0 times (or, for Dr. Tzianabos, 1.5 times) the sum of his base salary plus target annual bonus for the year of termination, (ii) payment of all bonuses earned but unpaid as of the date of termination, (iii) direct payment of or reimbursement for continued medical, dental or vision coverage pursuant to COBRA for up to 12 months (or, for Dr. Tzianabos, 18 months) and (iv) accelerated vesting of all unvested equity or equity-based awards held by the named executive officer that vest solely based on the passage of time, with any such awards that vest based on the attainment of performance-vesting conditions being governed by the terms of the applicable award agreement.

Each of our named executive officers has agreed to refrain from competing with us or soliciting our employees, in each case, while employed and following his termination of employment for any reason for a period of 12 months.

For purposes of the employment agreements, "cause" generally means the named executive officer's refusal to substantially perform the duties associated with his position with our company or to carry out the

reasonable and lawful instructions of his board of directors concerning duties or actions consistent with his position, his breach of a material provision of the employment agreement which remains uncured (to the extent capable of cure) for a period of 30 days following written notice from our company, his conviction, plea of no contest or *nolo contedere* or imposition of unadjudicated probation for any felony or crime involving moral turpitude, his unlawful use (including being under the influence) or possession of illegal drugs on our premises or while performing his duties and responsibilities under the employment agreement, or his commission of any act of fraud, embezzlement, misappropriation, willful misconduct, or breach of fiduciary duty against us.

For purposes of the employment agreements, "good reason" generally means, subject to certain cure rights, the named executive officer's termination of employment due to a reduction in salary or target bonus, a material decrease in authority or areas of responsibility, our company's breach of any one or more of the material provisions of the employment agreement, or a relocation by our company of the named executive officer's primary office to a location more than 25 miles from the named executive officer's primary office on the date of the agreement.

Incentive Plans

The following summarizes the material terms of the long-term incentive compensation plans in which our directors and named executive officers are eligible to participate following the consummation of this offering, and the 2015 Plan, under which we have previously made periodic grants of equity and equity-based awards to our directors and named executive officers.

2018 Incentive Award Plan

Our board of directors and stockholders have approved, effective the day prior to the first public trading date of our common stock, the 2018 Plan, under which we may grant cash and equity-based incentive awards to eligible service providers in order to attract, retain and motivate the persons who make important contributions to our company. The material terms of the 2018 Plan are summarized below.

Eligibility and Administration

Our employees, consultants and directors will be eligible to receive awards under the 2018 Plan. The 2018 Plan will be administered by our board of directors, which may delegate its duties and responsibilities to one or more committees of our directors and/or officers (referred to collectively as the plan administrator below), subject to the limitations imposed under the 2018 Plan, Section 16 of the Exchange Act, stock exchange rules and other applicable laws. The plan administrator will have the authority to take all actions and make all determinations under the 2018 Plan, interpret the 2018 Plan and award agreements, adopt, amend and repeal rules for the administration of the 2018 Plan as it deems advisable and correct any defects and ambiguities as it deems necessary or appropriate in its discretion. The plan administrator will also have the authority to grant awards, determine which eligible service providers receive awards, and set the terms and conditions of all awards under the 2018 Plan, including any vesting and vesting acceleration provisions, subject to the conditions and limitations in the 2018 Plan.

Shares Available for Awards

An aggregate of 3,186,205 shares of our common stock will initially be available for issuance under the 2018 Plan. The number of shares initially available for issuance will be increased by an annual increase on January 1 of each calendar year beginning in 2019 and ending in and including 2028, equal to the lesser of (A) 4% of the shares of common stock outstanding on the final day of the immediately preceding calendar year and (B) a smaller number of shares determined by our board of directors. No more than 20,887,347 shares of common stock may be issued under the 2018 Plan upon the exercise of incentive stock options. Shares issued under the 2018 Plan may be authorized but unissued shares, shares purchased on the open market or treasury shares.

If an award under the 2018 Plan or the 2015 Plan expires, lapses or is terminated, exchanged for cash, surrendered, repurchased, canceled without having been fully exercised or forfeited, any unused shares subject to the award will, as applicable, become or again be available for new grants under the 2018 Plan. Awards granted under the 2018 Plan in substitution for any options or other stock or stock-based awards granted by an entity before the entity's merger or consolidation with us or our acquisition of the entity's property or stock will not reduce the shares available for grant under the 2018 Plan, but may count against the maximum number of shares that may be issued upon the exercise of incentive stock options, or ISOs.

Awards

The 2018 Plan provides for the grant of stock options, including ISOs, nonqualified stock options, or NSOs, stock appreciation rights, or SARs, restricted stock, restricted stock units, or RSUs, and other stock or cash based awards. Certain awards under the 2018 Plan may constitute or provide for payment of "nonqualified deferred compensation" under Section 409A of the Code. All awards under the 2018 Plan will be set forth in award agreements, which will detail the terms and conditions of awards, including any applicable vesting and payment terms and post-termination exercise limitations. A brief description of each award type follows.

- *Stock Options and SARs*. Stock options provide for the purchase of shares of our common stock in the future at an exercise price set on the grant date. ISOs, by contrast to NSOs, may provide tax deferral beyond exercise and favorable capital gains tax treatment to their holders if certain holding period and other requirements of the Code are satisfied. SARs entitle their holder, upon exercise, to receive from us an amount equal to the appreciation of the shares subject to the award between the grant date and the exercise date. The plan administrator will determine the number of shares covered by each option and SAR, the exercise price of each option and SAR and the conditions and limitations applicable to the exercise of each option and SAR. The exercise price of a stock option or SAR will not be less than 100% of the fair market value of the underlying share on the grant date (or 110% in the case of ISOs granted to certain significant stockholders), except with respect to certain substitute awards granted in connection with a corporate transaction. The term of a stock option or SAR may not be longer than ten years (or five years in the case of ISOs granted to certain significant stockholders).

- *Restricted Stock and RSUs.* Restricted stock is an award of nontransferable shares of our common stock that remain forfeitable unless and until specified conditions are met and which may be subject to a purchase price. RSUs are contractual promises to deliver shares of our common stock in the future, which may also remain forfeitable unless and until specified conditions are met and may be accompanied by the right to receive the equivalent value of dividends paid on shares of our common stock prior to the delivery of the underlying shares. The plan administrator may provide that the delivery of the shares underlying RSUs will be deferred on a mandatory basis or at the election of the participant. The terms and conditions applicable to restricted stock and RSUs will be determined by the plan administrator, subject to the conditions and limitations contained in the 2018 Plan.

- *Other Stock or Cash Based Awards.* Other stock or cash based awards are awards of cash, fully vested shares of our common stock or other awards valued wholly or partially by referring to, or otherwise based on, shares of our common stock or other property. Other stock or cash based awards may be granted to participants and may also be available as a payment form in the settlement of other awards, as standalone payments and as payment in lieu of compensation to which a participant is otherwise entitled. The plan administrator will determine the terms and conditions of other stock or cash based awards, which may include any purchase price, performance goal, transfer restrictions and vesting conditions.

Performance Criteria

The plan administrator may select performance criteria for an award to establish performance goals for a performance period. Performance criteria under the 2018 Plan may include, but are not limited to, the following: net earnings or losses (either before or after one or more of interest, taxes, depreciation, amortization, and non-cash equity-based compensation expense); gross or net sales or revenue or sales or revenue growth; net income (either before or after taxes) or adjusted net income; profits (including but not limited to gross profits, net profits, profit growth, net operation profit or economic profit), profit return ratios or operating margin; budget or operating earnings (either before or after taxes or before or after allocation of corporate overhead and bonus); cash flow (including operating cash flow and free cash flow or cash flow return on capital); return on assets; return on capital or invested capital; cost of capital; return on stockholders' equity; total stockholder return; return on sales; costs, reductions in costs and cost control measures; expenses; working capital; earnings or loss per share; adjusted earnings or loss per share; price per share or dividends per share (or appreciation in or maintenance of such price or dividends); regulatory achievements or compliance; implementation, completion or attainment of objectives relating to research, development, regulatory, commercial, or strategic milestones or developments; market share; economic value or economic value added models; division, group or corporate financial goals; customer satisfaction/growth; customer service; employee satisfaction; recruitment and maintenance of personnel; human resources management; supervision of litigation and other legal matters; strategic partnerships and transactions; financial ratios (including those measuring liquidity, activity, profitability or leverage); debt levels or reductions; sales-related goals; financing and other capital raising transactions; cash on hand; acquisition activity; investment sourcing activity; and marketing initiatives, any of which may be measured in absolute terms or as compared to any incremental increase or decrease. Such performance goals also may be based solely by reference to the company's performance or the performance of a subsidiary, division, business segment or business unit of the company or a subsidiary, or based upon performance relative to performance of other companies or upon comparisons of any of the indicators of performance relative to performance of other companies. When determining performance goals, the plan administrator may provide for exclusion of the impact of an event or occurrence which the plan administrator determines should appropriately be excluded, including, without limitation, non-recurring charges or events, acquisitions or divestitures, changes in the corporate or capital structure, events unrelated to the business or outside of the control of management, foreign exchange considerations, and legal, regulatory, tax or accounting changes.

Certain Transactions

In connection with certain corporate transactions and events affecting our common stock, including a change in control, or change in any applicable laws or accounting principles, the plan administrator has broad discretion to take action under the 2018 Plan to prevent the dilution or enlargement of intended benefits, facilitate the transaction or event or give effect to the change in applicable laws or accounting principles. This includes canceling awards for cash or property, accelerating the vesting of awards, providing for the assumption or substitution of awards by a successor entity, adjusting the number and type of shares subject to outstanding awards and/or with respect to which awards may be granted under the 2018 Plan and replacing or terminating awards under the 2018 Plan. In addition, in the event of certain non-reciprocal transactions with our stockholders, the plan administrator will make equitable adjustments to outstanding awards as it deems appropriate to reflect the transaction.

Provisions of the 2018 Plan Relating to Director Compensation

The 2018 Plan provides that the plan administrator may establish compensation for non-employee directors from time to time subject to the 2018 Plan's limitations. Prior to commencing this offering, our stockholders approved the initial terms of our non-employee director compensation program, which is described below under the heading "Director Compensation." Our board of directors or its authorized committee may modify the non-employee director compensation program from time to time in the exercise of its business judgment, taking into account such factors, circumstances and considerations as it shall deem relevant from time

to time, provided that the sum of any cash compensation or other compensation and the grant date fair value of any equity awards granted under the 2018 Plan as compensation for services as a non-employee director during any fiscal year may not exceed $750,000 in the fiscal year of a non-employee director's initial service as a non-employee director or $500,000 in any subsequent fiscal year. The plan administrator may make exceptions to this limit for individual non-employee directors in extraordinary circumstances, as the plan administrator may determine in its discretion, subject to the limitations in the 2018 Plan.

Plan Amendment and Termination

Our board of directors may amend, suspend or terminate the 2018 Plan at any time; however, no amendment, other than an amendment that increases the number of shares available under the 2018 Plan, may materially and adversely affect an award outstanding under the 2018 Plan without the consent of the affected participant and stockholder approval will be obtained for any amendment to the extent necessary to comply with applicable laws. Further, the plan administrator cannot, without the approval of our stockholders, amend any outstanding stock option or SAR to reduce its price per share other than in the context of corporate transactions or equity restructurings, as described above. The 2018 Plan will remain in effect until the tenth anniversary of its effective date, unless earlier terminated by our board of directors. No awards may be granted under the 2018 Plan after its termination.

Foreign Participants, Claw-Back Provisions, Transferability and Participant Payments

The plan administrator may modify awards granted to participants who are foreign nationals or employed outside the United States or establish subplans or procedures to address differences in laws, rules, regulations or customs of such foreign jurisdictions. All awards will be subject to any company claw-back policy as set forth in such claw-back policy or the applicable award agreement. Except as the plan administrator may determine or provide in an award agreement, awards under the 2018 Plan are generally non-transferrable, except by will or the laws of descent and distribution, or, subject to the plan administrator's consent, pursuant to a domestic relations order, and are generally exercisable only by the participant. With regard to tax withholding obligations arising in connection with awards under the 2018 Plan and exercise price obligations arising in connection with the exercise of stock options under the 2018 Plan, the plan administrator may, in its discretion, accept cash, wire transfer or check, shares of our common stock that meet specified conditions, a promissory note, a "market sell order," or such other consideration as the plan administrator deems suitable or any combination of the foregoing.

2018 Employee Stock Purchase Plan

Our board of directors and stockholders have approved, effective the day prior to the first public trading date of our common stock, a 2018 Employee Stock Purchase Plan, or the 2018 ESPP. The material terms of the 2018 ESPP are summarized below.

Shares Available for Awards; Administration

A total of 353,980 shares of our common stock will initially be reserved for issuance under the 2018 ESPP. In addition, the number of shares available for issuance under the 2018 ESPP will be annually increased on January 1 of each calendar year beginning in 2019 and ending in and including 2028, by an amount equal to the lesser of (A) 1% of the shares outstanding on the final day of the immediately preceding calendar year and (B) such smaller number of shares as is determined by our board of directors, provided that no more than 4,778,738 shares of our common stock may be issued under the 2018 ESPP. Our board of directors or a committee of our board of directors will administer and will have authority to interpret the terms of the 2018 ESPP and determine eligibility of participants. We expect that the compensation committee will be the initial administrator of the 2018 ESPP.

Eligibility

Our employees are eligible to participate in the 2018 ESPP if they are customarily employed by us or a participating subsidiary for more than twenty hours per week and more than five months in any calendar year. However, an employee may not be granted rights to purchase stock under our 2018 ESPP if the employee, immediately after the grant, would own (directly or through attribution) stock possessing 5% or more of the total combined voting power or value of all classes of our stock.

Grant of Rights

The 2018 ESPP is intended to qualify under Section 423 of the Code and stock will be offered under the 2018 ESPP during offering periods. The length of the offering periods under the 2018 ESPP will be determined by the plan administrator and may be up to twenty-seven months long. Employee payroll deductions will be used to purchase shares on each purchase date during an offering period. The purchase dates for each offering period will be the final trading day in the offering period. Offering periods under the 2018 ESPP will commence when determined by the plan administrator. The plan administrator may, in its discretion, modify the terms of future offering periods.

The 2018 ESPP permits participants to purchase common stock through payroll deductions of up to a specified percentage of their eligible compensation. The plan administrator will establish a maximum number of shares that may be purchased by a participant during any offering period, which, in the absence of a contrary designation, will be 25,000 shares. In addition, no employee will be permitted to accrue the right to purchase stock under the 2018 ESPP at a rate in excess of $25,000 worth of shares during any calendar year during which such a purchase right is outstanding (based on the fair market value per share of our common stock as of the first day of the offering period).

On the first trading day of each offering period, each participant will automatically be granted an option to purchase shares of our common stock. The option will expire at the end of the applicable offering period, and will be exercised at that time to the extent of the payroll deductions accumulated during the offering period. The purchase price of the shares, in the absence of a contrary designation, will be 85% of the lower of the fair market value of our common stock on the first trading day of the offering period or on the purchase date. Participants may voluntarily end their participation in the 2018 ESPP at any time not later than a specified period prior to the end of the applicable offering period, and will be paid their accrued payroll deductions that have not yet been used to purchase shares of common stock. Participation ends automatically upon a participant's termination of employment.

A participant may not transfer rights granted under the 2018 ESPP other than by will or the laws of descent and distribution.

Certain Transactions

In the event of certain non-reciprocal transactions or events affecting our common stock the plan administrator will make equitable adjustments to the 2018 ESPP and outstanding rights. In the event of certain unusual or non-recurring events or transactions, including a change in control, the plan administrator may provide for (1) either the replacement of outstanding rights with other rights or property or termination of outstanding rights in exchange for cash, (2) the assumption or substitution of outstanding rights by the successor or survivor corporation or parent or subsidiary thereof, if any, (3) the adjustment in the number and type of shares of stock subject to outstanding rights, (4) the use of participants' accumulated payroll deductions to purchase stock on a new purchase date prior to the next scheduled purchase date and termination of any rights under ongoing offering periods or (5) the termination of all outstanding rights.

Plan Amendment

The plan administrator may amend, suspend or terminate the 2018 ESPP at any time. However, stockholder approval will be obtained for any amendment that increases the aggregate number or changes the type of shares that may be sold pursuant to rights under the 2018 ESPP, changes the corporations or classes of corporations whose employees are eligible to participate in the 2018 ESPP or changes the 2018 ESPP in any manner that would cause the 2018 ESPP to no longer be an employee stock purchase plan within the meaning of Section 423(b) of the Code.

2015 Stock Incentive Plan

Our board of directors and stockholders have approved the 2015 Plan, under which we may grant stock options and restricted stock awards to employees, directors and consultants or advisors of our company or its affiliates. A total of 3,225,346 shares of our common stock have been authorized for issuance under the 2015 Plan.

Following the effectiveness of the 2018 Plan, we will not make any further grants under the 2015 Plan. However, the 2015 Plan will continue to govern the terms and conditions of the outstanding awards granted under it. Shares of our common stock subject to awards granted under the 2015 Plan that are forfeited, lapse unexercised or are settled in cash and which following the effective date of the 2018 Plan are not issued under the 2015 Plan will be available for issuance under the 2018 Plan.

Administration. Our board of directors administers the 2015 Plan and has the authority to issue awards under the 2015 Plan, to interpret the 2015 Plan and awards outstanding thereunder, to prescribe, amend and rescind rules and regulations relating to the 2015 Plan, to determine the terms and provisions of award agreements under the 2015 Plan, to correct any defect, omission or inconsistency in the 2015 Plan or in any award agreement, and to make all other determinations in the judgment of the board of directors that are necessary and desirable for the administration of the 2015 Plan. The board of directors may delegate its authority under the 2015 Plan to a committee. Following the effectiveness of this offering, we anticipate that the board of directors will delegate its general administrative authority under the 2015 Plan to its Compensation Committee.

Types of Awards. The 2015 Plan provides for the grant of NSOs and ISOs and restricted stock awards to employees, directors and consultants or advisors of the company or its affiliates, except that stock options intended to qualify as ISOs under the Code may only be granted to employees. As of the date of this prospectus, awards of stock options and restricted stock are outstanding under the 2015 Plan.

Certain Transactions. If certain changes are made in, or events occur with respect to, our common stock, the 2015 Plan and outstanding awards will be adjusted in the class, number and, as applicable, exercise price of securities as determined by the board of directors. In the event of certain corporate transactions of our company, including a consolidation, merger, sale of all or substantially all of our assets or a liquidation, our board or the board of directors of any corporation assuming the obligations under the 2015 Plan, may, in its discretion, take any one or more of the following actions, as to some or all options outstanding under the 2015 Plan (and need not take the same action as to each such option): (i) provide for the assumption or substitution of the option; (ii) upon written notice to the optionee, provide for the termination of all unexercised options unless exercised within a specified period; (iii) upon written notice, provide that all unvested shares of restricted stock will be repurchased at cost, (iv) in the event of a merger in which stockholders receive cash payment for shares surrendered, make or provide for a cash payment to optionees based on the difference between (A) the merger consideration times the number of shares subject to outstanding options and (B) the aggregate exercise price of the outstanding options, in exchange for termination of such options; or (v) provide that all outstanding options will become exercisable in part or in full immediately prior to such event.

Amendment and Termination. The board of directors may terminate, modify or amend the 2015 Plan from time to time, provided that any amendment or modification may not adversely affect the rights of a holder

of an outstanding award without such holder's consent. The board of directors may amend or modify the 2015 Plan and any outstanding ISOs to the extent necessary to qualify any or all such options for favorable federal income tax treatment.

Director Compensation

Historically, our directors other than Dr. Gregory have not received compensation for their service on our board of directors. For 2017, we paid Dr. Gregory a $25,000 retainer for his services on our board of directors.

2017 Director Compensation Table

Name	Fees Earned or Paid in Cash ($)	Total ($)
Steven Gillis, Ph.D.	—	—
Richard J. Gregory, Ph.D.	25,000	25,000
Kush M. Parmar, M.D., Ph.D.	—	—
Mahendra G. Shah, Ph.D.	—	—
Cameron Wheeler, Ph.D.	—	—

The table below shows the aggregate numbers of option awards (exercisable and unexercisable) held as of December 31, 2017 by each director who was serving as of December 31, 2017. None of our directors held unvested stock awards as of December 31, 2017. The tables above and below exclude Mr. Patterson and Ms. Thistle because they joined our board in 2018.

Name	Options Outstanding
Steven Gillis, Ph.D.	—
Richard J. Gregory, Ph.D	10,807
Kush M. Parmar, M.D., Ph.D.	—
Mahendra G. Shah, Ph.D.	—
Cameron Wheeler, Ph.D	—
	—

Recent Developments Regarding Director Compensation

In March 2018, in anticipation and subject to the consummation of this offering, our board of directors approved the following grants of options to purchase shares of our common stock for our non-employee directors, effective on the date that the registration statement of which this prospectus forms a part becomes effective: Dr. Gillis: 31,160 shares; Dr. Gregory: 31,160 shares; Dr. Parmar, 31,160 shares; Dr. Shah, 31,160 shares; Ms. Thistle, 31,160 shares; Dr. Wheeler, 31,160 shares; and Mr. Patterson, 8,360 shares. The options will have an exercise price equal to the initial public offering price of our common stock and will vest in three equal installments beginning on the first anniversary of the effective date of grant.

In addition, effective on the effectiveness of the registration statement of which this prospectus forms a part, we adopted and, prior to commencing this offering, our stockholders approved a compensation program for our non-employee directors under which each non-employee director will receive the following amounts for their services on our board of directors:

- an option to purchase 31,160 shares of our common stock upon the director's initial election or appointment to our board of directors that occurs after our initial public offering,

- if the director has served on our board of directors for at least six months as of the date of an annual meeting of stockholders, an option to purchase 15,580 shares of our common stock on the date of the annual meeting,
- an annual director fee of $37,500, and
- if the director serves on a committee of our board of directors or in the other capacities stated below, an additional annual fee as follows:
    - chairman of the board or lead independent director, $35,000,
    - chairman of the audit committee, $15,000,
    - audit committee member other than the chairman, $7,500,
    - chairman of the compensation committee, $10,000,
    - compensation committee member other than the chairman, $5,000,
    - chairman of the nominating and corporate governance committee, $7,500, and
    - nominating and corporate governance committee member other than the chairman, $4,000.

Stock options granted to our non-employee directors under the program will have an exercise price equal to the fair market value of our common stock on the date of grant and will expire not later than ten years after the date of grant. The stock options granted upon a director's initial election or appointment will vest in three equal installments on each of the first three anniversaries of the date of grant. The stock options granted annually to directors will vest in a single installment on the earlier of the day before the next annual meeting or the first anniversary of the date of grant. In addition, all unvested stock options will vest in full upon the occurrence of a change in control.

Director fees under the program will be payable in arrears in four equal quarterly installments not later than the fifteenth day following the final day of each calendar quarter, provided that the amount of each payment will be prorated for any portion of a quarter that a director is not serving on our board and no fee will be payable in respect of any period prior to the effective date of the registration statement of which this prospectus is a part.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

The following includes a summary of transactions since January 1, 2014 to which we have been a party in which the amount involved exceeded or will exceed $120,000, and in which any of our directors, executive officers or, to our knowledge, beneficial owners of more than 5% of our capital stock or any member of the immediate family of any of the foregoing persons had or will have a direct or indirect material interest, other than equity and other compensation, termination, change in control and other arrangements, which are described under "Executive and Director Compensation." We also describe below certain other transactions with our directors, executive officers and stockholders.

Preferred Stock Financings and Convertible Notes Financing

Convertible Notes. From April 2015 to November 2015, we issued six convertible promissory notes in the aggregate principal amount of $2.5 million.

Series A Preferred Stock Financing. On December 22, 2015, we issued and sold to investors in a private placement 33,395,907 shares of our Series A preferred stock at a price per share of $0.71, for aggregate consideration of approximately $23.1 million, $20.5 million in cash proceeds plus the conversion of our promissory notes in the aggregate amount of approximately $2.6 million, which notes were converted at a discount to the Series A preferred stock price per share. On February 10, 2017, we issued and sold an additional 28,873,237 shares of our Series A preferred stock for aggregate consideration of approximately $20.5 million.

Series B Preferred Stock Financing. On July 28, 2017 and November 8, 2017, we issued and sold to investors in private placements an aggregate of 64,930,561 shares of our Series B preferred stock at a purchase price of $1.44 per share, for aggregate consideration of approximately $93.5 million.

The following table sets forth the aggregate number of shares of our capital stock acquired by beneficial owners of more than 5% of our capital stock in the financing transactions described above. Each share of our Series A preferred stock identified in the following table will convert into one share of common stock immediately prior to the closing of this offering. Each share of our Series B preferred stock identified in the following table will convert into one share of common stock immediately prior to the closing of this offering.

Participants	Series A Preferred Stock	Series B Preferred Stock
5% or Greater Stockholders(1)		
Entities affiliated with 5AM	22,128,302	6,250,000
Entities affiliated with ARCH	24,647,886	7,291,667
Entities affiliated with Deerfield	7,042,252	13,888,889
TLS Beta Pte. Ltd.	8,450,704	5,208,333
Novartis Institutes for BioMedical Research, Inc.	—	10,416,668

(1) Additional details regarding these stockholders and their equity holdings are provided in this prospectus under the caption "Principal Stockholders."

Some of our directors are associated with our principal stockholders as indicated in the table below:

Director	Principal Stockholder
Kush M. Parmar, M.D., Ph.D.	5AM Ventures
Steven Gillis, Ph.D.	ARCH Venture Partners
Cameron Wheeler, Ph.D.	Entities affiliated with Deerfield

Investors' Rights Agreement

We entered into an investors' rights agreement in December 2015, which was amended and restated in July 2017 with the holders of our preferred stock, including entities with which certain of our directors are

related. The agreement provides for certain rights relating to the registration of such holders' common stock, including shares issuable upon conversion of preferred stock, and a right of first refusal to purchase future securities sold by us. See "Description of Capital Stock—Registration Rights" for additional information.

Voting Agreement

We entered into an amended and restated voting agreement in December 2015, which was further amended and restated in July 2017 and further amended in March 2018, by and among us and certain of our stockholders, pursuant to which the following directors were elected to serve as members on our board of directors and, as of the date of this prospectus, continue to so serve: Steven Gillis, Ph.D., Richard J. Gregory, Ph.D., Kush M. Parmar, M.D., Ph.D., Matthew R. Patterson, Mahendra G. Shah, Ph.D., Mary Thistle, Arthur O. Tzianabos, Ph.D. and Cameron Wheeler, Ph.D. Dr. Tzianabos was initially selected to serve on our board of directors in his capacity as our chief executive officer. Drs. Parmar, Gillis, Wheeler, and Shah were initially selected to serve on our board of directors as representatives of holders of our preferred stock, as designated by entities affiliated with 5AM Ventures IV, L.P., ARCH Venture Fund VIII, L.P., entities affiliated with Deerfield, and Vivo Panda Fund, L.P., respectively. Dr. Gregory and Mr. Patterson were initially selected to serve on our board of directors as independent directors who are mutually acceptable to a majority of the other directors.

The voting agreement will terminate upon the closing of this offering, and members previously elected to our board of directors pursuant to this agreement will continue to serve as directors until they resign, are removed or their successors are duly elected by the holders of our common stock. The composition of our board of directors after this offering is described in more detail under "Management—Board Composition and Election of Directors."

Novartis Collaboration and License Agreement

In November 2017, we entered into a collaboration and license agreement with Novartis Institutes for BioMedical Research, Inc., or Novartis. For more information regarding the agreement with Novartis, see "Business—Strategic Collaborations."

Employment Agreements

We intend to enter into employment agreements with our named executive officers. For more information regarding the agreements with our named executive officers, see "Executive and Director Compensation—Executive Compensation Arrangements."

Indemnification Agreements

We intend to enter into indemnification agreements with each of our directors and executive officers. These agreements, among other things, require us or will require us to indemnify each director (and in certain cases their related venture capital funds) and executive officer to the fullest extent permitted by Delaware law, including indemnification of expenses such as attorneys' fees, judgments, fines and settlement amounts incurred by the director or executive officer in any action or proceeding, including any action or proceeding by or in right of us, arising out of the person's services as a director or executive officer. For further information, see "Executive and Director Compensation—Limitations of Liability and Indemnification."

Stock Option Grants to Executive Officers and Directors

We have granted stock options to our executive officers and one of our directors as more fully described in the section entitled "Executive and Director Compensation."

Participation in This Offering

Certain of our existing stockholders, including entities affiliated with certain of our directors, have indicated an interest in purchasing an aggregate of approximately $50.0 million in shares of our common stock in this offering at the initial public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, fewer or no shares in this offering to any or all of these stockholders, or any or all of these stockholders may determine to purchase more, fewer or no shares in this offering. The underwriters will receive the same underwriting discount on any shares purchased by these stockholders as they will on any other shares sold to the public in this offering.

Policies and Procedures for Related Person Transactions

Our board of directors has adopted a written related person transaction policy, to be effective upon the closing of this offering, setting forth the policies and procedures for the review and approval or ratification of related person transactions. This policy will cover, with certain exceptions set forth in Item 404 of Regulation S-K under the Securities Act, any transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships, in which we were or are to be a participant, where the amount involved exceeds $120,000 in any fiscal year and a related person had, has or will have a direct or indirect material interest, including without limitation, purchases of goods or services by or from the related person or entities in which the related person has a material interest, indebtedness, guarantees of indebtedness and employment by us of a related person. In reviewing and approving any such transactions, our audit committee is tasked to consider all relevant facts and circumstances, including, but not limited to, whether the transaction is on terms comparable to those that could be obtained in an arm's length transaction and the extent of the related person's interest in the transaction. All of the transactions described in this section occurred prior to the adoption of this policy.

PRINCIPAL STOCKHOLDERS

The following table sets forth information with respect to the beneficial ownership of our common stock, as of February 28, 2018 by:

- each person or group of affiliated persons known by us to beneficially own more than 5% of our common stock;
- each of our named executive officers;
- each of our directors; and
- all of our executive officers and directors as a group.

The number of shares beneficially owned by each stockholder is determined under rules issued by the Securities and Exchange Commission. Under these rules, beneficial ownership includes any shares as to which the individual or entity has sole or shared voting power or investment power. Applicable percentage ownership is based on 27,080,819 shares of common stock outstanding as of February 28, 2018, assuming the conversion of all outstanding shares of preferred stock into common stock. In computing the number of shares beneficially owned by an individual or entity and the percentage ownership of that person, shares of common stock subject to options, warrants or other rights held by such person that are currently exercisable or will become exercisable within 60 days of February 28, 2018 are considered outstanding, although these shares are not considered outstanding for purposes of computing the percentage ownership of any other person. Unless noted otherwise, the address of all listed stockholders is 45 Wiggins Avenue, Bedford, MA 01730. Each of the stockholders listed has sole voting and investment power with respect to the shares beneficially owned by the stockholder unless noted otherwise, subject to community property laws where applicable.

Certain of our existing stockholders, including entities affiliated with certain of our directors, have indicated an interest in purchasing an aggregate of approximately $50.0 million in shares of our common stock in this offering at the initial public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, fewer or no shares in this offering to any or all of these stockholders, or any or all of these stockholders may determine to purchase more, fewer or no shares in this offering. The underwriters will receive the same underwriting discount on any shares purchased by these stockholders as they will on any other shares sold to the public in this offering. The following table does not reflect any such potential purchases by these existing stockholders or their affiliated entities. If any shares are purchased by these stockholders, the number of shares of common stock beneficially owned after this offering and the percentage of common stock beneficially owned after this offering would increase from that set forth in the table below.

	Shares Beneficially Owned Prior to Offering		Shares Beneficially Owned After Offering	
Name of Beneficial Owner	Number	Percentage	Number	Percentage
5% or Greater Stockholders				
Entities affiliated with 5AM Ventures(1)	6,722,076	24.8%	6,722,076	19.9%
Entities affiliated with ARCH Venture Fund(2)	6,068,695	22.4	6,068,695	18.0
Entities affiliated with Deerfield(3)	3,977,035	14.7	3,977,035	11.8
Novartis Institutes for BioMedical Research, Inc.(4)	1,979,226	7.3	1,979,226	5.9
TLS Beta Pte. Ltd.(5)	2,595,293	9.6	2,595,293	7.7
Named Executive Officers and Directors				
Arthur O. Tzianabos, Ph.D.(6)	473,587	1.7	473,587	1.4
Bradford Smith(7)	49,456	*	49,456	*
Albert Seymour, Ph.D.(8)	234,617	*	234,617	*
Steven Gillis, Ph.D.(2)	6,068,695	22.4	6,068,695	18.0
Richard J. Gregory, Ph.D.(9)	7,879	*	7,879	*
Kush M. Parmar, M.D., Ph.D.(1)	6,722,076	24.8	6,722,076	19.9
Matthew R. Patterson	—	—	—	—
Mahendra G. Shah, Ph.D.(10)	659,742	2.4	659,742	2.0
Mary Thistle	—	—	—	—
Cameron Wheeler, Ph.D.(3)	3,977,035	14.7	3,977,035	11.8
All executive officers and directors as a group (11 persons)	18,431,884	68.0	18,431,884	54.6

* Less than 1%.

(1) Consists of 6,453,195 shares of common stock held by 5AM Ventures IV, L.P. (“Ventures IV”) and 268,881 shares of common stock held by 5AM Co-Investors IV, L.P. (“Co-Investors IV”). 5AM Partners IV, LLC (“Partners IV”) is the sole general partner of Ventures IV and Co-Investors IV. Dr. John Diekman, Andrew J. Schwab and Dr. Scott M. Rocklage, are the managing members of Partners IV, and have shared voting and investment power over the shares beneficially owned by Ventures IV and Co-Investors IV. Kush M. Parmar, M.D., Ph.D., one of our directors, is an affiliate of Ventures IV. Each of Partners IV, Dr. Diekman, Mr. Schwab and Dr. Rocklage disclaim beneficial ownership of such shares except to the extent of its or their recurring interest therein. The address of all entities affiliated with 5AM Ventures is 501 2nd Street, Suite 350, San Francisco, CA 94107.

(2) Consists of 4,871,868 shares of common stock held by ARCH Venture Fund VIII, L.P. (“ARCH Fund VIII”) and 1,196,827 shares of common stock held by ARCH Venture Fund VIII Overage, L.P. (“ARCH Fund Overage”). The sole general partner of ARCH Fund VIII is ARCH Venture Partners VIII, L.P. (“ARCH Partners VIII”), which may be deemed to beneficially own the shares held by ARCH Fund VIII. The sole general partner of ARCH Partners VIII and ARCH Fund Overage is ARCH Venture Partners VIII, LLC (“ARCH VIII LLC”), which may be deemed to beneficially own the shares held by ARCH Fund VIII and ARCH Fund Overage. ARCH Partners VIII and ARCH VIII LLC disclaim beneficial ownership of such shares, except to the extent of any pecuniary interest therein. The managing directors of ARCH VIII LLC are Keith L. Crandell, Clinton Bybee and Robert Nelsen, and they may be deemed to beneficially own the shares held by ARCH Fund VIII and ARCH Fund Overage. Messrs. Crandell, Bybee and Nelsen disclaim beneficial ownership of such shares, except to the extent of any pecuniary interest therein. Steven Gillis, M.D., Ph.D., one of our directors, is a managing director at ARCH Venture Partners. Director Steven Gillis owns an interest in ARCH Partners VIII but does not have voting or investment control over the shares held by ARCH Fund VIII, and disclaims beneficial ownership of such shares, except to the extent of any pecuniary interest therein. The address of ARCH Fund VIII and ARCH Fund Overage is 8755 West Higgins Road, Suite 1025, Chicago, Illinois 60631.

(3) Consists of 1,988,518 shares of common stock held by Deerfield Healthcare Innovations Fund, L.P. and 1,988,517 shares held by Deerfield Private Design Fund III, L.P. Deerfield Mgmt III, L.P. is the general partner of Deerfield Private Design Fund III, L.P., and Deerfield Mgmt HIF, L.P. is the general partner of Deerfield Healthcare Innovations Fund, L.P. Deerfield Management Company, L.P. is the investment manager of each of Deerfield Private Design Fund III, L.P. and Deerfield Healthcare Innovations Fund, L.P. Mr. James E. Flynn is the sole member of the general partner of each of Deerfield Mgmt III, L.P., Deerfield Mgmt HIF, L.P., and Deerfield Management Company, L.P. Deerfield Mgmt III, L.P., Deerfield Management Company, L.P., and Mr. James E. Flynn may be deemed to beneficially own the securities held by Deerfield Private Design Fund III, L.P. Deerfield Mgmt HIF, L.P., Deerfield Management Company, L.P. and Mr. James E. Flynn may be deemed to beneficially own the securities held by Deerfield Healthcare Innovations Fund, L.P. Dr. Wheeler, one of our directors, is the principal at Deerfield Management. The address of Deerfield Healthcare Innovations Fund, L.P., and Deerfield Private Design Fund III, L.P. is 780 Third Avenue, 37th Floor, New York, New York.

(4) Consists of 1,979,226 shares of common stock held by Novartis Institutes for BioMedical Research, Inc., or Novartis. Novartis is an indirect wholly-owned subsidiary of, and controlled by, Novartis AG. The address for Novartis is 250 Massachusetts Avenue, Cambridge, MA 02139.

(5) TLS Beta Pte. Ltd. is a direct wholly-owned subsidiary of Temasek Life Sciences Private Limited. Temasek Life Sciences Private Limited, is a direct wholly-owned subsidiary of Fullerton Management Pte Ltd, or FMPL, which in turn is a direct wholly-owned subsidiary of Temasek Holdings (Private) Limited. Temasek Life Sciences Private Limited, FMPL and Temasek Holdings (Private) Limited may be deemed to beneficially own the shares held by TLS Beta Pte. Ltd. The principal business address of Temasek Holdings (Private) Limited, FMPL, Temasek Life Sciences Private Limited and TLS Beta Pte. Ltd. is 60B Orchard Road #06-18 Tower 2, The Atrium@Orchard, Singapore 238891.

(6) Includes options to purchase 283,582 shares of common stock that are or will be immediately exercisable within 60 days of February 28, 2018.

(7) Consists of options to purchase 49,546 shares of common stock that are or will be immediately exercisable within 60 days of February 28, 2018.
(8) Includes options to purchase 6,367 shares of common stock that are or will be immediately exercisable within 60 days of February 28, 2018.
(9) Consists of options to purchase 7,879 shares of common stock that are or will be immediately exercisable within 60 days of February 28, 2018.
(10) Consists of 659,742 shares of common stock held by Vivo Panda Fund, L.P. ("Vivo LP"). Vivo Panda, LLC ("Vivo LLC") is the sole general partner of Vivo LP. Mahendra G. Shah, Ph.D., one of our directors, is a managing member of Vivo LLC and has shared voting and investment power over the shares beneficially owned by Vivo LP. Each of Vivo LLC and Dr. Shah disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. The address of all entities affiliated with Vivo LP is 505 Hamilton Street, Suite 207, Palo Alto, CA 94301.

DESCRIPTION OF CAPITAL STOCK

General

The following description summarizes some of the terms of our amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the closing of this offering, the investors' rights agreement and of the General Corporation Law of the State of Delaware. Because it is only a summary, it does not contain all the information that may be important to you. For a complete description, you should refer to our amended and restated certificate of incorporation, amended and restated bylaws and investors' rights agreement, copies of which have been or will be filed as exhibits to the registration statement of which this prospectus is a part, as well as the relevant provisions of the General Corporation Law of the State of Delaware. The description of our common stock and preferred stock reflects changes to our capital structure that will occur upon the closing of this offering.

Following the closing of this offering, our authorized capital stock will consist of 200,000,000 shares of common stock, par value $0.0001 per share, and 10,000,000 shares of preferred stock, par value $0.0001 per share.

As of December 31, 2017, there were 2,902,109 shares of our common stock outstanding (including 265,098 shares of unvested restricted stock) and 24,168,656 shares of our common stock issuable upon the automatic conversion of all outstanding shares of our preferred stock in connection with this offering, held of record by 80 stockholders.

Common Stock

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. An election of directors by our stockholders shall be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Subject to the supermajority votes for some matters, other matters shall be decided by the affirmative vote of our stockholders having a majority in voting power of the votes cast by the stockholders present or represented and voting on such matter. Our amended and restated certificate of incorporation and amended and restated bylaws also provide that our directors may be removed only for cause and only by the affirmative vote of the holders of at least two-thirds in voting power of the outstanding shares of capital stock entitled to vote thereon. In addition, the affirmative vote of the holders of at least two-thirds in voting power of the outstanding shares of capital stock entitled to vote thereon is required to amend or repeal, or to adopt any provision inconsistent with, several of the provisions of our amended and restated certificate of incorporation. See below under "—Anti-Takeover Effects of Delaware Law and Our Certificate of Incorporation and Bylaws—Amendment of Charter Provisions." Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of any series of preferred stock that we may designate and issue in the future.

In the event of our liquidation or dissolution, the holders of common stock are entitled to receive proportionately our net assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock. Holders of common stock have no preemptive, subscription, redemption or conversion rights. Our outstanding shares of common stock are, and the shares offered by us in this offering will be, when issued and paid for, validly issued, fully paid and nonassessable. The rights, preferences and privileges of holders of common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Preferred Stock

Under the terms of our amended and restated certificate of incorporation that will become effective upon the closing of this offering, our board of directors is authorized to direct us to issue shares of preferred stock in

one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock.

The purpose of authorizing our board of directors to issue preferred stock and determine its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions, future financings and other corporate purposes, could have the effect of making it more difficult for a third party to acquire, or could discourage a third party from seeking to acquire, a majority of our outstanding voting stock. Upon the closing of this offering, there will be no shares of preferred stock outstanding, and we have no present plans to issue any shares of preferred stock.

Options

As of December 31, 2017, options to purchase 1,971,711 shares of our common stock were outstanding under our 2015 Plan, all of which were exercisable and of which 189,760 were vested as of that date. Additionally, 731,757 shares of common stock issuable upon the exercise of options will be granted in connection with this offering under our 2018 Plan, which will become effective in connection with this offering, to certain of our directors, executive officers and employees, at an exercise price per share equal to the initial public offering price in this offering.

Registration Rights

Holders of 24,270,061 shares of our common stock are entitled to certain rights with respect to the registration of such shares for public resale under the Securities Act, pursuant to an amended and restated investors' rights agreement by and among us and certain of our stockholders, until the rights otherwise terminate pursuant to the terms of the investors' rights agreement. The registration of shares of common stock as a result of the following rights being exercised would enable holders to trade these shares without restriction under the Securities Act when the applicable registration statement is declared effective.

Form S-1 Registration Rights

If at any time beginning 180 days after the closing date of this offering the holders of registrable securities request in writing that we effect a registration with respect to all or part of such registrable securities then outstanding and having an anticipated aggregate offering price that would exceed $5,000,000, net of expenses, we may be required to register their shares. We are obligated to effect at most two registrations in response to these demand registration rights. If the holders requesting registration intend to distribute their shares by means of an underwriting, the managing underwriter of such offering will have the right to limit the numbers of shares to be underwritten for reasons related to the marketing of the shares.

Piggyback Registration Rights

If at any time after this offering we propose to register any shares of our common stock under the Securities Act, subject to certain exceptions, the holders of registrable securities will be entitled to notice of the registration and to include their shares of registrable securities in the registration. If our proposed registration involves an underwriting, the managing underwriter of such offering will have the right to limit the number of shares to be underwritten for reasons related to the marketing of the shares.

Form S-3 Registration Rights

If, at any time after we become entitled under the Securities Act to register our shares on a registration statement on Form S-3, the holders of the registrable securities request in writing that we effect a registration with respect to registrable securities at an aggregate price to the public in the offering of at least $5,000,000, we will be required to effect such registration; provided, however, that we will not be required to effect such a registration if, within any twelve month period, we have already effected two registrations on Form S-3 for the holders of registrable securities.

Expenses and Indemnification

Ordinarily, other than underwriting discounts and commissions, we will be required to pay all expenses incurred by us related to any registration effected pursuant to the exercise of these registration rights. These expenses may include all registration and filing fees, printing expenses, fees and disbursements of our counsel, reasonable fees and disbursements of a counsel for the selling security holders and blue sky fees and expenses. Additionally, we have agreed to indemnify selling stockholders for damages, and any legal or other expenses reasonably incurred, arising from or based upon any untrue statement of a material fact contained in any registration statement, an omission or alleged omission to state a material fact in any registration statement or necessary to make the statements therein not misleading, or any violation or alleged violation by the indemnifying party of securities laws, subject to certain exceptions.

Termination of Registration Rights

The registration rights terminate upon the earlier of three years after the effective date of the registration statement of which this prospectus is a part, the closing of a deemed liquidation event, as defined in the investors' rights agreement.

Anti-Takeover Effects of Delaware Law and Our Certificate of Incorporation and Bylaws

Some provisions of Delaware law, our restated certificate of incorporation and our restated bylaws could make the following transactions more difficult: an acquisition of us by means of a tender offer; an acquisition of us by means of a proxy contest or otherwise; or the removal of our incumbent officers and directors. It is possible that these provisions could make it more difficult to accomplish or could deter transactions that stockholders may otherwise consider to be in their best interest or in our best interests, including transactions which provide for payment of a premium over the market price for our shares.

These provisions, summarized below, are intended to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of the increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging these proposals because negotiation of these proposals could result in an improvement of their terms.

Undesignated Preferred Stock

The ability of our board of directors, without action by the stockholders, to issue up to 10,000,000 shares of undesignated preferred stock with voting or other rights or preferences as designated by our board of directors could impede the success of any attempt to change control of us. These and other provisions may have the effect of deferring hostile takeovers or delaying changes in control or management of our company.

Stockholder Meetings

Our restated bylaws provide that a special meeting of stockholders may be called only by our chairman of the board, chief executive officer or president (in the absence of a chief executive officer), or by a resolution adopted by a majority of our board of directors.

Requirements for Advance Notification of Stockholder Nominations and Proposals

Our restated bylaws establish advance notice procedures with respect to stockholder proposals to be brought before a stockholder meeting and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee of the board of directors.

Elimination of Stockholder Action by Written Consent

Our restated certificate of incorporation eliminates the right of stockholders to act by written consent without a meeting.

Staggered Board

Our board of directors is divided into three classes. The directors in each class will serve for a three-year term, one class being elected each year by our stockholders. For more information on the classified board, see "Management—Board Composition and Election of Directors." This system of electing and removing directors may tend to discourage a third party from making a tender offer or otherwise attempting to obtain control of us, because it generally makes it more difficult for stockholders to replace a majority of the directors.

Removal of Directors

Our restated certificate of incorporation provides that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of the holders of at least two-thirds in voting power of the outstanding shares of stock entitled to vote in the election of directors.

Stockholders Not Entitled to Cumulative Voting

Our restated certificate of incorporation does not permit stockholders to cumulate their votes in the election of directors. Accordingly, the holders of a majority of the outstanding shares of our common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they choose, other than any directors that holders of our preferred stock may be entitled to elect.

Delaware Anti-Takeover Statute

We are subject to Section 203 of the General Corporation Law of the State of Delaware, which prohibits persons deemed to be "interested stockholders" from engaging in a "business combination" with a publicly held Delaware corporation for three years following the date these persons become interested stockholders unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. Generally, an "interested stockholder" is a person who, together with affiliates and associates, owns, or within three years prior to the determination of interested stockholder status did own, 15% or more of a corporation's voting stock. Generally, a "business combination" includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. The existence of this provision may have an anti-takeover effect with respect to transactions not approved in advance by the board of directors.

Choice of Forum

Our restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative form, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for: (1) any derivative action or proceeding brought on our behalf; (2) any action asserting a claim of breach of a fiduciary duty or other wrongdoing by any of our directors, officers, employees or agents to us or our stockholders; (3) any action asserting a claim against us arising pursuant to any provision of the General Corporation Law of the State of Delaware or our certificate of incorporation or bylaws; (4) any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or bylaws; or (5) any action asserting a claim governed by the internal affairs doctrine. Our restated certificate of incorporation also provides that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock will be deemed to have notice of and to have consented to this choice of forum provision. It is possible that a court of law could rule that the choice of forum provision contained in our restated certificate of incorporation is inapplicable or unenforceable if it is challenged in a proceeding or otherwise.

Amendment of Charter Provisions

The amendment of any of the above provisions, except for the provision making it possible for our board of directors to issue preferred stock and the provision prohibiting cumulative voting, would require approval by holders of at least two-thirds in voting power of the outstanding shares of stock entitled to vote thereon.

The provisions of Delaware law, our restated certificate of incorporation and our restated bylaws could have the effect of discouraging others from attempting hostile takeovers and, as a consequence, they may also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions may also have the effect of preventing changes in the composition of our board and management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock will be American Stock Transfer & Trust Company, LLC.

Stock Exchange Listing

Our common stock has been approved for listing on The Nasdaq Global Select Market under the symbol “FIXX.”

SHARES ELIGIBLE FOR FUTURE SALE

Immediately prior to this offering, there was no public market for our common stock. Future sales of substantial amounts of common stock in the public market, or the perception that such sales may occur, could adversely affect the market price of our common stock.

Upon the closing of this offering, we will have outstanding an aggregate of 33,747,819 shares of common stock, assuming the issuance of 6,667,000 shares of common stock offered by us in this offering, the automatic conversion of all outstanding shares of our preferred stock into 24,168,656 shares of our common stock and no exercise of options after February 28, 2018. Of these shares, all shares sold in this offering will be freely tradable without restriction or further registration under the Securities Act, except for any shares purchased by our "affiliates," as that term is defined in Rule 144 under the Securities Act, whose sales would be subject to the Rule 144 resale restrictions described below, other than the holding period requirement.

The remaining 27,080,819 shares of common stock will be "restricted securities," as that term is defined in Rule 144 under the Securities Act. These restricted securities are eligible for public sale only if they are registered under the Securities Act or if they qualify for an exemption from registration under Rules 144 or 701 under the Securities Act, which are summarized below. We expect that substantially all of these shares will be subject to the 180-day lock-up period under the lock-up agreements described below. Upon expiration of the lock-up period, we estimate that approximately 27,080,819 shares will be available for sale in the public market, subject in some cases to applicable volume limitations under Rule 144.

In addition, of the 1,972,027 shares of our common stock that were subject to stock options outstanding as of February 28, 2018, options to purchase 166,329 shares of common stock were vested as of February 28, 2018 and, upon exercise, these shares will be eligible for sale subject to the lock–up agreements described below and Rules 144 and 701 under the Securities Act.

Lock-Up Agreements

We and each of our directors and executive officers and holders of substantially all of our outstanding capital stock have agreed that, without the prior written consent of Merrill Lynch, Pierce, Fenner & Smith Incorporated and Cowen and Company, LLC, we and they will not, subject to certain exceptions, during the period ending 180 days after the date of this prospectus, offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for common stock; or enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of our common stock, whether any transaction described above is to be settled by delivery of our common stock or such other securities, in cash or otherwise.

Upon the expiration of the applicable lock-up periods, substantially all of the shares subject to such lock-up restrictions will become eligible for sale, subject to the limitations discussed above. These lock-up restrictions may be waived at any time by Merrill Lynch, Pierce, Fenner & Smith Incorporated and Cowen and Company, LLC. For a further description of these lock-up agreements, please see "Underwriting."

Rule 144

Affiliate Resales of Restricted Securities

In general, beginning 90 days after the effective date of the registration statement of which this prospectus is a part, a person who is an affiliate of ours, or who was an affiliate at any time during the 90 days before a sale, who has beneficially owned shares of our common stock for at least six months would be entitled

to sell in "broker's transactions" or certain "riskless principal transactions" or to market makers, a number of shares within any three-month period that does not exceed the greater of:

- 1% of the number of shares of our common stock then outstanding, which will equal approximately 337,478 shares (or 347,478 shares if the underwriters exercise their option to purchase additional shares in full) immediately after this offering; or

- the average weekly trading volume in our common stock on the Nasdaq Global Select Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to such sale.

Affiliate resales under Rule 144 are also subject to the availability of current public information about us. In addition, if the number of shares being sold under Rule 144 by an affiliate during any three-month period exceeds 5,000 shares or has an aggregate sale price in excess of $50,000, the seller must file a notice on Form 144 with the Securities and Exchange Commission and Nasdaq concurrently with either the placing of a sale order with the broker or the execution directly with a market maker.

Non-Affiliate Resales of Restricted Securities

In general, beginning 90 days after the effective date of the registration statement of which this prospectus is a part, a person who is not an affiliate of ours at the time of sale, and has not been an affiliate at any time during the three months preceding a sale, and who has beneficially owned shares of our common stock for at least six months but less than a year, is entitled to sell such shares subject only to the availability of current public information about us. If such person has held our shares for at least one year, such person can resell under Rule 144(b)(1) without regard to any Rule 144 restrictions, including the 90-day public company requirement and the current public information requirement.

Non-affiliate resales are not subject to the manner of sale, volume limitation or notice filing provisions of Rule 144.

Rule 701

In general, under Rule 701, any of an issuer's employees, directors, officers, consultants or advisors who purchases shares from the issuer in connection with a compensatory stock or option plan or other written agreement before the effective date of a registration statement under the Securities Act is entitled to sell such shares 90 days after such effective date in reliance on Rule 144. An affiliate of the issuer can resell shares in reliance on Rule 144 without having to comply with the holding period requirement, and non-affiliates of the issuer can resell shares in reliance on Rule 144 without having to comply with the current public information and holding period requirements.

The Securities and Exchange Commission has indicated that Rule 701 will apply to typical stock options granted by an issuer before it becomes subject to the reporting requirements of the Exchange Act, along with the shares acquired upon exercise of such options, including exercises after an issuer becomes subject to the reporting requirements of the Exchange Act.

Equity Plans

We intend to file one or more registration statements on Form S-8 under the Securities Act to register all shares of common stock subject to outstanding stock options and common stock issued or issuable under our stock plans. We expect to file the registration statement covering shares offered pursuant to our stock plans shortly after the date of this prospectus, permitting the resale of such shares by non-affiliates in the public market without restriction under the Securities Act and the sale by affiliates in the public market, subject to compliance with the resale provisions of Rule 144.

Registration Rights

Upon the closing of this offering, the holders of 24,270,061 shares of common stock, which includes all of the shares of common stock issuable upon the automatic conversion of our preferred stock upon the closing of this offering, or their transferees will be entitled to various rights with respect to the registration of these shares under the Securities Act. Registration of these shares under the Securities Act would result in these shares becoming fully tradable without restriction under the Securities Act immediately upon the effectiveness of the registration, except for shares purchased by affiliates. See “Description of Capital Stock—Registration Rights” for additional information. Shares covered by a registration statement will be eligible for sale in the public market upon the expiration or release from the terms of the lock-up agreement.

MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES TO NON-U.S. HOLDERS

The following discussion is a summary of the material U.S. federal income tax consequences to non-U.S. holders (as defined below) of the purchase, ownership and disposition of the shares of common stock issued pursuant to this offering, but does not purport to be a complete analysis of all potential tax effects. The effects of other U.S. federal tax laws, such as estate and gift tax laws, and any applicable state, local or foreign tax laws are not discussed. This discussion is based on the Internal Revenue Code of 1986, as amended, or the Code, Treasury Regulations promulgated thereunder, judicial decisions, and published rulings and administrative pronouncements of the U.S. Internal Revenue Service, or IRS, in effect as of the date of this offering. These authorities may change or be subject to differing interpretations. Any such change or differing interpretation may be applied retroactively in a manner that could adversely affect a non-U.S. holder of our common stock. We have not sought and will not seek any rulings from the IRS regarding the matters discussed below. There can be no assurance the IRS or a court will not take a contrary position regarding the tax consequences of the purchase, ownership and disposition of our common stock.

This discussion is limited to non-U.S. holders that hold our common stock as a "capital asset" within the meaning of Section 1221 of the Code (property held for investment). This discussion does not address all U.S. federal income tax consequences relevant to a non-U.S. holder's particular circumstances, including the impact of the alternative minimum tax or the unearned income Medicare contribution tax. In addition, it does not address consequences relevant to holders subject to particular rules, including, without limitation:

- U.S. expatriates and certain former citizens or long-term residents of the United States;
- persons holding our common stock as part of a hedge, straddle or other risk reduction strategy or as part of a conversion transaction or other integrated investment;
- banks, insurance companies, and other financial institutions;
- brokers, dealers or traders in securities or currencies;
- "controlled foreign corporations," "passive foreign investment companies," and corporations that accumulate earnings to avoid U.S. federal income tax;
- partnerships or other entities or arrangements treated as partnerships for U.S. federal income tax purposes (and investors therein);
- tax-exempt organizations or governmental organizations;
- persons deemed to sell our common stock under the constructive sale provisions of the Code;
- persons for whom our common stock constitutes "qualified small business stock" within the meaning of Section 1202 of the Code;
- persons who hold or receive our common stock pursuant to the exercise of any employee stock option or otherwise as compensation;
- persons subject to special tax accounting rules as a result of any item of gross income with respect to our common stock being taken into account in an applicable financial statement; and
- tax-qualified retirement plans.

If a partnership (or other entity treated as a partnership for U.S. federal income tax purposes) holds our common stock, the tax treatment of a partner in the partnership will depend on the status of the partner, the

activities of the partnership and certain determinations made at the partner level. Accordingly, partnerships holding our common stock and the partners in such partnerships should consult their tax advisors regarding the U.S. federal income tax consequences to them.

THIS DISCUSSION IS FOR INFORMATION PURPOSES ONLY AND IS NOT INTENDED AS LEGAL OR TAX ADVICE. INVESTORS SHOULD CONSULT THEIR TAX ADVISORS WITH RESPECT TO THE APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS TO THEIR PARTICULAR SITUATIONS AS WELL AS ANY TAX CONSEQUENCES OF THE PURCHASE, OWNERSHIP AND DISPOSITION OF OUR COMMON STOCK ARISING UNDER THE U.S. FEDERAL ESTATE OR GIFT TAX LAWS OR UNDER THE LAWS OF ANY STATE, LOCAL OR NON-U.S. TAXING JURISDICTION OR UNDER ANY APPLICABLE INCOME TAX TREATY.

Definition of a Non-U.S. Holder

For purposes of this discussion, a "non-U.S. holder" is any beneficial owner of our common stock that is not a "U.S. person," a partnership or an entity disregarded as separate from its owner, each for U.S. federal income tax purposes. A U.S. person is any person that, for U.S. federal income tax purposes, is:

- an individual who is a citizen or resident of the United States;
- a corporation (or other entity treated as a corporation for U.S. federal income tax purposes) created or organized under the laws of the United States, any state thereof, or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust that (1) is subject to the primary supervision of a U.S. court and the control of one or more U.S. persons (within the meaning of Section 7701(a)(30) of the Code), or (2) has made a valid election under applicable Treasury Regulations to continue to be treated as a U.S. person.

Distributions

As described in the section entitled "Dividend Policy," we do not anticipate declaring or paying dividends to holders of our common stock in the foreseeable future. However, if we do make distributions on our common stock, such distributions of cash or property on our common stock will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Amounts not treated as dividends for U.S. federal income tax purposes will constitute a return of capital and first be applied against and reduce a non-U.S. holder's adjusted tax basis in its common stock, but not below zero. Any excess will be treated as capital gain and will be treated as described below in the section relating to the sale or disposition of our common stock. Because we may not know the extent to which a distribution is a dividend for U.S. federal income tax purposes at the time it is made, for purposes of the withholding rules discussed below we or the applicable withholding agent may treat the entire distribution as a dividend.

Subject to the discussion below on backup withholding and foreign accounts, dividends paid to a non-U.S. holder of our common stock that are not effectively connected with the non-U.S. holder's conduct of a trade or business within the United States will be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the dividends (or such lower rate specified by an applicable income tax treaty).

Non-U.S. holders will be entitled to a reduction in or an exemption from withholding on dividends as a result of either (a) an applicable income tax treaty or (b) the non-U.S. holder holding our common stock in connection with the conduct of a trade or business within the United States and dividends being effectively connected with that trade or business. To claim such a reduction in or exemption from withholding, the non-U.S.

holder must provide the applicable withholding agent with a properly executed (a) IRS Form W-8BEN or W-8BEN-E (or other applicable documentation) claiming an exemption from or reduction of the withholding tax under the benefit of an income tax treaty between the United States and the country in which the non-U.S. holder resides or is established, or (b) IRS Form W-8ECI stating that the dividends are not subject to withholding tax because they are effectively connected with the conduct by the non-U.S. holder of a trade or business within the United States, as may be applicable. These certifications must be provided to the applicable withholding agent prior to the payment of dividends and must be updated periodically. Non-U.S. holders that do not timely provide the applicable withholding agent with the required certification, but that qualify for a reduced rate under an applicable income tax treaty, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS.

If dividends paid to a non-U.S. holder are effectively connected with the non-U.S. holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the non-U.S. holder maintains a permanent establishment in the United States to which such dividends are attributable), then, although exempt from U.S. federal withholding tax (provided the non-U.S. holder provides appropriate certification, as described above), the non-U.S. holder will be subject to U.S. federal income tax on such dividends on a net income basis at the regular graduated U.S. federal income tax rates. In addition, a non-U.S. holder that is a corporation may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on its effectively connected earnings and profits for the taxable year that are attributable to such dividends, as adjusted for certain items. Non-U.S. holders should consult their tax advisors regarding their entitlement to benefits under any applicable income tax treaty.

Sale or Other Disposition of Common Stock

Subject to the discussions below on backup withholding and foreign accounts, a non-U.S. holder will not be subject to U.S. federal income tax on any gain realized upon the sale or other disposition of our common stock unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the non-U.S. holder maintains a permanent establishment in the United States to which such gain is attributable);
- the non-U.S. holder is a nonresident alien individual present in the United States for 183 days or more during the taxable year of the disposition and certain other requirements are met; or
- our common stock constitutes U.S. real property interests, or USRPIs, by reason of our status as a U.S. real property holding corporation, or USRPHC, for U.S. federal income tax purposes.

Gain described in the first bullet point above will generally be subject to U.S. federal income tax on a net income basis at the regular graduated U.S. federal income tax rates. A non-U.S. holder that is a foreign corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected gain, as adjusted for certain items.

A non-U.S. holder described in the second bullet point above will be subject to U.S. federal income tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on any gain derived from the disposition, which may be offset by certain U.S. source capital losses of the non-U.S. holder (even though the individual is not considered a resident of the United States) provided the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses.

With respect to the third bullet point above, we believe we are not currently and do not anticipate becoming a USRPHC. Because the determination of whether we are a USRPHC depends on the fair market value of our USRPIs relative to the fair market value of our other business assets and our non-U.S. real property

interests, however, there can be no assurance we are not a USRPHC or will not become one in the future. Even if we are or were to become a USRPHC, gain arising from the sale or other taxable disposition by a non-U.S. holder of our common stock will not be subject to U.S. federal income tax if our common stock is "regularly traded," as defined by applicable Treasury Regulations, on an established securities market, and such non-U.S. holder owned, actually and constructively, 5% or less of our common stock throughout the shorter of the five-year period ending on the date of the sale or other taxable disposition or the non-U.S. holder's holding period. If we are a USRPHC and either our common stock is not regularly traded on an established securities market or a non-U.S. holder holds more than 5% of our outstanding common stock, directly or indirectly, during the applicable testing period, such non-U.S. holder's gain on the disposition of shares of our common stock generally will be taxed in the same manner as gain that is effectively connected with the conduct of a U.S. trade or business, except that the branch profits tax generally will not apply. If we are a USRPHC and our common stock is not regularly traded on an established securities market, a non-U.S. holder's proceeds received on the disposition of shares will also generally be subject to withholding at a rate of 15%. Prospective investors are encouraged to consult their tax advisors regarding the possible consequences to them if we are, or were to become, a USRPHC.

Non-U.S. holders should consult their tax advisors regarding potentially applicable income tax treaties that may provide for different rules.

Information Reporting and Backup Withholding

Subject to the discussion below on foreign accounts, a non-U.S. holder will not be subject to backup withholding with respect to distributions on our common stock we make to the non-U.S. holder, provided the applicable withholding agent does not have actual knowledge or reason to know such holder is a U.S. person and the holder certifies its non-U.S. status, such as by providing a valid IRS Form W-8BEN, W-8BEN-E or W-8ECI, or other applicable certification. However, information returns generally will be filed with the IRS in connection with any distributions (including deemed distributions) made on our common stock to the non-U.S. holder, regardless of whether any tax was actually withheld. Copies of these information returns may also be made available under the provisions of a specific treaty or agreement to the tax authorities of the country in which the non-U.S. holder resides or is established.

Information reporting and backup withholding may apply to the proceeds of a sale or other taxable disposition of our common stock within the United States, and information reporting may (although backup withholding generally will not) apply to the proceeds of a sale or other taxable disposition of our common stock outside the United States conducted through certain U.S.-related financial intermediaries, in each case, unless the beneficial owner certifies under penalty of perjury that it is a non-U.S. holder on IRS Form W-8BEN or W-8BEN-E, or other applicable form (and the payor does not have actual knowledge or reason to know that the beneficial owner is a U.S. person) or such owner otherwise establishes an exemption. Proceeds of a disposition of our common stock conducted through a non-U.S. office of a non-U.S. broker generally will not be subject to backup withholding or information reporting.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against a non-U.S. holder's U.S. federal income tax liability, provided the required information is timely furnished to the IRS.

Additional Withholding Tax on Payments Made to Foreign Accounts

Withholding taxes may be imposed under the Foreign Account Tax Compliance Act, or FATCA, on certain types of payments made to non-U.S. financial institutions and certain other non-U.S. entities. Specifically, a 30% withholding tax may be imposed on dividends (including deemed dividends) paid on our common stock, or gross proceeds from the sale or other disposition of our common stock paid to a "foreign financial institution" or a "non-financial foreign entity" (each as defined in the Code), unless (1) the foreign financial institution

undertakes certain diligence and reporting obligations, (2) the non-financial foreign entity either certifies it does not have any "substantial United States owners" (as defined in the Code) or furnishes identifying information regarding each substantial United States owner, or (3) the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from these rules. If the payee is a foreign financial institution and is subject to the diligence and reporting requirements in (1) above, it must enter into an agreement with the U.S. Department of the Treasury requiring, among other things, that it undertake to identify accounts held by certain "specified United States persons" or "United States-owned foreign entities" (each as defined in the Code), annually report certain information about such accounts, and withhold 30% on certain payments to non-compliant foreign financial institutions and certain other account holders. Foreign financial institutions located in jurisdictions that have an intergovernmental agreement with the United States governing FATCA may be subject to different rules.

Under the applicable Treasury Regulations and administrative guidance, withholding under FATCA generally applies to payments of dividends (including deemed dividends) paid on our common stock, and will apply to payments of gross proceeds from the sale or other disposition of common stock on or after January 1, 2019. Because we may not know the extent to which a distribution is a dividend for U.S. federal income tax purposes at the time it is made, for purposes of these withholding rules we or the applicable withholding agent may treat the entire distribution as a dividend. Prospective investors should consult their tax advisors regarding the potential application of these withholding provisions.

UNDERWRITING

Merrill Lynch, Pierce, Fenner & Smith Incorporated, Cowen and Company, LLC and Evercore Group L.L.C. are acting as representatives of each of the underwriters named below. Subject to the terms and conditions set forth in an underwriting agreement among us and the underwriters, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the number of shares of common stock set forth opposite its name below.

Underwriter	Number of Shares
Merrill Lynch, Pierce, Fenner & Smith Incorporated	
Cowen and Company, LLC	
Evercore Group L.L.C.	
BTIG, LLC	
Total	6,667,000

Subject to the terms and conditions set forth in the underwriting agreement, the underwriters have agreed, severally and not jointly, to purchase all of the shares sold under the underwriting agreement if any of these shares are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the nondefaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the shares, and other conditions contained in the underwriting agreement, such as the receipt by the underwriters of officer's certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commissions and Discounts

The representatives have advised us that the underwriters propose initially to offer the shares to the public at the public offering price set forth on the cover page of this prospectus and to dealers at that price less a concession not in excess of $ per share. After the initial offering, the public offering price, concession or any other term of the offering may be changed.

The following table shows the public offering price, underwriting discount and proceeds before expenses to us. The information assumes either no exercise or full exercise by the underwriters of their option to purchase additional shares.

	Per Share	Without Option	With Option
Public offering price	$	$	$
Underwriting discount	$	$	$
Proceeds, before expenses, to us	$	$	$

The expenses of the offering, not including the underwriting discount, are estimated at $2.9 million and are payable by us. We have also agreed to reimburse the underwriters for their expenses relating to clearance of this offering with the Financial Industry Regulatory Authority in an amount up to $50,000.

Option to Purchase Additional Shares

We have granted an option to the underwriters, exercisable for 30 days after the date of this prospectus, to purchase up to 1,000,050 additional shares at the public offering price, less the underwriting discount. If the underwriters exercise this option, each will be obligated, subject to conditions contained in the underwriting agreement, to purchase a number of additional shares proportionate to that underwriter's initial amount reflected in the above table.

No Sales of Similar Securities

We, our executive officers and directors and substantially all of our other existing security holders have agreed not to sell or transfer any common stock or securities convertible into, exchangeable for, exercisable for, or repayable with common stock, for 180 days after the date of this prospectus without first obtaining the written consent of Merrill Lynch, Pierce, Fenner & Smith Incorporated and Cowen and Company, LLC. Specifically, we and these other persons have agreed, with certain limited exceptions, not to directly or indirectly:

- offer, pledge, sell or contract to sell any common stock,
- sell any option or contract to purchase any common stock,
- purchase any option or contract to sell any common stock,
- grant any option, right or warrant for the sale of any common stock,
- lend or otherwise dispose of or transfer any common stock,
- request or demand that we file a registration statement or make a confidential submission related to the common stock, or
- enter into any swap or other agreement that transfers, in whole or in part, the economic consequence of ownership of any common stock whether any such swap or transaction is to be settled by delivery of shares or other securities, in cash or otherwise.

This lock-up provision applies to common stock and to securities convertible into or exchangeable or exercisable for or repayable with common stock. It also applies to common stock owned now or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition. Merrill Lynch, Pierce, Fenner & Smith Incorporated and Cowen and Company, LLC, in their sole discretion, may release the common stock and other securities subject to the lock-up agreements described above in whole or in part at any time with or without notice. In addition, in the event that any stockholder holding in excess of five percent of our outstanding shares, or a Major Holder, is granted an early release from the lock-up restrictions with respect to our securities in an aggregate amount in excess of one percent of our issued and outstanding shares (whether in one or multiple releases), then each other Major Holder automatically will be granted an equivalent early release from its obligations under the lock-up agreement on a pro-rata basis. Such release shall not be applicable in the event of an underwritten primary or secondary public offering or sale of our common stock during the period ending 180 days after the date of this prospectus.

Nasdaq Global Select Market Listing

Our common stock has been approved for listing on the Nasdaq Global Select Market, subject to notice of issuance, under the symbol "FIXX."

Before this offering, there has been no public market for our common stock. The initial public offering price will be determined through negotiations between us and the representatives. In addition to prevailing market conditions, the factors to be considered in determining the initial public offering price are

- the valuation multiples of publicly traded companies that the representatives believe to be comparable to us,
- our financial information,
- the history of, and the prospects for, our company and the industry in which we compete,
- an assessment of our management, its past and present operations, and the prospects for, and timing of, our future revenues,
- the present state of our development, and
- the above factors in relation to market values and various valuation measures of other companies engaged in activities similar to ours.

An active trading market for the shares may not develop. It is also possible that after the offering the shares will not trade in the public market at or above the initial public offering price.

The underwriters do not expect to sell more than 5% of the shares in the aggregate to accounts over which they exercise discretionary authority.

Price Stabilization, Short Positions and Penalty Bids

Until the distribution of the shares is completed, SEC rules may limit underwriters and selling group members from bidding for and purchasing our common stock. However, the representatives may engage in transactions that stabilize the price of the common stock, such as bids or purchases to peg, fix or maintain that price.

In connection with the offering, the underwriters may purchase and sell our common stock in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering. “Covered” short sales are sales made in an amount not greater than the underwriters’ option to purchase additional shares described above. The underwriters may close out any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option granted to them. “Naked” short sales are sales in excess of such option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of shares of common stock made by the underwriters in the open market prior to the completion of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Similar to other purchase transactions, the underwriters’ purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a

decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. The underwriters may conduct these transactions on the Nasdaq Global Select Market, in the over-the-counter market or otherwise.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. In addition, neither we nor any of the underwriters make any representation that the representatives will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Electronic Distribution

In connection with the offering, certain of the underwriters or securities dealers may distribute prospectuses by electronic means, such as e-mail.

Other Relationships

Some of the underwriters and their affiliates have engaged in, and may in the future engage in, investment banking and other commercial dealings in the ordinary course of business with us or our affiliates. They have received, or may in the future receive, customary fees and commissions for these transactions.

In addition, in the ordinary course of their business activities, the underwriters and their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Notice to Prospective Investors in the European Economic Area

In relation to each member state of the European Economic Area, no offer of ordinary shares which are the subject of the offering has been, or will be made to the public in that Member State, other than under the following exemptions under the Prospectus Directive:

(a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;

(b) to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), subject to obtaining the prior consent of the Representatives for any such offer; or

(c) in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of ordinary shares referred to in (a) to (c) above shall result in a requirement for the Company or any Representative to publish a prospectus pursuant to Article 3 of the Prospectus Directive, or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

Each person located in a Member State to whom any offer of ordinary shares is made or who receives any communication in respect of an offer of ordinary shares, or who initially acquires any ordinary shares will be deemed to have represented, warranted, acknowledged and agreed to and with each Representative and the Company that (1) it is a “qualified investor” within the meaning of the law in that Member State implementing Article 2(1)(e) of the Prospectus Directive; and (2) in the case of any ordinary shares acquired by it as a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, the ordinary shares acquired by it in

the offer have not been acquired on behalf of, nor have they been acquired with a view to their offer or resale to, persons in any Member State other than qualified investors, as that term is defined in the Prospectus Directive, or in circumstances in which the prior consent of the Representatives has been given to the offer or resale; or where ordinary shares have been acquired by it on behalf of persons in any Member State other than qualified investors, the offer of those ordinary shares to it is not treated under the Prospectus Directive as having been made to such persons.

The Company, the Representatives and their respective affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgments and agreements.

This prospectus has been prepared on the basis that any offer of shares in any Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus for offers of shares. Accordingly any person making or intending to make an offer in that Member State of shares which are the subject of the offering contemplated in this prospectus may only do so in circumstances in which no obligation arises for the Company or any of the Representatives to publish a prospectus pursuant to Article 3 of the Prospectus Directive in relation to such offer. Neither the Company nor the Representatives have authorized, nor do they authorize, the making of any offer of shares in circumstances in which an obligation arises for the Company or the Representatives to publish a prospectus for such offer.

For the purposes of this provision, the expression an “offer of ordinary shares to the public” in relation to any ordinary shares in any Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the ordinary shares to be offered so as to enable an investor to decide to purchase or subscribe the ordinary shares, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, the expression “Prospectus Directive” means Directive 2003/71/EC (as amended) and includes any relevant implementing measure in each Member State.

The above selling restriction is in addition to any other selling restrictions set out below.

Notice to Prospective Investors in the United Kingdom

In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are “qualified investors” (as defined in the Prospectus Directive) (i) who have professional experience in matters relating to investments falling within Article 19 (5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the “Order”) and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as “relevant persons”). This document must not be acted on or relied on in the United Kingdom by persons who are not relevant persons. In the United Kingdom, any investment or investment activity to which this document relates is only available to, and will be engaged in with, relevant persons.

Notice to Prospective Investors in Switzerland

The shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange (“SIX”) or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, the Company, or the shares have been or will be filed with or approved by any Swiss regulatory authority. In

particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA (FINMA), and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes ("CISA"). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares.

Notice to Prospective Investors in the Dubai International Financial Centre

This prospectus relates to an Exempt Offer in accordance with the Offered Securities Rules of the Dubai Financial Services Authority ("DFSA"). This prospectus is intended for distribution only to persons of a type specified in the Offered Securities Rules of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus nor taken steps to verify the information set forth herein and has no responsibility for the prospectus. The shares to which this prospectus relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the shares offered should conduct their own due diligence on the shares. If you do not understand the contents of this prospectus you should consult an authorized financial advisor.

Notice to Prospective Investors in Australia

No placement document, prospectus, product disclosure statement or other disclosure document has been lodged with the Australian Securities and Investments Commission ("ASIC"), in relation to the offering. This prospectus does not constitute a prospectus, product disclosure statement or other disclosure document under the Corporations Act 2001 (the "Corporations Act"), and does not purport to include the information required for a prospectus, product disclosure statement or other disclosure document under the Corporations Act.

Any offer in Australia of the shares may only be made to persons (the "Exempt Investors") who are "sophisticated investors" (within the meaning of section 708(8) of the Corporations Act), "professional investors" (within the meaning of section 708(11) of the Corporations Act) or otherwise pursuant to one or more exemptions contained in section 708 of the Corporations Act so that it is lawful to offer the shares without disclosure to investors under Chapter 6D of the Corporations Act.

The shares applied for by Exempt Investors in Australia must not be offered for sale in Australia in the period of 12 months after the date of allotment under the offering, except in circumstances where disclosure to investors under Chapter 6D of the Corporations Act would not be required pursuant to an exemption under section 708 of the Corporations Act or otherwise or where the offer is pursuant to a disclosure document which complies with Chapter 6D of the Corporations Act. Any person acquiring shares must observe such Australian on-sale restrictions.

This prospectus contains general information only and does not take account of the investment objectives, financial situation or particular needs of any particular person. It does not contain any securities recommendations or financial product advice. Before making an investment decision, investors need to consider whether the information in this prospectus is appropriate to their needs, objectives and circumstances, and, if necessary, seek expert advice on those matters.

Notice to Prospective Investors in Hong Kong

The shares have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or (b) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance. No advertisement, invitation or

document relating to the shares has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the Securities and Futures Ordinance and any rules made under that Ordinance.

Notice to Prospective Investors in Japan

The shares have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948, as amended) and, accordingly, will not be offered or sold, directly or indirectly, in Japan, or for the benefit of any Japanese Person or to others for re-offering or resale, directly or indirectly, in Japan or to any Japanese Person, except in compliance with all applicable laws, regulations and ministerial guidelines promulgated by relevant Japanese governmental or regulatory authorities in effect at the relevant time. For the purposes of this paragraph, "Japanese Person" shall mean any person resident in Japan, including any corporation or other entity organized under the laws of Japan.

Notice to Prospective Investors in Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the "SFA"), (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275, of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

(a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

(b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares pursuant to an offer made under Section 275 of the SFA except:

(a) to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;

(b) where no consideration is or will be given for the transfer;

(c) where the transfer is by operation of law;

(d) as specified in Section 276(7) of the SFA; or

(e) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

Notice to Prospective Investors in Canada

The shares may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 *Prospectus Exemptions* or subsection 73.3(1) of the *Securities Act* (Ontario), and are permitted clients, as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*. Any resale of the shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 (or, in the case of securities issued or guaranteed by the government of a non-Canadian jurisdiction, section 3A.4) of National Instrument 33-105 *Underwriting Conflicts* (**NI 33-105**), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by Latham & Watkins LLP. Certain legal matters in connection with this offering will be passed upon for the underwriters by Shearman & Sterling LLP.

EXPERTS

The financial statements included in this Prospectus have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report appearing herein. Such financial statements are included in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the Securities and Exchange Commission a registration statement on Form S-1 under the Securities Act with respect to the shares of common stock offered hereby. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement or the exhibits and schedules filed therewith. For further information about us and the common stock offered hereby, we refer you to the registration statement and the exhibits and schedules filed thereto. Statements contained in this prospectus regarding the contents of any contract or any other document that is filed as an exhibit to the registration statement are not necessarily complete, and each such statement is qualified in all respects by reference to the full text of such contract or other document filed as an exhibit to the registration statement. Upon completion of this offering, we will be required to file periodic reports, proxy statements, and other information with the Securities and Exchange Commission pursuant to the Securities Exchange Act of 1934. You may read and copy this information at the Public Reference Room of the Securities and Exchange Commission, 100 F Street, N.E., Room 1580, Washington, District of Columbia. 20549. You may obtain information on the operation of the public reference rooms by calling the Securities and Exchange Commission at 1-800-SEC-0330. The Securities and Exchange Commission also maintains an Internet website that contains reports, proxy statements and other information about registrants, like us, that file electronically with the Securities and Exchange Commission. The address of that site is *www.sec.gov*.

HOMOLOGY MEDICINES, INC.

INDEX TO FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of Homology Medicines, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Homology Medicines, Inc. and its subsidiary (the "Company") as of December 31, 2017 and 2016, and the related consolidated statements of operations, comprehensive loss, convertible preferred stock and stockholders' deficit, and cash flows for the years then ended and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2017 and 2016, and the results of its operations and its cash flows for the years then ended, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Deloitte & Touche LLP

Boston, Massachusetts

February 23, 2018 (March 19, 2018 as to the effects of the reverse stock split and other matters described in Note 17)

We have served as the Company's auditor since 2017.

HOMOLOGY MEDICINES, INC.

CONSOLIDATED BALANCE SHEETS
AS OF DECEMBER 31, 2017 AND 2016

	December 31, 2017	December 31, 2016	Pro Forma December 31, 2017 (unaudited)
ASSETS			
CURRENT ASSETS:			
Cash and cash equivalents	$ 51,574,932	$ 11,392,207	$ 51,574,932
Short-term investments	78,083,604	—	78,083,604
Prepaid expenses and other current assets	1,944,751	481,794	1,944,751
Deferred rent	—	113,260	—
Total current assets	131,603,287	11,987,261	131,603,287
Property and equipment, net	3,154,205	1,956,054	3,154,205
Deferred offering costs	1,000,262	—	1,000,262
Restricted cash	1,772,587	276,000	1,772,587
TOTAL ASSETS	$ 137,530,341	$ 14,219,315	$ 137,530,341
LIABILITIES, CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' DEFICIT			
CURRENT LIABILITIES:			
Accounts payable	$ 2,538,057	$ 893,673	$ 2,538,057
Accrued expenses and other liabilities	2,860,025	1,237,726	2,860,025
Deferred rent	122,601	—	122,601
Deferred revenue	3,341,063	—	3,341,063
Convertible preferred stock tranche liability	—	4,247,000	—
Total current liabilities	8,861,746	6,378,399	8,861,746
NON-CURRENT LIABILITIES:			
Deferred rent, net of current portion	290,923	340,627	290,923
Deferred revenue, net of current portion	30,069,563	—	30,069,563
Total liabilities	39,222,232	6,719,026	39,222,232
COMMITMENTS AND CONTINGENCIES (NOTE 8)			
CONVERTIBLE PREFERRED STOCK:			
Series A convertible preferred stock, $0.0001 par value; 62,304,354 and 62,269,145 shares authorized as of December 31, 2017 and 2016, respectively; 62,269,144 and 33,395,907 shares issued and outstanding as of December 31, 2017 and 2016, respectively; aggregate liquidation preference of $44,211,092 and $23,711,094 as of December 31, 2017 and 2016, respectively, no shares issued or outstanding, pro forma (unaudited)	42,994,550	17,392,062	—
Series B convertible preferred stock, $0.0001 par value; 64,930,561 shares authorized, issued and outstanding as of December 31, 2017; aggregate liquidation preference of $93,500,008 as of December 31, 2017, no shares issued or outstanding, pro forma (unaudited)	94,767,610	—	—
Total convertible preferred stock	137,762,160	17,392,062	—
STOCKHOLDERS' (DEFICIT) EQUITY:			
Common stock, $0.0001 par value; 170,000,000 and 86,000,000 shares authorized as of December 31, 2017 and 2016, respectively; 2,902,109 and 2,943,199 shares issued as of December 31, 2017 and 2016, respectively; and 2,637,011 and 2,121,156 shares outstanding as of December 31, 2017 and 2016, respectively, 27,070,765 shares issued and 26,805,667 shares outstanding, pro forma at December 31, 2017 (unaudited)	264	212	2,681
Additional paid-in capital	799,859	298,018	138,559,602
Accumulated other comprehensive loss	(73,308)	—	(73,308)
Accumulated deficit	(40,180,866)	(10,190,003)	(40,180,866)
Total stockholders' (deficit) equity	(39,454,051)	(9,891,773)	98,308,109
TOTAL LIABILITIES, CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' DEFICIT	$ 137,530,341	$ 14,219,315	$ 137,530,341

See notes to consolidated financial statements.

HOMOLOGY MEDICINES, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS
FOR THE YEARS ENDED DECEMBER 31, 2017 AND 2016

	Year Ended December 31, 2017	2016
OPERATING EXPENSES:		
Research and development	$ 21,378,154	$ 5,694,997
General and administrative	8,279,344	4,305,021
Total operating expenses	29,657,498	10,000,018
LOSS FROM OPERATIONS	(29,657,498)	(10,000,018)
OTHER INCOME (EXPENSE):		
Changes in fair value of convertible preferred stock tranche liability	(876,000)	1,929,000
Interest income	542,635	24,201
Total other income (expense)	(333,365)	1,953,201
Net loss and net loss attributable to common stockholders-basic and diluted	$(29,990,863)	$ (8,046,817)
Net loss per share attributable to common stockholders-basic and diluted	$ (12.10)	$ (4.23)
Weighted average common shares outstanding-basic and diluted	2,479,432	1,900,531
Pro forma net loss per share attributable to common stockholders-basic and diluted (unaudited)	$ (1.57)	
Pro forma weighted average common shares outstanding-basic and diluted (unaudited)	18,602,429	

See notes to consolidated financial statements.

HOMOLOGY MEDICINES, INC.

CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
FOR THE YEARS ENDED DECEMBER 31, 2017 AND 2016

	Year Ended December 31, 2017	2016
Net loss	$ (29,990,863)	$ (8,046,817)
Other comprehensive loss:		
Unrealized losses on available for sale securities, net	(73,308)	—
Total other comprehensive loss	(73,308)	—
Comprehensive loss	$ (30,064,171)	$ (8,046,817)

See notes to consolidated financial statements.

HOMOLOGY MEDICINES, INC.

CONSOLIDATED STATEMENTS OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' DEFICIT
FOR THE YEARS ENDED DECEMBER 31, 2017 AND 2016

	Convertible Preferred Stock $0.0001 Par Value Series A		Convertible Preferred Stock $0.0001 Par Value Series B		Common Stock $0.0001 Par Value		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Deficit
	Shares	Amount	Shares	Amount	Shares	Amount				
BALANCE, January 1, 2016	33,395,907	$ 17,392,062	—	$ —	1,689,261	$ 169	$ 720	$ —	$ (2,143,186)	$ (2,142,297)
Issuance of common stock to licensor	—	—	—	—	256,241	26	121,348	—	—	121,374
Vesting of common stock from option exercise	—	—	—	—	45,034	4	13,611	—	—	13,615
Vesting of founders restricted common stock	—	—	—	—	130,620	13	63,581	—	—	63,594
Stock-based compensation	—	—	—	—	—	—	98,758	—	—	98,758
Net loss	—	—	—	—	—	—	—	—	(8,046,817)	(8,046,817)
BALANCE, December 31, 2016	33,395,907	$ 17,392,062	—	$ —	2,121,156	$ 212	$ 298,018	$ —	$ (10,190,003)	$ (9,891,773)
Issuance of Series A convertible preferred stock, net of issuance costs of $ 20,511	28,873,237	20,479,488	—	—	—	—	—	—	—	—
Reclassification of tranche liability upon issuance of convertible preferred stock	—	5,123,000	—	—	—	—	—	—	—	—
Issuance of Series B convertible preferred stock, net of issuance costs of $ 399,065	—	—	64,930,561	93,100,943	—	—	—	—	—	—
Allocation of collaboration proceeds to carrying value of Series B convertible preferred stock	—	—	—	1,666,667	—	—	—	—	—	—
Vesting of common stock from option exercise	—	—	—	—	483,200	49	224,626	—	—	224,675
Vesting of founders restricted common stock	—	—	—	—	32,655	3	20,622	—	—	20,625
Stock-based compensation	—	—	—	—	—	—	256,593	—	—	256,593
Comprehensive loss					—	—	—	(73,308)	—	(73,308)
Net loss	—	—	—	—	—	—	—	—	(29,990,863)	(29,990,863)
BALANCE, December 31, 2017	62,269,144	$ 42,994,550	64,930,561	$ 94,767,610	2,637,011	$ 264	$ 799,859	$ (73,308)	$ (40,180,866)	$ (39,454,051)

See notes to consolidated financial statements.

HOMOLOGY MEDICINES, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS
FOR THE YEARS ENDED DECEMBER 31, 2017 AND 2016

	December 31, 2017	2016
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net loss	$ (29,990,863)	$ (8,046,817)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities:		
Depreciation	684,214	239,797
Stock-based compensation	277,201	162,283
Accretion on short-term investments	(85,740)	
Change in fair value associated with convertible preferred stock tranche liability	876,000	(1,929,000)
Research and development expense funded through share issuance	—	121,374
Abandonment of leasehold improvements	—	39,829
Changes in operating assets and liabilities:		
Prepaid expense and other current assets	(1,462,957)	(477,602)
Accounts payable	1,719,926	517,971
Accrued expenses and other liabilities	864,200	660,743
Deferred revenue	33,410,626	—
Deferred rent	186,157	227,367
Net cash provided by (used in) operating activities	6,478,764	(8,484,055)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Purchases of short-term investments	(78,071,172)	—
Purchases of property and equipment	(1,957,908)	(1,989,333)
Changes in restricted cash	(1,496,587)	(276,000)
Net cash used in investing activities	(81,525,667)	(2,265,333)
CASH FLOWS FROM FINANCING ACTIVITIES:		
Proceeds from issuance of restricted common stock	—	378,312
Repurchase of unvested common stock	(17,470)	
Proceeds from issuance of Series A convertible preferred stock, net of issuance costs	20,479,488	—
Proceeds from issuance of Series B convertible preferred stock, net of issuance costs	94,767,610	—
Net cash provided by financing activities	115,229,628	378,312
INCREASE (DECREASE) IN CASH AND CASH EQUIVALENTS	40,182,725	(10,371,076)
CASH AND CASH EQUIVALENTS, BEGINNING OF YEAR	11,392,207	21,763,283
CASH AND CASH EQUIVALENTS, END OF YEAR	$ 51,574,932	$ 11,392,207
SUPPLEMENTAL DISCLOSURES OF NONCASH INVESTING AND FINANCING ACTIVITIES:		
Reclassification of liability for common stock vested	$ 224,675	$ 13,615
Property and equipment additions included in accounts payable	$ 167,594	$ 243,137
Deferred offering costs included in accrued expenses	$ 1,000,262	$ —
Reclassification of tranche liability upon issuance of convertible preferred stock	$ 5,123,000	$ —

See notes to consolidated financial statements.

HOMOLOGY MEDICINES, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
AS OF AND FOR THE YEAR ENDED DECEMBER 31, 2017 AND 2016

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 efforts to research and development activities, raising capital and recruiting skilled personnel for the pursuit of translating proprietary gene editing and gene therapy technology into novel treatments for patients with rare genetic diseases. 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.

Basis of Presentation—The accompanying consolidated financial statements are prepared in conformity with accounting principles generally accepted in the United States of America ("U.S. GAAP") and have been prepared on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. 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. During the year ended December 31, 2017, the Company incurred a net loss of $30.0 million and has $40.2 million in accumulated deficit. The Company has financed its operations to date primarily through the issuance of convertible preferred stock (see Note 11) and with proceeds from its collaboration and license agreement with Novartis (see Note 16). The Company expects to incur additional operating losses and negative operating cash flows for the foreseeable future.

Management believes that existing cash, cash equivalents and short-term investments will allow the Company to continue its operations for at least a year from the issuance date of these consolidated financial statements. 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.

2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Principles of Consolidation—In December 2015, the Company formed Homology Medicines Securities Corporation ("HMSC"), a wholly owned Massachusetts corporation, for the sole purpose of buying, selling, and holding securities on the Company's behalf. The Company's consolidated financial statements include the accounts of the Company and HMSC. All intercompany balances and transactions have been eliminated in the 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 consolidated financial statements include, but are not limited to, 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.

Unaudited Pro Forma Information—The unaudited pro forma balance sheet as of December 31, 2017 assumes the automatic conversion of all outstanding preferred stock into shares of common stock and the reclassification of the Company's outstanding Series A convertible preferred stock ("Series A Preferred Stock"), and Series B convertible preferred stock ("Series B Preferred Stock") from temporary to permanent equity classification, in each case occurring upon the closing of the Company's proposed initial public offering ("IPO"), as if these transactions had occurred on December 31, 2017.

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

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

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 our 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), net.

Restricted Cash—The Company had restricted cash of $1.8 million and $276,000 as of December 31, 2017 and 2016, respectively, which represents cash serving as collateral for letters of credit issued for security deposits for the Company's facility leases in Bedford, Massachusetts.

Concentrations of Credit Risk—Financial instruments that potentially subject us to significant concentration of credit risk consist primarily of cash, cash equivalents, short-term investments and restricted cash. Periodically, the Company may maintain deposits in financial institutions in excess of government insured limits. We believe that we are not exposed to significant credit risk as our deposits are held at financial institutions that management believes to be of high credit quality and the Company has not experienced any losses on these deposits. We regularly invest excess cash with major financial institutions in money market funds, U.S. government and corporate debt securities and commercial paper, all of which can be readily purchased and sold using established markets. As of December 31, 2017, the Company's cash and cash equivalents were held with two financial institutions. We believe that the market risk arising from our holdings of these financial instruments is mitigated based on the fact that many of these securities are either government backed or of high credit rating.

Deferred Offering Costs—The Company capitalizes incremental legal, professional accounting and other third-party fees that are directly associated with our planned IPO as other non-current assets until the IPO is consummated. After consummation of the IPO, these costs will be recorded in stockholders' deficit as a reduction of additional paid-in capital generated as a result of the offering. If the Company terminates its plan for an IPO, any costs deferred will be expensed immediately.

Guarantees and Indemnifications—As permitted under Delaware law, the Company indemnifies its officers, directors, consultants and employees for certain events or occurrences that happen by reason of the relationship with, or position held at, the Company. Through December 31, 2017, the Company had not experienced any losses related to these indemnification obligations, and no claims were outstanding. The Company does not expect significant claims related to these indemnification obligations and, consequently, concluded that the fair value of these obligations is negligible, and no related liabilities have been established.

Property and Equipment—Property and equipment are recorded at cost. Expenditures for repairs and maintenance are expensed as incurred. When assets are retired or disposed of, the assets and related accumulated depreciation are derecognized from the accounts, and any resulting gain or loss is included in the determination of net loss. Depreciation is provided using the straight-line method over the estimated useful lives of the related assets. Leasehold improvements are amortized over the shorter of the lease term or the estimated useful life of the asset.

Computer equipment and software	3 years
Laboratory equipment and office furniture	5 years
Leasehold improvements	Shorter of the lease term or estimated useful life

Impairment of Long-Lived Assets—The Company evaluates its long-lived assets, which consist primarily of property and equipment, for impairment whenever events or changes in circumstances indicate that the carrying amount of such assets may not be recoverable. Recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset to the future undiscounted net cash flows expected to be generated by the asset. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the carrying amount of the asset exceeds the fair value of the asset. To date, no impairments have been recognized for these assets.

Derivative Instruments—The Company has determined that its obligation to issue, and the Company's investors' obligation to purchase, additional shares of Series A convertible preferred stock in the second of two tranches represents 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 (expense) in the statements of operations at each period end while such instruments were outstanding. The liability was valued using an income approach, specifically the discounted cash flow method. On February 10, 2017, the Company issued 28,873,237 shares of Series A Preferred Stock at $0.71 per share upon the achievement of certain development milestones, resulting in net proceeds of $20.5 million. Accordingly, the convertible preferred stock tranche liability was re-measured at fair value on February 10, 2017 using an income approach and then derecognized with a corresponding amount recorded to Series A Preferred Stock.

Research and Development Costs—Research and development costs are charged to expense as incurred. Research and development expense consists of expenses incurred in performing research and development activities, including salaries and benefits, materials and supplies, preclinical expenses, stock-based compensation expense, depreciation of equipment, contract services, and other outside expenses. Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information provided to the Company by its vendors on their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the consolidated financial statements as prepaid expense or accrued research and development expense.

Income Taxes—The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the Company's consolidated financial statements and tax returns. Deferred tax assets and liabilities are determined based upon the differences between the financial statement carrying amounts and the tax bases of existing assets and liabilities and for loss and credit

carryforwards, using enacted tax rates expected to be in effect in the year in which the differences are expected to reverse. Deferred tax assets are reduced by a valuation allowance if it is more likely than not that these assets may not be realized. The Company determines whether it is more likely than not that a tax position will be sustained upon examination. If it is not more likely than not that a position will be sustained, none of the benefit attributable to the position is recognized. The tax benefit to be recognized for any tax position that meets the more-likely-than-not recognition threshold is calculated as the largest amount that is more than 50% likely of being realized upon resolution of the contingency. The Company accounts for interest and penalties related to uncertain tax positions as part of its provision for income taxes.

Common Stock Valuation—Due to the absence of an active market for the Company's common stock, the Company utilized methodologies in accordance with the framework of the American Institute of Certified Public Accountants Technical Practice Aid, Valuation of Privately-Held Company Equity Securities Issued as Compensation, to estimate the fair value of its common stock. In determining the exercise prices for options granted, the Company has considered the estimated fair value of the common stock as of the measurement date. The estimated fair value of the common stock has been determined at each grant date based upon a variety of factors, including 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 other factors are the Company's financial position and historical financial performance, the status of technological developments within the Company's research, the composition and ability of the current research and management team, an evaluation or benchmark of the Company's competition, and the current business climate in the marketplace. Significant changes to the key assumptions underlying the factors used could result in different fair values of common stock at each valuation date.

Convertible Preferred Stock—The Company has classified convertible preferred stock ("preferred stock") as temporary equity in the accompanying consolidated balance sheets due to certain change in control events that are outside of the Company's control, including sale or transfer of control of the Company, as holders of the preferred stock could cause redemption of the shares in these situations. The Company does not accrete the carrying values of the preferred stock to the redemption values since a liquidation event was not considered probable as of December 31, 2017 and 2016. Subsequent adjustments of the carrying values to the ultimate redemption values will be made only when it becomes probable that such a liquidation event will occur.

Segment Information—Operating segments are identified as components of an enterprise about which separate discrete financial information is made available for evaluation by the chief operating decision maker ("CODM") in making decisions regarding resource allocation and assessing performance. The CODM is the Company's Chief Executive Officer. The Company manages its operations as a single segment for the purposes of assessing performance and making operating decisions. The Company's singular focus is dedicated to translating proprietary gene editing and gene therapy technology into novel treatments for patients with rare genetic diseases. All of the Company's tangible assets are held in the United States.

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 16). 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 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.

Stock-based Compensation—The Company recognizes compensation expense for awards to employees based on the grant date fair value of stock-based awards on a straight-line basis over the period during which an award holder provides service in exchange for the award. The Company accounts for stock-based compensation for awards granted to nonemployees by re-measuring the fair value of the awards over the vesting period as the services are provided.

Fair Value Measurements—Certain assets and liabilities are reported on a recurring basis at fair value. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

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

Net Loss per Share and Unaudited Pro Forma 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, convertible preferred stock, convertible preferred stock tranche liability and the potential issuance of stock upon the conversion of the Company's convertible notes.

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. When a gain is recorded pursuant to a change in fair value of the preferred stock tranche liability during the period, the Company assesses whether the impact of reversing the gain and including the additional securities is dilutive, and if so, will adjust dilutive net loss per share. The Company reported a net loss attributable to common stockholders for the year ended December 31, 2017 and 2016.

Unaudited pro forma net loss per share applicable to common stockholders is computed using the weighted-average number of common shares outstanding after giving effect to the conversion of all outstanding convertible preferred stock into shares of common stock as if such conversion had occurred on January 1, 2017, or the date of original issuance, if later.

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 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 16). 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 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 to employees. ASU No. 2016-09 is effective for the Company beginning January 1, 2018, with early application permitted. 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. The Company is in the process of evaluating the impact of the adoption of ASU No. 2016-09 on the Company's 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 is in the process of evaluating the impact that this standard will have on its consolidated financial statements.

3. CASH AND CASH EQUIVALENTS

The Company held $51.6 million and $11.4 million in cash and cash equivalents as of December 31, 2017 and 2016, respectively. From time to time, the Company may have cash balances in financial institutions in excess of federal deposit insurance limits. The Company has never experienced any losses related to these balances. The Company considers only those investments that are highly liquid, readily convertible to cash, and that mature within three months from date of purchase to be cash equivalents.

The following table summarizes the Company's cash and cash equivalents as of December 31, 2017 and 2016:

	As of December 31,	
	2017	2016
Cash	$ 7,393,176	$ 5,336,103
Money market funds	44,181,756	6,056,104
Total cash and cash equivalents	$ 51,574,932	$ 11,392,207

4. SHORT-TERM INVESTMENTS

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

The following table summarizes the Company's short-term investments as of December 31, 2017:

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
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	$78,156,912	$ —	$ (73,308)	$78,083,604

As of December 31, 2017, we do not consider those securities that are in an unrealized loss position to be other-than-temporarily impaired, as we have the ability to hold such investments until recovery of the fair

value. We utilize the specific identification method in computing realized gains and losses. We had no realized gains and losses on our available-for-sale securities for the year ended December 31, 2017.

The Company did not hold any short-term investments as of December 31, 2016.

5. PROPERTY AND EQUIPMENT

Property and equipment, net as of December 31, 2017 and 2016 consist of the following:

	2017	2016
Laboratory equipment	$ 3,713,912	$ 1,922,104
Computers and purchased software	252,436	198,625
Furniture and fixtures	51,379	25,038
Leasehold improvements	34,120	23,715
Property and equipment, at cost	4,051,847	2,169,482
Less accumulated depreciation and amortization	(897,642)	(213,428)
Property and equipment—net	$ 3,154,205	$ 1,956,054

Depreciation and amortization expense for the years ended December 31, 2017 and 2016 was $684,214 and $239,797, respectively. Maintenance and repairs are charged to expense as incurred and any additions or improvements are capitalized.

6. FAIR VALUE MEASUREMENTS

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

The following table presents the fair value of the Company's financial assets and liabilities determined using the inputs defined.

Description	December 31, 2017	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Other Observable Inputs (Level 3)
Assets				
Money market funds, included in cash equivalents	$ 44,181,756	$ 44,181,756	$ —	$ —
Short-term investments	78,083,604	—	78,083,604	—
Total financial assets	$122,265,360	$ 41,181,756	$ 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.

Description	December 31, 2016	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Other Observable Inputs (Level 3)
Assets				
Money market funds, included in cash equivalents	$ 6,056,104	$ 6,056,104	$ —	$ —
Total financial assets	$ 6,056,104	$ 6,056,104	$ —	$ —
Liabilities				
Convertible preferred stock tranche liability	$ 4,247,000	$ —	$ —	$ 4,247,000
Total financial liabilities	$ 4,247,000	$ —	$ —	$ 4,247,000

The convertible preferred stock tranche liability is stated at fair value and is measured using a Level 3 input because the fair value measurement is based, in part, on significant inputs not observed in the market. The Company determined the fair value of the convertible preferred stock tranche liability as described in Note 11.

The reconciliations of changes in the fair value of financial instruments based on Level 3 inputs for the years ended December 31, 2017 and 2016 consisted of:

Fair value as of January 1, 2016	$ 6,176,000
Change in fair value of convertible preferred stock tranche liability	(1,929,000)
Fair value as of December 31, 2016	$ 4,247,000
Change in fair value of convertible preferred stock tranche liability	876,000
Reduction in tranche liability due to preferred stock issuance	(5,123,000)
Fair value as of December 31, 2017	$ —

There have been no transfers between fair value measure levels during the years ended December 31, 2017 and 2016, respectively.

7. ACCRUED EXPENSES

Accrued expenses at December 31, 2017 and 2016 consist of the following:

	2017	2016
Accrued professional fees	$ 1,119,959	$ 149,005
Accrued compensation and benefits	1,435,015	612,035
Accrued unvested common stock subject to repurchase	122,551	364,713
Accrued research and development expenses	182,500	111,973
Total accrued expenses	$ 2,860,025	$ 1,237,726

8. COMMITMENTS AND CONTINGENCIES

Operating Leases—In February 2016, the Company entered into an operating lease for office and laboratory space in Lexington, Massachusetts, which originally was scheduled to expire in January 2019. This lease was cancelled effective November 2016, without penalty.

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 December 31, 2017, 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 December 31, 2017 are as follows:

Years Ending December 31	Amount
2018	$ 1,546,251
2019	3,505,225
2020	3,750,149
2021	3,696,598
2022	2,928,014
Thereafter	13,177,338
Total future minimum lease payments	$ 28,603,575

A letter of credit was established as a security deposit for the facility lease in the amount of $1.5 million. The letter of credit is secured by restricted cash of $1.5 million. The lease agreement 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.

Rent expense for the years ended December 31, 2017 and 2016 was $947,822 and $367,310, respectively. The Company maintains letters of credit, secured by restricted cash, for security deposits totaling $1.8 million and $276,000 as of December 31, 2017 and 2016, respectively, in conjunction with its current leases.

Loan and Security Agreement—In September 2016, the Company entered into a Loan and Security Agreement (the “Agreement”) with a bank. Under the terms of the Agreement, the Company could draw down up to $2.5 million in the form of term loans through June 30, 2017. The Agreement, expired on June 30, 2017 with no borrowings drawn or outstanding balance.

9. LICENSE AGREEMENTS

City of Hope

In April 2016, the Company entered into a license agreement with City of Hope (“COH”), an academic research and medical center. In consideration for the right to develop, manufacture, and commercialize products based on certain of COH’s intellectual property, the Company paid a one-time, non-refundable license fee of $75,000 and issued 154,837 shares of common stock, with a fair value of $73,342. The total consideration of $148,342 is recorded in research and development expense in the consolidated statement of operations for the year ended December 31, 2016. The license term extends until the last to expire patent, unless terminated earlier by either party under certain provisions. The Company is required to pay an annual license fee of $25,000, reimburse COH for patent costs incurred, pay amounts up to $3.2 million upon the achievement of certain development and commercialization milestones for each product under the license, pay royalties on future sales in the low single- digits and royalties on sublicense revenue in the low double-digits, if any.

As a result of the execution of the Collaboration Agreement with Novartis (see Note 16), the Company paid $4.5 million to COH in December 2017, under the terms of the license agreement.

In May 2015, the Company entered into a sponsored research agreement with COH with a goal to identify potential treatments for diseases in humans. The agreed upon commitment for research and development services is for $1,064,628 which continues through 2019. Under this agreement, the Company has recorded $76,250 and $256,282 in research and development expense for the years ended December 31, 2017 and 2016, respectively, of which $140,000 and $98,891 is recorded as accrued research and development expenses as of December 31, 2017 and 2016, respectively.

The Company's future contractual obligation under the sponsored research agreement is $791,128 as of December 31, 2017.

California Institute of Technology

In September 2016, the Company entered into a co-exclusive license agreement with the California Institute of Technology ("Caltech"), an academic research institute. In consideration for the right to develop, manufacture, and commercialize products based on certain Caltech intellectual property, the Company paid a one-time, non-refundable license fee of $100,000 and issued 101,405 shares of common stock, with a fair value of $48,032 The total consideration of $148,032 has been recorded in research and development expense in the consolidated statement of operations for the year ended December 31, 2016. The license term extends until the expiration, revocation, invalidation or unenforceability of the licensed patent rights. The Company is required to pay an annual minimal royalty fee of $20,000, reimburse for patent costs incurred, pay an amount up to $7.2 million upon the achievement of certain milestones and pay royalties on future sales in the low single-digits and royalties on sublicense revenue in the mid to high single-digits, if any.

As a result of the execution of the Collaboration Agreement with Novartis (see Note 16), the Company paid $0.1 million to Caltech in December 2017, under the terms of the license agreement.

10. INCOME TAXES

A reconciliation of the income tax expense computed using the federal statutory income tax rate to the Company's effective income tax rate is as follows:

	Year Ended December 31,	
	2017	2016
Income tax computed at federal statutory rate	34.0%	34.0%
Tax credits	4.8%	1.7%
State taxes, net of federal tax benefit	5.0%	6.3%
Change in tranche liability	(1.0%)	7.9%
Non-deductible expenses	(1.8%)	(0.6%)
Impact of federal rate change	(15.2%)	0.0%
Change in valuation allowance	(25.8%)	(49.3%)
Effective income tax rate	0.0%	0.0%

The principal components of the Company's deferred tax assets and liabilities consist of the following at December 31, 2017 and 2016:

	As of December 31, 2017	2016
Deferred tax assets:		
Net operating losses	$ 9,179,589	$ 2,400,386
R&D credits	1,775,534	234,850
Capitalized R&D costs	1,362,333	2,188,801
Accrued expense and other	196,272	89,833
Equity compensation	26,837	12,078
Deferred rent	112,974	89,310
Total deferred tax assets	12,653,539	5,015,258
Deferred tax liabilities:		
Depreciation	(165,712)	(270,590)
Total deferred tax liabilities	(165,712)	(270,590)
Valuation allowance	(12,487,827)	(4,744,668)
Net deferred taxes	$ —	$ —

In December 2017, the Tax Cuts and Jobs Act, or the Tax Act ("TCJA"), was signed into law. Among other things, the Tax Act permanently lowers the corporate federal income tax rate to 21% from the statutory rate of 34%, effective for tax years including or commencing January 1, 2018. As a result of the reduction of the corporate federal income tax rate to 21%, U.S. GAAP requires companies to revalue their deferred tax assets and deferred tax liabilities as of the date of enactment, with the resulting tax effects accounted for in the reporting period of enactment. This revaluation resulted in an overall reduction of deferred taxes of $4,558,258 and a corresponding reduction in the valuation allowance. As a result, there was no net impact to the Company's statement of operations as a result of the reduction in tax rates.

The Company has no income tax expense due to the operating loss incurred for the years ended December 31, 2017 and 2016. The Company has provided a valuation allowance for the full amount of the net deferred tax assets as the realization of the net deferred tax assets is not determined to be more likely than not.

At December 31, 2017, the Company has $33,429,262 and $34,168,424 of federal and state net operating loss carryforwards, respectively, that expire at various dates through 2037. At December 31, 2016, the Company has $6,142,640 and $5,906,973 of federal and state net operating loss carryforwards, respectively, that expire at various dates through 2036. At December 31, 2017, the Company has $1,148,562 and $793,635 of federal and state research and development credit carryforwards, respectively, that expire at various dates through 2037. At December 31, 2016, the Company has $82,365 and $231,037 of federal and state research and development credit carryforwards, respectively, that expire at various dates through 2036. The valuation allowance increased in 2017 and 2016 by $7,743,159 and $4,129,679, respectively, due to the increase in the deferred tax assets by the same amounts, primarily due to net operating loss carryforwards and research and development tax credits not utilized.

Realization of the future tax benefits is dependent on many factors, including the Company's ability to generate taxable income within the net operating loss carryforward period. Under the provisions of the Internal Revenue Code, certain substantial changes in the Company's ownership, including a sale of the Company or significant changes in ownership due to sales of equity, may have limited, or may limit in the future, the amount of net operating loss carryforwards that could be used annually to offset future taxable income. The Company has not completed a study to assess whether a change of control has occurred or whether there have been multiple changes of control since the Company's formation due to the significant complexity and cost associated with

such study and because there could be additional changes in control in the future. As a result, the Company is not able to estimate the effect of the change in control, if any, on the Company's ability to utilize net operating loss and research and development credit carryforwards in the future.

The Company files tax returns in the United States and Massachusetts. All tax years since inception remain open to examination by the major taxing jurisdictions to which the Company is subject, as carryforward attributes generated in years past may still be adjusted upon examination by the Internal Revenue Service (IRS) or other authorities if they have or will be used in a future period. The Company is not currently under examination by the IRS or any other jurisdictions for any tax years.

As of December 31, 2017, the Company had no uncertain tax positions. The Company has elected to recognize interest and penalties related to income tax matters as a component of income tax expense, of which no interest or penalties were recorded for the years ended December 31, 2017 and 2016.

11. CONVERTIBLE PREFERRED STOCK

In December 2015, the Company authorized the sale and issuance of up to 62,269,145 shares of Series A preferred stock. The Series A preferred financing was structured to close in two tranches. The first tranche closed on December 22, 2015 with the issuance of 28,873,237 shares at $0.71 per share resulting in gross cash proceeds of $20.5 million. Issuance costs totaled $143,033. As part of the closing on December 22, 2015, the Company also issued 4,522,670 shares of Series A in connection with the conversion of notes payable to investors that were originally issued in 2015.

The investors in the first tranche were granted the right to purchase additional 28,873,237 shares of Series A preferred stock to be offered in the second tranche at $0.71 per share. The Company determined that the right of the investors to purchase Series A preferred stock in the second tranche meets the definition of a freestanding financial instrument and therefore was recognized as a liability at fair value until the tranche right was exercised.

Upon the first tranche closing, the Company recognized a liability of $6.2 million for the fair value of the convertible preferred stock tranche liability representing the future obligation. The convertible preferred stock tranche liability was re-measured with a fair value of $5.1 million and $4.2 million as of February 9, 2017 and December 31, 2016, respectively. The fair value of the convertible preferred stock tranche liability was determined using an option pricing model with the following assumptions:

	February 9, 2017	December 31, 2016
Probability of milestone closing	99.9%	85.0%
Expected years closing	0.0	0.08
Discount rate	1.0%	15.0%
Risk-free interest rate	0.84%	0.94%
Expected dividend yield	0.0%	0.0%

The Company 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. During the years ended December 31, 2017 and 2016, the Company recognized total other income (expense) of $(876,000) and $1,929,000, respectively, related to changes in the fair value of the convertible preferred stock tranche liability.

On February 10, 2017, the Company issued 28,873,237 shares of Series A preferred stock at $0.71 per share for gross proceeds of $20.5 million. Issuance costs were $20,511. Accordingly, the convertible preferred stock tranche liability was re-measured at fair value and then derecognized with a corresponding amount of $5.1 million reclassified to Series A preferred stock.

On July 28, 2017, the Company authorized the sale of 64,930,561 shares of Series B convertible preferred stock and issued 57,986,116 shares of Series B convertible preferred stock at $1.44 per share, for gross proceeds of $83.5 million upon closing. Total issuance costs were $399,065. All holders of Series A convertible preferred stock participated in the Series B issuance along with new investors.

On November 6, 2017, the Company entered into a Collaboration and License Agreement with Novartis for the development and commercialization of products using the Company's gene editing technology for the treatment of certain ophthalmic targets and sickle cell disease (see Note 16). Under the terms of the Collaboration Agreement, Novartis invested $10.0 million to purchase 6,944,445 shares of Series B convertible preferred stock. The difference between the cash proceeds received from Novartis for the purchase of Series B preferred stock and the $11.7 million estimated fair value of the Series B at the time of purchase was allocated from the collaboration proceeds to Series B preferred stock.

The following is a summary of the rights and privileges of the Series A and Series B convertible preferred stock holders as of December 31, 2017.

Conversion—Each share of Series A and Series B preferred stock may be converted into shares of common stock and subject to adjustment in accordance with anti-dilution provisions. Each share of Series A and Series B preferred stock is convertible on a one-for-5.263 basis into common stock. The Series A and Series B preferred shares automatically convert into shares of common stock at the earlier of the closing of an initial public offering of the Company's common stock with gross proceeds to the Company of at least $50.0 million or at the election of the holders of at least 71.5% of the then-outstanding shares of Series A and Series B convertible preferred stock, voting together as a single class.

Liquidation Preference—Upon liquidation, dissolution, or winding-up of the Company, Series A and Series B preferred shareholders are entitled to receive a liquidation preference in priority to holders of common stock at the greater of the original Series A and Series B preferred stock original issue price plus any declared but unpaid dividends, or such amount per share as would have been payable had all shares of preferred stock been converted into common stock immediately prior to such liquidation, dissolution or winding up of the Company or deemed liquidation event. No dividends have been declared to date. If assets available for distribution are insufficient to satisfy the liquidation payment to holders in full, assets available for distribution will be allocated among holders based on their pro rata holdings. When holders are satisfied in full, any excess assets available for distribution will be allocated ratably among common stockholders based on their pro rata holdings.

Dividends—Holders are entitled to non-cumulative dividends at the rate of 8% of the original issue price per share when and if declared by the Board of Directors. No dividends have been declared through December 31, 2017.

Voting Rights—Preferred stock and common stock vote together as one class on an as converted basis. Common stock voting rights on certain matters are subject to the powers, preferences, and rights of the preferred stock. Holders are entitled to vote on all matters and shall have the number of votes equal to the number of shares of common stock into which the shares of preferred stock held by such holder are then convertible. At any time where there are at least 5,000,000 shares of preferred stock outstanding, certain actions such as mergers, acquisition, liquidation, dissolution, wind up of business and deemed liquidation events, must be approved by at least 71.5% of the then outstanding shares of preferred stock.

12. STOCKHOLDERS' EQUITY

Common Stock—Voting, dividend and liquidation rights of the holders of the common stock are subject to and qualified by the rights, powers and preferences of the holders of the preferred stock.

Voting—Each holder of outstanding shares of common stock shall be entitled to one vote in respect of each share. The holders of outstanding shares of common stock, voting together as a single class, shall be entitled to elect one director. The number of authorized shares of common stock may be increased or decreased by the affirmative vote of a majority of the outstanding shares of common stock and preferred stock voting together as a single class.

Dividends—Subject to the payment in full of all preferential dividends to which the holders of the preferred stock are entitled, the holders of common stock shall be entitled to receive dividends out of funds legally available therefore at such times and in such amounts as the Board of Directors may determine in its sole discretion, with holders of preferred stock and common stock sharing pari passu in such dividends.

Liquidation Rights—In the event of any voluntary or involuntary liquidation, dissolution or winding-up of the Company, after the payment or provision for payment of all debts and liabilities of the Company and all preferential amounts to which the holders of preferred stock are entitled with respect to the distribution of assets in liquidation, the holders of common stock shall be entitled to share ratably in the remaining assets of the Company available for distribution.

Reserved Shares—As of December 31, 2017, the Company has reserved the following shares of common stock for potential conversion of the outstanding convertible preferred stock and exercise of stock options:

	December 31, 2017
Convertible preferred stock	24,168,656
2015 stock option plan	2,432,028
Total	26,600,684

Restricted Common Stock—During 2015, the Company issued 522,515 shares of founders' restricted common stock to the scientific founders of the Company for an aggregate consideration of $275. The purchase price of the founders' restricted common stock was the estimated fair value at the issuance date. The shares were subject to vesting over a period of two years, and vesting could have been accelerated upon a change in control, as defined. If the holders ceased to have a business relationship with the Company during the vesting period, the Company could have repurchased any unvested founders' restricted common stock held by these individuals at their original purchase price. The Company recognized a liability in accrued expenses of $17 for the unvested portion of the founders' restricted common stock as of December 31, 2016. During March 2017, the founders' restricted common stock fully vested. A summary of the Company's unvested founders' restricted common stock and changes during the year ended December 31, 2017 as follows:

	Shares	Grant Date Fair Value
Unvested—January 1, 2017	32,655	$ 0.0001
Issued	—	—
Vested	(32,655)	0.0001
Unvested—December 31, 2017	—	$ —

The total fair value of the founders' restricted common stock that vested during the year ended December 31, 2017 was $21.

13. STOCK OPTION 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 issue 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 December 31, 2017, there were 460,317 shares available for future grant under the 2015 Plan.

Total stock-based compensation expense recorded as research and development and general and administrative expenses, respectively, for employees, directors and non-employees during the years ended December 31, 2017 and 2016 is as follows:

	2017	2016
Research and development	$115,094	$39,794
General and administrative	141,499	58,964
	$256,593	$98,758

As of December 31, 2017, there was $3.8 million of unrecognized compensation expense related to unvested employee and non-employee share-based compensation arrangements granted under the 2015 Plan. The unrecognized compensation expense is estimated to be recognized over a period of 3.7 years at December 31, 2017.

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 has considered the fair value of the common stock as of the measurement date. The fair value of the common stock has been determined by the Board of Directors 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 years ended December 31, 2017 and 2016 were as follows:

	2017	2016
Expected volatility	52.73% - 59.40%	53.05% - 63.63%
Weighted-average risk-free interest rate	2.04% - 2.37%	1.49% - 2.07%
Expected dividend yield	-%	-%
Expected term (in years)	5.9 - 8.6	6.25 - 9.4
Underlying common stock fair value	$0.63 - $6.63	$0.63

A summary of option activity under the 2015 Plan during the year ended December 31, 2017 is as follows:

	Number of Options	Weighted-Average Exercise Price per Share	Weighted Average Remaining Contractual Term (in Years)	Aggregate Intrinsic Value
Outstanding as of January 1, 2017	669,511	$ 0.46	9.3	$ 121,807
Granted	1,302,200	$ 5.23		
Exercised	—	$ —		
Cancelled/Forfeited	—	$ —		
Outstanding as of December 31, 2017	1,971,711	$ 3.61	9.3	$5,977,162
Exercisable at December 31, 2017	189,760	$ 0.40	8.2	$1,182,904
Vested and expected to vest at December 31, 2017	1,971,711	$ 3.61	9.3	$5,977,162

The total intrinsic value of options exercised during the year ended December 31, 2016 was $16,920. There were no option exercises in 2017. The weighted-average grant date fair value of options granted during the years ended December 31, 2017 and 2016 was $2.78 and $0.26, 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 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, 2017	789,380
Vested	(483,200)
Repurchased	(41,082)
Unvested shares—December 31, 2017	265,098

As of December 31, 2017 and 2016, 265,098 and 789,380 shares, respectively, remained subject to a repurchase right by the Company, with a related liability included in accrued expenses and other liabilities in the consolidated balance sheet of $122,551 and $364,696, respectively.

14. NET LOSS PER SHARE AND UNAUDITED PRO FORMA NET LOSS PER SHARE

Net Loss Per Share-Basic and diluted net loss per share attributable to common stockholders was calculated as follows:

	Year Ended December 31, 2017	Year Ended December 31, 2016
Numerator:		
Net loss attributable to common stockholders	$(29,990,863)	$(8,046,817)
Denominator:		
Weighted average common shares outstanding—basic and diluted	2,479,432	1,900,531
Net loss per share attributable to common stockholders—basic and diluted	$ (12.10)	$ (4.23)

The Company's potential dilutive securities, which include convertible preferred stock tranche rights, restricted stock, 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 December 31, 2017 and 2016, 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 December 31, 2017	2016
Convertible preferred shares (as converted to common stock)	24,168,656	6,345,409
Unvested restricted common stock	—	32,655
Unvested common stock from early exercise of options	265,098	789,380
Stock options to purchase common stock	1,971,711	669,511
	26,405,465	7,836,955

Unaudited Pro Forma Net Loss Per Share

The unaudited pro forma basic and diluted net loss per share attributable to common stockholders for the year ended December 31, 2017 has been prepared to give effect to adjustments arising upon the completion of a qualified initial public offering. The unaudited pro forma net loss attributable to common stockholders used in the calculation of unaudited pro forma basic and diluted net loss per share attributable to common stockholders does not include the effects of the preferred stock tranche liability because the calculation gives effect to the automatic conversion of all shares of convertible preferred stock outstanding as of December 31, 2017 into shares of common stock as if the proposed initial public offering had occurred on the later of January 1, 2017 or the issuance date of the convertible preferred stock.

The unaudited pro forma basic and diluted weighted average common shares outstanding used in the calculation of unaudited pro forma basic and diluted net loss per share attributable to common stockholders for the year ended December 31, 2017 has been prepared to give effect, upon a qualified initial public offering, to the automatic conversion of all outstanding shares of convertible preferred stock into common stock as if the proposed initial public offering had occurred on the later of January 1, 2017 or the issuance date of the convertible preferred stock. Pro forma basic and diluted net loss per share attributable to common stockholders was calculated as follows:

	Year Ended December 31, 2017 (unaudited)
Numerator:	
Net loss attributable to common stockholders	$ (29,990,863)
Change in fair value of convertible preferred stock tranche liability	876,000
Pro forma net loss attributable to common stockholders	$ (29,114,863)
Denominator:	
Weighted average common shares outstanding—basic and diluted	2,479,432
Pro forma adjustment to reflect automatic conversion of convertible preferred stock to common stock upon the completion of the proposed initial public offering	16,122,997
Pro forma weighted average common shares outstanding—basic and diluted	18,602,429
Pro forma net loss per share attributable to common stockholders—basic and diluted	$ (1.57)

15. DEFINED CONTRIBUTION PLAN

The Company has a 401(k) defined contribution plan (the "401(k) Plan") for all of its employees. Eligible employees may make pretax contributions to the 401(k) Plan up to statutory limits. There was no discretionary match made under the 401(k) Plan as of December 31, 2017 and 2016.

16. 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. any *in vivo* hemoglobinipathy product, 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 million in development milestone payments, up to $275 million in regulatory milestone payments and up to $350 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 will be 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 will commence revenue recognition upon delivery of the final deliverable included in the combined unit of accounting. As of December 31, 2017, all deliverables included in the combined unit of accounting have commenced except for the manufacturing services, which are expected to commence early in 2018. Accordingly no amounts of revenue have been recognized as of December 31, 2017. All payments due or received from Novartis as of December 31, 2017, including amounts due for research activities performed, have been recorded as deferred revenue as of December 31, 2017.

17. SUBSEQUENT EVENTS

The Company evaluated subsequent events for financial statement purposes through February 23, 2018, the date these consolidated financial statements were originally issued. The Company also evaluated subsequent events through March 19, 2018, the date on which the retroactively revised consolidated financial statements were reissued (as a result of the reverse stock split discussed below).

Reverse Stock Split

On March 12, 2018, the Company's Board of Directors approved 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 (see Note 11). 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.

Equity Incentive Plan

On March 12, 2018, the Company's Board of Directors adopted and the Company's stockholders approved the Homology Medicines, Inc. 2018 Incentive Plan (the "2018 Plan"), which will become effective upon the effectiveness of the registration statement on Form S-1 for the Company's initial public offering. The 2018 Plan provides for the grant of incentive stock options, nonstatutory stock options, restricted stock awards, restricted stock units, stock appreciation right and other stock-based awards initially equal to 3,186,205 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) 4% of the aggregate number of shares of common stock outstanding on the final day of the immediately preceding calendar year and (ii) such smaller number of shares of common stock as determined by the Board of Directors (but no more than 20,887,347 shares may be issued upon the exercise of incentive stock options), plus any shares that are subject to awards outstanding under the 2015 Plan as of the effective date of the 2018 Plan which are forfeited, expire, lapse for any reason or are settled for cash without the issuance of shares.

* * * * * *

Through and including , 2018 (the 25th day after the date of this prospectus), all dealers effecting transactions in the Common Stock, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to a dealer's obligation to deliver a prospectus when acting as an underwriter and with respect to an unsold allotment or subscription.

6,667,000 Shares

Common Stock

PROSPECTUS

BofA Merrill Lynch

Cowen

Evercore ISI

BTIG

, 2018

Part II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 13. Other Expenses of Issuance and Distribution.

The following table indicates the expenses to be incurred in connection with the offering described in this registration statement, other than underwriting discounts and commissions, all of which will be paid by us. All amounts are estimated except the Securities and Exchange Commission registration fee, the Financial Industry Regulatory Authority, Inc., or FINRA, filing fee and the Nasdaq listing fee.

	Amount
Securities and Exchange Commission registration fee	$ 15,273
FINRA filing fee	18,900
Nasdaq initial listing fee	150,000
Accountants' fees and expenses	750,000
Legal fees and expenses	1,500,000
Blue Sky fees and expenses	15,000
Transfer Agent's fees and expenses	4,500
Printing and engraving expenses	285,000
Miscellaneous	111,327
Total expenses	$ 2,850,000

Item 14. Indemnification of Directors and Officers.

Section 102 of the General Corporation Law of the State of Delaware permits a corporation to eliminate the personal liability of directors of a corporation to the corporation or its stockholders for monetary damages for a breach of fiduciary duty as a director, except where the director breached his duty of loyalty, failed to act in good faith, engaged in intentional misconduct or knowingly violated a law, authorized the payment of a dividend or approved a stock repurchase in violation of Delaware corporate law or obtained an improper personal benefit. Our restated certificate of incorporation provides that no director of the Registrant shall be personally liable to it or its stockholders for monetary damages for any breach of fiduciary duty as a director, notwithstanding any provision of law imposing such liability, except to the extent that the General Corporation Law of the State of Delaware prohibits the elimination or limitation of liability of directors for breaches of fiduciary duty.

Section 145 of the General Corporation Law of the State of Delaware provides that a corporation has the power to indemnify a director, officer, employee, or agent of the corporation, or a person serving at the request of the corporation for another corporation, partnership, joint venture, trust or other enterprise in related capacities against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by the person in connection with an action, suit or proceeding to which he was or is a party or is threatened to be made a party to any threatened, ending or completed action, suit or proceeding by reason of such position, if such person acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the corporation, and, in any criminal action or proceeding, had no reasonable cause to believe his conduct was unlawful, except that, in the case of actions brought by or in the right of the corporation, no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or other adjudicating court determines that, despite the adjudication of liability but in view of all of the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Court of Chancery or such other court shall deem proper.

Our restated certificate of incorporation provides that we will indemnify each person who was or is a party or threatened to be made a party to any threatened, pending or completed action, suit or proceeding (other than an action by or in the right of us) by reason of the fact that he or she is or was, or has agreed to become, a director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (all such persons being referred to as an "Indemnitee"), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding and any appeal therefrom, if such Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, our best interests, and, with respect to any criminal action or proceeding, he or she had no reasonable cause to believe his or her conduct was unlawful. Our restated certificate of incorporation provides that we will indemnify any Indemnitee who was or is a party to an action or suit by or in the right of us to procure a judgment in our favor by reason of the fact that the Indemnitee is or was, or has agreed to become, a director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise, or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees) and, to the extent permitted by law, amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding, and any appeal therefrom, if the Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, our best interests, except that no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to us, unless a court determines that, despite such adjudication but in view of all of the circumstances, he or she is entitled to indemnification of such expenses. Notwithstanding the foregoing, to the extent that any Indemnitee has been successful, on the merits or otherwise, he or she will be indemnified by us against all expenses (including attorneys' fees) actually and reasonably incurred in connection therewith. Expenses must be advanced to an Indemnitee under certain circumstances.

We have entered into indemnification agreements with each of our directors and officers. These indemnification agreements may require us, among other things, to indemnify our directors and officers for some expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by a director or officer in any action or proceeding arising out of his or her service as one of our directors or officers, or any of our subsidiaries or any other company or enterprise to which the person provides services at our request.

We maintain a general liability insurance policy that covers certain liabilities of directors and officers of our corporation arising out of claims based on acts or omissions in their capacities as directors or officers.

In any underwriting agreement we enter into in connection with the sale of common stock being registered hereby, the underwriters will agree to indemnify, under certain conditions, us, our directors, our officers and persons who control us within the meaning of the Securities Act of 1933, as amended, or the Securities Act, against certain liabilities.

Item 15. Recent Sales of Unregistered Securities.

Set forth below is information regarding shares of capital stock issued by us within the past three years. Also included is the consideration received by us for such shares and information relating to the section of the Securities Act, or rule of the Securities and Exchange Commission, under which exemption from registration was claimed.

(a) Issuance of Capital Stock.

From December 22, 2015 through November 8, 2017, the registrant issued an aggregate of 62,269,144 shares of Series A Preferred Stock for aggregate consideration of $44.2 million to accredited investors and 64,930,561 shares of Series B Preferred Stock for aggregate consideration of $93.5 million pursuant to Section 4(a)(2) of the Securities Act and Rule 506 as a transaction not involving a public offering.

(b) Equity Grants.

Since May 5, 2015, the registrant granted stock options to purchase an aggregate of 2,837,294 shares of its common stock with exercise prices ranging between $0.0263 and $6.63 per share, and 834,395 shares of restricted common stock to employees, non-employees, and directors from the early exercise of stock options in connection with services provided to the registrant by such parties.

In March 2018, the registrant granted stock options to purchase an aggregate of 731,757 shares of common stock, which will become effective in connection with this offering, to certain of the registrant's directors, executive officers and employees, at an exercise price per share equal to the initial public offering price in this offering in connection with services provided to the registrant.

The issuances of such stock options, the shares of common stock issuable upon the exercise of such options and such restricted shares of common stock were issued pursuant to written compensatory plans or arrangements with the registrant's employees, directors and consultants, in reliance on the exemption provided by Rule 701 promulgated under the Securities Act, or pursuant to Section 4(a)(2) under the Securities Act, relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required.

(c) Warrants.

On October 6, 2016, the registrant issued a warrant to purchase up to an aggregate of 6,690 shares of Series A preferred stock to Silicon Valley Bank pursuant to Section 4(a)(2) of the Securities Act as a transaction not involving a public offering. The warrant never became exercisable for any shares and, in November 2017, the warrant was terminated.

(d) Issuance of Notes.

From April 2015 to November 2015, the registrant issued six unsecured convertible loan notes for aggregate consideration of $2,500,000.

Item 16. Exhibits and Financial Statement Schedules.

(a) Exhibits.

Exhibit Number	Description of Exhibit
1.1**	Form of Underwriting Agreement
3.1**	Certificate of Incorporation of the Registrant, as amended (currently in effect)
3.2**	Bylaws of the Registrant (currently in effect)
3.3**	Form of Restated Certificate of Incorporation of the Registrant (to be effective upon the closing of this offering)
3.4**	Form of Restated Bylaws of the Registrant (to be effective upon the closing of this offering)
4.1**	Amended and Restated Investors' Rights Agreement dated July 28, 2017, among the Registrant and the investors named therein
4.2**	Specimen Stock Certificate evidencing the shares of common stock
5.1**	Opinion of Latham & Watkins LLP
10.1#**	2015 Stock Incentive Plan, as amended, and form of option agreements thereunder

Exhibit Number	Description of Exhibit
10.2#**	2018 Incentive Award Plan and form of option agreements thereunder
10.3#**	2018 Employee Stock Purchase Plan
10.4#**	Non-Employee Director Compensation Program
10.5#**	Form of Indemnification Agreement for Directors and Officers
10.6**	Lease Agreement, dated August 31, 2016, between the Registrant and ARE-MA Region No. 24, LLC
10.7**	Lease Agreement, dated December 21, 2017, between the Registrant and Bedford Patriots Park, LLC
10.8**	Offer Letter to Siyamak (Sam) Rasty, dated December 7, 2015
10.9**	Offer Letter to Albert Seymour, dated February 14, 2016
10.10**	Offer Letter to Arthur O. Tzianabos, dated March 31, 2016
10.11**	Employment Agreement, by and between the Registrant and Siyamak (Sam) Rasty (to be effective upon the closing of this offering)
10.12**	Employment Agreement, by and between the Registrant and Albert Seymour (to be effective upon the closing of this offering)
10.13**	Employment Agreement, by and between the Registrant and Bradford Smith (to be effective upon the closing of this offering)
10.14**	Employment Agreement, by and between the Registrant and Arthur Tzianabos, Ph.D. (to be effective upon the closing of this offering)
10.15†	Collaboration and License Agreement, dated November 6, 2017, between the Registrant and Novartis Institutes for BioMedical Research, Inc.
10.16†**	Exclusive License Agreement, dated April 28, 2016, between the Registrant and City of Hope
10.17.1†**	License Agreement, dated September 14, 2016, between the Registrant and California Institute of Technology
10.17.2†**	First Amendment to License Agreement, dated May 16, 2017, between the Registrant and California Institute of Technology
10.17.3†**	Letter Agreement, dated November 14, 2017, between the Registrant and California Institute of Technology
21.1**	Subsidiaries of the Registrant
23.1	Consent of Deloitte & Touche LLP
23.2**	Consent of Latham & Watkins LLP (included in Exhibit 5.1)
24.1**	Power of Attorney (included on signature page)

** Previously filed.
# Indicates management contract or compensatory plan.
† Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment pursuant to Rule 406 under the Securities Act of 1933, as amended.

(b) Financial Statement Schedules. Schedules not listed above have been omitted because the information required to be set forth therein is not applicable or is shown in the consolidated financial statements or notes thereto.

Item 17. Undertakings.

The undersigned registrant hereby undertakes to provide to the underwriter, at the closing specified in the underwriting agreement, certificates in such denominations and registered in such names as required by the underwriter to permit prompt delivery to each purchaser.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

The undersigned hereby undertakes that:

(1) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.

(2) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

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SIGNATURES

Pursuant to the requirements of the Securities Act, the registrant has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Bedford, Commonwealth of Massachusetts, on this 23rd day of March, 2018.

HOMOLOGY MEDICINES, INC.

By: /s/ Arthur O. Tzianabos, Ph.D.
Arthur O. Tzianabos, Ph.D.
President and Chief Executive Officer

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities held on the dates indicated.

Signature	Title	Date
/s/ Arthur O. Tzianabos, Ph.D. Arthur O. Tzianabos, Ph.D.	President, Chief Executive Officer and Director (principal executive officer)	March 23, 2018
/s/ Bradford Smith Bradford Smith	Chief Financial Officer, Treasurer and Secretary (principal financial officer and principal accounting officer)	March 23, 2018
* Kush M. Parmar, M.D., Ph.D.	Chairman of the Board of Directors	March 23, 2018
* Steven Gillis, Ph.D.	Director	March 23, 2018
* Richard J. Gregory, Ph.D.	Director	March 23, 2018
* Matthew R. Patterson	Director	March 23, 2018

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Signature	Title	Date
*	Director	
Mahendra G. Shah, Ph.D.		March 23, 2018
*	Director	
Mary Thistle		March 23, 2018
*	Director	
Cameron Wheeler, Ph.D.		March 23, 2018

*By: /s/ Bradford Smith
Attorney-in-fact

Exhibit 10.15

Confidential Treatment Requested by Homology Medicines, Inc.

Execution Version

COLLABORATION AND LICENSE AGREEMENT

BY AND BETWEEN

HOMOLOGY MEDICINES, INC.

AND

NOVARTIS INSTITUTES FOR BIOMEDICAL RESEARCH, INC.

DATED NOVEMBER 6, 2017

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Exhibits and Schedules

Exhibit A – Form of Invoice
Schedule 1.130 – HMI Platform Patent Rights
Schedule 1.165 – Knowledge of HMI
Schedule 3.4.1 – General Research Plan
Schedule 4.5 – Third Party License Terms
Schedule 14.2 – Exception to Representations and Warranties
Schedule 14.2.1 – HMI Patent Rights
Schedule 14.2.2 – Third Party Licenses of HMI

Confidential Portions of this Exhibit marked as [***] have been omitted pursuant to a request for confidential treatment and have been filed separately with the Securities and Exchange Commission.

COLLABORATION AND LICENSE AGREEMENT

THIS **COLLABORATION AND LICENSE AGREEMENT** (this "**Agreement**") is entered into this 6th day of November, 2017 (the "**Effective Date**"), by and between Homology Medicines, Inc., a corporation organized under the laws of the State of Delaware, having a business address at 45 Wiggins Avenue, Bedford, MA 01730 ("**HMI**"), and Novartis Institutes for BioMedical Research, Inc., a corporation organized under the laws of the State of Delaware, having a business address at 250 Massachusetts Avenue, Cambridge, MA 02139 ("**NVS**"). HMI and NVS are sometimes referred to herein individually as a "**Party**" and collectively as the "**Parties**."

WHEREAS, HMI is a biopharmaceutical company focused on the research and development of genome editing products targeting genetically-defined diseases with unmet medical needs;

WHEREAS, NVS is a global pharmaceutical company focused on developing and commercializing pharmaceutical and biopharmaceutical products;

WHEREAS, NVS wishes to fund a research program that will include the identification and synthesis by HMI of genome editing products that Modulate certain gene targets; and

WHEREAS, NVS desires to obtain a license under the HMI Patent Rights and the HMI Know-How to Develop, Manufacture, and Commercialize Products, under the terms and conditions set forth herein, and HMI desires to grant such a license.

NOW, THEREFORE, the Parties agree as follows:

Article 1. DEFINITIONS

The following terms, whether used in the singular or plural, will have the following meanings:

1.1. "**AAA**" has the definition set forth in Section 17.1.2 (Full Arbitration).

1.2. "**AAV**" means any recombinant adeno-associated viral vector.

1.3. "**AAV Candidate Design**" means the [***]

1.4. "**AAV Gene Editing Technology**" means [***].

1.5. "**Accounting Standards**" means, with respect to HMI, GAAP and, with respect to NVS, IFRS, in each case, as generally and consistently applied throughout the Party's organization. Each Party shall promptly notify the other in the event that it changes the Accounting Standards pursuant to which its records are maintained, it being understood that each Party may only use internationally recognized accounting principles (*e.g.*, IFRS, US GAAP, etc.).

1.6. "**Acquiror**" has the definition set forth in Section 4.12.1 (Exception to Exclusivity).

1.7. "**Adverse Event**" means any untoward medical occurrence in a human clinical study subject or in a patient who is administered a Product, whether or not considered related to such Product, including any undesirable sign (including abnormal laboratory findings of clinical concern), symptom, or disease associated with the use of a Product.

1.8. "**Affiliate**" means, with respect to any Person, any Person controlling, controlled by or under common control with such Person. For purposes of this Section 1.8 (Affiliate), the term "control" (including, with correlative meaning, the terms "controlled by" and "under common control with"), means the possession, directly or indirectly, of more than 50% of the voting stock or other ownership interest of such Person, or the possession, directly or indirectly, of the power to direct or cause the direction of the affairs or management and policies of such Person or the power to elect or appoint more than 50% of the members of the governing body of such Person. The Parties acknowledge that in the case of certain entities organized under the laws of certain countries outside the United States, the maximum percentage ownership permitted by Applicable Law for a foreign investor may be less than fifty percent (50%), and that in such case such lower percentage will be substituted in the preceding sentence; *provided*, that such foreign investor has the power to direct the management and policies of such entity.

1.9. "**Agreement**" has the definition set forth in the Preamble.

1.10. "**Alliance Manager**" has the definition set forth in Section 5.3 (Alliance Managers).

1.11. "**Applicable Law**" means any applicable federal, state, local, municipal, foreign or other law, statute, legislation, principle of common law, ordinance, code, rule, regulation, or other pronouncement issued, enacted, adopted, passed, approved, promulgated, made, implemented or otherwise put into effect by or under the authority of any Governmental Authority, and will include the applicable regulations and guidance of the FDA and European Union (and national implementations thereof) that constitute cGLP practices, cGMP practices and cGCP practices (and, if and as appropriate under the circumstances, International Conference on Harmonization (ICH) guidance or other comparable regulation and guidance of any applicable Governmental Authority).

1.12. "**Arbitration**" has the definition set forth in Section 17.1.2 (Full Arbitration).

1.13. "**Assigned Know-How**" means HMI Assigned Know-How or NVS Assigned Know-How.

1.14. "**Assigned Patent Rights**" means HMI Assigned Patent Rights or NVS Assigned Patent Rights.

1.15. "**Assigned Regulatory Submissions**" has the definition set forth in Section 7.6.1 (U.S. BLA for U.S. SCD Products).

1.16. "**At-Will Opt-Out Date**" has the definition set forth in Section 4.14 (HMI Commercialization Opt-Out Rights for U.S. SCD Products).

1.17. "**Audited Party**" has the definition set forth in Section 11.10 (Records and Audits).

1.18. "**Auditing Party**" has the definition set forth in Section 11.10 (Records and Audits).

1.19. "**Auditor**" has the definition set forth in Section 11.10 (Records and Audits).

1.20. "**Bankrupt Party**" has the definition set forth in Section 16.2.3 (Termination for Bankruptcy).

1.21. "**Bankruptcy Code**" has the definition set forth in Section 17.15 (Rights in Bankruptcy).

1.22. "[***] **Out-license**" has the definition set forth in Section 4.13.1 ([***]).

1.23. "[***] **Package**" means, with respect to a [***] Product, a summary of the information or data generated by or on behalf of HMI with respect to any Research, Manufacturing, Development, or Commercialization of such [***] Product, as applicable to the stage of Development or Commercialization of such [***] Product, along with any Regulatory Submissions provided by or on behalf of HMI or its Affiliates to any Regulatory Authority for such [***] Product.

1.24. "[***] **Product**" means [***].

1.25. "[***] **Target**" means [***] A [***] Target does not include [***].

1.26. "**Biosimilar Application**" has the definition set forth in Section 12.6.5(a) (Receipt of Application; Responsibilities).

1.27. "**BLA**" means, as applicable, a Biologics License Application (as defined in 21 C.F.R. 600 et seq.), or a New Drug Application (as defined in 21 C.F.R. Parts 314 et seq.) or, in each case, its successor regulation.

1.28. "**Breach Opt-Out Date**" the date on which NVS exercises its special remedy in lieu of terminating this Agreement pursuant to Section 16.5 (Special Remedy for HMI's Uncured Material Breach) due to HMI's breach with respect to the Sickle Cell Target in the [***] Field.

1.29. "**Brief**" has the definition set forth in Section 17.1.3(a) (Expedited Arbitration).

1.30. "**Business Day**" means a day that is not a Saturday, Sunday, or a day on which banking institutions in Basel, Switzerland or Boston, Massachusetts are authorized or required by Applicable Law to remain closed.

1.31. "**C.F.R.**" means the U.S. Code of Federal Regulations.

1.32. "**Calendar Quarter**" means each period of 3 consecutive calendar months ending on March 31, June 30, September 30, or December 31, except that the first Calendar Quarter of the Term will commence on the Effective Date, and the last Calendar Quarter of the Term will end on the effective date of the termination or expiration of this Agreement.

1.33. "**Calendar Year**" means each period of 12 consecutive calendar months commencing on January 1 and ending on December 31, except that the first Calendar Year of the Term will commence on the Effective Date, and the last Calendar Year of the Term will end on the effective date of the termination or expiration of this Agreement.

1.34. "**Caltech**" means California Institute of Technology, a not-for-profit corporation duly organized and existing under the laws of the State of California with an address at 1200 East California Boulevard, MC 6-32, Pasadena, California 91125.

1.35. "**Caltech License**" means that certain License Agreement dated September 14, 2016 by and between Caltech and HMI.

1.36. "**Caltech Patent Rights**" means those Patent Rights licensed to HMI under the Caltech License.

1.37. "**Caltech Side Letter**" means that certain Amendment and Stand-By License Arrangement to be entered into by and among NVS, HMI, and Caltech in accordance with Section 14.4.3 (Caltech License).

1.38. "**Candidate**" means a Sickle Cell Candidate or an Ophthalmic Candidate.

1.39. "**cGCP**" means the then-current ethical, scientific and quality standards as required by FDA for designing, conducting, recording, and reporting trials that involve the participation of human subjects, as set forth in FDA regulations in 21 C.F.R. Parts 11, 50, 54, 56, and 312 and related FDA guidance documents, and by the International Conference on Harmonization E6: Good Clinical Practices Consolidated Guideline, or as otherwise required by Applicable Law.

1.40. "**cGLP**" means the then-current good laboratory practice as required by the FDA under 21 C.F.R. Part 58 and all applicable FDA rules, regulations, orders, and guidances, and the requirements with respect to current good laboratory practices prescribed by the European Community, the OECD (Organization for Economic Cooperation and Development Council) and the ICH Guidelines, or as otherwise required by Applicable Law.

1.41. "**cGMP**" means the then-current good manufacturing practices as required by the FDA under provisions of 21 C.F.R. Parts 210 and 211 and all applicable FDA rules, regulations, orders, and guidances, and the requirements with respect to current good manufacturing practices prescribed by the European Community under provisions of "The Rules Governing Medicinal Products in the European Community, Volume 4, Good Manufacturing Practices, Annex 13, Manufacture of Investigational Medicinal Products, July 2003," or as otherwise required by Applicable Law.

1.42. "**Change of Control**" means, with respect to a Party, (a) a merger or consolidation of such Party with a Third Party that results in the voting securities of such Party outstanding immediately prior thereto, or any securities into which such voting securities have been converted or exchanged, ceasing to represent at least 50% of the combined voting power of the surviving entity or the parent of the surviving entity immediately after such merger or consolidation, (b) a transaction or series of related transactions in which a Third Party, together with its Affiliates, becomes the direct or indirect beneficial owner of more than 50% of the combined voting power of the outstanding securities of such Party, or (c) the sale or other transfer to a Third Party of all or substantially all of such Party's and its controlled Affiliates' assets.

1.43. "**Claim**" has the definition set forth in Section 17.1.1 (Escalation).

1.44. "**Clinical Development**" means all Development activities in humans for a Candidate or Product undertaken from and after Initiation of the first Phase I Clinical Trial for such Candidate or Product, including conduct of each Clinical Trial.

1.45. "**Clinical Trial**" means a Phase I Clinical Trial, Phase I/II Clinical Trial, Phase II Clinical Trial, Phase III Clinical Trial, or such other study in humans that is conducted in accordance with cGCP and is designed to generate data in support or maintenance of an IND or MAA, or other similar marketing application.

1.46. "**CMC**" means chemistry, manufacturing, and controls.

1.47. "**COC Opt-Out**" has the definition set forth in Section 4.12.2 (Change of Control).

1.48. "**COC Opt-Out Date**" has the definition set forth in Section 4.12.2 (Change of Control).

1.49. "**COH**" means City of Hope, a California nonprofit public benefit corporation located at 1500 East Duarte Road, Duarte, California, 91010.

1.50. "**COH Indemnitees**" means COH and its Affiliates, officers, directors, shareholders, employees, and agents.

1.51. "**COH License**" means that certain Exclusive License Agreement dated April 28, 2016 by and between COH and HMI.

1.52. "**COH Losses**" has the definition set forth in Schedule 4.5 (Third Party License Terms).

1.53. "**COH Patent Rights**" means those Patent Rights licensed to HMI under the COH License.

1.54. "**COH Side Letter**" means that certain Stand-by License Arrangement, dated November 6, 2017, by and among NVS, HMI, and COH.

1.55. "**Combination Product**" means any single pharmaceutical product in finished form containing as active ingredients both a Product and one or more Other Components.

1.56. "**Commercial Quality Assurance Agreement**" means the quality assurance agreement entered into by the Parties that addresses the quality related obligations of the Parties with respect to Candidates and Products supplied under the Commercial Supply Agreement.

1.57. "**Commercial Supply Agreement(s)**" has the definition set forth in Section 8.4 (Commercial Supply Agreement).

1.58. "**Commercialization**" or "**Commercialize**" any and all processes and activities conducted to establish and maintain sales for any product, including to market, advertise, promote, import, export, offer to sell (including pricing and reimbursement activities), detail, or sell any product or conduct other commercialization activities, and, where applicable, Medical Affairs. "Commercialization" shall have the correlative meaning with respect to such activities; *provided*, *however*, that Commercialize shall exclude Development and Manufacturing activities (including Manufacturing activities related to Commercialization). When used as a verb, "to Commercialize" and "Commercializing" means to engage in Commercialization and "Commercialized" has a corresponding meaning.

1.59. "**Commercialization Budget**" means the budget of Commercialization Costs established by the JSC covering all Commercialization activities in the [***] set forth in the approved [***] portion of the [***] or the approved [***], as applicable, as such budget may be updated and approved by the JSC, from year to year.

1.60. "**Commercialization Costs**" means all costs incurred by or on behalf of the Commercialization Party or its Affiliates, or in the case of NVS, any Sublicensees, during the Term in connection with the Commercialization activities conducted in support of Commercialization of **[***]** in accordance with the approved Commercialization Budget, including (to the extent reasonably related to Commercialization of [***] costs directly allocable to costs of [***] (before and after Regulatory Approval of a [***] and other substantially similar activities reasonably related to marketing and promoting [***]. Such costs will include [***]. "Commercialization Costs" shall also include all direct costs incurred by or on behalf of the Commercializing Party or its Affiliates, or in the case of NVS, any Sublicensees, in pursuing activities related to sales and marketing in support of Commercializing [***] including activities directly relating to [***] and other similar marketing expenses, but shall specifically exclude the costs of activities that [***] except to the extent a portion of such Commercialization Costs is reasonably allocated to the Product in accordance with such Party's cost accounting policies, as consistently applied across such Party's entire portfolio and approved pursuant to this Agreement.

1.61. "**Commercializing Party**" means (a) NVS (or is Affiliates or Sublicensees) for all Ophthalmic Products, all Sickle Cell Products for the Ex-Vivo Fields, and all In-Vivo SCD Products outside the U.S.; and (b) HMI for all In-Vivo SCD Products in the U.S.; *provided*, that upon the SCD Opt-Out Date, NVS (or its Affiliates or Sublicensees) shall become the Commercializing Party for such In-Vivo SCD Products in the U.S.

1.62. "**Commercially Reasonable Efforts**" means, with respect to the efforts to be expended by a Party or its Affiliates with respect to any objective or activity under this Agreement, [***] by a [***] as such [***] with respect to [***] at a [***] in its [***] taking into account all [***] and [***] and [***] and [***] the [***] including the [***] of [***] and [***]. It is [***] that the [***] in the [***] of the [***].

1.63. "**Competing Infringement**" has the definition set forth in Section 12.6.1 (Notice).

1.64. "**Competing Product**" means a product or biological agent, other than a Product, that [***] (a) [***] or (b) [***].

1.65. "**Confidential Information**" means, with respect to each Party, Know-How, inventions, Materials, and other proprietary information including data and all other scientific, pre-clinical, clinical, regulatory, Manufacturing, marketing, financial and commercial information or data that is disclosed, made available to, or provided by or on behalf of such Party to the other Party or to any of the Receiving Party's employees, consultants, Affiliates, or Sublicensees, whether or not specifically marked or designated by the disclosing Party as confidential.

1.66. "**Confidentiality Agreements**" has the definition set forth in Section 13.1.2 (Confidential Information of Each Party).

1.67. "**Control**" or "**Controlled**" means with respect to any Regulatory Submissions, Marketing Approvals, Intellectual Property Rights, or Materials, the possession by a Party (or an Affiliate of such Party, as applicable) of the right to grant a license or sublicense to such Regulatory Submissions, Marketing Approvals, Intellectual Property Rights, or Materials (as applicable) as provided herein without violating the terms of any agreement or arrangement with, or misappropriating the proprietary or trade secret information of, any Third Party and without violating any Applicable Law. Notwithstanding anything to the contrary set forth in this Agreement, a Party (or an Affiliate of a Party, as applicable) will not be deemed to Control any Regulatory Submission, Marketing Approval, Intellectual Property Right, or Materials (a) solely by virtue of the license grants set forth in this Agreement, or (b) if [***] or [***] of such [***] and such [***] were not [***] except (i) with respect to [***] from [***] by [***] or [***] with this Agreement after such Change of Control,] (ii) to the [***] any such [***] of this [***] after such [***] or (iii) for [***] to the [***] or the [***] to such [***] by any [***] of the [***].

1.68. "**Cover**," "**Covers**," or "**Covered**" means, with respect to a Product or other subject matter at issue and a relevant Patent Right, that the Manufacture, use, sale, offer for sale or importation of such Product or other subject matter by such Person would fall within the scope of a claim in such Patent Right.

1.69. "**CPI**" means the Consumer Price Index – Urban Wage Earners and Clerical Workers, U.S. City Average, All Items, 1982-84 = 100, published by the U.S. Department of Labor, Bureau of Labor Statistics (or its successor equivalent index).

1.70. "**Designated CMO**" means any Third Party contract manufacturer mutually agreed upon by the Parties, such agreement not to be unreasonably withheld, conditioned, or delayed.

1.71. "**Development**" or "**Develop**" means to develop any candidate or product, including conducting non-clinical studies or Clinical Trials prior to or after receiving Regulatory Approval and otherwise engaging in activities related to obtaining or maintaining Regulatory Approval, including, where applicable, the conduct of Medical Affairs. Developing does not include Research or Manufacturing. When used as a verb, "Developing" means to engage in Development and "Developed" has a corresponding meaning.

1.72. "**Development and Commercialization License**" has the definition set forth in Section 4.1.2 (Development and Commercialization License).

1.73. "**Development Budget**" has the definition set forth in Section 6.3 (Development Plans).

1.74. "**Development Milestone Event**" means an Ophthalmic Development Milestone Event, an In-Vivo Sickle Cell Development Milestone Event, or an Ex-Vivo Sickle Cell Development Milestone Event, as applicable.

1.75. "**Development Milestone Payment**" means an Ophthalmic Development Milestone Payment, an In-Vivo Sickle Cell Development Milestone Payment or an Ex-Vivo Sickle Cell Development Milestone Payment, as applicable.

1.76. "**Development Plan**" has the definition set forth in Section 6.3 (Development Plans).

1.77. "**Development Quality Assurance Agreement**" means the quality assurance agreement entered into by the Parties that addresses the quality related obligations of the Parties with respect to Candidates and Products supplied under the Development Supply Agreement.

1.78. "**Development Report**" has the definition set forth in Section 6.4 (Development Reporting).

1.79. "**Development Supply Agreement**" has the definition set forth in Section 8.3 (Development Supply Agreement).

1.80. "**Disclosing Party**" has the definition set forth in Section 13.1.1 (General).

1.81. "**Dose Expansion Cohort**" means in a [***], as applicable, after the initial confirmation of safety and efficacy in a small patient group, the start of recruiting additional patients with same or different eligibility criteria, to collect additional information in order to better characterize the toxicity profile or identify early signs of efficacy within a specific disease population.

1.82. "**Dose Initiation**" means, with respect to any Clinical Trial, the date on which the first volunteer or patient in such trial receives his or her initial dose in such Clinical Trial.

1.83. "**Effective Date**" has the definition set forth in the Preamble.

1.84. "**EMA**" means the European Medicines Agency or any successor agency or authority thereto.

1.85. "**Establishing Committee**" has the definition set forth in Section 5.4.2 (Operational Teams).

1.86. "**Executive Officer**" has the definition set forth in Section 17.1.1 (Escalation).

1.87. "**Expedited Arbitration**" has the definition set forth in Section 17.1.3 (Expedited Arbitration).

1.88. "**Expedited Dispute**" has the definition set forth in Section 17.1.3 (Expedited Arbitration).

1.89. "**Exploratory Reagents**" means reagents resulting from the Exploratory Research Activities, including [***] but specifically excluding [***].

1.90. "**Exploratory Research Activities**" has the definition set forth in Section 3.4.2 (Exploratory Research Plan).

1.91. "**Exploratory Research Budget**" has the definition set forth in Section 3.4.2 (Exploratory Research Plan).

1.92. "**Exploratory Research Plan**" has the definition set forth in Section 3.4.2 (Exploratory Research Plan).

1.93. "**Exploratory Research Report**" has the definition set forth in Section 3.6.4 (Exploratory Research Report).

1.94. "**External Costs**" mean expenses paid to Third Parties (or payable to Third Parties and accrued in accordance with Accounting Standards) by a Party (or its Affiliate) and incurred in the performance of activities under this Agreement; such expenses to have been recorded as income statement items in accordance with Accounting Standards, [***].

1.95. "**Ex-Vivo Field**" means [***] by cells that are [***].

1.96. "**Ex-Vivo Sickle Cell Development Milestone Event**" has the definition set forth in Section 11.4.2(a) (Events).

1.97. "**Ex-Vivo Sickle Cell Development Milestone Payment**" has the definition set forth in Section 11.4.2(a) (Events).

1.98. "**Ex-Vivo Sickle Cell Sales Milestone Event**" has the definition set forth in Section 11.5.2 (Ex-Vivo Sickle Cell Products).

1.99. "**Ex-Vivo Sickle Cell Sales Milestone Payment**" has the definition set forth in Section 11.5.2 (Ex-Vivo Sickle Cell Products).

1.100. "**FDA**" means the United States Food and Drug Administration and any successor agency or authority thereto.

1.101. "**First Commercial Sale**" means, on a [***], the date of the first sale by a Party, any Sublicensee, or any of their Affiliates, of a Product to a Third Party for end use or consumption of such Product following receipt of any required Regulatory Approval and Pricing Approval (where applicable) for such Product in the country in which such Product is sold, excluding any named patient sales or any sale or other distribution at cost or less than cost for use in any Clinical Trial, for *bona fide* charitable purposes, test marketing program, or for compassionate use.

1.102. "**Force Majeure**" means any occurrence beyond the reasonable control of a Party that prevents or substantially interferes with the performance by such Party of any of its obligations hereunder, including by reason of any act of God, flood, fire, explosion, earthquake, strike, lockout, labor dispute (except for any strike, lockout, or labor dispute involving a Party's own employees), casualty or accident, or war, revolution, civil commotion, act of terrorism, blockage or embargo, or any injunction, law, order, proclamation, regulation, ordinance, demand, or requirement of any Governmental Authority.

1.103. "**FTE**" means the equivalent of a full-time individual's work, performed by one or more individuals, at [***] hours per year for a 12 month period, performing activities pursuant to this Agreement. For clarity, indirect personnel (including support functions such as managerial, financial, legal or business development) shall not constitute FTEs. In the case that any full-time personnel of a Party works partially on work pursuant to this Agreement and partially on other work in a given time period, then the full-time equivalent to be attributed to such individual's work hereunder will be calculated based upon (a) the percentage of such individual's total work time in such time period that such individual spent working under this Agreement and (b) the percentage of a 12 month period that such time period equals. Each Party will track FTEs using its standard practice and normal systems and methodologies.

1.104. "**FTE Rate**" means the rate of $[***] per FTE per Calendar Year, which rate shall be prorated on a daily basis as necessary, and which [***] in each [***] by the [***] of the [***] of the [***] with the [***] to be [***]. For the avoidance of doubt, such FTE Rate shall be the [***] and is intended to cover the cost of [***]. Notwithstanding the foregoing, for any Calendar Year during the Term that is less than a full year, the above referenced rate will be proportionately reduced to reflect such portion of such full Calendar Year.

1.105. "**GAAP**" means accounting principles generally accepted in the United States of America, as in effect from time to time, consistently applied.

1.106. "**General Research Plan**" has the definition set forth in Section 3.4.1 (Target Research Plans).

1.107. "**Generic Product**" means, with respect to a Product in a country, a [***] product (a) [***] is sold in such country by a Third Party and (b) has achieved Regulatory Approval from a Regulatory Authority in such country jurisdiction in reliance on data supporting a prior approval of such Product by such Regulatory Authority.

1.108. "**Global Brand Plan**" has the definition set forth in Section 10.6 (Global Brand Plan and Promotional Materials for In-Vivo SCD Products).

1.109. "**Global In-Vivo SCD Commercialization Plan**" has the definition set forth in Section 10.3.1 (In-Vivo SCD Commercialization Plans).

1.110. "**Global In-Vivo SCD Development Costs**" means [***] in implementing the Development Plan for In-Vivo SCD Products for the purpose of Developing Sickle Cell Candidates and obtaining Regulatory Approval throughout the Territory for In-Vivo SCD Products, calculated in accordance with Accounting Standards consistently applied and reflected in such Party's audited financial statements.

1.111. "**Global Medical Affairs Plan**" has the definition set forth in Section 9.1 (Medical Affairs Plans).

1.112. "**Global Trade Control Laws**" means the U.S. Export Administration Regulations, the U.S. International Traffic in Arms Regulations, the economic sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Control, E.U. Council Regulations on export controls, including Nos. 428/2009, 267/2012, other E.U. Council sanctions regulations, as implemented in the E.U. member states, United Nations sanctions policies, and all relevant regulations made under any of the foregoing.

1.113. "**Global Trademark**" means any Trademark selected by NVS, its Affiliates, or Sublicensees under which a Party, its Affiliates, or Sublicensees markets any Product, and all trademark registrations and applications therefor, and all goodwill associated therewith. Global Trademarks exclude all Local Trademarks and all NVS Housemarks.

1.114. "**GLP Toxicology Study**" means a toxicology study (a) in species that satisfies applicable regulatory requirements and (b) that employs applicable cGLP so as to meet the standard necessary for submission as part of an IND filing with the applicable Regulatory Authority.

1.115. "**Governmental Authority**" means any arbitrator, court, judicial, legislative, administrative or regulatory authority, commission, department, board, bureau, or body or other government authority or instrumentality or any Person exercising executive, legislative, judicial, regulatory, or administrative functions of or pertaining to government, whether foreign or domestic, whether federal, state, provincial, municipal, or other.

1.116. "**HMI**" has the definition set forth in the Preamble.

1.117. "**HMI Assigned Know-How**" has the definition set forth in Section 12.1.2 (Assigned Technology).

1.118. "**HMI Assigned Patent Rights**" has the definition set forth in Section 12.1.2 (Assigned Technology).

1.119. "**HMI Assigned Technology**" means any HMI Assigned Patent Rights and HMI Assigned Know-How that are invented (a) by or on behalf of NVS jointly with HMI or its Affiliates or Third Party subcontractors; or (b) solely by or on behalf of NVS, in the case of each of (a) and (b), without the use of any non-public HMI Know-How.

1.120. "**HMI Genus Patent Rights**" means all HMI Product Patent Rights, other than HMI Product-Specific Patent Rights.

1.121. "**HMI Housemarks**" means (a) the corporate logo of HMI or any of its Affiliates, (b) the Trademarks "Homology Medicines" and "AmENDR," (c) any other Trademark containing the word "Homology," (d) any other Trademark used by HMI to identify HMI or its Affiliates, (e) all registrations, applications for registrations, and other Intellectual Property Rights associated with any and all of the foregoing clauses (a) through (d), and (f) all goodwill associated with any and all of the foregoing in clauses (a) through (e).

1.122. "**HMI Indemnitees**" has the definition set forth in Section 15.1 (Indemnification of HMI by NVS).

1.123. "**HMI Know-How**" means any Know-How that is Controlled by HMI or any of its Affiliates as of the Effective Date or during the Term (other than Joint Know-How) that is necessary or useful to Research, Develop, Manufacture, or Commercialize any Candidate or Product, but in each case, *excluding* Know-How directed to [***]. For clarity, HMI Know-How includes HMI Materials, HMI Program Know-How, HMI Platform Know-How, HMI Product Know-How, HMI Manufacturing Know-How, and HMI Assigned Know-How (in each case *excluding* Know-How directed to [***]. For clarity, HMI Know-How includes Know-How Controlled by HMI or any of its Affiliates regarding the [***] of the Candidates.

1.124. "**HMI Licensed Technology**" means the HMI Know-How, HMI Patent Rights, and HMI's rights under the Joint Know-How and Joint Patent Rights.

1.125. "**HMI Manufacturing Know-How**" has the definition set forth in Section 8.6.2 (Manufacturing Technology Transfer to NVS).

1.126. "**HMI Materials**" means any seed stocks of cell lines, cell banks, plasmids, and viruses (including AAV vectors) that are not readily available as standard commercial items, that are, in each case, (a) Controlled by HMI, and (b) necessary or useful to Manufacture any Product, and in each case, *excluding* any NVS Materials.

1.127. "**HMI Necessary Rights**" has the definition set forth in Section 11.7.2(c)(i) (Third Party Licenses).

1.128. "**HMI Patent Rights**" means any Patent Rights Controlled by HMI or any of its Affiliates as of the Effective Date or during the Term (other than Joint Patent Rights) that are necessary or useful to Research, Develop, Manufacture, or Commercialize any Candidate or Product, but in each case, *excluding* Patent Rights to the extent they Cover [***]. For clarity, HMI Patent Rights include HMI Program Patent Rights, HMI Platform Patent Rights, HMI Product Patent Rights, and HMI Assigned Patent Rights (in each case, *excluding* Patent Rights to the extent they Cover [***]. For clarity, HMI Patent Rights include Patent Rights Controlled by HMI or any of its Affiliates that Cover the [***] of the Candidates.

1.129. "**HMI Platform Know-How**" means all HMI Know-How that (a) is licensed to HMI under the COH License, or (b) relates to AAV Gene Editing Technology generally (including all HMI Assigned Know-How).

1.130. "**HMI Platform Patent Rights**" means all HMI Patent Rights that (a) as of the Effective Date are identified on Schedule 1.130 (HMI Platform Patent Rights), including the COH Patent Rights, Caltech Patent Rights, and all Patent Rights claiming priority thereto, or (b) during the Term Cover HMI Platform Know-How (including all HMI Assigned Patent Rights).

1.131. "**HMI Platform Technology**" means the HMI Platform Know-How and the HMI Platform Patent Rights.

1.132. "**HMI Product Know-How**" means HMI Product-Specific Know-How and other HMI Know-How that relates to one or more Candidates or Products (including Know-How that would be applicable to candidates or products that Modulate targets other than the Targets), but excluding HMI Platform Know-How.

1.133. "**HMI Product Patent Rights**" means HMI Product-Specific Patent Rights and other HMI Patent Rights that Cover one or more Candidates or Products (including Patent Rights that would Cover candidates or products that Modulate targets other than the Targets), but excluding HMI Platform Patent Rights.

1.134. "**HMI Product-Specific Know-How**" means HMI Know-How that relates to one or more Candidates or Products but would not be applicable to candidates or products that Modulate targets other than the Targets, but excluding any HMI Platform Know-How.

1.135. "**HMI Product-Specific Patent Rights**" means HMI Patent Rights that Cover a Candidate or Product, but would not Cover any candidate or product that Modulates targets other than the Targets, but excluding any HMI Platform Patent Rights.

1.136. "**HMI Program Know-How**" means Know-How that is invented, conceived, discovered, created, or otherwise developed solely by employees, agents, contractors, or Sublicensees of HMI in the performance of activities under this Agreement, other than NVS Assigned Know-How.

1.137. "**HMI Program Patent Rights**" means Patent Rights that Cover any invention that is conceived or otherwise invented solely by employees, agents, contractors, or Sublicensees of HMI in the performance of activities under this Agreement, other than NVS Assigned Patent Rights.

1.138. "**HMI Research Costs**" has the definition set forth in Section 3.8.1 (Support).

1.139. "**HMI Third Party Obligations**" has the definition set forth in Section 11.7.2(c)(iii) (Third Party Licenses).

1.140. "**IFRS**" means International Financial Reporting Standards, the set of accounting standards and interpretations as promulgated by the International Standards Accounting Board and as they may be updated for time to time, as consistently applied.

1.141. "**IND**" means an investigational new drug application filed with the FDA with respect to a Product, or equivalent application filed with the Regulatory Authority of a country in the Territory other than the U.S. (such as an application for a Clinical Trial Authorization in the E.U.).

1.142. "**Indemnitee**" has the definition set forth in Section 15.4 (Conditions to Indemnification).

1.143. "**Indication**" means SCD in the In-Vivo Field, SCD in the Ex-Vivo Field, and all Ophthalmic Indications.

1.144. "**Infringement Action**" has the definition set forth in Section 12.6.2 (NVS' Rights).

1.145. "**Initiation**" means, with respect to any Clinical Trial, [***].

1.146. "**Intellectual Property Rights**" means any Know-How, Patent Rights, Trademarks, copyrights, trade secrets, and any other intellectual property rights however denominated throughout the world.

1.147. "**Interest Rate**" has the definition set forth in Section 11.12 (Late Fees).

1.148. "**Interim Report**" has the definition set forth in Section 3.6.2 (Interim Reports).

1.149. "**Internal Costs**" means, for any period, the product obtained by *multiplying* (a) the actual total FTEs (or portion thereof) devoted to the performance of activity under this Agreement during such period, *by* (b) the applicable FTE Rate.

1.150. "**In-Vivo Field**" means [***] by **[***]**.

1.151. "**In-Vivo SCD Commercial Supply Agreement**" has the definition set forth in Section 8.5 (In-Vivo SCD Commercial Supply Agreement).

1.152. "**In-Vivo SCD Products**" mean Sickle Cell Products for use in the In-Vivo Field.

1.153. "**In-Vivo SCD Quality Assurance Agreement**" has the definition set forth in Section 8.5 (In-Vivo SCD Commercial Supply Agreement).

1.154. "**In-Vivo Sickle Cell Development Milestone Event**" has the definition set forth in Section 11.4.3(a) (Events).

1.155. "**In-Vivo Sickle Cell Development Milestone Payment**" has the definition set forth in Section 11.4.3(a) (Events).

1.156. "**In-Vivo Sickle Cell Sales Milestone Event**" has the definition set forth in Section 11.5.3 (In-Vivo SCD Products).

1.157. "**In-Vivo Sickle Cell Sales Milestone Payment**" has the definition set forth in Section 11.5.3 (In-Vivo SCD Products).

1.158. "**Joint Know-How**" has the definition set forth in Section 12.1.3 (Ownership).

1.159. "**Joint Manufacturing Committee**" or "**JMC**" has the definition set forth in Section 5.2.1 (Formation and Purpose of the JMC).

1.160. "**Joint Patent Rights**" has the definition set forth in Section 12.1.3 (Ownership).

1.161. "**Joint Steering Committee**" or "**JSC**" has the definition set forth in Section 5.1.1 (Formation and Purpose of the JSC).

1.162. "**Joint Technology**" means all Joint Know-How and Joint Patent Rights.

1.163. "**Jointly-Agreed Regulatory Submissions**" means, for each U.S. SCD Product, (a) the IND and all material amendments thereto, (b) the pre-BLA meeting request and materials, (c) the BLA and all material amendments thereto, (d) substantive responses to questions from or negotiations with the FDA relating to the BLA or amendments or any of the meetings set forth in clause (g), (e) advisory committee materials, and material submissions related to any REMS program or Product labeling, or any post marketing requirements or commitments in each case, in the U.S, (f) the equivalent of (a) through (e) with respect to EMA, and (g) all substantive materials and filings submitted in connection with or otherwise related to any IND-related Type A meetings, Type B Pre-IND meetings, Type B End of Phase I Clinical Trial meetings, Type B End of Phase II Clinical Trial meetings, and Type C meetings.

1.164. "**Know-How**" means any proprietary records, Materials, know-how, processes, techniques, show-how, design information, information, formulations, technology, practices, trade secrets, inventions, methods, data (including animal data, clinical data, and quality control data) and results in any form whatsoever, whether or not patented or patentable.

1.165. "**Knowledge of HMI**" means the actual knowledge of the [***]; or a [***] of HMI, in each case, without any other duty of investigation or inquiry; *provided*, that in the case of the [***] such knowledge includes the information identified in the searches set forth on Schedule 1.165 (Knowledge of HMI).

1.166. "**Large Pharma Company**" means any pharmaceutical company or biotechnology company that ranks among the top [***] pharmaceutical companies or biotechnology companies in terms of annual revenue in the Calendar Year immediately prior to the Calendar Year in which a Change of Control occurs.

1.167. "**Local Trademarks**" has the definition set forth in Section 10.7.2 (Trademarks for In-Vivo **SCD** Products).

1.168. "**Loss of Market Exclusivity**" means, on a [***], (a) one or more Generic Products for which such Product is the reference product are being marketed in such country; and (b) Net Sales of such Product in such country in any Calendar Quarter following the initial sale of the first such Generic Product(s) in such country decreases to less than [***]% of the average Net Sales of such Product in such country during the [***] Calendar Quarters preceding the initial sale of such Generic Product(s).

1.169. "**Losses**" has the definition set forth in Section 15.1 (Indemnification of HMI by NVS).

1.170. "**MAA**" means (a) any BLA filed with the FDA to gain approval to market a biopharmaceutical product in the U.S., (b) a marketing authorization application filed with (i) the EMA under the centralized EMA filing procedure to gain approval to market a biopharmaceutical or diagnostic product in the E.U., or (ii) a Regulatory Authority in any E.U. country if the centralized EMA filing procedure is not used to gain approval to market a biopharmaceutical or diagnostic product in the E.U., or (c) any other equivalent or related Regulatory Submission filed in support of approval to market a biopharmaceutical or diagnostic product in any country outside the U.S. or E.U., and, in each case ((a) through (c)), including any amendments thereto, and supplemental applications, but excluding Pricing Approval applications.

1.171. "**Major European Country**" means the [***].

1.172. "**Manufacture**" or "**Manufacturing**" means all activities related to the manufacture of candidates and products, including test method development, stability testing, CMC activities, formulation, process development, manufacturing scale-up, analytical method validation, manufacturing process validation, cleaning validation, manufacturing supplies for Research, Development, Commercialization, packaging, in-process and finished product testing, release of product or any component or ingredient thereof, quality assurance and quality control activities related to manufacturing and release of product, ongoing stability tests, storage, shipment, and regulatory activities related to any of the foregoing. When used as a verb, "Manufacturing" means to engage in Manufacture and "Manufactured" has the corresponding meaning.

1.173. "**Manufacturing Costs**" means, with respect to a Candidate or Product, the [***] cost incurred by either Party or any of their respective Affiliates in Manufacturing such Candidate or Product (including all activities related to CMC, formulation and process development, and scale-up) in accordance with this Agreement and consistent with the applicable Research Plan, Development Plan, Development Supply Agreement, Commercial Supply Agreement, or In-Vivo SCD Commercial Supply Agreement [***], including: (a) to the extent that such Candidate or Product is Manufactured by a Third Party contract manufacturer: (i) the [***] External Costs paid by a Party or its Affiliates to the Third Party contract manufacturer (or to a Party, if one Party supplies to the other Party Candidate or Product Manufactured by a Third Party contract manufacturer) for the Manufacture and supply thereof (including packaging and labeling), determined in accordance with the books and records of such Party or its Affiliates maintained in accordance with Accounting Standards, *plus* (ii) a [***] amount to cover such Party's Internal Costs incurred in engaging and overseeing such Third Party contract manufacturer; and (b) to the extent that such Candidate or Product is Manufactured by a Party or its Affiliates: [***] material costs, depreciation of capital expenditures, External Costs, and Internal Costs attributable to the Manufacture of such Candidate or Product, determined in accordance with the books and records of such Party or its Affiliates maintained in accordance with Accounting Standards and as consistently applied to other products Manufactured by the Party Manufacturing; *provided*, that Manufacturing Costs calculated in accordance with clause (b) will not include any allocation of [***].

1.174. "**Marketing Approval**" means receipt of Regulatory Approval, and, in any country in the Territory where a Governmental Authority or Regulatory Authority approves or determines pricing for pharmaceutical products for reimbursement or otherwise, receipt of Pricing Approval.

1.175. "**Materials**" means any tangible compositions of matter, articles of manufacture, assays, chemical, biological or physical materials, and other similar materials.

1.176. "**Medical Affairs**" means activities conducted by a Party's medical affairs departments, including communications with key opinion leaders, medical education, symposia, advisory boards (to the extent related to medical affairs or clinical guidance), activities performed in connection with patient registries, and other medical programs and communications, including educational grants, research grants (including conducting investigator-initiated studies), and charitable donations to the extent related to medical affairs and not to other activities that do not involve the promotion, marketing, sale, or other Commercialization of Products and are not conducted by a Party's medical affairs departments.

1.177. "**Modulate**" or "**Modulation**" means to edit, engineer, modify, or modulate a gene or locus, including by means of gene knock-out, gene tagging, gene disruption, gene mutation, gene insertion, gene deletion, gene activation, gene silencing, or gene knock-in, which includes knock-in of a heterologous gene to a genomic locus, for example, a safe harbor genomic locus or a target genomic locus.

1.178. "**Net Profit"** or **"Net Loss**" means, for a given period of time, [***] during such [***] of: (a) [***] by [***] and [***] from [***] in accordance with [***] (b) [***] and its [***] for the [***] during such [***]; and (c) [***] or [***] during such [***] from [***] in accordance with [***] will be [***] of any [***]. For clarity, [***] are the [***] and shall [***] in the [***] If the [***].

1.179. "**Net Sales**" means the net sales recorded by a Party or any of its Affiliates or Sublicensees (excluding Third Party Distributors) for any Product sold to Third Parties (including Third Party Distributors) other than Sublicensees as determined in accordance with Accounting Standards as consistently applied, less a deduction of [***]% for direct expenses related to the sales of Products, distribution and warehousing expenses, and uncollectible amounts on previously sold Product. The deductions booked on an accrual basis by a Party and its Affiliates under Accounting Standards to calculate the recorded net sales from gross sales are as follows:

1.179.1. [***] and [***];

1.179.2. [***];

1.179.3. [***] and [***] and [***] (including [***] and [***]);

1.179.4. [***] through [***] and other [***];

1.179.5. [***] or [***] related to [***] and [***] or [***];

1.179.6. [***] for [***] for any [***] (including [***] and [***]); and

1.179.7. [***] or [***] for reasons [***] to [***] above to the [***] in accordance with [***].

[***] of any [***] or [***] such [***] or [***] to a [***] or is [***] shall be [***] at the [***] In the case [***] or other [***] of the [***] of such [***]. [***] the [***] (1) [***] will **[***]**; (2) [***] to the [***] of a [***]; and (3) [***] or [***] or [***] or [***] or [***] or [***] is [***] or any [***].

In the event [***] will be [***] the [***] in the [***] of the [***] in [***] is the [***] as the [***] Regarding [***] for [***] to such [***] in [***] of the [***] If the **[***]** the [***] then the [***] will be [***] on the [***] by each [***] not to be [***] or [***]).

1.180. "**Non-Bankrupt Party**" has the definition set forth in Section 16.2.3 (Termination for Bankruptcy).

1.181. "**Non-Withholding Party**" has the definition set forth in Section 11.14 (Withholding Taxes).

1.182. "**NVS**" has the definition set forth in the Preamble.

1.183. "**NVS Assigned Know-How**" has the definition set forth in Section 12.1.2 (Assigned Technology).

1.184. "**NVS Assigned Patent Rights**" has the definition set forth in Section 12.1.2 (Assigned Technology).

1.185. "**NVS Audit Team**" means a team of no more than [***] individuals who will have access to the HMI Manufacturing Know-How in connection with their audit and inspection responsibilities with respect to Candidates and Products Manufactured by or on behalf of HMI.

1.186. "**NVS CMC Sub-Team**" means a team of no more than [***] individuals with expertise in different fields who will have access to the HMI Manufacturing Know-How to ensure compliance with regulatory and quality obligations with respect to NVS' Development and Commercialization of Candidates and Products.

1.187. "**NVS Housemarks**" means (a) the corporate logo of Novartis Institutes for BioMedical Research, Inc., (b) any other Trademark containing the word "Novartis," (c) any other Trademark of NVS used by NVS to identify NVS or its Affiliates, (d) all registrations, applications for registrations, and other Intellectual Property Rights associated with any and all of the foregoing in clauses (a) through (c), and (e) all goodwill associated with any and all of the foregoing in clauses (a) through (d).

1.188. "**NVS Indemnitees**" has the definition set forth in Section 15.2 (Indemnification of NVS by HMI).

1.189. "**NVS Know-How**" means all Know-How that is Controlled by NVS or any of its Affiliates as of the Effective Date or during the Term (other than Joint Know-How) that is necessary or useful to Research, Develop, Manufacture, or Commercialize any Candidate or Product, including NVS Program Know-How, Know-How included within NVS Proprietary Technology, and NVS Assigned Know-How.

1.190. "**NVS Manufacturing Date**" means the date on which NVS is permitted to Manufacture a Candidate or Product itself or through its Affiliates or a Designated CMO in accordance with Section 8.1.2(b) (Transfer of HMI Manufacturing Responsibilities).

1.191. "**NVS Manufacturing Improvements**" means those improvements, modifications, or enhancements made by NVS or its Affiliates to the specific HMI Manufacturing Know-How in the form transferred to NVS by HMI as of the NVS Manufacturing Date for such Target, excluding NVS Materials owned or Controlled by NVS or its Affiliates.

1.192. "**NVS Materials**" means any tangible compositions of matter, articles of manufacture, assays, chemical, biological or physical materials, and other similar materials owned or Controlled by NVS, including seed stocks of cell lines, cell banks, plasmids, and viruses, *but excluding* all HMI Materials.

1.193. "**NVS Patent Rights**" means all Patent Rights that are Controlled by NVS or any of its Affiliates as of the Effective Date or during the Term (other than Joint Patent Rights) that are necessary or useful to Research, Develop, Manufacture, or Commercialize any Candidate or Product, including NVS Program Patent Rights, Patent Rights included within NVS Proprietary Technology, and NVS Assigned Patent Rights.

1.194. "**NVS Products**" means all Products for which NVS is the Commercializing Party.

1.195. "**NVS Program Know-How**" means Know-How that is invented, conceived, discovered, created, or otherwise developed solely by employees, agents, contractors, or Sublicensees of NVS in the performance of activities under this Agreement and specifically related to a Candidate or Product, other than HMI Assigned Know-How and Joint Know-How.

1.196. "**NVS Program Patent Rights**" means Patent Rights that Cover any invention that is conceived or otherwise invented solely by employees, agents, contractors, or Sublicensees of NVS in the performance of activities under this Agreement and specifically related to a Candidate or Product, other than HMI Assigned Patent Rights and Joint Patent Rights.

1.197. "**NVS Program Technology**" means NVS Program Know-How and NVS Program Patent Rights.

1.198. "**NVS Proprietary Technology**" means all Patent Rights or Know-How Controlled by NVS or any of its Affiliates as of the Effective Date or during the Term and generated independently of this Agreement that are provided to HMI for use in connection with this Agreement and include Know-How and related Patent Rights [***]*; provided* that solely with respect to any Patent Rights or Know-How Controlled by NVS or any of its Affiliates [***], NVS or its applicable Affiliate will identify such information as NVS Proprietary Technology when disclosing the same to HMI or its Affiliates.

1.199. "**NVS Quality Requirements**" has the definition set forth in Section 8.1.2 (Transfer of HMI Manufacturing Responsibilities).

1.200. "**NVS Technology**" means the NVS Know-How, the NVS Patent Rights, and NVS' rights under the Joint Know-How and Joint Patent Rights; but *excluding*, in all events, any Intellectual Property Rights in or to any Other Component.

1.201. "**Objective Criteria**" has the definition set forth in Section 8.1.3 (Objective Criteria).

1.202. "**Occupied Target**" means, with respect to NVS' selection of a potential Ophthalmic target, [***] with respect [***] to any [***] such proposed [***].

1.203. "**OFAC**" means the Office of Foreign Assets Control of the United States Department of the Treasury or any successor agency thereto.

1.204. "**Operational Team**" has the definition set forth in Section 5.4.2 (Operational Teams).

1.205. "**Ophthalmic Candidate**" means an AAV gene editing vector that Modulates an Ophthalmic Target that (a) is designed and optimized under the applicable Target Research Plan using HMI Platform Technology during the Research Term or (b) otherwise uses HMI Licensed Technology, in each case ((a) and (b)), for the [***] of Ophthalmic Indications.

1.206. "**Ophthalmic Development Milestone Event**" has the definition set forth in Section 11.4.1(a) (Events).

1.207. "**Ophthalmic Development Milestone Payment**" has the definition set forth in Section 11.4.1(a) (Events).

1.208. "**Ophthalmic Indication**" means any [***].

1.209. "**Ophthalmic Internal Program**" means, with respect to [***] with an [***] or its [***] have [***].

1.210. "**Ophthalmic Product**" means any product containing an Ophthalmic Candidate, or in the case of the [***], a cell-based product generated through genetic modification using an Ophthalmic Candidate.

1.211. "**Ophthalmic Sales Milestone Event**" has the definition set forth in Section 11.5.1 (Ophthalmic Products).

1.212. "**Ophthalmic Sales Milestone Payment**" has the definition set forth in Section 11.5.1 (Ophthalmic Products).

1.213. "**Ophthalmic Target**" means a gene, the Modulation of which would lead to treatment or prevention of an Ophthalmic Indication, which genes will be [***].

1.214. "**Other Components**" means other pharmaceutically active compounds or substances (including products that contain [***] other than those included in such Product) that [***], that are [***] within a single box or sales unit or that are sold separately but approved (or being developed for approval) for use in [***], whether sold at a single price point or under separate price points or as part of a course [***], in each case, which compounds or substances are not a Product, are not Covered by an HMI Patent Right, and do not embody HMI Know-How.

1.215. "**Party**" means either HMI or NVS; "**Parties**" means both HMI and NVS.

1.216. "**Party Vote**" has the definition set forth in Section 5.6.1 (Committee Decisions).

1.217. "**Patent Challenge**" means any challenge to the validity or enforceability of a Patent Right by commencing any opposition proceeding, post-grant review, *inter partes* review, or declaratory action, or any foreign equivalent thereof, in any court, arbitration proceeding, or other tribunal, including the United States Patent and Trademark Office and any foreign counterpart thereof.

1.218. "**Patent Rights**" means all rights, title and interests in and to (a) all national, regional and international patents and patent applications filed in any country of the world including provisional patent applications and all supplementary protection certificates, (b) all patent applications filed either from such patents, patent applications or provisional applications or from an application claiming priority to any of the foregoing, including any continuation, continuation-in part, divisional, provisional, converted provisionals and continued prosecution applications, or any substitute applications, (c) any patent issued with respect to or in the future issued from any such patent applications, including utility models, petty patents, design patents and certificates of invention, and (d) any and all extensions or restorations by existing or future extension or restoration mechanisms, including revalidations, reissues, reexaminations and extensions (including any supplementary protection certificates and the like) of the foregoing patents or patent applications.

1.219. "**Person**" means an individual, sole proprietorship, partnership, limited partnership, limited liability partnership, corporation, limited liability company, business trust, joint stock company, trust, incorporated association, joint venture or similar entity or organization, including any Governmental Authority (or any department, agency, or political subdivision thereof).

1.220. "**Pharmacovigilance Agreement**" has the definition set forth in Section 7.7 (Pharmacovigilance Agreement).

1.221. "**Phase I Clinical Trial**" means a clinical trial of an investigational product in patients with the primary objective of characterizing its safety, tolerability, and pharmacokinetics and identifying a recommended dose and regimen for future studies as described in 21 C.F.R. 312.21(a), or a comparable Clinical Trial prescribed by the relevant Regulatory Authority in a country other than the United States. The investigational product can be administered to patients as a single agent or in combination with other investigational or marketed agents.

1.222. "**Phase I/II Clinical Trial**" means a combined Phase I Clinical Trial and Phase II Clinical Trial.

1.223. "**Phase II Clinical Trial**" means a clinical trial of an investigational product in patients with the primary objective of characterizing its activity in a specific disease state as well as generating more detailed safety, tolerability, pharmacokinetics, and dosing information as described in 21 C.F.R. 312.21(b), or a comparable Clinical Trial prescribed by the relevant Regulatory Authority in a country other than the United States including a human clinical trial that is also designed to satisfy the requirements of 21 C.F.R. 312.21(a) or corresponding foreign regulations and is subsequently optimized or expanded to satisfy the requirements of 21 C.F.R. 312.21(b) (or corresponding foreign regulations) or otherwise to enable a Phase III Clinical Trial (*e.g.*, a Phase I/II Clinical Trial). The investigational product can be administered to patients as a single agent or in combination with other investigational or marketed agents.

1.224. "**Phase III Clinical Trial**" means any clinical trial of an investigational product in patients that incorporates accepted endpoints for confirmation of statistical significance of efficacy and safety with the aim to obtain Regulatory Approval in any country as described in 21 C.F.R. 312.21(c), or a comparable Clinical Trial prescribed by the relevant Regulatory Authority in a country other than the United States. The investigational product can be administered to patients as a single agent or in combination with other investigational or marketed agents.

1.225. "**Pivotal Clinical Trial**" means a human clinical trial in any country that is prospectively designed to generate data intended to satisfy the requirements of 21 C.F.R. § 312.21(c) (as amended) in the U.S. or a similar clinical study prescribed by a Regulatory Authority from another country, from time to time, pursuant to Applicable Law.

1.226. "**Pivotal Clinical Trial Trigger Point**" means, with respect to a U.S. SCD Product, the date that is [***] months prior to the anticipated Initiation of a Pivotal Clinical Trial for such U.S. SCD Product as provided in the Development Plan for such U.S. SCD Product.

1.227. "**Preclinical Development**" means all pre-clinical and non-clinical Development activities for a Candidate or Product undertaken prior to the commencement of the first Clinical Trial for such Candidate or Product, including non-clinical studies and other material Development activities to be undertaken to generate data sufficient to enable the filing of an IND.

1.228. "**Pricing Approval**" means any approval, agreement, determination, or decision establishing prices that can be charged to consumers for a pharmaceutical product or that will be reimbursed by Governmental Authorities for a pharmaceutical product, in each case, in a country in the Territory where Governmental Authorities or Regulatory Authorities approve or determine pricing for pharmaceutical products for reimbursement or otherwise.

1.229. "**Product**" means any Sickle Cell Product or Ophthalmic Product.

1.230. "**Product Trademarks**" means the Global Trademarks and Local Trademarks (excluding the HMI Housemarks and NVS Housemarks).

1.231. "**Professional Requirements**" includes (a) FDA's regulations, guidance, and enforcement letters concerning the advertising of prescription drug products, (b) the American Medical Association's Guidelines on Gifts to Physicians from Industry, (c) the Accreditation Council for Continuing Medical Education (ACCME) Standards for Commercial Support of Continuing Medical Education, (d) the Pharmaceutical Supply Chain Initiative (PSCI) and Pharmaceutical Industry Principles for Responsible Supply Chain Management, (e) the Code on Interactions with Healthcare Professionals promulgated by the Pharmaceutical Research and Manufacturers of America, (f) the Department of Health and Human Services Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers, and (g) all other accepted national and international pharmaceutical industry codes of practice in and for the relevant countries in the Territory, as any of the foregoing may be amended from time-to-time.

1.232. "**Profit Share Payments**" has the definition set forth in Section 11.6.3 (Net Profits).

1.233. "**Profit Share Report**" has the definition set forth in Section 11.6.5 (Profit Share Reports; Payments).

1.234. "**Program Technology**" means HMI Program Patent Rights, HMI Program Know-How, NVS Program Patent Rights, and NVS Program Know-How.

1.235. "**Quality Agreements**" mean the Development Quality Assurance Agreement(s), the Commercial Quality Assurance Agreement(s), and the In-Vivo SCD Quality Assurance Agreement.

1.236. "**Receiving Party**" has the definition set forth in Section 13.1.1 (General).

1.237. "**Regulatory Approval**" means, with respect to a Product in any country or jurisdiction, any approval (excluding any Pricing Approval), registration, license, or authorization from a Regulatory Authority in a country or other jurisdiction that is necessary to market and sell such Product in such country or jurisdiction.

1.238. "**Regulatory Authority**" means any Governmental Authority or authority responsible for granting Regulatory Approvals, including the FDA, EMA, and any corresponding national or regional regulatory authorities, or Pricing Approvals for Products.

1.239. "**Regulatory Exclusivity**" means, with respect to a Product, the ability to exclude Third Parties from Commercializing a product in a country, either through data exclusivity rights, orphan drug designation, or such other rights conferred by a Regulatory Authority in such country, other than through Patent Rights.

1.240. "**Regulatory Executive**" has the definition set forth in Section 7.2.2 (Responsibility).

1.241. "**Regulatory Responsible Party**" means [***].

1.242. "**Regulatory Submissions**" means any regulatory application, submission, notification, communication, correspondence, registration, Regulatory Approvals, and other filings, made to, received from or otherwise conducted with a Regulatory Authority related to Developing, Manufacturing, obtaining marketing authorization, or otherwise Commercializing a product in a particular country or jurisdiction, including all INDs, CTAs, BLAs, MAAs, and all applications for Regulatory Approval together with all supplements or amendments to any of the foregoing.

1.243. "**Reimbursement Cap**" has the definition set forth in Section 3.8.1 (Support).

1.244. "**Research**" means computational biology, bioinformatics, and basic research and discovery activities, including molecular biology, biochemistry, and pre-clinical pharmacology, *in vitro* assays, and *in vivo* assays that Modulate the identification of new biological agents including activities related to the synthesis, discovery, identification, screening, optimization or design of recombinant adeno-associated virus-based vectors. "Research" excludes Development, Manufacture, and Commercialization. When used as a verb, "Researching" means to engage in Research.

1.245. "**Research Activities**" means the Exploratory Research Activities and the Target Research Activities.

1.246. "**Research Budget**" means the Exploratory Research Budget and any Target Research Budget.

1.247. "**Research License**" has the definition set forth in Section 4.1.1 (Research License).

1.248. "**Research Plans**" means the Exploratory Research Plan and the Target Research Plans.

1.249. "**Research Term**" means the period of time commencing on the Effective Date and concluding, (a) with respect to the Exploratory Research Activities, on the 3rd anniversary of the Effective Date, and (b) with respect to the Target Research Activities, on the 5th anniversary of the Effective Date, in each case of (a) and (b), as such period may be extended upon agreement of the Parties.

1.250. "**ROFN Exercise Notice**" has the definition set forth in [***]).

1.251. "**Royalties**" has the definition set forth in Section 11.7.1 (Royalty Rates).

1.252. "**Royalty Floor**" has the definition set forth in Section 11.7.3 (Cumulative Effect of Royalty Reductions).

1.253. "**Royalty Patent Rights**" means [***].

1.254. "**Royalty Rates**" has the definition set forth in Section 11.7.1 (Royalty Rates).

1.255. "**Royalty Report**" has the definition set forth in Section 11.8 (Royalty Reports; Payments).

1.256. "**Royalty Term**" means, on a Product-by-Product and country-by-country basis, the period commencing on the date of First Commercial Sale of a Product in a country and ending on the latest of (a) 10 years following the First Commercial Sale of such Product in such country, (b) the expiration of the last Valid Claim of the Royalty Patent Rights Covering such Product in such country, or (c) the expiration of the first Regulatory Exclusivity obtained for such Product in such country.

1.257. "**Sales Milestone Events**" means any of the Ophthalmic Sales Milestone Events, Ex-Vivo Sickle Cell Sales Milestone Events, or In-Vivo Sickle Cell Sales Milestone Events.

1.258. "**Sales Milestone Payments**" means any of the Ophthalmic Sales Milestone Payments, Ex-Vivo Sickle Cell Sales Milestone Payments, or In-Vivo Sickle Cell Sales Milestone Payments.

1.259. "**SCD**" means Sickle Cell Disease.

1.260. "[***]" has the definition set forth in Section [*******].

1.261. "[***]" has the definition set forth in Section [*******].

1.262. "**SCD Opt-Out Date**" means, with respect to a U.S. SCD Product, as applicable, (a) the COC Opt-Out Date, (b) the Breach Opt-Out Date, or (c) the At-Will Opt-Out Date.

1.263. "**Selected Third Party Agreements**" means, with respect to any Terminated Candidate or Terminated Product, any agreement entered into by and between NVS or any of its Affiliates or its Sublicensees, on the one hand, and one or more Third Parties, on the other hand, that is necessary to Develop, Manufacture, or Commercialize such Terminated Candidate or Terminated Product in the Territory and that does not relate to any compound or product other than any Terminated Candidates or Terminated Products.

1.264. "**Sickle Cell Candidate**" means an AAV gene editing vector that Modulates the Sickle Cell Target that (a) is designed and optimized under the applicable Target Research Plan using HMI Platform Technology during the Research Term or (b) otherwise uses the HMI Licensed Technology, in each case ((a) and (b)), for the treatment of SCD.

1.265. "**Sickle Cell Product**" means a product containing a Sickle Cell Candidate, or in the case of the Ex-Vivo Field, a cell-based product generated through genetic modification using a Sickle Cell Candidate.

1.266. "**Sickle Cell Target**" means any gene, the Modulation of which would lead to [***] of SCD.

1.267. "**Subcommittee**" has the definition set forth in Section 5.1.5(q) (Specific Responsibilities of the JSC).

1.268. "**Sublicensee**" means any Person, other than a Party or an Affiliate or Third Party Distributor of a Party, to which a Party grants a sublicense of the licenses granted to such Party by the other Party under this Agreement.

1.269. "**Success Criteria**" means, with respect to a Candidate that Modulates a given Target, [***] in order to [***] the [***] from the [***] or a [***].

1.270. "**Success Criteria Report**" has the definition set forth in Section 3.6.3 (Success Criteria Reports).

1.271. "**Target**" means the Sickle Cell Target for the In-Vivo Field, the Sickle Cell Target for the Ex-Vivo Field, and each Ophthalmic Target.

1.272. "**Target Fee**" has the definition set forth in Section 11.3 (Target Fee).

1.273. "**Target Fee Trigger**" has the definition set forth in Section 3.7 (Candidates).

1.274. "**Target Fee Trigger Date**" has the definition set forth in Section 11.3 (Target Fee).

1.275. "**Target Reagents**" means reagents resulting from the Target Research Activities, including cell lines and animal models, but specifically excluding AAV vectors, plasmids, working cell banks, master cell banks and manufacturing raw materials, components, or helpers.

1.276. "**Target Research Activities**" has the definition set forth in Section 3.4.1 (Target Research Plans).

1.277. "**Target Research Budget**" has the definition set forth in Section 3.4.1 (Target Research Plans).

1.278. "**Target Research Plan**" has the definition set forth in Section 3.4.1 (Target Research Plans).

1.279. "**Term**" has the definition set forth in Section 16.1 (Term).

1.280. "**Terminated Candidates**" has the definition set forth in Section 16.3 (Effects of Termination for NVS Breach, Patent Challenge, or for Convenience by NVS).

1.281. "**Terminated Products**" has the definition set forth in Section 16.3 (Effects of Termination for NVS Breach, Patent Challenge, or for Convenience by NVS).

1.282. "**Terminated Target**" means any Target that is terminated pursuant to Section 16.2 (Termination).

1.283. "**Territory**" means all countries of the world and all territories and possessions thereof.

1.284. "**Third Party**" means any Person other than a Party or an Affiliate of a Party.

1.285. "**Third Party Distributor**" means any Third Party, other than a Sublicensee, that distributes (but does not Develop or Manufacture) a Product directly to customers.

1.286. "**Third Party Infringement**" has the definition set forth in Section 12.7.1 (Notice).

1.287. "**Third Party Infringement Losses**" has the definition set forth in Section 15.3.2 (Third Party Infringement).

1.288. "**Third Party License**" means a written agreement between a Party or its Affiliates and a Third Party to license or acquire Third Party Intellectual Property Rights for use in connection with the Research, Development, Manufacture, or Commercialization of a Candidate or Product, including for clarity, any such agreement entered into as a result of settlement of any claims for infringement of Third Party Intellectual Property Rights. For clarity, the COH License and the Caltech License constitute Third Party Licenses of HMI.

1.289. "**Trademarks**" means all registered and unregistered trademarks, service marks, trade dress, trade names, logos, insignias, symbols, designs, and all other indicia of ownership, and combinations thereof.

1.290. "**U.S. BLA Transfer Date**" has the definition set forth in Section 7.6.1 (U.S. BLA for In-Vivo SCD Products).

1.291. "**U.S. In-Vivo SCD Commercialization Plan**" has the definition set forth in Section 10.3.1 (In-Vivo SCD Commercialization Plans).

1.292. "**U.S. Medical Affairs Plan**" has the definition set forth in Section 9.1 (Medical Affairs Plans).

1.293. "**U.S. SCD HMI Assumed IP Costs**" mean [***] to a U.S. SCD Product pursuant to [***] to a U.S. SCD Product pursuant to the [***] with respect to [***] U.S. SCD Product.

1.294. "**U.S. SCD Product**" means any In-Vivo SCD Product Commercialized in the U.S.

1.295. "**U.S. SCD Shared IP Costs**" mean [***] U.S. SCD Product [***] into to [***] U.S. SCD Product [***] to [***] U.S. SCD Product [***] or its [***] any [***] of such U.S. SCD Product including [***] (a) and (b), [***]

1.296. "**Valid Claim**" means a claim of (a) an issued patent within the Royalty Patent Rights in the U.S. or in a jurisdiction outside the U.S., as applicable, that has not expired, lapsed, or been cancelled, or been dedicated to the public, or held unenforceable, invalid, revoked or cancelled by a court or Governmental Authority of competent jurisdiction in an order or decision from which no appeal has can be taken, including through opposition, reexamination, reissue, disclaimer, *inter partes* review, post grant procedures, or similar proceedings; or (b) a pending patent application for a patent included in the Royalty Patent Rights that has not been finally abandoned or finally rejected by a Governmental Authority action from which no appeal can be taken and that has been pending for no more than [***] from the date of filing of the earliest patent application to which such pending patent application is entitled to claim priority.

1.297. "**Withholding Party**" has the definition set forth in Section 11.14 (Withholding Taxes).

Article 2. Overview of Collaboration

2.1. **Overview of Research Activities**. During the Research Term for the Target Research Activities and in accordance with the terms and conditions of this Agreement, the Parties will collaborate to identify and synthesize Candidates that Modulate each Target according to the applicable Target Research Plan for such Target, with the aim of identifying IND-ready Candidates for treatment of the corresponding Indication for such Target. As of the Effective Date, the Parties anticipate that the Target Research Activities will result in the identification, synthesis, and further advancement of at least [***] IND-ready Candidate that Modulates each Target, which Candidate(s) NVS may elect to take forward into Clinical Development. In addition, during the Research Term for the Exploratory Research Activities, the Parties will collaborate and HMI will perform research

activities in accordance with the terms of this Agreement and the Exploratory Research Plan to determine the feasibility of applying the HMI Licensed Technology to identify any applications with respect to available targets other than the Targets (but not to provide to NVS any candidates that manipulate, or AAV gene editing vectors that Modulate, in each case, any such other targets, unless otherwise agreed to in writing by the Parties). [***].

2.2. **Overview of Development and Commercialization**. If NVS elects to Develop any Candidate(s) for a particular Target in accordance with the terms of this Agreement, then, subject to HMI's performance of any Research Activities (which may include performing IND-enabling toxicology studies requested by NVS) with respect to such Target and HMI's Manufacturing obligations under Article 8 (Manufacturing and Technology Transfer), NVS will thereafter have the sole right to conduct and be responsible for, at its cost and expense (other than HMI's share of the Global In-Vivo SCD Development Costs), all Development and Commercialization of such Candidates and any associated Products (other than HMI's Commercialization of In-Vivo SCD Products in the U.S.) for the remainder of the Term in accordance with the terms of this Agreement.

Article 3. Research Term

3.1. **Targets**.

3.1.1 **SCD Target**. During the Research Term, NVS will have the right to identify one or more genes, the Modulation of which would lead to [***] of SCD, as a Sickle Cell Target. Any such identified genes shall be reflected in an update to the Research Plan.

3.1.2 **Ophthalmic Target Selection and Substitution**. As of the Effective Date, NVS has selected [***] as its first Ophthalmic Target under this Agreement. NVS will have the right to (a) select the [***] no later than the [***] of the Effective Date; and (b) make up to [***] substitutions of an Ophthalmic Target (in aggregate) during the first [***] of the Research Term by providing written notice to HMI; *provided*, *however*, that in the case of each of (a) and (b), NVS may not select any target except as expressly permitted under this Section 3.1.2 (Ophthalmic Target Selection and Substitution). If, at the time of HMI's receipt of such notice, the proposed ophthalmic target is an Occupied Target, then NVS may select another proposed target (and another if such other proposed target is an Occupied Target and so on) until such time that NVS selects an ophthalmic target that is not an Occupied Target, at which point such proposed ophthalmic target will be added as an Ophthalmic Target under this Agreement. If NVS in good faith questions why a proposed ophthalmic target is an Occupied Target, then upon request HMI shall promptly provide reasonable evidence as to why such target is an Occupied Target, which evidence may be provided by HMI to NVS' outside counsel or another outside consultant engaged by NVS to confirm such status. Such outside counsel or consultant engaged by NVS will be permitted to disclose to NVS only whether or not it agrees with HMI's determination that the proposed ophthalmic target is an Occupied Target. In the event of a dispute with regard to any proposed ophthalmic target, such dispute shall be resolved by Expedited Arbitration. Upon substitution of an Ophthalmic Target, the original target will no longer be an Ophthalmic Target for purposes of this Agreement. NVS will have no further right to substitute any Ophthalmic Target once it has made [***] substitutions under this Section 3.1.2 (Ophthalmic Target Selection and Substitution). If HMI has granted any Third Party any non-exclusive rights with respect to any non-Occupied Target that NVS selects as an Ophthalmic Target, then HMI will disclose to NVS the nature of such granted non-

exclusive rights at the time of NVS' proposal of such target, and if (i) NVS does not withdraw its proposal of such target, then when such target becomes an Ophthalmic Target, the rights granted by HMI to NVS under this Agreement with respect to such Ophthalmic Target will be subject to such non-exclusive rights; and (ii) NVS does withdraw its proposal of such target, then such proposal shall not qualify as one of the [***] permitted substitutions under this Agreement.

3.2. **Success Criteria**. NVS will propose to the JSC for review, discussion, and approval (a) a draft of the Success Criteria for Sickle Cell Candidates and the Success Criteria for Ophthalmic Candidates that Modulate the initial Ophthalmic Target, and the JSC may modify and will approve the final Success Criteria within [***] month after the Effective Date; and (b) the draft Success Criteria for Ophthalmic Candidates that Modulate [***], any other additional substituted Ophthalmic Target, or any new SCD Target, and the JSC may modify and will approve the final Success Criteria no later than [***] month after NVS' selection of [***], such substitution Ophthalmic Target, or such new SCD Target, as applicable.

3.3. **Conduct of Research Activities**.

3.3.1 **Research Diligence Obligations**. Subject to the JSC's review and approval of each Research Plan, the Parties will [***] perform (themselves or through their Affiliates or any subcontractor) the Target Research Activities in accordance with the applicable Target Research Plan and the Exploratory Research Activities in accordance with the Exploratory Research Plan.

3.3.2 **Additional Development Support**. HMI's obligations to perform any Research Activities will conclude at the end of the Research Term. If NVS wishes HMI to conduct any additional activities with respect to any Candidate or Product at any time during the Term after the conclusion of the Research Term, then the Parties will negotiate in good faith to agree upon the scope of any such additional activities and other [***] terms with respect to such activities, including compensation. Notwithstanding the foregoing, subject to reasonable availability, HMI will cooperate with NVS by answering NVS' questions and sharing HMI Product Know-How relating to the Candidates [***]; *provided, however*, [***].

3.4. **Research Plans and Budgets**.

3.4.1 **Target Research Plans**. The principal objectives of the activities to be undertaken by both Parties during the Research Term with respect to each Target will be based substantially on the research plan attached hereto as Schedule 3.4.1 (the "**General Research Plan**"). The Parties will jointly create a research plan for each such Target based on the General Research Plan (each, a "**Target Research Plan**"). Each Target Research Plan will set forth for such Target: (a) the specific activities to be performed by each Party during the Research Term to Research and conduct Preclinical Development on Candidates that Modulates such Target, including the Manufacture of research grade vectors (the "**Target Research Activities**"); (b) the anticipated number of HMI FTEs to be dedicated to performing the Target Research Activities for such Target; and (c) a budget setting out by Calendar Year the estimated Internal Costs and External Costs (including Manufacturing Costs) to be incurred by HMI and its Affiliates in the conduct of the Target Research Activities for such Target during the upcoming Calendar Year (each, a "**Target Research Budget**"). The Parties shall develop and submit the initial Target Research Plan to the JSC for its review and approval (i) for the first Sickle Cell

Target and the first Ophthalmic Target, no later than [***] month after the Effective Date, and (ii) for the [***], any substitution Ophthalmic Target, or any new Sickle Cell Target, as applicable, no later than [***] month after NVS' selection of such Target.

3.4.2 **Exploratory Research Plan**. The principal objectives of the activities to be undertaken by HMI during the Research Term to determine the feasibility of applying the HMI Licensed Technology to identify novel applications with respect to available targets other than the Targets will be defined in a research plan based substantially on the General Research Plan (the "**Exploratory Research Plan**"). The Exploratory Research Plan will set forth: (a) the specific activities to be performed by HMI during the Research Term using the HMI Platform Technology to conduct vector design or vector assessment activities to determine the feasibility of applying the HMI Licensed Technology to identify novel applications with respect to available targets other than the Targets, including the Manufacture of research grade vectors (the "**Exploratory Research Activities**"); (b) the anticipated number of HMI FTEs to be dedicated to performing the Exploratory Research Activities; and (c) a budget setting out by Calendar Year the estimated Internal Costs and External Costs (including Manufacturing Costs) to be incurred by HMI and its Affiliates in the conduct of the Exploratory Research Activities in the upcoming Calendar Year (the "**Exploratory Research Budget**"). NVS will develop and submit the initial Exploratory Research Plan to the JSC for its review and approval no later than [***] month after the Effective Date and in any event in advance of HMI being responsible for the performance of any such Exploratory Research Activities.

3.4.3 **Amendments to the Research Plans and Research Budgets**. During the Research Term, the Parties will jointly develop and submit an update to each applicable Research Plan (including each applicable Research Budget) no later than [***] of each Calendar Year (or more frequently as may be determined by the JSC) and the JSC may modify and will approve each updated Research Plan no later than [***]. HMI will not be required to perform any work that would impose any additional financial obligations beyond those that would not be fully reimbursed by NVS pursuant to Section 3.8 (Research Funding), unless NVS agrees to provide funding for such additional work in writing, and such additional work is included in an amendment approved by the JSC. Following such review and approval by the JSC, each amended Research Plan and Research Budget will become effective immediately and will supersede the applicable previous Research Plan and Research Budget.

3.5. Results of Exploratory and Target Activities. Upon NVS' reasonable request, HMI will transfer to NVS all Exploratory Reagents and Target Reagents. For clarity, HMI Materials shall be transferred to NVS in accordance with Section 4.6 (Knowledge and Technology Transfer) and Section 8.6 (Manufacturing Know-How Transfer and Technology Transfer), as applicable.

3.6. Research Records and Reports.

3.6.1 **Records**. HMI will maintain, or cause to be maintained, records of its Research Activities in sufficient detail and in a good scientific manner appropriate for scientific, patent, and regulatory purposes, which records will reasonably reflect work performed by HMI under each Research Plan. NVS will have the right to audit and request a copy of such records from time to time during the Term.

3.6.2 **Interim Reports**. During the Research Term, in advance of each meeting of the JSC (unless otherwise agreed by the JSC), the Parties will jointly create and submit to the JSC for its review and discussion a written report that includes: (a) a summary of the Research Activities completed during the most recently completed Calendar Quarter; (b) a copy of all material results generated during such period related to each Target; and (c) both Parties' progress against the timeline and budget set forth in each Research Plan, with appropriate documentation to substantiate all such activities and results (each, an "**Interim Report**").

3.6.3 **Success Criteria Reports**. During the Research Term, if HMI reasonably believes that any Candidate has achieved the Success Criteria for Candidates that Modulate such Target, HMI will submit to the JSC for its review and approval a report that: (a) identifies all such Candidate(s); and (b) provides all data and documentation that supports HMI's determination of achievement of the Success Criteria for Candidates that Modulate such Target (each, a "**Success Criteria Report**").

3.6.4 **Exploratory Research Report**. No later than [***] after the end of the Research Term, HMI will prepare and submit to the JSC for its review and discussion a final written report that provides information summarizing the Exploratory Research Activities undertaken and all accomplishments achieved during the Research Term (the "**Exploratory Research Report**"). The Exploratory Research Report will contain a copy of all results generated during the Research Term in the performance of the Exploratory Research Activities, including a description of all Exploratory Reagents, in hard copy or electronic format with appropriate documentation to substantiate such results.

3.7. **Candidates**. During the Research Term, (a) NVS and the JSC will assess the results provided in each Interim Report; (b) the JSC will review and determine whether each Candidate identified in the Success Criteria Report has achieved the Success Criteria for the Target that such Candidate Modulates; and (c) NVS will determine whether it wishes to Develop any Candidate, regardless of whether such Candidate has achieved the applicable Success Criteria. NVS will have the right to Develop and Commercialize [***] arising from the Target Research Activities. On a Target-by-Target basis, upon the earlier of (i) the JSC's approval of the first Candidate that meets the applicable Success Criteria for the Target that such Candidate Modulates, or (ii) [***] with respect to such Candidate ((i) or (ii), the "**Target Fee Trigger**"), NVS will pay the Target Fee to HMI in accordance with Section 11.3 (Target Fee); [***].

3.8. **Research Funding**.

3.8.1 **Support**. During the Research Term, as support for work performed by or on behalf of HMI in accordance with this Agreement and each Research Plan, NVS will be responsible for all Internal Costs and External Costs, in each case, incurred by HMI in accordance with the JSC-approved Research Plans (collectively, the "**HMI Research Costs**"), to the extent such amounts are within [***]% of each applicable Research Budget for such Calendar Year or otherwise approved in advance in writing by NVS. Notwithstanding the foregoing, NVS will not be responsible for any Internal Costs or External Costs incurred by HMI in performance of any Research Activities, including any Manufacturing Costs with respect to Candidates or Products Manufactured for use in connection with such Research Activities, in excess of $[***] in the aggregate (the "**Reimbursement Cap**") or that exceed [***]% of the approved Research Budget for such Calendar Year, in each case, unless otherwise approved by

NVS in writing. HMI will not be required to perform any Research Activities under any Research Plan, including incurring any Manufacturing Costs with respect to Candidates or Products Manufactured for use in connection with such Research Activities to the extent that HMI's performance of such activities would exceed the Reimbursement Cap, unless NVS agrees in writing to provide additional funding over the Reimbursement Cap to reimburse HMI for the Internal Costs and External Costs (including Manufacturing Costs, as applicable) incurred by HMI in connection with performing such Research Activities.

3.8.2 **Research Payments**. No later than [***] after the conclusion of each Calendar Quarter, HMI will provide to NVS a report of the HMI Research Costs actually incurred in performing its activities under each Research Plan during the most recently completed Calendar Quarter, which will include a breakdown of Internal Costs and External Costs actually incurred by HMI during such Calendar Quarter, including the applicable Manufacturing Costs along with a written invoice for the amount due in accordance with this Section 3.8 (Research Funding) for such Calendar Quarter. NVS will pay to HMI the undisputed amounts set forth in any such invoice within [***] of NVS' receipt of such invoice.

Article 4. Licenses; Exclusivity

4.1. License Grants to NVS.

4.1.1 **Research License**. Subject to the terms of this Agreement, HMI hereby grants to NVS and its Affiliates, (a) during the Research Term, a worldwide, non-exclusive research license, with the right to grant sublicenses through multiple tiers in accordance with Section 4.3 (Sublicensing Rights), under the HMI Licensed Technology solely to perform its responsibilities under any Research Plan; (b) a worldwide license, with the right to grant sublicenses through multiple tiers in accordance with Section 4.3 (Sublicensing Rights), under the HMI Licensed Technology to conduct Preclinical Development activities with respect to Candidates and Products (including the use of Target Reagents), which license will be (i) co-exclusive (with HMI) during the Research Term; and (ii) exclusive during the remainder of the Term; and (c) a worldwide, non-exclusive, perpetual, irrevocable license, without the right to grant sublicenses, to use Exploratory Reagents and Target Reagents, and any improvements, modifications, or derivatives resulting from the use thereof, solely for its internal research purposes ((a) – (c) together the "**Research License**").

4.1.2 **Development and Commercialization License**. Subject to the terms of this Agreement, HMI hereby grants to NVS and its Affiliates an exclusive, royalty-bearing license (with the right to grant sublicenses through multiple tiers in accordance with Section 4.3 (Sublicensing Rights)) under the HMI Licensed Technology to Develop and Commercialize (a) Ophthalmic Candidates and Ophthalmic Products worldwide, (b) Sickle Cell Candidates and Sickle Cell Products worldwide in the Ex-Vivo Field, and (c) Sickle Cell Candidates and In-Vivo SCD Products worldwide, excluding the Commercialization thereof in the United States (the "**Development and Commercialization License**"). Subject to the terms of this Agreement, effective as of the SCD Opt-Out Date, HMI hereby grants to NVS and its Affiliates an exclusive license (with the right to grant sublicenses through multiple tiers in accordance with Section 4.3 (Sublicensing Rights)) under the HMI Licensed Technology to Commercialize U.S. SCD Products.

4.1.3 **Manufacturing License**. Subject to the terms of this Agreement, HMI hereby grants to NVS and its Affiliates a royalty-bearing license (with the right to grant sublicenses to Designated CMOs in accordance with Section 4.3 (Sublicensing Rights)) under the HMI Licensed Technology to Manufacture or have Manufactured (a) Ophthalmic Candidates and Ophthalmic Products worldwide and (b) Sickle Cell Candidates and Sickle Cell Products in the In-Vivo Field and in the Ex-Vivo Field worldwide, in each case, in accordance with Article 8 (Manufacturing and Technology Transfer). The foregoing license will be (i) co-exclusive (with HMI) as of the Effective Date with respect to Candidates and Products, (ii) exclusive as of the NVS Manufacturing Date for the applicable Candidate and Product (other than any U.S. SCD Product), and (iii) co-exclusive (with HMI) as of the NVS Manufacturing Date for any U.S. SCD Product. [***]

4.1.4 **Assigned Technology License**. HMI hereby grants to NVS and its Affiliates, a worldwide, non-exclusive, perpetual, irrevocable, royalty-free, and fully-paid up license with the right to grant sublicenses under the HMI Assigned Technology in connection with the research, development, manufacturing, commercialization, or other exploitation of products or services by or on behalf of NVS or its Affiliates. Notwithstanding anything to the contrary set forth in this Agreement, the license granted under this Section 4.1.4 (Assigned Technology License) do not grant NVS or its Affiliates any rights or licenses under HMI Licensed Technology (other than the HMI Assigned Technology) beyond those granted as part of the Research License, the Development and Commercialization License, or under Section 4.1.3 (Manufacturing License).

4.2. License Grant to HMI.

4.2.1 **Non-Exclusive Research License**. Subject to the terms of this Agreement, NVS hereby grants to HMI during the Research Term, a worldwide, non-exclusive license, with the right to grant sublicenses through multiple tiers in accordance with Section 4.3 (Sublicensing Rights) under the NVS Technology solely to perform its Research Activities under the applicable Research Plan.

4.2.2 **Exclusive Commercial License**. Subject to the terms of this Agreement, NVS hereby grants to HMI during the Term of this Agreement, a worldwide exclusive license without the right to sublicense under the NVS Program Patent Rights, the NVS Program Know-How, and NVS' interest in the Joint Know-How and Joint Patent Rights, in each case, to Commercialize In-Vivo SCD Products in the U.S.

4.2.3 **Non-Exclusive NVS Manufacturing Improvements License**. NVS will and hereby does, grant to HMI a non-exclusive, royalty-bearing, perpetual, irrevocable, worldwide, sublicensable license under all NVS Manufacturing Improvements (if any) to Manufacture and have Manufactured candidates and products that are created using HMI Platform Technology; *provided*, that the Parties agree to negotiate [***] financial terms for such license, subject to Expedited Arbitration if the Parties are unable to agree on such financial terms within [***] following NVS' receipt of written notice from HMI requesting such license.

4.3. Sublicensing and Licensing Rights.

4.3.1 **Research License**. Subject to Section 4.3.4 (Sublicense and License Requirements), (a) NVS may sublicense the rights granted to it under clauses (a) and (b) of Section 4.1.1 (Research License); and (b) HMI may (i) license or sublicense its rights under clause (b)(i) of Section 4.1.1 (Research License) and (ii) sublicense the rights granted to it under Section 4.2.1 (Non-Exclusive Research License), in each of (a) or (b), to any Third Party service provider performing services for the benefit of such sublicensing Party without the other Party's prior written consent. NVS may not sublicense the rights granted to it under clause (c) of Section 4.1.1 (Research License) without HMI's prior written consent.

4.3.2 **Development and Commercialization Licenses**. Subject to Section 4.3.4 (Sublicense and License Requirements), NVS may sublicense its rights under Section 4.1.2 (Development and Commercialization License) without HMI's prior written consent (a) to any Third Party service provider performing services for the benefit of NVS in connection with the Development or Commercialization of any Candidate or Product, or (b) to any Third Party to whom NVS desires to sublicense Development or Commercialization rights in any and all jurisdictions; *provided*, [***].

4.3.3 **Manufacturing License**. Subject to Section 4.3.4 (Sublicense and License Requirements), (a) NVS may sublicense its rights under Section 4.1.3 (Manufacturing License); and (b) HMI may license or sublicense its rights under clauses (i) and (iii) under Section 4.1.3 (Manufacturing License), in each of (a) and (b), to any Designated CMO. For clarity, the use of Third Party service providers engaged to perform services in connection with Manufacturing, including analytics service providers, will be deemed subcontractors and not Sublicensees.

4.3.4 **Sublicense and License Requirements**. Each Party will ensure that all permitted sublicenses granted under this Agreement: (a) are consistent with the terms of this Agreement, (b) include an obligation of the Sublicensee to assign to such Party all Know-How and Patent Rights invented, discovered, created, or otherwise developed by the Sublicensee that would fall within the definition of Assigned Know-How or Assigned Patent Rights if they were invented, discovered, created, or otherwise developed by such Party or its Affiliates, (c) include an obligation of the Sublicensee to assign or grant a sublicensable license to such Party of all Know-How and Patent Rights invented, discovered, created, or otherwise developed by the Sublicensee that would fall within the definition of Program Technology if they were invented, discovered, created, or otherwise developed solely by such Party or its Affiliates, (d) to the extent a Party engages a Sublicensee to Commercialize a Product, include an obligation of such Sublicensee to account for and report its Net Sales of each such Product, and (e) require the Sublicensee to comply with the obligations of the sublicensing Party contained in this Agreement, including the confidentiality and non-use obligations set forth in Article 13 (Confidentiality). Each Party will remain responsible and liable for the performance of all Affiliates and Sublicensees under their respective sublicensed rights to the same extent as if such activities were conducted by the sublicensing Party. In no event will any sublicense relieve the sublicensing Party of any of its obligations under this Agreement. The sublicensing Party will deliver to the other Party a copy of any executed sublicense agreement (redacted as necessary to protect confidential information that is not necessary to confirm compliance with this Agreement) no later than [***] following the execution thereof. Any termination of the licenses granted to a Party hereunder will cause all of the applicable Sublicensees of such Party to automatically lose the same rights under any sublicense. For clarity, any licenses or sublicenses by HMI or its Affiliates (other than to NVS and its Affiliates under this Agreement) of HMI Licensed Technology [***] licensed to NVS hereunder shall be treated as a sublicense and subject to the terms of this 4.3.4 (Sublicense and License Requirements).

4.4. **Subcontractors**. Each Party may perform any of its obligations under this Agreement through one or more subcontractors; *provided*, that (a) the subcontracting Party remains fully responsible for the work allocated to, and payment to, such subcontractors to the same extent it would if it had done such work itself; (b) the subcontractor undertakes in writing obligations of confidentiality and non-use applicable to the Confidential Information that are at least as stringent as those set forth in Article 13 (Confidentiality); and (c) the subcontractor agrees in writing to assign all inventions and other Intellectual Property Rights developed in the course of performing any such work under this Agreement that are specifically related to Candidates or Products to the Party retaining such subcontractor and a sublicensable license under and to all other inventions and other Intellectual Property Rights that are developed by the subcontractor in the course of performing such work under this Agreement, and to cooperate and sign any documents to confirm or perfect such assignment.

4.5. **Third Party Licenses**. All rights licensed to a Party from a Third Party and sublicensed to the other Party under this Agreement will be subject to and subordinate to the terms of the applicable Third Party License. Each Party will comply with the terms of any such Third Party License, [***]. Schedule 4.5 (Third Party License Terms) sets forth certain obligations under (a) the COH License that apply to certain COH Patent Rights and (b) the Caltech License that apply to certain Caltech Patent Rights, and NVS will comply with those terms applicable to sublicensees under such licenses that have been [***] disclosed to NVS by HMI.

4.6. **Knowledge and Technology Transfer**. Within [***] of NVS' request, HMI will deliver to NVS copies of (a) the written HMI Product Know-How related to each Candidate or Product, (b) documents and files related to the HMI Product Patent Rights, and (c) any other HMI Know-How that is necessary or useful for the Development or Commercialization of Candidates and Products in accordance with this Agreement; *provided*, that any HMI Know-How relating to Manufacturing shall only be provided to NVS in accordance with Article 8 (Manufacturing and Technology Transfer). In addition, as part of such Know-How transfer, HMI will transfer to NVS HMI Materials related to a Candidate or Product to the extent necessary for NVS to exercise the rights granted to it under this Agreement with respect to the HMI Product Know-How related to such Candidate or Product. Any HMI Materials provided by HMI in connection with the transfer of the HMI Product Know-How will remain the sole property of HMI. Thereafter, on a continuing basis during the Term, HMI shall [***], and at a minimum no less frequently than on a [***] basis through the JSC, as applicable, disclose to NVS all additional HMI Product Know-How (including providing any such HMI Materials) related to a Candidate or Product that comes into existence since the prior disclosure. HMI will provide [***] assistance to NVS in connection with understanding and using all such HMI Product Know-How for purposes consistent with the licenses and rights granted to NVS hereunder. NVS will use and transfer all documents and files related to the HMI Product Know-How related to each Candidate or Product including HMI Materials and HMI Product Patent Rights only for purposes of exercising its rights and licenses with respect to applicable Candidates and Products in accordance with this Agreement, and for no other purpose. NVS will be responsible for all reasonable documented costs and expenses associated with the transfer to NVS of such documentation and any HMI Product Know-How.

4.7. **Covenant Not to Sue NVS**. During the Term, HMI hereby covenants not to assert or cause to be asserted, and will cause its Affiliates, licensees, and sublicensees not to assert or cause to be asserted, against NVS or any of NVS' Affiliates or Sublicensees, any claim of infringement,

misappropriation, or other violation of Intellectual Property Rights Controlled by HMI or its Affiliates, including any Intellectual Property Rights relating to [***], with respect to the Research, Development, Manufacturing, or Commercialization of any Candidate or Product in accordance with this Agreement.

4.8. **No Implied Licenses**. Each Party acknowledges that the rights and licenses granted under this Agreement are limited to the scope expressly granted herein. Except for the rights expressly granted under this Agreement, no rights, title, licenses, or other interests of any nature whatsoever are granted whether by implication, estoppel, reliance, or otherwise, by either Party to the other Party. Accordingly, NVS will not practice or exploit the HMI Know-How and HMI Patent Rights other than as expressly licensed in this Agreement, and likewise HMI will not practice or exploit the NVS Know-How and NVS Patent Rights other than as expressly licensed in this Agreement. Each Party specifically reserves all rights not expressly granted to the other Party hereunder.

4.9. **Retained Rights**. Notwithstanding the licenses granted to NVS in Section 4.1 (License Grants to NVS), but subject to Section 4.13 (ROFNs [***]), HMI (a) retains the exclusive right to practice the HMI Licensed Technology to Develop and Commercialize [***], and (b) NVS will not Research, Develop, Manufacture, Commercialize, or otherwise exploit any Sickle Cell Candidate or Sickle Cell Product for the treatment of [***].

4.10. **U.S. Government Rights**. The Parties acknowledge that the Patent Rights and Know-How licensed to HMI under the COH License and Caltech License are each subject to retained rights of the U.S. Government in such HMI Licensed Technology pursuant to 35 U.S.C. §§ 200-212 and applicable U.S. government regulations and the right of such Third Party licensors and other non-profit academic or research institutions to practice such HMI Licensed Technology for non-profit educational and research uses; *provided*, that HMI covenants that such uses will not include research sponsored by any for-profit Third Parties.

4.11. **Exclusivity**. During the Term, HMI and its Affiliates will not itself or with or through any Third Party, directly or indirectly, Research, Manufacture, Develop, or Commercialize (a) Candidates or Products except in the performance of activities under this Agreement; or (b) [***].

4.12. **Change of Control**.

4.12.1 **Exception to Exclusivity**. Notwithstanding the exclusivity granted under Section 4.11 (Exclusivity), if HMI, as a result of a Change of Control, is acquired by an entity that, as of the time of such transaction, directly or through an Affiliate, is Researching, Developing, Manufacturing, Commercializing, or otherwise exploiting a [***], [***] of such Change of Control, [***] such [***] may continue to [***] and otherwise [***] (without such [***]) so long as: (a) [***]; and (b) [***] (i) does [***] (including any [***]) or [***] involved in the [***] (*provided*, that the foregoing [***] but do not [***] or are not otherwise [***] involved in the [***] and (ii) [***] to ensure that such [***]. In addition, [***] (other than [***]) with respect to [***] with respect to [***].

4.12.2 **Change of Control** 4.12.3. Without limiting Section 4.12.1 (Exception to Exclusivity): (a) where the Acquiror is [***] any [***] then [***] with respect to [***] shall [***] of such Change of Control; (b) where [***] notwithstanding any other provision of this Agreement, [***] with respect to [***] and (c) at [***] will no longer [***] it is then [***] of such [***]. Upon the [***] (i) the [***] pursuant to **[***]**

with respect to such [***] and [***], (ii) [***] shall be [***] for such [***], (iii) **[***]** with respect to such [***] or any [***] in the [***] the same [***] as such [***] with respect to [***] shall [***] including [***] or any [***] with respect to [***] including [***] with respect to [***] shall instead [***] including [***], in each case, as with respect to [***]; and (iv) [***] and [***] with respect to [***] and [***], and all [***] in such [***].

4.13. ROFNs For [***].

4.13.1 **HMI** [***] **Products**. HMI will ensure that any [***] Product Researched, Developed, or Commercialized by or on behalf of HMI or its Affiliates is done so in a manner distinct from any Sickle Cell Product.

(a) If at any point HMI or its Affiliates receives or intends to make a *bona fide* offer from or to a Third Party with respect to the transfer, assignment, grant of a license, or other disposition of rights to Develop or Commercialize any [***] ("[***] **Out-license**"), then HMI will notify NVS in writing of such offer, and simultaneously provide NVS with the [***]. NVS will have an [***] exercisable no later than [***] days after receipt of any such written notice from HMI to notify HMI in writing as to whether NVS desires to negotiate for a license to Develop and Commercialize [***] owned by HMI or its Affiliates (the "**ROFN Exercise Notice**"). If NVS provides such ROFN Exercise Notice to HMI within such [***] period indicating its desire to negotiate for such rights, then (i) upon NVS' request, HMI will (A) within [***] of NVS' request, provide NVS with other information and documentation reasonably requested by NVS in HMI's or its Affiliate's Control relating to such [***]; and (B) afford NVS and its representatives reasonable access during normal business hours to HMI's personnel; and (ii) NVS will have the [***] from the date of HMI's receipt of the ROFN Exercise Notice to negotiate with HMI a definitive license agreement setting forth the terms of a license to Develop and Commercialize such [***].

(b) If either (i) NVS does not provide such written notice to HMI within such [***] period, or (ii) NVS and HMI do not enter into a definitive license agreement within the [***] negotiation period after having conducted such negotiations in good faith, then, in each case ((i) and (ii)), for a period of [***] following such [***] or [***] period, as applicable, and subject to the terms of this Agreement, HMI will be free to enter into negotiations and an agreement with one or more Third Parties relating to any license, grant, or other transfer of rights with respect to such [***] (or to further develop and commercialize any such product itself), without further obligation to NVS; *provided*, that (A) [***]; and (B) [***] in accordance with the provisions of this Section 4.13.1 (HMI [***]).

4.13.2 **NVS Development and Commercialization of Sickle Cell Products for** [***]. If NVS wishes to Research, Develop, and Commercialize a Sickle Cell Product for the treatment of [***], then NVS will notify HMI in writing of such desire. Upon HMI's receipt of such notice from NVS, the Parties will negotiate [***] terms of an amendment to this Agreement or another separate agreement to grant NVS the rights to Research, Develop, and Commercialize the applicable Sickle Cell Product for the treatment of [***], including additional financial consideration to be paid to HMI with respect to a grant of such rights. If HMI and NVS do not agree on commercially reasonable terms within [***] of the commencement of such negotiation, then NVS will not Research, Develop or Commercialize such Sickle Cell Product for the treatment of [***]; [***].

4.14. **HMI Commercialization Opt-Out Rights for U.S.** SCD **Products**. HMI shall have the right to elect not to Commercialize an In-Vivo SCD Product in the U.S. by written notice to NVS given any time. Such election shall become effective as of [***] after the date of NVS' receipt of such notice (such date, the "**At-Will Opt-Out Date**"). As of the At-Will Opt-Out Date with respect to a U.S. SCD Product: (a) the licenses granted to HMI pursuant to Section 4.2.2 (Exclusive Commercial License) and Section 10.7.3 (Trademark License) with respect to such U.S. SCD Product shall terminate and revert to NVS, (b) NVS shall be the Commercializing Party for such U.S. SCD Product, (c) all rights granted to HMI under this Agreement with respect to such U.S. SCD Product or any Sickle Cell Products in the Ex-Vivo Field incorporating the same Candidate as such U.S. SCD Product that differ from the rights granted to HMI under this Agreement with respect to the Ophthalmic Products shall terminate, including rights at the JSC or any Subcommittee and rights with respect to regulatory matters, including any rights with respect to Jointly-Agreed Regulatory Submissions, and HMI shall instead receive the same rights, including review and discussion rights and access to reports provided to HMI under this Agreement, in each case, as with respect to the Ophthalmic Products; and (d) HMI hereby assigns to NVS all of its right, title, and interest in and to any Local Trademarks used by HMI with respect to such In-Vivo SCD Product, including the right to sue and recover for past, present, or future infringement, dilution, or other violation thereof, and all goodwill contained in such Local Trademarks. For clarity, notwithstanding HMI's election not to Commercialize an In-Vivo SCD Product in the U.S., [***].

Article 5. Governance

5.1. **Joint Steering Committee**.

5.1.1 **Formation and Purpose of the JSC**. Promptly, but no later than [***] days after the Effective Date, the Parties will establish a Joint Steering Committee ("**JSC**"), which JSC will coordinate and oversee or monitor the Parties' activities hereunder in accordance with this Section 5.1 (Joint Steering Committee). The JSC will have the responsibilities set forth herein and will dissolve upon the expiration of the Term.

5.1.2 **Membership**. Each Party will designate up to [***] representatives with appropriate expertise and seniority to serve as members of the JSC, and who have the authority to bind such Party with respect to matters within the purview of the JSC. Each Party may replace its JSC representatives at any time upon written notice to the other Party. HMI will designate one of its JSC members as one of the co-chairpersons of the JSC and NVS will designate one of its members as the other co-chairperson of the JSC. Every [***] months the co-chairpersons will alternate serving in the role of "lead co-chairperson." The lead co-chairperson or his or her designee, in collaboration with the Alliance Managers, will be responsible for calling meetings, preparing and circulating an agenda in advance of each meeting, and preparing and issuing minutes of each meeting within [***] thereafter. Such minutes will be deemed finalized unless any JSC member objects to the accuracy of such minutes within [***] of receipt of such minutes.

5.1.3 **Meetings**. The JSC will hold meetings at such times as it elects to do so, but in no event will such meetings be held less frequently than [***], unless otherwise agreed by the Parties. The JSC will meet alternatively at NVS' facilities in Cambridge, Massachusetts and HMI's facilities in Bedford, Massachusetts, or at such locations as the Parties may otherwise agree. Meetings of the JSC may be held by audio or video teleconference with the consent of each Party; *provided*, *however*, that at least [***] JSC meeting per year will be held in person. The Alliance Manager of each Party will attend each meeting of the JSC as a non-voting participant. Each Party will be responsible for all of its own expenses of participating in any JSC meeting.

5.1.4 **Meeting Agendas**. Each Party will disclose to the other Party the proposed agenda items along with appropriate information at least [***] in advance of each meeting of the JSC. Notwithstanding the foregoing, under exigent circumstances requiring JSC input, a Party may provide its agenda items to the other Party within a lesser period of time in advance of the meeting, or may propose that there not be a specific agenda for a particular meeting, so long as such other Party consents to such later addition of such agenda items or the absence of a specific agenda for such JSC meeting.

5.1.5 **Specific Responsibilities of the JSC**. The responsibilities of the JSC will be to:

(a) oversee the overall strategic relationship between the Parties;

(b) review, discuss, and approve each Research Plan (including the applicable Research Budget set forth therein), and each amendment or update thereto;

(c) review, discuss, develop, and approve the Success Criteria (or any modification thereto) for Candidates that Modulate each Target;

(d) review and discuss each Interim Report, each Success Criteria Report, and the Exploratory Research Report;

(e) review, discuss, and determine whether any Candidate identified in the Success Criteria Report has achieved the Success Criteria for Candidates that Modulate such Target;

(f) facilitate the flow of information (including Development Reports) between the Parties with respect to the Development and Commercialization of Ophthalmic Candidates, Ophthalmic Products, Sickle Cell Candidates in the Ex-Vivo Field, and Sickle Cell Products in the Ex-Vivo Field;

(g) review and discuss any proposed sublicenses to whom NVS proposes to grant rights to Develop or Commercialize In-Vivo SCD Products;

(h) review and discuss the Development Plan for In-Vivo SCD Products and all material amendments or updates thereto;

(i) develop, discuss, and approve the initial high-level summary (including the associated budget) of marketing strategy and Commercialization activities for In-Vivo SCD Products, and each material amendment or update to such plans and budgets;

(j) review, discuss, and approve the Global In-Vivo SCD Commercialization Plan and the U.S. In-Vivo SCD Commercialization Plan (including the applicable Commercialization Budgets set forth therein), and all material amendments or updates to such plans and budgets;

(k) review and discuss the status and progress of regulatory activities for In-Vivo SCD Products and provide any comments to NVS with respect to any Jointly-Agreed Regulatory Submissions for In-Vivo SCD Products;

(l) review, discuss, and approve each Global Medical Affairs Plan and U.S. Medical Affairs Plan, progress under such plans, and all material amendments or updates thereto;

(m) review, discuss, and approve the initial Global Brand Plan for In-Vivo SCD Products, and each material amendment and update thereto;

(n) upon request of a Party, develop and discuss whether to approve a Territory-specific brand plan for U.S. SCD Products;

(o) review, discuss and coordinate the Parties' scientific presentation and publication strategy relating to In-Vivo SCD Products in the Territory;

(p) review and discuss reports from the JMC and provide guidance to any Subcommittee to resolve any other disputes or disagreements arising from any such Subcommittee;

(q) establish additional subcommittees, and other operational committees or *ad hoc* subcommittees, on an "as needed" basis to oversee particular projects or activities (the JMC, and such other operational committees and subcommittees, each a "**Subcommittee**"); and

(r) perform such other functions as appropriate to further the purposes of this Agreement as determined by the Parties.

5.2. Joint Manufacturing Committee

5.2.1 **Formation and Purpose of the JMC**. Promptly, but not more than [***] after the Parties establish the JSC, the JSC will establish a Joint Manufacturing Committee ("**JMC**"), which JMC will be a Subcommittee of the JSC and will have the responsibilities provided for herein. The JMC will dissolve upon the earlier of (a) expiration of the Term, or (b) such time as otherwise determined by the JSC.

5.2.2 **Membership and Meetings of the JMC**. Each Party will designate up to [***] representatives with appropriate expertise and seniority to serve as members of the JMC, and who have the authority to bind such Party with respect to matters within the purview of the JMC. HMI will designate a co-chairperson of the JMC and NVS will designate a co-chairperson of the JMC. Each Party may replace its JMC representatives and co-chairpersons at any time upon written notice to the other Party. The JMC will hold meetings at such times as it elects to do so (but in any event at least on a Calendar [***] basis, unless the Parties agree otherwise), and at such locations as the Parties may agree upon or, if agreed by the Parties, by audio or video teleconference. Each Party will be responsible for all of its own expenses of participating in any JMC meeting.

5.2.3 **Specific Responsibilities of the JMC**. The responsibilities of the JMC will be to:

(a) generally facilitate flow of information between the Parties with respect to technical development and Manufacturing clinical supply of Candidates and Products to NVS, and, if applicable, commercial supply;

(b) coordinate and oversee the complete Manufacturing Know-How transfer related to each Candidate and Product to the NVS CMC Sub-Team, including with respect to host cell line history, raw materials used for cultivation, available licenses for commercial use, details about vectors, and process and analytical methods applied to Candidates and Products;

(c) coordinate, oversee, and approve the type and amount of assistance to be provided by or on behalf of HMI to NVS for any HMI Manufacturing Know-How transfer support requested by NVS pursuant to Section 8.6.2 (Manufacturing Technology Transfer to NVS) to permit NVS to Manufacture such Candidate(s) and Product(s);

(d) update NVS about the progress of the HMI facility build-up, or the need to engage Designated CMOs, as appropriate;

(e) provide transparency on planning and budget requirements with respect to preclinical and clinical supplies of Candidates and Products to permit each Party to meet its internal budget and planning processes;

(f) facilitate and align the Parties' activities related to any NVS quality assurance audits of HMI's and Designated CMOs' facilities, including following up on critical audit findings and supporting the identification and implementations of potential solutions;

(g) select and approve the list of Designated CMOs;

(h) advise on the material terms of agreements entered into between HMI and Designated CMOs;

(i) oversee negotiation of the Development Supply Agreement, Commercial Supply Agreement, In-Vivo SCD Commercial Supply Agreement, and Quality Agreements, as appropriate; and

(j) perform such other functions as appropriate to further the purposes of this Agreement as determined by the Parties.

5.3. **Alliance Managers**. Each of the Parties will appoint a single individual to coordinate communications regarding Research, Development, Manufacturing, and Commercialization obligations between the Parties (each, an "**Alliance Manager**"). The role of the Alliance Manager is to act as a single point of contact between the Parties to ensure a successful relationship under this Agreement. The Alliance Managers will attend any JSC meetings and may

attend any Subcommittee meetings. Alliance Managers will be non-voting participants in all JSC and Subcommittee meetings that they attend; *provided*, *however*, that an Alliance Manager may bring any matter to the attention of the JSC or any Subcommittee if such Alliance Manager reasonably believes that such matter warrants such attention. Each Party will designate its initial Alliance Manager promptly after the Effective Date and each Party may change its designated Alliance Manager at any time upon written notice to the other Party. Any Alliance Manager may designate a substitute to temporarily perform the functions of that Alliance Manager by written notice to the other Party. Each Alliance Manager will also: (a) be the point of first referral in all matters of conflict resolution; (b) provide a single point of communication for seeking consensus between the Parties regarding key strategy and plan issues; (c) identify and bring disputes to the attention of the JSC in a timely manner; and (d) plan and coordinate cooperative efforts.

5.4. Additional Committees.

5.4.1 **JSC Subcommittees**. Each such Subcommittee, other than the JMC, which will be established and will operate as provided for above, will be constituted and will operate as the JSC determines. HMI will designate a co-chairperson of each Subcommittee and NVS will designate a co-chairperson of each Subcommittee, each of whom will be a Party's representative who is a member of such Subcommittee. Every [***] the co-chairpersons of each Subcommittee will alternate serving in the role of "lead co-chairperson." The lead co-chairperson or his or her designee will be responsible for calling meetings, preparing and circulating an agenda in advance of each meeting, and preparing and issuing minutes of each meeting within [***] thereafter. Such minutes shall be deemed finalized unless any applicable Subcommittee member objects to the accuracy of such minutes within [***] of receipt of such minutes. Each Party may replace its representatives and co-chairpersons on each such Subcommittee at any time upon written notice to the other Party. Each Party will be responsible for all of its own expenses of participating in any Subcommittee meeting. Each Subcommittee and its activities will be subject to the oversight of the JSC. No Subcommittee's authority may exceed that specified for such Subcommittee in this Article 5 (Governance). Any disagreement between the representatives of the Parties on a Subcommittee will be resolved in accordance with Section 5.6 (Decision-Making).

5.4.2 **Operational Teams**. From time-to-time, the JSC or any Subcommittee may establish and delegate specific matters or duties within its responsibilities to directed teams (each, an "**Operational Team**"), the composition, operation, and responsibilities of which will be determined by the JSC or the applicable establishing Subcommittee (the "**Establishing Committee**"). Operational Teams may be established on an *ad hoc* basis for purposes of a specific activity or on such other basis as the applicable Establishing Committee may determine. Each Operational Team will report to, and its activities will be subject to the oversight of, the applicable Establishing Committee. No Operational Team's authority may exceed that specified for the applicable Establishing Committee. Any disagreement between the representatives of the Parties on any Operational Teams will be referred to the applicable Establishing Committee for resolution in accordance with Section 5.6 (Decision-Making).

5.5. Additional Participants. With the consent of the other Party, not to be unreasonably withheld, conditioned, or delayed, other employees of either Party or any of its Affiliates involved in the Research, Development, Manufacturing, or Commercialization of any Candidates or Products may attend meetings of the JSC or any Subcommittee as non-voting participants. In addition, with the consent of each Party, consultants, representatives, or advisors involved in the Research,

Development, Manufacturing, or Commercialization of any Candidates or Products may attend meetings of the JSC or any Subcommittee as non-voting observers; *provided*, *however*, that such Third Party participants and observers are under written obligations of confidentiality and non-use applicable to the Confidential Information of each Party that are at least as stringent as those set forth in Article 13 (Confidentiality).

5.6. Decision-Making.

5.6.1 **Committee Decisions**. Each Party's representatives on the JSC and each Subcommittee will, collectively, have one vote (the "**Party Vote**") on all matters brought before such committee for a decision by consensus. The JSC and each Subcommittee will make decisions as to matters within its jurisdiction by unanimous Party Vote, which Party Vote may either be reflected in the minutes of the committee meeting or by an action by written consent signed by the co-chairperson appointed by each Party or his or her designee identified in writing. No vote will be binding on either Party unless each Party has at least one representative in attendance.

5.6.2 **Scope of Committee Authority**. For the avoidance of doubt, matters that are specified in this Article 5 (Governance) only to be reviewed and discussed (as opposed to reviewed, discussed, and approved) do not require any agreement or decision by either Party and are not subject to the voting and decision-making procedures set forth in this Section 5.6 (Decision-Making).

5.6.3 **Escalation**. If the representatives of HMI and NVS are unable to agree on or resolve any matter requiring the approval of the JSC, the JMC or any other Subcommittee after the use of good faith efforts, then, at the election of either Party, such Party may refer such matter to the Party's respective Executive Officer. The Executive Officers will use good faith efforts to resolve any such disagreement so referred to them as soon as practicable, and any final decision that the Executive Officers agree to in writing will be conclusive and binding on the Parties. If the Executive Officers are unable to resolve any disagreement so referred within a period of [***] after such matter is referred to them (or such longer period as the Executive Officers may agree upon), then:

(a) If such disagreement refers to any amendment to any Research Plan (including any Research Budget) that would (a) materially change the objectives of the activities to be conducted during the Research Term from those set forth in Section 2.1 (Overview of Research Activities), or (b) otherwise conflict with the terms and conditions of the Agreement, then [***];

(b) If such disagreement refers to any additional payments in excess of the Reimbursement Cap to compensate HMI for the additional Internal Costs and External Costs (including Manufacturing Costs), as applicable, to be incurred by HMI as required to complete any Research Activities in accordance with any JSC approved Research Plan, then [***];

(c) If such disagreement refers to the initial U.S. In-Vivo SCD Commercialization Plan (or the Commercialization Budget set forth therein), or any amendment or update thereto, then [***] with respect to the aspects of such U.S. In-Vivo SCD Commercialization Plan upon which the Parties are unable to agree, *provided*, that such decision is not reasonably likely to have a material adverse effect on (i) [***] or (ii) [***];

(d) If such disagreement refers to a Territory-specific brand strategy for U.S. SCD Products, then [***] with respect to the aspects of such Territory-specific brand strategy upon which the Parties are unable to agree that solely relates to the U.S., *provided*, that such decision is not reasonably likely to have a material adverse effect on (i) [***] or (ii) [***]; and

(e) [***].

5.7. **General Authority**. The JSC and each Subcommittee and Alliance Manager will have solely the powers expressly assigned to them in this Article 5 (Governance) and elsewhere in this Agreement. In conducting themselves on the JSC and any other Subcommittee, and as Alliance Managers, and in exercising their rights under this Article 5 (Governance), all representatives of each Party will consider diligently, reasonably, and in good faith all input received from the other Party, and will use good faith efforts to reach unanimity, where required, on all matters before them. Notwithstanding anything to the contrary set forth in this Agreement, neither the JSC nor any Subcommittee will have the right to make any decisions:

5.7.1 to amend or modify this Agreement, or waive compliance with this Agreement;

5.7.2 in a manner that excuses such Party from any obligation specifically enumerated under this Agreement;

5.7.3 in a manner that negates any consent right or other right specifically allocated to the other Party under this Agreement;

5.7.4 to resolve any dispute involving the breach or alleged breach of this Agreement;

5.7.5 to resolve a matter if the provisions of this Agreement specify that agreement of the Parties, including consent of each Party, is required for such matter;

5.7.6 in a manner that would require the other Party to perform any act that would cause such Party to violate any Applicable Law or the requirements of any Regulatory Authority, or otherwise breach any of its obligations hereunder;

5.7.7 impose any obligation on either Party that would be in violation of such Party's written standard operating procedures, written business policies, or written compliance policies or procedures; or

5.7.8 otherwise expand the rights or reduce the obligations of either Party under this Agreement.

Article 6. Development

6.1. **Development Diligence**. Subject to Article 8 (Manufacturing and Technology Transfer), NVS will use Commercially Reasonable Efforts to Develop and obtain Marketing Approval for at least [***] Sickle Cell Product in each of the In-Vivo Field and Ex-Vivo Field and for at least [***] Ophthalmic Product that Modulates each Ophthalmic Target.

6.2. **Candidate and Product Development Responsibilities**. Subject to HMI's performance of its Research Activities and HMI's Manufacturing obligations under Article 8 (Manufacturing and Technology Transfer), NVS will [***] at its sole cost and expense (other than HMI's share of the Global In-Vivo SCD Development Costs), the Development of each Candidate and Product.

6.3. **Development Plans**. Within [***] In-Vivo SCD Product, NVS will develop a written development plan setting forth the Development activities for such In-Vivo SCD Product (as such plan may be amended from time-to-time, the "**Development Plan**"). Such Development Plan will include in reasonable detail: (a) the anticipated overall program of Development for the In-Vivo SCD Product, including pre-clinical studies, Clinical Trials, and other material Development activities to be undertaken to achieve Regulatory Approval for such In-Vivo SCD Product, along with any anticipated dates for filing for Regulatory Approvals thereof; and (b) the anticipated costs and expenses associated with those Development activities (the "**Development Budget**"). NVS will submit the initial Development Plan for Development of the In-Vivo SCD Product to the JSC for its review and approval, and NVS will use [***] to consider and implement any reasonable comments received from the JSC on any such initial Development Plan. NVS will update the Development Plan (including the Development Budget therein) on an annual basis (or more frequently as may be determined by NVS or the JSC, as applicable), and submit all material amendments to the Development Plan for review and approval by the JSC. NVS will provide the JSC with a copy of each finalized Development Plan, as amended.

6.4. **Development Reporting**. With respect to each Calendar Year in which NVS conducts any Development activities (a) for any Candidates or any Products other than an In-Vivo SCD Product, NVS will, on or before December 30th of such Calendar Year, provide to HMI (through the JSC) for its review and discussion, [***] report summarizing (i) NVS' and its Affiliates' and Sublicensees' material Development and regulatory activities with respect to each such Product over the prior Calendar Year, and (ii) any planned future Development and regulatory activities, including those activities it anticipates to initiate or have initiated for the following Calendar Year; and (b) for any In-Vivo SCD Products, NVS will, on or before May 31st and December 30th of such Calendar Year, provide to HMI (through the JSC) for its review and discussion, [***] report summarizing (i) NVS' and its Affiliates' and Sublicensees' material Development and regulatory activities with respect to each In-Vivo SCD Product during the prior 6 month period; and (ii) any planned future Development and regulatory activities, including those activities it anticipates to initiate or have initiated during the following 6 month period (each of (a) and (b), a "**Development Report**").

Article 7. Regulatory Affairs.

7.1. **Regulatory Submissions**. From and after the Effective Date, NVS will[***] be responsible for (a) preparing, filing, and submitting, directly or through its Affiliates and permitted Sublicensees, all Regulatory Submissions for all Products in the Territory, and each material amendment or update thereto, in its name other than Jointly-Agreed Regulatory Submissions; and (b) interfacing, corresponding and meeting with Regulatory Authorities relating to Regulatory Submissions in the Territory for such Products; *provided*, that Regulatory Submissions and correspondence made to, and meetings held with, the FDA and EMA with respect to (i) [***] or (ii) [***] in each of (i) and (ii), will be prepared or conducted, as applicable, in collaboration with a representative from HMI's regulatory team in accordance with this Article 7 (Regulatory Affairs); *provided further* that in all cases, such rights shall expressly exclude and not apply with

respect to any data in Regulatory Submissions, correspondence, or meetings relating to any Other Components. Subject to Section 7.6 (Transfer of U.S. BLA for In-Vivo SCD Products), all Regulatory Approvals and Pricing Approvals for Products will be [***] owned by [***]. For all Products, NVS will timely inform HMI regarding the submission, receipt or denial of Regulatory Approval for such Product obtained or denied; *provided*, *however*, that NVS will inform HMI of such event prior to public disclosure of such event by NVS.

7.2. Collaboration With Respect to Regulatory Interactions.

7.2.1 **Correspondence**. The Parties' regulatory teams will collaborate with respect to substantive correspondence in support of (a) that portion of Jointly-Agreed Regulatory Submissions related to any In-Vivo SCD Product; and (b) that portion of Regulatory Submissions related to Manufacturing by HMI or its Designated CMO of Candidates and Products, in the case of each of ((a) and (b)), excluding any portion of such correspondence that contains any data or information relating to any Other Components. In addition, NVS will, in a timely manner, provide HMI with (i) copies of any material written correspondence submitted to or received from Regulatory Authorities with the FDA or EMA, and (ii) summaries of any material oral communications with the FDA or EMA, in each case of (i) and (ii), relating to Regulatory Submissions or Development of any In-Vivo SCD Product with the FDA or EMA, or Regulatory Submissions to the extent relating to the Manufacture of Products by or on behalf of HMI (including its Designated CMO), but excluding in all cases, any portion of such copies or summaries that contain any data or information relating to any Other Components.

7.2.2 **Responsibility**. Notwithstanding Section 7.1 (Regulatory Submissions) or Section 7.2.1 (Correspondence Related to In-Vivo SCD Products), NVS will be responsible for, and will have final decision-making authority on the content of, all Regulatory Submissions, communications, and other dealings with the Regulatory Authorities in the applicable countries in the Territory relating to Development of Candidates and Products other than Jointly-Agreed Regulatory Submissions; *provided* that NVS will consider [***] comments from HMI with respect to any Regulatory Submissions with the Regulatory Authorities to the extent related to the Manufacture of any Product by or on behalf of HMI (including its Designated CMO). The Parties will [***] agree on the content of each Jointly-Agreed Regulatory Submissions for In-Vivo SCD Products excluding any portion of any such submission that relates solely to any data or information relating to any Other Components. Any disagreement between the Parties' regulatory teams with respect to the contents of any such Jointly-Agreed Regulatory Submission that cannot be resolved after good faith efforts will, at the election of either Party, be submitted for resolution to each Party's head of regulatory affairs (each, a "**Regulatory Executive**"). If, after good faith efforts, the Regulatory Executives are unable to resolve any such disagreement within a period of [***], then, at the election of either Party, a Party may refer such matter to the Parties' respective Executive Officers for resolution in accordance with Section 17.1.1 (Escalation). If the Parties' Executive Officers are unable to reach agreement on the content of such Jointly-Agreed Regulatory Submission within a period of [***], then the Regulatory Responsible Party will have final decision-making authority with respect to the content of such Jointly-Agreed Regulatory Submission. At least [***] In-Vivo SCD Product, the Parties' regulatory teams will meet and agree on the strategy and procedures for reviewing, approving, and submitting Jointly-Agreed Regulatory Submissions for In-Vivo SCD Products. For clarity, any review, discussion, and approval rights with respect to Jointly-Agreed Regulatory Submissions shall exclude in all cases, such portions relating to any Other Components.

7.3. **Regulatory Meetings**. NVS will use good faith efforts to invite up to [***] representatives of HMI's regulatory team to attend and act as non-participating observers at any substantive meetings relating to (a) Regulatory Submissions for Development of In-Vivo SCD Products with the FDA or EMA (including the following meetings, to the extent held by NVS: [***], and (b) Regulatory Submissions with respect to Manufacturing by HMI or its Designated CMO of Candidates and Products, in the case of each of (a) and (b), to the extent (i) such meetings are scheduled in advance, (ii) HMI's attendance is not prohibited by Applicable Law or the FDA or EMA; and (iii) such meetings do not involve Other Components. In addition, (A) attendance by HMI representatives will not prevent participation of a NVS representative due to restrictions imposed by the FDA or EMA on the number of attendees; and (B) NVS will not be obligated to change the schedule of such meetings in order to accommodate the schedule of HMI's representatives. HMI will follow NVS' reasonable instructions with respect to any such meeting that it attends, and will not discuss the contents of any such meeting with any Third Party or Regulatory Authority except as required by Applicable Law or authorized by NVS in writing.

7.4. **Rights of Reference; Further Assurances**. NVS hereby grants to HMI a "Right of Reference," as that term is defined in 21 C.F.R. § 314.3(b) and any analogous law, rule, or regulation outside of the U.S., to the data included in any Regulatory Submissions for an In-Vivo SCD Product or a Sickle Cell Product in the Ex-Vivo Field that incorporates the same Candidate as the In-Vivo SCD Product to the extent necessary for HMI's Commercialization of such In-Vivo SCD Product in the U.S. HMI hereby grants to NVS a "Right of Reference," as that term is defined in 21 C.F.R. § 314.3(b) and any analogous law, rule, or regulation outside of the U.S., to any data included in any Regulatory Submission for an In-Vivo SCD Product in the U.S. to the extent necessary for NVS' Development, Manufacturing, or Commercialization of In-Vivo SCD Products outside of the U.S. or Sickle Cell Products in the Ex-Vivo Field incorporating the same Candidate as the In-Vivo SCD Product. The Party granting the right of reference under this Section 7.4 (Rights of Reference; Further Assurances) will execute and deliver, or will cause to be executed and delivered, to the non-granting Party such endorsements, assignments, and other documents as may be reasonably necessary to effect the foregoing right to reference. Such actions may include providing a signed statement that the non-granting Party may rely on, and that the Regulatory Authority may access, in support of the non-granting Party's application for Regulatory Approval or providing any underlying raw data or information submitted by the granting Party to the Regulatory Authority with respect to any Regulatory Submissions or Regulatory Approval Controlled by the granting Party or its Affiliates that relate to In-Vivo SCD Products, in each case, to the extent provided under this Section 7.4 (Rights of Reference; Further Assurances); *provided*, *further*, that in all cases, such right shall expressly exclude any data in Regulatory Submissions or Regulatory Approvals relating to any Other Components.

7.5. **Cooperation**. The Parties will cooperate with each other to achieve the regulatory objectives contemplated herein in a timely, accurate, and responsive manner, including using reasonable efforts to coordinate the regulatory strategy for In-Vivo SCD Products such that it is consistent with the overall objective of facilitating Regulatory Approvals of one or more In-Vivo SCD Products in the U.S. HMI will assist NVS as is reasonably necessary, in order for NVS to obtain and maintain each applicable Marketing Approval for each Product in the Territory, including in connection with the preparation, filing, and submission of all Regulatory Submissions by NVS and as reasonably requested in connection with (a) CMC data and the preparation and filing of Regulatory Submissions related to the Manufacture of the Candidates and Products in the Territory, or (b) any other activities conducted by or on behalf of HMI or its Affiliates under this

Agreement with respect to the Research and Preclinical Development of such Candidates and Products (including with respect to any AAV Candidate Design for a Candidate or Product), including in the case of each of (a) and (b), providing any expert testimony in support thereof with Regulatory Authorities to the extent required in connection with such Regulatory Submissions. Without limiting the generality of the foregoing, if requested by a Regulatory Authority in the Territory in connection with the receipt of any Regulatory Approval for a Product, or if reasonably requested by NVS in connection with any Regulatory Submission for a Product, HMI will communicate with, and provide any available information in HMI's Control regarding the HMI Platform Know-How and HMI Platform Patent Rights to the applicable Regulatory Authority as necessary to obtain Regulatory Approval for such Product from the applicable Regulatory Authority.

7.6. Transfer of U.S. BLA for In-Vivo SCD Products.

7.6.1 **U.S. BLA for In-Vivo SCD Products**. In advance of the anticipated date of receipt of Regulatory Approval for an In-Vivo SCD Product from the FDA in the U.S., the Parties' regulatory teams will meet and agree on process for timely transferring over the BLA for the U.S. SCD Product following receipt of such BLA from FDA along with the necessary dossier for such Product to allow for the prompt Commercialization of such U.S. SCD Product. As soon as reasonably practicable following the date of receipt of Regulatory Approval for an In-Vivo SCD Product from the FDA in the U.S. and in accordance with the mutually agreed timetable for such transfer, which, in any event will be no later than [***] days following the date of receipt of Regulatory Approval for such In-Vivo SCD Product from the FDA in the U.S., NVS will submit a letter or other document informing the FDA that all rights to the BLA filed for such In-Vivo SCD Product have been transferred to HMI (the date of such transfer of the BLA, the "**U.S. BLA Transfer Date**"). NVS will transfer to HMI copies (in electronic or other format) of such BLA and any other Regulatory Submissions owned or Controlled by NVS or its Affiliates as of the U.S. BLA Transfer Date to the extent not already in HMI's or its Affiliates possession that are exclusively related to In-Vivo SCD Products in the U.S., excluding any such data relating to any Other Components (the "**Assigned Regulatory Submissions**") in accordance with the timeline mutually agreed upon by the Parties.

7.6.2 **Ex-Vivo Related Regulatory Submissions**. To the extent that any portion of any Regulatory Submissions Controlled by NVS as of the U.S. BLA Transfer Date relating to the Development, Manufacture, or Commercialization of Sickle Cell Products in the Ex-Vivo Field that incorporate the same Candidate as that in the U.S. SCD Product are necessary for the Commercialization of such U.S. SCD Product, then, after the U.S. BLA Transfer Date, upon HMI's reasonable request and at HMI's expense, but subject to Applicable Law, NVS will provide copies of such portions of such material to HMI (excluding any data in such Regulatory Submissions relating to any Other Components).

7.6.3 **Further Assurances**. HMI will bear all Third Party expenses in connection with the transfer and assignment of all Assigned Regulatory Submissions, and any other copies of Regulatory Submissions provided to HMI pursuant to this Article 7 (Regulatory Affairs). Subject to the terms and conditions of this Agreement, upon HMI's written reasonable request, NVS will execute and deliver, or will cause to be executed and delivered, to HMI such endorsements, assignments and other documents as may be reasonably necessary to assign, convey, transfer, and deliver

to HMI all of NVS' rights, title, and interests in and to the Assigned Regulatory Submissions, including submitting to the FDA a letter or other necessary documentation (with copy to HMI) notifying the FDA of the transfer of ownership of each Assigned Regulatory Submission assigned to HMI pursuant to Section 7.6.1 (U.S. BLA for In-Vivo SCD Products).

7.7. **Pharmacovigilance Agreement**. The Parties will cooperate with regard to the reporting and handling of safety information, including Adverse Events, involving In-Vivo SCD Products in accordance with Applicable Law on pharmacovigilance and clinical safety. Following the Effective Date but prior to the U.S. BLA Transfer Date and within such time to ensure that all regulatory requirements are met, the Parties will negotiate in good faith and execute a pharmacovigilance agreement on reasonable terms that will define the pharmacovigilance responsibilities of the Parties and safety data exchange procedures between the Parties to enable each Party to comply with all of its respective legal and regulatory obligations relating to In-Vivo SCD Products, including safety data exchange procedures for information relating to (a) Sickle Cell Products in the Ex-Vivo Field that incorporate the same Candidate as the In-Vivo SCD Product and (b) other Products manufactured using the HMI Platform Technology, to the extent reasonably likely to impact the safety of any Product (the "**Pharmacovigilance Agreement**"); it being understood that NVS will take the lead for safety and hold the global safety database on behalf of both Parties for each In-Vivo SCD Product while such Product is being Developed.

7.8. **Clinical Trial Holds; Recalls**.

7.8.1 **Clinical Trial Holds**. NVS will timely inform HMI in the event that any Clinical Trial for an In-Vivo SCD Product is suspended, put on hold, or terminated in its respective Territory prior to completion as a result of any action by a Regulatory Authority or by NVS voluntarily.

7.8.2 **Recalls**. Each Party will timely notify the other Party upon its determination that any event, incident, or circumstance has occurred that may result in the need for a recall, market withdrawal, or stock recovery of any In-Vivo SCD Product in accordance with the timelines agreed to in the applicable supply agreement or Quality Agreement. For all recalls of In-Vivo SCD Products, the Parties will reasonably consult with each other with respect to the actions to be taken to address such recall, market withdrawal, or stock recovery, [***], and [***]. Subject to the foregoing, and the terms set forth in any manufacturing, supply, quality, or pharmacovigilance agreement (including the Pharmacovigilance Agreement) between the Parties, (a) for all recalls, market withdrawals, and stock recoveries that are taken in the U.S. with respect to any In-Vivo SCD Product, so long as HMI is the Commercializing Party for such In-Vivo SCD Product in the U.S., HMI will be responsible for execution at its cost and expense, and NVS will take such actions as reasonably requested by HMI at HMI's cost in connection therewith and otherwise reasonably cooperate in all such efforts, and (b) for all other recalls, market withdrawals, and stock recoveries with respect to any In-Vivo SCD Product, NVS will be responsible for execution at its cost and expense, and HMI will take such actions as reasonably requested by NVS in connection therewith and otherwise reasonably cooperate in all such efforts at NVS' cost. All [***] incurred by the Commercializing Party in connection with any recall, market withdrawal, or stock recovery for any In-Vivo SCD Product in the U.S. (including expenses for notification, destruction, and return of the affected In-Vivo SCD Product and any refund to customers of amounts paid for such In-Vivo SCD Product) will be a [***].

Article 8. Manufacturing and Technology Transfer

8.1. Manufacturing Responsibilities.

8.1.1 **HMI Responsibilities**. Subject to the oversight of the JSC or JMC, as applicable, HMI will be responsible for Manufacturing: (a) Candidates for each Target for Research Activities in accordance with the applicable Target Research Plan; and (b) subject to Sections 8.1.3 (Objective Criteria) and 8.6.1 (Manufacturing Related Rights), Candidates and Products in accordance with the Development Supply Agreement(s), Commercial Supply Agreement(s), and applicable Quality Agreements, as applicable. For clarity, with respect to any Products in the Ex-Vivo Field, HMI's responsibility for Manufacturing such Products will be limited to Manufacturing of the applicable Candidate for such Product.

8.1.2 **Transfer of HMI Manufacturing Responsibilities**.

(a) As part of the Parties' negotiations of each of the Development Supply Agreement(s), Development Quality Assurance Agreement(s), Commercial Supply Agreement(s), or Commercial Quality Assurance Agreement(s), as applicable to a Candidate or Product, if [***] determines, based on those criteria set out in Section 8.1.3 below (Objective Criteria), that [***] (i) [***] or (ii) [***], then (A) subject to Section 8.1.3 (Objective Criteria) and the JMC's approval or the Executive Officer's agreement (or, in the event of any disagreement by the JMC and the Executive Officers as to whether the Objective Criteria have been met, the determination by the arbitrators that such Objective Criteria have not been met in accordance with Section 8.1.4 (Dispute Resolution)), HMI will contract with and transfer Manufacturing for such Candidate or Product to that Designated CMO agreed upon by the Parties; and (B) [***]. In HMI's agreement with each applicable Designated CMO, HMI shall ensure that (1) NVS has the same rights in respect of the Designated CMO that NVS has under Section 8.6.1 (Manufacturing Related Rights), (2) NVS is a Third Party beneficiary to all such agreements with the right to enforce provisions contained therein, and (3) NVS is permitted to order such Candidate or Product directly from the Designated CMO pursuant to the terms of such HMI-Designated CMO agreement.

(b) In the event that NVS reasonably determines, based on those criteria set out in Section 8.1.3 (Objective Criteria) below, that the available Designated CMOs are unable to Manufacture or supply such Candidate or Product (i) [***] or (ii) [***], then (A) the NVS Manufacturing Date shall be deemed to occur with respect to such Candidate or Product; and (B) NVS shall be entitled to Manufacture such Candidate or Product, as applicable, itself. Notwithstanding NVS' right to Manufacture Candidates and Products itself commencing on the NVS Manufacturing Date, NVS shall also be entitled, where the Parties have agreed that a Designated CMO is capable of Manufacturing or supplying such Candidate or Product and such Designated CMO becomes able to Manufacture or supply such Candidate or Product (1) [***] or (2) [***] to have such Candidate and Product Manufactured by such alternative Designated CMO.

8.1.3 **Objective Criteria**. As part of the Parties' negotiations of the Development Supply Agreement, Development Quality Assurance Agreement, Commercial Supply Agreement, or Commercial Quality Assurance Agreement, as applicable to such Candidate or Product, the Parties will jointly define a set of criteria that will be used to determine whether HMI or the applicable Designated CMO is able to Manufacture or supply such Candidate or Product (i) [***] or (ii) [***] (the "**Objective Criteria**"), which Objective Criteria will include the following listed criteria (as applicable, based on the phase of Development or Commercialization of such Candidate or Product):

(a) whether HMI or the Designated CMO has [***] to Manufacture such Candidate or Product so as to meet: (i) [***]; (ii) [***]; and (iii) [***];

(b) whether HMI or the Designated CMO has [***] to Manufacture such Candidate or Product so that they will be [***] in materials, ingredients, workmanship, appearance and finish;

(c) whether HMI or the Designated CMO has [***] to Manufacture such Candidate or Product in accordance with all applicable authorizations;

(d) whether the Manufacturing site (i) has (or is capable of obtaining [***]) all permits, licenses, equipment, approvals, and other authorizations that are required under Applicable Law relating to the performance of Manufacturing and the provision of such Candidate and Product; (ii) has received (or is capable of obtaining [***]) approval to Manufacture Candidates and Products by the applicable Regulatory Authorities; and (iii) has been subject to any warning letters or other regulatory actions; and

(e) whether HMI or the Designated CMOs have [***] to supply, and the quantities to be Manufactured and supplied are likely to be capable of meeting [***] requirements.

8.1.4 **Dispute Resolution**.

(a) If the Parties are unable to agree upon the terms of any Development Supply Agreement, Development Quality Assurance Agreement, Commercial Supply Agreement, or Commercial Quality Assurance Agreement, as applicable, then neither Party will be obligated to enter into any such agreement with respect to which the Parties fail to reach agreement and HMI will not be obligated to Manufacture Candidates and Products under the Development Supply Agreement (if the Parties fail to reach agreement on the terms of the Development Supply Agreement or the Development Quality Assurance Agreement) or the Commercial Supply Agreement (if the Parties fail to reach agreement on the terms of the Commercial Supply Agreement or the Commercial Quality Assurance Agreement), as applicable, until the Parties reach agreement on the terms of the applicable agreements.

(b) Any dispute between the Parties as to whether the Objective Criteria have been met shall first be discussed by the representatives of HMI and NVS at the JMC, and if the JMC, after the use of good faith efforts, is unable to agree on or resolve such disputed terms within a period of [***] after discussing such issue (or such longer period as the JMC may agree), then the Parties shall submit the issue(s) in dispute to each Party's respective Executive Officer. If the Executive

Officers are unable to agree on or resolve such issue within a period of [***] after discussing such issue, then the Parties shall submit the issues for Arbitration in accordance with Section 17.1.2 (Full Arbitration); *provided*, that the arbitrators selected will have the technical expertise, experience, and capability to impartially resolve disputes with respect to AAV manufacturing and supply and quality matters, including whether the Manufacture or supply of such Candidates and Products provided hereunder meet the Objective Criteria.

8.2. **Manufacturing Costs**. During the period that HMI is responsible for Manufacturing any Candidate or Product, NVS will be responsible for the documented Manufacturing Costs actually incurred by HMI directly in connection with the Manufacture and supply of such Candidate and Product in accordance with the Research Plans, Development Supply Agreement(s), and Commercial Supply Agreement(s), as applicable; *provided*, *further*, that: (a) Manufacturing Costs for Candidates shall (i) continue until the end of [***], (ii) be set forth in the applicable JSC approved Research Budget, and (iii) be subject to the [***]; (b) Candidates and Products Manufactured and supplied pursuant to the applicable Development Supply Agreement shall be supplied to NVS at a transfer price equal to [***]; and (c) Candidates and Products Manufactured for Pivotal Clinical Trials and Commercialization activities and supplied pursuant to the Commercial Supply Agreement shall be supplied to NVS at a transfer price equal to [***].

8.3. **Development Supply Agreement**. At such time as directed by the JMC following identification of any Candidates and Products and subject to the oversight of the JMC, the Parties will negotiate in good faith a definitive supply agreement for HMI to Manufacture and supply Candidates and Products to NVS for use in conducting Preclinical Development and Clinical Development of such Candidates and Products until the completion of the Phase I/II Clinical Trial for Candidates and Products that Modulate such Target in accordance with this Agreement ("**Development Supply Agreement(s)**") along with the associated Development Quality Assurance Agreement (which Development Quality Assurance Agreement will contain terms related to HMI's rights and obligations as the Manufacturer of such Product(s) as well as terms related to NVS' rights and obligations as the Regulatory Responsible Party for such Product(s), including each Party's respective review, comment, and approval rights thereunder). The Development Supply Agreement and the Development Quality Assurance Agreement will provide for customary terms and conditions, including quality requirements, those provisions required under Sections 8.1.3 (Objective Criteria) and 8.6.1 (Manufacturing Related Rights), forecasting, ordering, delivery, technical criteria to be met, payment, and supply, in accordance with the terms of this Agreement.

8.4. **Commercial Supply Agreement**. Provided that HMI is still Manufacturing Candidates and Products under the applicable Development Supply Agreement and Development Quality Assurance Agreement, at such time as directed by the JMC prior to the Initiation of the first Pivotal Clinical Trial for such Target, the Parties will negotiate in good faith the terms of a new supply agreement for Candidates and Products ("**Commercial Supply Agreement(s)**"), along with the associated Commercial Quality Assurance Agreement(s) to cover supply of Candidates and Products for the Pivotal Clinical Trial, Product launch, and NVS' Commercialization requirements (which Commercial Quality Assurance Agreement will contain terms related to HMI's rights and obligations as the Manufacturer of such Product(s) as well as terms related to NVS' rights and obligations as the Regulatory Responsible Party for such Product(s), including each Party's respective review, comment, and approval rights thereunder). The Commercial Supply Agreement and Commercial Quality Assurance Agreement will provide for customary terms and conditions, including quality requirements, those provisions required under Sections 8.1.3 (Objective Criteria) and 8.6.1 (Manufacturing Related Rights), forecasting, ordering, delivery, technical requirements and criteria to be met, payment, and supply and will be consistent with the terms of this Agreement, [***].

8.5. **In-Vivo SCD Commercial Supply Agreement**. If (a) NVS is Manufacturing such In-Vivo SCD Product for use outside the U.S. and (b) no Designated CMO is, at such time, able to (or within a timely manner would be capable of) Manufacture and supply such In-Vivo SCD Products, then at HMI's request and at the appropriate time directed by the JMC, the Parties will negotiate in good faith a definitive supply agreement for NVS to supply to HMI In-Vivo SCD Products for Commercialization in the U.S. in accordance with this Agreement ("**In-Vivo SCD Commercial Supply Agreement**") along with a quality assurance agreement covering quality related obligations of such supply ("**In-Vivo SCD Quality Assurance Agreement**") (which In-Vivo SCD Quality Assurance Agreement will contain terms related to NVS' rights and obligations as the Manufacturer of such In-Vivo SCD Product as well as terms related to each Party's rights and obligations as the Regulatory Responsible Party for such In-Vivo SCD Product, including each Party's respective review, comment, and approval rights thereunder). The In-Vivo SCD Commercial Supply Agreement and In-Vivo SCD Quality Assurance Agreement will provide for customary terms and conditions, including forecasting, ordering, delivery, manufacturing costs, termination at will rights for both Parties with reasonable advance notice periods, reasonable volume caps with a mechanism to address adjustments to such cap over time, technical criteria to be met, payment, and supply, and will be consistent with the terms of this Agreement. The transfer price paid by HMI for In-Vivo SCD Products under the In-Vivo SCD Commercial Supply Agreement shall be equal to [***]. If the Parties are unable to agree upon the terms of the In-Vivo SCD Commercial Supply Agreement, then neither Party will be obligated to enter into such agreement, and NVS will not be obligated to Manufacture In-Vivo SCD Products under the In-Vivo SCD Commercial Supply Agreement until the Parties reach agreement on the terms of such agreement.

8.6. **Manufacturing Know-How Transfer and Technology Transfer**.

8.6.1 **Manufacturing Related Rights**. Commencing upon NVS' commencement of Preclinical Development of a Candidate or Product, HMI will grant, or in the case of any Designated CMO, shall procure the granting, to the NVS CMC Sub-Team or NVS Audit Team, as applicable, the rights below for the purposes of enabling NVS to comply fully with its regulatory and quality obligations in relation to such Candidate or Product Manufactured by HMI or a Designated CMO, including the release of such Candidate and Product:

(a) access to all information relating to HMI Manufacturing Know-How with respect to such Candidate and Product, including the Manufacturing process for such Candidate or Product and access to CMC data for such Candidates and Products (*i.e.*, cell line history, vector sequences, media composition, summary of animal derived material used during the course of technical Research and Development, details about Manufacturing process and analytical methods applied or under Development, etc.);

(b) a right (either itself or through an authorized representative), pursuant to the audit right provided under Section 8.7 below (Audit and Inspection), to inspect and audit any facility in which such Candidate or Product is Manufactured with advance reasonable notice, which inspection or audit shall not occur more than once per Calendar Year per Manufacturing facility, subject to any for-cause audits or any follow-up audit required to ensure compliance with prior audit findings;

(c) a right to approve any Designated CMO used by HMI for the Manufacture of such Candidate or Product;

(d) a right to access records regarding the selection and engagement of any Third Party supplier of any materials, components, excipients, or processing aids necessary for the Manufacture of such Candidate or Product, including traceability requirements to ensure compliance under pedigree requirements; and

(e) access to any other relevant information or materials [***] to satisfy its regulatory or other quality related obligations with respect to such Candidate or Product, including access to and inspection and audit rights for any Third Party subcontractors or suppliers, each as mutually agreed upon in the applicable Development Supply Agreement, Commercial Supply Agreement, or Quality Agreement.

Thereafter, on a continuing basis during the Term, HMI shall [***], and at a minimum no less frequently than on a [***] basis, disclose to the NVS CMC Sub-Team all additional HMI Product Know-How relating to such Candidate or Product that comes into existence from time to time. Subject to Section 13.1.3 (Exceptions to Confidentiality), the NVS CMC Sub-Team and NVS Audit Team will not disclose any HMI Manufacturing Know-How to other personnel of NVS or its Affiliates; *provided*, that the foregoing shall not apply to any [***] of NVS or its Affiliates where the information received is of a general nature regarding the progress of the Development, Manufacturing, or Commercialization activities of any Candidate or Product and does not disclose specific technical information contained within such HMI Manufacturing Know-How. HMI will provide reasonable assistance to NVS, at NVS' expense, in connection with understanding and using all such HMI Product Know-How to Manufacture Candidates and Products in accordance with the licenses and rights granted to NVS pursuant to this Agreement.

8.6.2 **Manufacturing Technology Transfer to NVS**. On or after the NVS Manufacturing Date, HMI will make available to NVS all additional HMI Know-How [***] to enable NVS or its Affiliates to Manufacture the applicable Candidate and Product that NVS has the right to Manufacture pursuant to this Agreement (the "**HMI Manufacturing Know-How**"), including by providing copies or samples of relevant documentation, HMI Materials, and other embodiments of such HMI Manufacturing Know-How. Without limiting the foregoing, the transfer shall include (a) transferring copies of technical documentation, specifications, patents and procedures, and tangible embodiments of the HMI Manufacturing Know-How; (b) providing access to a sufficient number of qualified scientists, production and quality assurance personnel and engineers, as well as quality control personnel; (c) allowing reasonable access to the Manufacturing sites, Designated CMO's and Affiliates involved in the Manufacture and Development of the applicable Candidates and Products; and (d) any other support or training reasonably requested by NVS to facilitate such transfer. Any HMI Materials provided by HMI in connection with the transfer of the HMI Manufacturing Know-How will remain the sole property of HMI. NVS will (i) use such HMI Materials only in the fulfillment of obligations or exercise of rights under this Agreement, and (ii) not use such HMI Manufacturing Know-How or HMI Materials or deliver the same to any Third Party, other than Designated CMOs or Third Party sub-contractors or permitted

Sublicensees used in connection with Manufacturing, without HMI's prior written consent, not to be unreasonably withheld, conditioned, or delayed. Each Party will bear its own Internal Costs in connection with such transfer support, *provided* that NVS will reimburse HMI those actual documented and agreed upon Internal Costs incurred by HMI in connection with any HMI Manufacturing Know-How transfer support requested by NVS that exceed the number of hours of transfer support approved by the JMC. NVS will be responsible for any reasonable documented Third Party expenses incurred by either Party in connection with the requested HMI Manufacturing Know-How transfer. HMI will invoice NVS for its Internal Costs incurred under this Section 8.6.2 (Manufacturing Technology Transfer to NVS), which Internal Costs NVS is responsible for paying no later than [***] after the conclusion of each Calendar Quarter, and NVS will pay to HMI the undisputed amount set forth in such invoice within [***] of NVS' receipt of such invoice.

8.7. **Audit and Inspection**. Where HMI is Manufacturing, HMI grants NVS, and where a Designated CMO is Manufacturing, HMI will secure for NVS the right, upon execution of the Designated CMO's standard site visit confidentiality agreement and other customary protections to protect the confidentiality of any visible Third Party confidential information, in each case, at reasonable times (but not to exceed [***] audit per site per Calendar Year except with respect to any for-cause audits or any follow-up audit required to ensure compliance with prior audit findings), with reasonable prior written notice, and for a reasonable period of time, to inspect HMI's or such Designated CMO's production facilities to (a) perform a pre-qualification audit, (b) confirm HMI's or such Designated CMO's or such Third Party's compliance with cGMP, NVS Quality Requirements, the applicable specifications, and Applicable Law, and (c) review relevant Manufacturing records with respect to Candidates and Products, in each case, in accordance with the Development Quality Assurance Agreement or Commercial Quality Assurance Agreement, as applicable. Unless otherwise agreed by the Parties, NVS will have the right to have up to [***] NVS representatives of the NVS Audit Team at any such audit or inspection and any such audit must take place in the presence of HMI personnel. If NVS observes a condition [***] that any Candidates or Products are not being Manufactured in accordance with cGMP, NVS Quality Requirements, or the applicable specifications or Applicable Law, then the Parties will discuss and agree on any appropriate corrective actions to address such non-compliance, and HMI will and will cause the Designated CMO to implement any such corrective action, in each case, in accordance with the Development Quality Assurance Agreement or Commercial Quality Assurance Agreement, as applicable. If any Regulatory Authority or any other Governmental Authority conducts or gives notice of its intent to conduct any audit or inspection at any offices or facilities (including Manufacturing facilities) of HMI or any Designated CMO where such audit or inspection relates to any Candidates or Products, then HMI will [***] give notice thereof to NVS and, to the extent such audit or inspection relates to a Candidate or Product and to the extent practicable and not prohibited by Applicable Law, secure for NVS through the NVS CMC Sub-Team or the NVS Audit Team, in NVS' discretion, the right to participate in any such audit or inspection. HMI shall ensure that all such rights set forth in this Section 8.7 (Audit and Inspection) apply to those Third Party subcontractors and suppliers as agreed upon by the Parties in the applicable Development Quality Assurance Agreement or Commercial Quality Assurance Agreement.

8.8. **Additional Obligations**. Product sold in the United States will be manufactured substantially in the United States to the extent required by 35 U.S.C. §§ 200-212 with respect to HMI Patent Rights licensed to HMI by any Third Party licensors.

Article 9. Medical Affairs

9.1. **Medical Affairs Plans**. NVS will prepare a reasonably detailed, annual plan for global Medical Affairs with respect to In-Vivo SCD Products (the "**Global Medical Affairs Plan**"), and HMI will prepare a reasonably detailed, annual plan for Medical Affairs with respect to In-Vivo SCD Products in the U.S. (the "**U.S. Medical Affairs Plan**"), in each case, no later than [***] or an In-Vivo SCD Product. The strategic objectives in the U.S. Medical Affairs Plan will be consistent with the strategic objectives in the Global Medical Affairs Plan, unless otherwise agreed by the Parties. In order to ensure consistency between the Global Medical Affairs Plan and the U.S. Medical Affairs Plan and coordination and alignment between the Parties with respect to the Medical Affairs to be conducted by NVS with respect to In-Vivo SCD Products pursuant to the Global Medical Affairs Plan and by HMI with respect to U.S. SCD Products pursuant to the U.S. Medical Affairs Plan (including with respect to each Party's communications with key opinion leaders in the Territory), the Global Medical Affairs Plan and the U.S. Medical Affairs Plan, and any material amendments or updates thereto will be reviewed and discussed by the JSC, with the first such review and discussion occurring no later than [***] for an In-Vivo SCD Product. Any subsequent review and discussion, to the extent required, will occur annually thereafter at an appropriate time as agreed by the JSC, or more frequently as may be required during the Term.

9.2. **Medical Affairs Activities**. HMI will be responsible for Medical Affairs with respect to In-Vivo SCD Products in the U.S., and will conduct such activities in accordance with the U.S. Medical Affairs Plan; and NVS will be responsible for Medical Affairs with respect to In-Vivo SCD Products outside of the U.S., and will conduct such activities in accordance with the Global Medical Affairs Plan. NVS will also be responsible for Medical Affairs with respect to all NVS Products throughout the Territory. Each Party will (a) conduct all Medical Affairs in a professional and ethical business manner and in compliance with Applicable Law and applicable Professional Requirements; (b) provide the other Party with reasonable cooperation, support, and assistance with respect to preparing such Party's Medical Affairs plan, and conducting activities under each such plan, in order to coordinate Medical Affairs with respect to In-Vivo SCD Products throughout the Territory, at the requesting Party's cost and expense; and (c) provide updates (through the JSC) summarizing its Medical Affairs with respect to In-Vivo SCD Products and progress under the Global Medical Affairs Plan (with respect to NVS) and the U.S. Medical Affairs Plan (with respect to HMI) during the period since the last JSC meeting.

Article 10. Commercialization

10.1. **Commercialization Responsibilities**.

10.1.1 **Of NVS**. During the Term, subject to Article 8 (Manufacturing and Technology Transfer), NVS will be solely responsible, at its cost and expense, for Commercializing all NVS Products in the Territory (including booking all sales for such products).

10.1.2 **Of HMI**. During the Term, so long as HMI is the Commercializing Party for the U.S. SCD Products and subject to Article 8 (Manufacturing and Technology Transfer), HMI will be solely responsible, at its cost and expense, for Commercializing all In-Vivo SCD Products in the U.S. (including booking all sales for such In-Vivo SCD Products in the U.S.).

10.2. Commercialization Diligence Obligations.

10.2.1 **Of NVS**. During the Term, subject to Article 8 (Manufacturing and Technology Transfer), NVS will [***] Commercialize each NVS Product in the Territory for which Marketing Approval has been obtained.

10.2.2 **Of HMI**. During the Term, so long as HMI is the Commercializing Party for the U.S. SCD Product and subject to Article 8 (Manufacturing and Technology Transfer), HMI will [***] Commercialize each In-Vivo SCD Product in the U.S. following the receipt of Marketing Approval from the FDA in the U.S. for such In-Vivo SCD Product.

10.3. Commercialization Plans.

10.3.1 **In-Vivo SCD Commercialization Plans**. Subject to Applicable Law, NVS will prepare and provide to HMI (through the JSC): (a) an initial high-level summary of the anticipated Commercialization strategy and activities to be conducted for an In-Vivo SCD Product; and (b) an associated budget, no later than [***] for such In-Vivo SCD Product. In addition, NVS will prepare and provide to the JSC a Commercialization plan for each In-Vivo SCD Product that contemplates the commercial launch of, and the Commercialization activities to be taken in the first [***] after the First Commercial Sale of, such In-Vivo SCD Product in the Territory excluding the U.S. if HMI is the Commercializing Party and including the U.S. if NVS is the Commercializing Party (the "**Global In-Vivo SCD Commercialization Plan**"). If HMI is the Commercializing Party, then HMI will prepare and provide to the JSC a Commercialization plan for each In-Vivo SCD Product that contemplates the commercial launch of, and the Commercialization activities to be taken in the first [***] after the First Commercial Sale of, such In-Vivo SCD Product in the U.S. (the "**U.S. In-Vivo SCD Commercialization Plan**"). If HMI is the Commercializing Party, then each Party will provide the applicable Commercialization plan to the other Party no later than [***] such In-Vivo SCD Product in such Party's territory. Subject to Applicable Law, (i) the strategic objectives and activities in the U.S. In-Vivo SCD Commercialization Plan will be consistent with the strategic objectives and activities in the Global In-Vivo SCD Commercialization Plan, unless otherwise agreed by the Parties; and (ii) the Global In-Vivo SCD Commercialization Plan and the U.S. In-Vivo SCD Commercialization Plan will each be reviewed, discussed, and approved by the JSC. Thereafter, at least once each [***], NVS will submit an updated Global In-Vivo SCD Commercialization Plan for each In-Vivo SCD Product, and HMI will submit an updated U.S. In-Vivo SCD Commercialization Plan, in each case, to the JSC for review, discussion, and approval.

10.3.2 **In-Vivo SCD Commercialization Activities**. Each Party will provide the other Party with reasonable cooperation, support, and assistance requested by the other Party, at the requesting Party's expense, with respect to preparing such Party's Commercialization plan for In-Vivo SCD Products in order to coordinate Commercialization with respect to such In-Vivo SCD Products throughout the Territory; *provided*, that any such cooperation, support, and assistance shall be limited to that permitted under Applicable Law.

10.4. Reimbursement. The Commercializing Party will be responsible for, and will have sole authority and the final decision-making right with respect to, any payor and pricing studies related to obtaining and maintaining Pricing Approval in each country in its respective Territory (where required), and all submissions, communications, meetings, and other dealings with

Governmental Authorities, payors, and other Third Parties relating to pricing and reimbursement of In-Vivo SCD Products in such Commercializing Party's territory. Notwithstanding the foregoing, in the U.S., upon the non-Commercializing Party's reasonable request, the Commercializing Party will allow a representative from the non-Commercializing Party to attend meetings with such Governmental Authorities, payors, and other Third Parties relating to pricing and reimbursement of In-Vivo SCD Products in the U.S. (unless prohibited by Applicable Law, or the applicable Governmental Authorities, payors, or other Third Party and excluding in all cases, that portion involving communications involving Other Components). In addition, so long as HMI is the Commercializing Party for In-Vivo SCD Products in the U.S. and there has not been an HMI Change of Control, upon HMI's request, NVS will consent to allow a representative from HMI to attend meetings with Governmental Authorities, payors, and other Third Parties relating to pricing and reimbursement for In-Vivo SCD Products in Canada and the EU, such NVS consent not to be unreasonably withheld, conditioned, or delayed (unless prohibited by Applicable Law, or the applicable Governmental Authorities, payors, or other Third Party and excluding in all cases, that portion involving communications involving Other Components). If a non-Commercializing Party is not allowed to attend any such meeting in the U.S., then the Commercializing Party will provide the other Party with an update summarizing such meeting reasonably promptly after such meeting. Upon either Party's reasonable request, but subject to local anti-competition laws and any obligations of confidentiality between a Party and any Third Party, the Parties will share key market research and relevant sections of national reimbursement dossiers (or their equivalent) for In-Vivo SCD Products, as well as other relevant Commercialization information as may be agreed by the Parties.

10.5. Commercialization Reporting.

10.5.1 **NVS Obligations**. On or before May 31st and December 30th of each Calendar Year in which NVS conducts any Commercialization activities for any NVS Product, NVS will provide to the JSC for its review and discussion a summary of the material Commercialization activities it has, or its Affiliates or Sublicensees have, performed, or caused to be performed, since the preceding report, and the future activities it expects to initiate with respect to any NVS Product for the following [***].

10.5.2 **HMI Obligations**. On or before May 31st and December 30th of each Calendar Year in which HMI conducts any Commercialization activities for any In-Vivo SCD Product in the U.S., HMI will provide to the JSC for its review and discussion a summary of the material Commercialization activities it has, or its Affiliates have, performed since the preceding report, and the future activities it expects to initiate with respect to any In-Vivo SCD Product in the U.S. for the following [***].

10.6. Global Brand Plan and Promotional Materials for In-Vivo SCD Products. No later than [***] months [***] the first In-Vivo SCD Product, NVS will submit to the JSC for review and discussion a global brand plan, which plan will include the global key positioning and global messaging strategy for such In-Vivo SCD Product (the "**Global Brand Plan**"). NVS may amend or update the Global Brand Plan from time-to-time and will submit material amendments and updates to the JSC for review and discussion. All promotional materials for any In-Vivo SCD Product used by HMI or its Affiliates in the U.S. must be consistent with the Global Brand Plan, unless the JSC develops and approves a Territory-specific brand strategy for such In-Vivo SCD Product in the U.S., including any positioning or key messaging for such In-Vivo SCD Product in the U.S. that is inconsistent with the Global Brand Plan. With respect to any such Territory-specific brand strategy that is either approved by the JSC or HMI or NVS, as applicable, pursuant to Section 5.6.3 (Escalation), in each case, HMI will implement such Territory-specific brand

strategy in lieu of the applicable strategy under the Global Brand Plan for In-Vivo SCD Products in the U.S. If HMI seeks to use any promotional materials for any In-Vivo SCD Product that have content or messaging that is inconsistent with the Global Brand Plan or any Territory-specific brand strategy, then, in each case, HMI will obtain NVS' prior written approval with respect to such materials prior to HMI's use thereof. Upon NVS' reasonable request, HMI will provide samples of HMI's promotional materials for the U.S. for NVS' review to determine consistency with the Global Brand Plan or any Territory-specific brand strategy, and other content or format approved by NVS. Upon HMI's reasonable request, NVS will provide to HMI samples of NVS' core promotional materials for In-Vivo SCD Products outside the U.S.

10.7. Trademarks and International Nonproprietary Name.

10.7.1 **NVS Product Trademarks**. NVS will have the right, in its sole discretion, to select all Trademarks to be used in connection with each NVS Product to be sold by NVS, and to design and produce any and all promotional materials for each such NVS Product, including package inserts, data sheets, leaflets, advertisements, and labeling. HMI will have the right to use any Product Trademarks selected by NVS on HMI's websites and corporate communications for the purpose of promoting HMI's association with NVS under this Agreement with NVS' prior written consent, not to be unreasonably withheld, conditioned, or delayed and in accordance with any Trademark usage guidelines provided by NVS.

10.7.2 **Trademarks for In-Vivo SCD Products**. NVS, in collaboration with HMI, will select, and submit to the JSC for its review and discussion, the global brand name for each In-Vivo SCD Product and the applicable Trademarks for use in the Territory. HMI will Commercialize each In-Vivo SCD Product in the U.S. under the Global Trademarks using the global brand name for such In-Vivo SCD Product selected by NVS in the Global Brand Plan and under the trade dress set forth in the Global Brand Plan, unless HMI reasonably believes that the use or registration of any Global Trademark in the U.S. (a) would be inappropriate due to the linguistic or cultural particularities in the U.S. or would violate Applicable Law in the U.S., (b) is reasonably likely to be rejected by the FDA, or (c) is in conflict with any Third Party's Intellectual Property Rights in the U.S. If HMI is unable to use any Global Trademark for any of the foregoing reasons ((a) through (c)), then HMI will use one of the alternative Trademarks (which Trademarks will include trademarks and trade dress) for In-Vivo SCD Products in the U.S. selected by NVS in the Global Brand Plan, or if such alternative Trademarks are unacceptable for the reasons set forth in the preceding sentence, then HMI will use other Trademarks (including trademarks and trade dress) to be agreed upon by HMI and NVS (the "**Local Trademarks**"). HMI will own all such Local Trademarks, including all trademark registrations and applications therefor and all goodwill associated therewith. Once the brand name for an In-Vivo SCD Product has been selected for a country in the Territory pursuant to this Section 10.7.2 (Trademarks for In-Vivo SCD Products), NVS will be responsible for obtaining Regulatory Approval of such brand name for use in the Commercialization of such In-Vivo SCD Product in the U.S. HMI will Commercialize In-Vivo SCD Products in the U.S. only under the applicable Product Trademarks for such In-Vivo SCD Product and HMI's Housemarks, and no other Trademarks (*provided*, that NVS Housemarks may be included with NVS' prior written consent).

10.7.3 **Trademark License**. Subject to the terms and conditions of this Agreement, NVS hereby grants and agrees to grant to HMI (a) an exclusive, royalty-free limited license with the right to sublicense to Sublicensees (in accordance with Section 4.3.2 (Development and Commercialization Licenses)) to use the Global Trademark for each In-Vivo SCD Product in the U.S. in accordance with this Agreement, and (b) subject to NVS' prior written consent, not to be unreasonably withheld, conditioned, or delayed, a non-exclusive, royalty-free limited license to use NVS Housemarks, with the right to sublicense to Sublicensees (in accordance with Section 4.3.2 (Development and Commercialization Licenses)), in the case of each of (a) and (b), solely in connection with the Commercialization of the applicable In-Vivo SCD Product in the U.S. in accordance with this Agreement.

10.7.4 **International Non-Proprietary Name**. NVS will, [***], be responsible for the selection and filing of the international nonproprietary name for any Sickle Cell Candidate and In-Vivo SCD Product with the World Health Organization and any Regulatory Authorities in the Territory, to which names HMI will have the right to reference in the U.S. in connection with its Commercialization activities for such In-Vivo SCD Product. NVS will, using Commercially Reasonable Efforts, be responsible for the selection and filing of the international nonproprietary name for each other Candidate and Product with the World Health Organization and any Regulatory Authorities in the Territory.

Article 11. Consideration; Financial Terms

11.1. **Equity Investment**. On the Effective Date, NVS will enter into a separate stock purchase agreement with HMI pursuant to which NVS will make a $10,000,000 equity investment through the sale and issuance to NVS of Series B Preferred Stock of HMI on the same terms as set forth in the Series B Preferred Stock Purchase Agreement dated as of July 28, 2017 by and between the Parties. NVS also made a $5,000,000 equity investment pursuant to the terms set forth in such Series B Preferred Stock Purchase Agreement dated as of July 28, 2017.

11.2. **Upfront Payment**. In partial consideration for the performance by HMI of the Research Activities during the Research Term and in partial consideration for the exclusivity granted in favor of NVS under Section 4.11 (Exclusivity) and the Research License granted to NVS under Section 4.1.1 (Research License), no later than [***] after receipt of an invoice from HMI, which invoice shall be substantially in the form of Exhibit A, NVS will pay to HMI a one-time payment of $35,000,000 in immediately available funds by wire transfer, in accordance with wire instructions to be given by HMI to NVS.

11.3. **Target Fee**. NVS will provide HMI with written notice within [***] of the date of the occurrence of the Target Fee Trigger for a Target (the "**Target Fee Trigger Date**"). Following occurrence of the Target Fee Trigger, HMI will submit an invoice to NVS for the Target Fee. No later than [***] after NVS' receipt of an invoice from HMI for the Target Fee, NVS will pay to HMI a one-time payment of $[***] with respect to the applicable Target (for each Target, a "**Target Fee**") in immediately available funds by wire transfer, in accordance with wire instructions to be given by HMI to NVS. For the avoidance of doubt, the Target Fee shall be payable (a) only once for each Target, regardless of the number of Candidates that meet the applicable Success Criteria for the Target that such Candidate Modulates, and (b) only if the Target Fee Trigger conditions are met.

11.4. **Development Milestones Payments**.

11.4.1 **Ophthalmic Products**.

(a) **Events**. Subject to Section 11.4.4 (Development Milestone Payment Terms), NVS will pay to HMI the corresponding milestone payment set forth in Table 11.4.1 (each an "**Ophthalmic Development Milestone Payment**") upon achievement of each applicable milestone event listed in Table 11.4.1 below (each, an "**Ophthalmic Development Milestone Event**") [***].

Table 11.4.1 – Ophthalmic Development Milestones

	***Ophthalmic Development Milestone Event* [***]**	***Ophthalmic Development Milestone Payment***
1.	[***]	$ [***]
2.	[***] [***]	$ [***]
3.	[***]	$ [***]
4.	[***]	$ [***]
5.	[***]	$ [***]
6.	[***]	$ [***]
7.	[***]	$ [***]
8.	[***]	$ [***]
9.	[***]	$ [***]

(b) **Other Payment Conditions**. Each Ophthalmic Development Milestone Payment shall be payable only on the first occurrence of the applicable Ophthalmic Development Milestone Event for each of the [***] Ophthalmic Targets, and none of the Ophthalmic Development Milestone Payments shall be payable more than once with respect to an Ophthalmic Target, regardless of the number of Ophthalmic Products Developed or Commercialized.

Confidential Portions of this Exhibit marked as [***] have been omitted pursuant to a request for confidential treatment and have been filed separately with the Securities and Exchange Commission.

11.4.2 **Sickle Cell Products in the Ex-Vivo Field**.

(a) **Events**. Subject to Section 11.4.4 (Development Milestone Payment Terms), NVS will pay to HMI the corresponding milestone payment set forth in Table 11.4.2 (each an "**Ex-Vivo Sickle Cell Development Milestone Payment**") upon achievement of each applicable milestone event listed in Table 11.4.2 below (each, an "**Ex-Vivo Sickle Cell Development Milestone Event**") for solely the first Sickle Cell Product in the Ex-Vivo Field that Modulates the Sickle Cell Target.

Table 11.4.2 – Ex-Vivo Sickle Cell Development Milestones

	Ex-Vivo Sickle Cell Development Milestone Event	*Ex-Vivo Sickle Cell Development Milestone Payment*
1.	[***]	$ [***]
2.	[***]	$ [***]
3.	[***]	$ [***]
4.	[***]	$ [***]
5.	[***]	$ [***]
6.	[***]	$ [***]
7.	[***]	$ [***]
8.	[***]	$ [***]
9.	[***]	$ [***]

(b) **Other Payment Conditions**. Each Ex-Vivo Sickle Cell Development Milestone Payment shall be payable only once upon the first occurrence of the applicable Ex-Vivo Sickle Cell Development Milestone Event, and none of the Ex-Vivo Sickle Cell Development Milestone Payments shall be payable more than once, regardless of the number of Sickle Cell Products for the Ex-Vivo Field Developed or Commercialized.

Confidential Portions of this Exhibit marked as Sickle Cell have been omitted pursuant to a request for confidential treatment and have been filed separately with the Securities and Exchange Commission.

11.4.3 **In-Vivo SCD Products**.

(a) **Events**. Subject to Section 11.4.4 (Development Milestone Payment Terms), NVS will pay to HMI the corresponding milestone payment set forth in Table 11.4.3 (each an "**In-Vivo Sickle Cell Development Milestone Payment**") upon achievement of each applicable milestone event listed in Table 11.4.3 below (each, an "**In-Vivo Sickle Cell Development Milestone Event**") for solely the first In-Vivo SCD Product that Modulates the Sickle Cell Target.

Table 11.4.3 – In-Vivo Sickle Cell Development Milestones

	In-Vivo Sickle Cell Development Milestone Event	*In-Vivo Sickle Cell Development Milestone Payment*
1.	[***]	$ [***]
2.	[***] [***]	$ [***]
3.	[***]	$ [***]
4.	[***]	$ [***]
5.	[***]	$ [***]
6.	[***]	$ [***]
7.	[***]	$ [***]
8.	[***]	$ [***]
9.	[***]	$ [***]

(b) **Other Payment Conditions**. Each In-Vivo Sickle Cell Development Milestone Payment shall be payable only once upon the first occurrence of the applicable In-Vivo Sickle Cell Development Milestone Event, and none of the In-Vivo Sickle Cell Development Milestone Payments shall be payable more than once, regardless of the number of In-Vivo SCD Products Developed or Commercialized.

11.4.4 **Development Milestone Payment Terms**.

(a) **Payment Terms.** NVS will notify HMI within [***] after achievement of each Development Milestone Event. After receipt of notice of achievement of such Development Milestone Event, HMI shall submit an invoice to NVS substantially in the form of Exhibit A for the corresponding Development Milestone Payment. NVS will pay to HMI the corresponding milestone payment set forth in the applicable table within [***] of receipt of such invoice.

Confidential Portions of this Exhibit marked as [***] have been omitted pursuant to a request for confidential treatment and have been filed separately with the Securities and Exchange Commission.

(b) **Once Per Target**. If Development of a Product for which a Development Milestone Payment is due is terminated after it achieves a Development Milestone Event, then the Development Milestone Payment will remain due and payable with respect to such terminated Product, but the corresponding Development Milestone Payment will not be due on any subsequent achievement of the same Development Milestone Event by a subsequent Product for such Target.

11.4.5 **Skipped Milestones**. If a Development Milestone Event for a Target is skipped (*i.e.*, a later Development Milestone Event for a Target is payable before the achievement of an earlier Development Milestone Event for such Target), then the Development Milestone Payments for such earlier-listed and skipped Development Milestone Events for such Target will be deemed to have been achieved upon the achievement of the subsequent Development Milestone Event; [***].

11.5. Sales Milestone Payments.

11.5.1 **Ophthalmic Products**. In conjunction with the Royalty Reports, NVS will notify HMI [***] after the end of each Calendar Quarter in which the date on which NVS', its Affiliates', and its Sublicensees' cumulative Net Sales of all Ophthalmic Products for a Target in a given Calendar Year first reach the respective thresholds indicated below in Table 11.5.1 below (each, an "**Ophthalmic Sales Milestone Event**"). Upon receipt of such notice, HMI shall submit an invoice to NVS substantially in the form of Exhibit A for the corresponding one-time milestone payments set forth below in Table 11.5.1 (each, an "**Ophthalmic Sales Milestone Payment**"). NVS will pay to HMI the corresponding Ophthalmic Sales Milestone Payment no later than [***] after receipt of such invoice.

Table 11.5.1 – Ophthalmic Sales Milestones

Ophthalmic Sales Milestone Event	*Ophthalmic Sales Milestone Payment*
1. [***]	$ [***]
2. [***]	$ [***]
3. [***]	$ [***]

For clarity, only Net Sales of Ophthalmic Products that Modulate the applicable Ophthalmic Target shall count towards achievement of the applicable Ophthalmic Sales Milestone Event for such Ophthalmic Target.

11.5.2 **Ex-Vivo Sickle Cell Products**. In conjunction with the Royalty Reports, NVS will notify HMI [***] after the end of each Calendar Quarter in which the date on which NVS', its Affiliates', and its Sublicensees' cumulative Net Sales of all Sickle Cell Products in the Ex-Vivo Field in a given Calendar Year first reach the respective thresholds indicated below in Table 11.5.2 below (each, an "**Ex-Vivo Sickle Cell**

Sales Milestone Event"). Upon receipt of such notice, HMI shall submit an invoice to NVS substantially in the form of Exhibit A for the corresponding one-time milestone payments set forth below in Table 11.5.2 (each, an "**Ex-Vivo Sickle Cell Sales Milestone Payment**"). NVS will pay to HMI the corresponding Ex-Vivo Sickle Cell Sales Milestone Payment no later than [***] after receipt of such invoice.

Table 11.5.2 – Ex-Vivo Sickle Cell Sales Milestones

	Ex-Vivo Sickle Cell Sales Milestone Event	**Ex-Vivo Sickle Cell Sales Milestone Payment**
1.	[***]	$ [***]
2.	[***]	$ [***]
3.	[***]	$ [***]

11.5.3 **In-Vivo SCD Products**. In conjunction with the Royalty Reports, NVS will notify HMI [***] after the end of each Calendar Quarter in which the date on which NVS', its Affiliates', and its Sublicensees' cumulative Net Sales of all In-Vivo SCD Products in all countries in the Territory other than the U.S. in a given Calendar Year first reach the respective thresholds indicated below in Table 11.5.3 below (each, an "**In-Vivo Sickle Cell Sales Milestone Event**"). Upon receipt of such notice, HMI shall submit an invoice to NVS substantially in the form of Exhibit A for the corresponding one-time milestone payments set forth below in Table 11.5.3 (each, an "**In-Vivo Sickle Cell Sales Milestone Payment**"). NVS will pay to HMI the corresponding In-Vivo Sickle Cell Sales Milestone Payment no later than [***] after receipt of such invoice.

Table 11.5.3 – In-Vivo Sickle Cell Sales Milestones

	In-Vivo Sickle Cell Sales Milestone Event	***In-Vivo Sickle Cell Sales Milestone Payment***
1.	[***]	$ [***]
2.	[***]	$ [***]
3.	[***]	$ [***]

11.5.4 **Achievement of Multiple Sales Milestones**. If 2 or more of Sales Milestone Events are achieved in the same Calendar Quarter or the same Calendar Year, then NVS will pay each corresponding Sales Milestone Payments during the Calendar Quarter in which it is achieved, in conjunction with royalty payments due for such Calendar Quarter.

Confidential Portions of this Exhibit marked as [***] have been omitted pursuant to a request for confidential treatment and have been filed separately with the Securities and Exchange Commission.

11.6. Payments for U.S. SCD Products.

11.6.1 **Development Cost Reimbursement to NVS**. Within [***] after each Calendar Quarter during which NVS incurred Global In-Vivo [***] Development Costs, NVS shall provide HMI with a report setting forth the amount of Global In-Vivo [***] Development Costs incurred by or on behalf of NVS in such Calendar Quarter. Subject to Section 11.6.2 ([***]), HMI shall be obligated to reimburse NVS for 30% of such Global In-Vivo [***] Development Costs by payment of such amount to NVS within [***] after receipt of such report.

11.6.2 [***]. With respect to [***] of its [***] related to [***] and, in such case, [***] that would have [***] pursuant to [***] in the absence [***] of such [***] at any [***] and become [***] (a) [***], (b) [***] in the [***], and (c) in accordance with [***], in the event of [***]. In order to [***] with respect to [***] prior to [***] for such [***]. [***] shall be [***] following [***]. In the event [***] with respect to [***], subject to [***] and [*******upon the [***] (i) [***] of such [***] or (ii) [***] with respect to [***] shall be [***] for (A) [***] in the case [***] of such [***] shall be [***]:

(a) in the case of [***] provided above [***] of the [***]; it being [***] for such [***] with respect [***], which shall [***] in accordance with [***] or

(b) in the case of [***] with respect to [***] or any [***] of any [***] in respect of [***]; it being understood that [***] with respect to [***].

11.6.3 **Net Profits**. Subject to Section 16.4 (Effects of Termination for Bankruptcy or HMI's Uncured Material Breach), with respect to each U.S. SCD Product, commencing with the Calendar Quarter in which the First Commercial Sale of such U.S. SCD Product occurs, the Commercializing Party will pay to the non-Commercializing Party an amount equal to 50% of the Net Profit for such U.S. SCD Product for each Calendar Quarter (the "**Profit Share Payments**").

11.6.4 **Net Losses**. The non-Commercializing Party will not be responsible for any Net Losses in a given Calendar Quarter during the Term, and the Commercializing Party may carry forward Net Losses in any Calendar Quarter for deduction from Net Sales in the calculation of Net Profits earned in a subsequent Calendar Quarter.

11.6.5 **Profit Share Reports; Payments**. Within [***] after the end of each Calendar Quarter commencing with the first Calendar Quarter in which any of the amounts set forth in Section 11.6.3 (Net Profits) and Section 11.6.4 (Net Losses) are received or incurred, the Commercializing Party will provide to the other Party a [***] report of (a) the total monthly sales calculation of Net Sales of the U.S. SCD Product, and (b) Commercialization Costs and Manufacturing Costs incurred by the Commercializing Party or its Affiliates and in the case of NVS, Sublicensees, and (c) U.S. SCD Shared IP Costs, in accordance with this Agreement in such Calendar Quarter, which report will be in such form as the Parties may agree from time-to-time (the "**Profit Share Report**"). Without limiting the generality of the foregoing, the Commercializing Party will require its Affiliates and in the case of NVS, Sublicensees, to account for Net Sales and will include their Net Sales in the Profit Share Report as if such sales were made by the Commercializing Party. If no Net Profit is due to the other Party for a given Calendar Quarter, then the applicable Profit Share Report will so state. Concurrently with

the Profit Share Report, the Commercializing Party will make a payment to the other Party of the applicable Profit Share Payment due pursuant to Section 11.6.3 (Net Profits), in each case for such Calendar Quarter. For the avoidance of doubt, no cost or expense will be counted more than once in calculating Manufacturing Costs, Commercialization Costs, or U.S. SCD Shared IP Costs, even if such cost or expense falls into more than one of the cost categories that comprise such costs.

11.7. Royalty Payments.

11.7.1 **Royalty Rates**. In further consideration of the licenses and other rights granted to NVS under this Agreement, during the Royalty Term for a Product in a country (other than for U.S. SCD Products), NVS will pay HMI royalties based on the aggregate Net Sales by NVS, its Affiliates, and its Sublicensees in a Calendar Year of (a) all Ophthalmic Products during the Royalty Term for each such Product in such country at the rates set forth in Table 11.7.1(a) below, (b) all Sickle Cell Products in the Ex-Vivo Field during the Royalty Term for each such Product in such country at the rates set forth in Table 11.7.1(b) below, and (c) all In-Vivo SCD Products outside of the U.S. during the Royalty Term for each such Product in such country at the rates set forth in Table 11.7.1(c) below. The royalty payments made pursuant to this Section 11.7.1 (Royalty Rates), the "**Royalties**" and the rates set forth in Table 11.7.1(a), Table 11.7.1(b), and Table 11.7.1(c), the "**Royalty Rates**."

Table 11.7.1(a) – Royalty Rates for Ophthalmic Products

Net Sales of all Ophthalmic Products	***Royalty Rate***	***Royalty Floor***
[***]	[***]%	[***]%
[***]	[***]%	[***]%
[***]	[***]%	[***]%

Table 11.7.1(b) – Royalty Rates for Sickle Cell Products in the Ex-Vivo Field

Net Sales of all Sickle Cell Products in the Ex-Vivo Field	***Royalty Rate***	***Royalty Floor***
[***]	[***]%	[***]%
[***]	[***]%	[***]%
[***]	[***]%	[***]%

Table 11.7.1(c) – Royalty Rates for In-Vivo SCD Products

Net Sales of all In-Vivo SCD Products outside of the U.S.	***Royalty Rate***	***Royalty Floor***
[***]	[***]%	[***]%
[***]	[***]%	[***]%
[***]	[***]%	[***]%

Confidential Portions of this Exhibit marked as [***] have been omitted pursuant to a request for confidential treatment and have been filed separately with the Securities and Exchange Commission.

By way of example only, if NVS receives $[***] in Net Sales of all Ophthalmic Products during a given Calendar Year, then the Royalties payable by NVS under this Section 11.7.1 (Royalty Rates) with respect to such Ophthalmic Products during such Calendar Year would be calculated as follows:

Royalty = [***] = $[***]
+ [***] = $[***]
+ [***] = $[***]
= $[***]

11.7.2 **Adjustments to Royalties**.

(a) **Lack of Valid Claims**. Subject to Section 11.7.3 (Cumulative Effect of Royalty Reductions), on a Product-by-Product and country-by-country basis in the Territory, during any period of the Royalty Term for a Product in such country (other than any U.S. SCD Product) in which such Product is not Covered by a Valid Claim in such country, then Royalties due to HMI under Section 11.7.1 (Royalty Rates) for such Product in such country will be reduced by [***]% during any such period until the expiration of the Royalty Term for such Product in such country.

(b) **Loss of Market Exclusivity**. Subject to 11.7.3 (Cumulative Effect of Royalty Reductions), on a Product-by-Product and country-by-country basis, if an event of a Loss of Market Exclusivity for a Product in any country has occurred, then the Royalties due to HMI pursuant to Section 11.7.1 (Royalty Rates) with respect to such Product in such country will be reduced by [***]%.

(c) **Third Party Licenses**.

(i) If NVS reasonably determines that rights to a Third Party's Intellectual Property Rights are [***] in connection with the Development, Manufacture or Commercialization of a Candidate or Product, then NVS will have the right to enter into a Third Party License in order to permit such Development, Manufacture or Commercialization. Notwithstanding the foregoing, where NVS reasonably determines that rights to a Third Party's Patent Rights or Third Party Know-How are [***] for NVS to practice the HMI Platform Technology in accordance with the licenses granted to NVS pursuant to Section 4.1 (License Grants to NVS) (such Third Party Patent Rights "**HMI Necessary Rights**"), NVS will first provide HMI with written notice of any such Third Party License that it intends to enter, and HMI will have the right to enter into such Third Party License itself within [***] of HMI's receipt of such notice on terms and conditions determined by HMI with HMI responsible for all costs and expenses incurred in connection with securing any such license. If HMI fails to enter into any such Third Party License within such [***] period, then will NVS have the right to enter into any such Third Party License itself. If NVS does enter into such Third Party License in accordance with this paragraph, then NVS may determine the terms and conditions of any such Third Party License and subject to this remainder of this Section 11.7.2(c) (Third Party Licenses), will be responsible for all costs and expenses incurred in connection with securing any such license.

(ii) Subject to Section 11.7.3 (Cumulative Effect of Royalty Reductions), the amount of any Royalties due to HMI pursuant to Section 11.7.1 (Royalty Rates) with respect to the applicable Product in such country during such Calendar Quarter will be reduced, on a Product-by-Product and country-by-country basis, by an amount equal to:

(A) [***]% of any royalty or other payments paid by NVS or its Affiliates pursuant to any (1) Third Party License entered into by NVS or its Affiliates for; or (2) Third Party Infringement Losses incurred by or on behalf of NVS and its Affiliates with respect to any Product (excluding In-Vivo SCD Products in the U.S.) for in each of (1) and (2), HMI Necessary Rights with respect to a Product in the applicable country; and

(B) [***]% of any royalty or other payments paid by NVS or its Affiliates pursuant to any (1) other Third Party License entered into by NVS or its Affiliates with respect to such Product in such country or (2) Third Party Infringement Losses incurred by or on behalf of NVS or its Affiliates with respect to any Product (excluding In-Vivo SCD Products in the U.S.), in each of (1) and (2), other than with respect to the HMI Necessary Rights.

(iii) Notwithstanding anything to the contrary in this Agreement, HMI shall remain solely responsible for the payment of any royalty, milestone, and other payment obligations, if any, due to Third Parties in connection with any HMI Licensed Technology or Third Party Licenses that (A) has been licensed to HMI or its Affiliates and is sublicensed to NVS under this Agreement, or (B) relates to covenants or other obligations agreed by HMI or its Affiliates prior to the Effective Date with any Third Party relating to any HMI Licensed Technology or any Candidate or Product, (collectively, the "**HMI Third Party Obligations**"), including pursuant to the COH License and the Caltech License. All such payments in respect of the HMI Third Party Obligations shall be made promptly by HMI in accordance with the terms of the applicable Third Party License.

11.7.3 **Cumulative Effect of Royalty Reductions**. On a country-by-country basis, in no event will the royalty reductions for Products that Modulate a given Target permitted under Section 11.7.2(a) (Lack of Valid Claims), Section 11.7.2(b) (Loss of Market Exclusivity), or Section 11.7.2(c)(i) (Third Party Licenses), alone or together, reduce the Royalties due to HMI for Products that Modulate such Target pursuant to Section 11.7.1 (Royalty Rates) in a country in a given Calendar Quarter to less than the applicable royalty floor set forth in Table 11.7.1 in such country in such

Calendar Quarter (the "**Royalty Floor**"). [***] Notwithstanding the Royalty Floor or any other limitations set forth in this Section 11.7.3 (Cumulative Effect of Royalty Reductions) and without limiting HMI's obligations hereunder, if a Third Party threatens to either terminate or diminish the scope or exclusivity of the licenses granted to NVS under any HMI Licensed Technology under a Third Party License to which HMI or its Affiliates is a party, then [***]

11.8. **Royalty Reports; Payments**. Commencing on the First Commercial Sale of a Product (other than a U.S. SCD Product) and for so long as Royalties are due under this Agreement, no later than [***] after the end of each Calendar Quarter, NVS will provide to HMI a written report (each, a "**Royalty Report**"), which Royalty Report will set forth: (a) the Net Sales (in local currency and United States Dollars) for such Calendar Quarter on a country-by-country and Product-by-Product basis; (b) the amount of any adjustments to such Royalties in accordance with Section 11.7.2 (Adjustments to Royalties); (c) the resulting total Royalties for the relevant Calendar Quarter in United States Dollars; and (d) if, applicable, Sales Milestone Payments owed to HMI listed by category. All Royalty Reports will be the Confidential Information of NVS. Upon receipt of such Royalty Report, HMI shall issue an invoice to [***]. Royalty payments for each Calendar Quarter will be due within [***] of receipt of such written invoice by HMI for the Calendar Quarter.

11.9. **Other Payments**. Subject to the terms and conditions of this Agreement, each Party will pay to the other Party any other undisputed amounts due under this Agreement no later than [***] after receipt of such invoice.

11.10. **Records and Audits**.

11.10.1 **Books and Records**. Each Party shall (a) keep complete, true, and accurate books and records in accordance with its Accounting Standards in relation to this Agreement, including in relation to HMI Research Costs, Global In-Vivo SCD Development Costs, Commercialization Costs, Manufacturing Costs, the number of units of Product sold or otherwise disposed of, the gross amount billed or invoiced for Products sold or otherwise disposed of, Net Sales of Products and the deductions taken in the calculation of Net Sales in sufficient detail to enable amounts owed or payable to the other Party hereunder to be determined; and (b) maintain such books and records for at least [***] following the Calendar Year to which they pertain. Each Party (the "**Auditing Party**") may, upon written request, cause an internationally-recognized independent accounting firm (the "**Auditor**"), that is reasonably acceptable to the other Party (the "**Audited Party**") to inspect the relevant records of such Audited Party and its Affiliates to verify the payments made and amounts reported by the Audited Party and the related reports, statements, and books of accounts, as applicable.

11.10.2 **Audit Procedure**. Before beginning its audit, the Auditor shall execute a written agreement acceptable to the Audited Party by which the Auditor agrees to keep confidential all information reviewed during the audit, which agreement shall contain terms of non-disclosure and non-use no less stringent than those set forth in this Agreement. The Auditor shall have the right to disclose to the Auditing Party only its conclusions regarding any payments owed under this Agreement. Each Party and its Affiliates shall make their records available for inspection by the Auditor during regular business hours at such place or places where such records are customarily kept, upon receipt of reasonable advance notice from the Auditing Party. The records shall

be reviewed solely to verify the accuracy of the Audited Party's Royalties and other payment obligations and compliance with the financial terms of this Agreement, including (a) with respect to HMI's right to audit, Royalty Reports and the reports provided for in Section 11.6.1 (Development Cost Reimbursement to NVS), and (b) with respect to NVS' right to audit, the reports of HMI Research Costs provided for in Section 3.8.2 (Research Payments), and information set forth in the Profit Share Reports provided for in Section 11.6.5 (Profit Share Reports; Payments) including Net Sales for U.S. SCD Products, Commercialization Costs, and Manufacturing Costs.

11.10.3 **Frequency; Overpayments and Underpayments**. Such inspection right shall not be exercised more than [***] without cause in any Calendar Year and not more frequently than [***] without cause with respect to records covering any specific period of time. In addition, the Auditing Party shall only be entitled to audit the books and records of the Audited Party for the [***] prior to the Calendar Year in which the audit request is made. The Auditing Party agrees to hold in strict confidence all information received and all information learned in the course of any audit or inspection, except to the extent necessary to enforce its rights under this Agreement or to the extent required to comply with any Applicable Law or judicial order. The Auditor shall provide its audit report and basis for any determination to the Audited Party at the time such report is provided to the Auditing Party before it is considered final. In the event that the final result of the inspection reveals an underpayment or overpayment by either Party, the underpaid or overpaid amount shall be settled promptly plus interest due on any underpayments at the Interest Rate. The Auditing Party shall pay for such inspections, as well as its expenses associated with enforcing its rights with respect to any payments hereunder; *provided*, that if an underpayment of more than [***]% of the total payments due hereunder for the applicable year is discovered, then the fees and expenses charged by the Auditor shall be paid by Audited Party.

11.11. **Currency of Payment**. All amounts to be paid by NVS pursuant to this Agreement will be made in United States Dollars. When conversion of payments from any foreign currency is required to be undertaken by NVS, the United States Dollar equivalent shall be calculated using NVS' then-current standard exchange rate methodology as applied in its external reporting for the conversion of foreign currency sales into United States Dollars.

11.12. **Late Fees**. Each paying Party will pay the other Party interest on any undisputed payments that are not paid on or before the date such payments are due under this Agreement at [***] or the maximum applicable legal rate, if less (the "**Interest Rate**"), calculated on the total number of days that the payment is delinquent.

11.13. **Currency Restrictions**. In the event that, by reason of Applicable Law in any country, it becomes impossible or illegal for a Party to transfer, or have transferred on its behalf, payments owed the other Party hereunder, such Party will promptly notify the other Party of the conditions preventing such transfer and such payments will be deposited in local currency in the relevant country to the credit of the other Party in a recognized banking institution designated by the other Party or, if none is designated by the other Party within a period of [***], in a recognized banking institution selected by the transferring Party, as the case may be, and identified in a written notice given to the other Party.

11.14. **Withholding Taxes**. Either Party (a "**Withholding Party**") may withhold from payments due to the other Party (a "**Non-Withholding Party**") amounts for payment of any withholding tax that is required by Applicable Law to be paid to any taxing authority with respect to such payments, which shall be remitted in accordance with Applicable Law. The Withholding Party will provide to the Non-Withholding Party all relevant documents and correspondence, and will also provide to the Non-Withholding Party any other cooperation or assistance on a reasonable basis as may be necessary to enable the Non-Withholding Party to claim exemption from such withholding taxes and to receive a refund of such withholding tax or claim a foreign tax credit. The Withholding Party will give proper evidence from time to time as to the payment of any such tax. The Parties will cooperate with each other in seeking deductions under any double taxation or other similar treaty or agreement from time to time in force. Such cooperation may include the Withholding Party making payments from a single source in the U.S., where possible.

Article 12. Intellectual Property

12.1. **Ownership of Inventions**.

12.1.1 **Background Intellectual Property**. As between the Parties, and subject to the licenses granted under this Agreement, each Party retains all rights, title, and interests in and to all Intellectual Property Rights that such Party owns or Controls as of the Effective Date or that it develops or otherwise acquires after the Effective Date outside the performance of the activities under this Agreement. Without limiting the generality of the foregoing, as between the Parties, HMI owns all rights, title, and interests in and to the HMI Platform Technology, and NVS owns all rights, title, and interest in and to the NVS Proprietary Technology.

12.1.2 **Assigned Technology**. Notwithstanding anything to the contrary set forth in this Agreement, (a) HMI will own (i) all inventions and other Know-How invented, discovered, created, or otherwise developed by or on behalf of a Party (or jointly by the Parties or their Affiliates) in the performance of activities under this Agreement that constitutes an improvement, modification, or enhancement of HMI Platform Technology, which invention or other Know-How arises from the use of such [***].

12.1.3 **Ownership**. Subject to Section 12.1.2 (Assigned Technology) with respect to Assigned Know-How and Assigned Patent Rights, (a) each Party, as between such Party and the other Party, will own (i) [***] that is invented, discovered, created, or otherwise developed solely by employees, agents, or contractors of such Party in the performance of the activities under this Agreement, and (ii) [***], and (b) both Parties will jointly own (i) all [***] that is invented, discovered, created, or otherwise developed jointly by or on behalf of the Parties in the performance of the activities under this Agreement ("Joint Know-How"), and (ii) [***] ("Joint Patent Rights"). Each Party will own a joint undivided interest in the Joint Technology, and, subject to any licenses granted by one Party to the other Party under this Agreement, and Section 4.11 (Exclusivity), each Party will have [***]. To the extent any further consent by either Party is required in connection with any permitted exploitation or licensing of the Joint Technology by the other Party, then such Party will promptly provide such consent on request. To the extent necessary in any jurisdiction to give effect to the intent of this Section 12.1.3 (Ownership), but subject to the licenses granted under this Agreement, each Party hereby grants and agrees to grant to the other Party a nonexclusive, royalty-free, fully-paid, worldwide, irrevocable, perpetual license, with the right to grant sublicenses through multiple tiers, to practice the Joint Technology for any and all purposes, subject to any licenses granted by one Party to the other under this Agreement and Section 4.11 (Exclusivity). [***].

12.1.4 **Covenants and Licenses in Support of Ownership**. NVS (on behalf of itself and its Affiliates) will and hereby does assign to HMI all rights, title, and interests in and to the HMI Assigned Know-How and HMI Assigned Patent Rights in order to give effect to the ownership of such HMI Assigned Patent Rights and HMI Assigned Know-How set forth in Section 12.1.2 (Assigned Technology), together with the right to file or own applications for any HMI Assigned Patent Rights. HMI (on behalf of itself and its Affiliates) will and hereby does assign to NVS all rights, title, and interests in and to the NVS Assigned Know-How and NVS Assigned Patent Rights in order to give effect to the ownership of such NVS Assigned Patent Rights and NVS Assigned Know-How set forth in Section 12.1.2 (Assigned Technology), together with the right to file or own applications for any NVS Assigned Patent Rights. Upon a Party's request, the other Party will provide all further cooperation that the requesting Party reasonably determines is necessary to give effect to the ownership of the Assigned Know-How and Assigned Patent Rights set forth in Section 12.1.2 (Assigned Technology) and to ensure the requesting Party the full and quiet enjoyment of the applicable Assigned Know-How and Assigned Patent Rights, including executing and delivering further assignments, consents, releases, and other commercially reasonable documentation, and providing good faith testimony by affidavit, declaration, deposition, in person, or other proper means, and otherwise assisting the requesting Party in support of any effort by the requesting Party to establish, perfect, defend, or enforce its rights in the Assigned Know-How and Assigned Patent Rights, in accordance with this Agreement. Upon a Party's request, the other Party will require the cooperation of the individual inventors of any inventions disclosed in the Assigned Know-How and Assigned Patent Rights, including (a) obtaining signatures of such inventors on any patent applications or other documentation reasonably necessary to obtain patent protection for such inventions, and (b) procuring (at the requesting Party's cost and expense) such inventors' good faith testimony by affidavit, declaration, deposition in person, or other proper means in support of the requesting Party's efforts in establishing, perfecting, defending, or enforcing Patent Rights to such inventions.

12.2. **Notice of Inventions**. Each Party will notify the other of the invention, creation, development, or reduction to practice of any Joint Technology, and NVS will promptly notify HMI of the invention, creation, development, or reduction to practice of any HMI Assigned Know-How and HMI Assigned Patent Rights, NVS Program Know-How, and NVS Program Patent Rights, and HMI will promptly notify NVS of the invention, creation, development, or reduction to practice of any HMI Program Know-How, HMI Program Patent Rights, NVS Assigned Know-How, and NVS Assigned Patent Rights. Each Party will ensure that its Affiliates, Sublicensees, and subcontractors enable such disclosure.

12.3. **Invention Protection**. Each Party will ensure that employees and independent contractors (excluding Sublicensees, who are subject to Section 4.3.4 (Sublicense and License Requirements) and subcontractors, who are subject to Section 4.4 (Subcontractors)) of such Party or its respective Affiliates performing work under this Agreement will, prior to commencing such work, be bound by written invention assignment obligations, requiring: (a) prompt reporting of any Intellectual Property Rights arising from such work; (b) assignment to the applicable Party or Affiliate all of his or her rights, title, and interests in and to any Intellectual Property Rights arising from such work; (c) cooperation in the preparation, filing, prosecution, maintenance, and enforcement of any Patent Right that is required to be assigned under this Agreement; and (d) performance of all acts and signing, executing, acknowledging, and delivering any and all documents required for effecting the obligations and purposes of this Agreement.

12.4. Prosecution and Maintenance of Patent Rights.

12.4.1 **HMI Patent Rights**. HMI will be responsible for the preparation, filing, prosecution, and maintenance of all [***]; *provided*, that the overall strategy for such preparation, filing, prosecution, and maintenance of the [***] will be consistent with the strategy determined for such Patent Rights by the Parties either directly or through the JSC (or corresponding Subcommittee). The HMI External Costs incurred to obtain, prosecute, and maintain (a) [***] will be borne [***]% by HMI and [***]% by NVS; [***]. HMI will invoice NVS for those agreed upon External Costs incurred to obtain, prosecute and maintain [***] on a Calendar Quarterly basis, and NVS will pay all such undisputed invoices no later than [***] after receipt thereof. HMI will provide copies of draft filings and material communications with any patent authority related to all pending [***] in advance of submission for review and comment by the NVS. HMI, its agents and attorneys will consider in good faith all comments timely provided to HMI by NVS on such filings and communications related to Candidates and Products (*provided*, that NVS does so promptly and consistent with any applicable filing deadlines) and, in all events, HMI will provide NVS with copies of all such filings and material communications submitted to or received from any patent authority. If HMI elects to abandon any HMI Patent Right, then NVS will have the option to continue to prosecute and maintain such Patent Right in HMI's name and at NVS' expense; *provided*, *however*, that if HMI does so and NVS exercises its option to continue to prosecute any such [***], then (i) NVS will [***] and (ii) [***].

12.4.2 [***]. NVS will be responsible for the preparation, filing, prosecution, and maintenance of the [***]; *provided*, that the overall strategy for such preparation, filing prosecution and maintenance of [***] will be consistent with the strategy determined for such Patent Rights by the Parties either directly or through the JSC (or corresponding Subcommittee). The External Costs incurred to obtain, prosecute, and maintain the [***] will be borne [***]% by NVS. The External Costs incurred to obtain, prosecute, and maintain [***] will be borne [***]% by HMI and [***]% by NVS. NVS will invoice HMI for those agreed upon External Costs incurred to obtain, prosecute and maintain [***] on a Calendar Quarterly basis, and HMS will pay all such undisputed invoices no later than [***] after receipt thereof. NVS will provide copies of draft filings and material communications with any patent authority related to all pending [***] in advance of submission for review and comment by HMI. NVS, its agents and attorneys will consider in good faith all comments timely provided to NVS by HMI on such filings and communications (*provided*, that HMI does so promptly and consistent with any applicable filing deadlines), and in all events, NVS will provide HMS with copies of all such filings and material communications submitted to or received from any patent authority. If NVS decides to abandon any [***], then HMI will have the option to continue to prosecute and maintain such [***] in HMI's name at HMI's expense. If NVS decides to abandon any [***], then HMI will have the option to continue to prosecute and maintain such [***] in both Parties' names, with such External Costs incurred to obtain, prosecute, and maintain such [***] still borne [***]% by HMI and [***]% by NVS; *provided*, that if NVS opts to no longer pay for such External Costs, then HMI will have the option to continue to prosecute and maintain such [***] in HMI's name and at HMI's sole cost, in which case NVS will assign its joint interest in the [***] to HMI and HMI grants NVS a non-exclusive, worldwide, transferable, perpetual, and irrevocable license and right under such former [***].

12.4.3 **Cooperation and Discussion**. On a [***] basis, each Party's internal or external patent counsel(s) will provide an update and discuss (a) the status of all pending [***], (b) any material updates regarding the prosecution and maintenance of the [***], including the strategy for the preparation, filing, prosecution, and maintenance of such Patent Rights (in each case (a) and (b), with HMI's representative providing an update on all [***] and NVS' representative providing an update on all [***]), (c) any inventions disclosed by either Party to the other pursuant to Section 12.2 (Notice of Inventions) since the prior meeting, and (d) any Third Party Licenses that each Party is considering entering into, including any such Third Party License to any HMI Necessary Rights. In addition, the Parties shall, and shall cause their Affiliates to, cooperate and implement reasonable Patent Right filing and prosecution strategies (including filing divisionals, continuations, or otherwise) so that, to the extent reasonably feasible, [***] are pursued in mutually exclusive patent applications.

12.4.4 **Patent Term Extension**. NVS will have the right to elect and file for patent term restorations or extensions, supplemental protection certificates, or any of their equivalents with respect to [***], and HMI will have the right to elect and file for patent term restorations or extensions, supplemental protection certificates, or any of their equivalents with respect to all [***] other than [***]; *provided*, that each Party shall take into account reasonable and timely requests by the other Party to make any such elections or filings with respect to any such Patent Right if a Party's failure to so act in such country would impair the other Party's ability to obtain any such restoration, extension, supplemental protection certificate, or any of their equivalents for the same relating to any Patent Right for which such Party controls the prosecution and maintenance thereof. The Parties will cooperate and shall take the other Party's reasonable input into account in determining whether to obtain such patent term restoration or extension, supplemental protection certificate, or equivalent thereof. Upon the request by a Party, such other Party will reasonably cooperate in the implementation of such requesting Party's decisions made in a manner with this Section 12.4.4 (Patent Term Extension).

12.5. Interference, Opposition, Reexamination, and Reissue.

12.5.1 **Notice**. During the Term, each Party will promptly notify the other Party but in any case not more than [***] following the discovery by the discovering Party of any request for, or the filing or declaration of, any Patent Challenge, with respect to any [***], along with the determination by the Parties either directly or through the JSC (or corresponding Subcommittee) that any such Patent Right should be reissued, reexamined, or reviewed via supplemental examination to avert invalidity or unenforceability thereof or reissued to permissibly broaden such [***].

12.5.2 **HMI's and NVS' Role**. During the Term, HMI will have the right (but not the obligation) to undertake any course of action to defend or prosecute any such Patent Challenge with respect to any [***] unless HMI determines in its sole discretion not to undertake any such course of action to defend or prosecute any such Patent Challenge, in which case NVS will have the right (but not the obligation) to undertake any course of action to defend or prosecute any such Patent Challenge with respect to any [***]. During the Term, NVS will have the right (but not the obligation) to

undertake any course of action to defend or prosecute any such Patent Challenge with respect to any [***], unless NVS determines in its sole discretion not to undertake any such course of action to defend or prosecute any such Patent Challenge, in which case HMI shall have the right (but not the obligation) to undertake any course of action to defend or prosecute any such Patent Challenge with respect to any such [***]. NVS will be responsible for (a) [***]% of the External Costs incurred by NVS in connection with any course of action taken to defend or prosecute any such Patent Challenge with respect to [***] and (b) [***]% of the External Costs incurred in connection with any course of action taken to defend or prosecute any Patent Challenge with respect to [***]. NVS will invoice HMI for all such External Costs to be borne by HMI on a Calendar Quarterly basis, and HMI will pay all such undisputed invoices no later than [***] after receipt thereof. During and after the Term, NVS will have the sole right (but not the obligation) to undertake any course of action to defend or prosecute any such Patent Challenge with respect to any [***] at its own expense.

12.5.3 **Cooperation; Coordination**. The Parties will cooperate fully with each other and each will provide to the other any information or assistance that the other may reasonably request with respect to any course of action taken under this Section 12.5 (Interference, Opposition, Reexamination, and Reissue) with respect to [***]. The applicable Party will (a) keep the other Party reasonably informed of all developments in such proceeding, including to the extent permissible, the status of any settlement negotiations and the terms of any offer related thereto, (b) provide to the other Party for its review and discussion, copies of all material submissions or agreements arising in connection with such proceeding sufficiently in advance of their filing, due date, or execution date so as to give the other Party sufficient time to comment thereon, and (c) give good faith consideration to the other Party's comments. Each Party and its respective Affiliates will promptly supply or execute all papers and instruments, or require their respective employees to supply or execute such papers and instruments, as may be necessary and appropriate for purposes of assisting the applicable Party in any course of action taken with respect to [***] under this Section and will promptly inform the other Party of matters that may, in such Party's reasonable judgment, affect any course of action taken with respect thereto.

12.6. Enforcement Against Third Party Infringement.

12.6.1 **Notice**. If either Party (a) becomes aware of any actual or threatened infringement, misappropriation, or other violation by a Third Party of any [***] as a result of the manufacture, use, sale, or import of any compound or product that is or is reasonably expected to be competitive with any Product (including alleged or threatened infringement based on the Development, Manufacturing, Commercialization or an application to market a product that is competitive with any Product in the Territory) (each, a "**Competing Infringement**"), then such Party will promptly notify the other Party (in all instances, such timeframe to be sufficiently prompt to provide the other Party the opportunity to respond to such proceedings) and provide it with all details of such Competing Infringement of which it is aware. The Parties will promptly meet to review and discuss the Competing Infringement and the strategy for patent enforcement with respect to such Competing Infringement.

12.6.2 **NVS' Rights**. NVS will have the right (but not the obligation) to initiate an infringement, misappropriation, or other appropriate suit (an "**Infringement Action**") anywhere in the world against any Third Party as to [***] at its cost and expense; *provided*, that (a) NVS will keep HMI reasonably informed about any such Infringement Action, (b) HMI will provide reasonable cooperation to NVS in connection with such Infringement Action, including, to the extent the Infringement Action relates to any [***], by promptly supplying or executing all papers and instruments, or requiring its employees to supply or execute such papers and instruments, as may be necessary for purposes of initiating and pursuing such Infringement Action, at NVS' cost and expense, (c) NVS will not take any position with respect to, or settle, such Infringement Action in any way that would adversely affect the scope, validity, or enforceability of any [***] without the prior written consent of HMI, such consent not to be unreasonably withheld, conditioned, or delayed, and (d) if NVS determines not to institute an Infringement Action with respect to a Competing Infringement, or determines to cease to pursue any such Infringement Action, then, in each case, it will promptly inform HMI of the same and pursuant to Section 12.6.3 (HMI's Rights), HMI may have the right to pursue such Infringement Action.

12.6.3 **HMI's Rights**.

(a) HMI will have the right (but not the obligation) to initiate an Infringement Action anywhere in the world against any Third Party as to any Competing Infringement of any [***] at its cost and expense; *provided*, that (i) HMI will keep NVS reasonably informed about any such Infringement Action, (ii) NVS will provide reasonable cooperation to HMI in connection with such Infringement Action, including by promptly supplying or executing all papers and instruments, or requiring its employees to supply or execute such papers and instruments, as may be necessary for purposes of initiating and pursuing such Infringement Action, at HMI's cost and expense, (iii) HMI will not take any position with respect to, or settle, such Infringement Action in any way that would adversely affect the scope, validity, or enforceability of any [***] without the prior written consent of NVS, such consent not to be unreasonably withheld, conditioned, or delayed, and (iv) if HMI determines not to institute an Infringement Action with respect to a Competing Infringement, or determines to cease to pursue any such Infringement Action, then, in each case, it will promptly inform NVS of the same and NVS may have the right to pursue such Infringement Action.

(b) If NVS informs HMI that it does not intend to prosecute an Infringement Action in respect of any [***] as to a Competing Infringement anywhere in the Territory pursuant to Section 12.6.2 (NVS' Rights), or NVS determines to cease to pursue any such Infringement Action in respect of any [***] with respect to such Competing Infringement, and, in each case, if NVS' use of [***] would lead to prosecuting or continuing to pursue such Infringement Action, then HMI will have the right (but not the obligation), upon notice to NVS, to take appropriate action to address such Competing Infringement in respect of any [***], including by initiating its own Infringement Action or taking over prosecution of any Infringement Action initiated by NVS. In such event, (i) HMI will keep NVS reasonably informed about such Infringement Action and will consult with NVS before taking any major steps during the conduct of such Infringement Action, (ii) NVS will provide reasonable cooperation to HMI in connection with such Infringement Action, at HMI's cost and expense, and (iii) HMI will not take any position with respect to, or settle, such Infringement Action in any way that would adversely affect the scope, validity, or enforceability of the [***] without NVS' prior written consent, which consent will not be unreasonably withheld, conditioned, or delayed.

(c) HMI will have the sole right (but not the obligation) to initiate an Infringement Action anywhere in the world against any Third Party as to any Competing Infringement of any [***] at its cost and expense; *provided*, that (i) HMI will keep NVS reasonably informed about any such Infringement Action, and (ii) NVS will provide reasonable cooperation to HMI, at HMI's cost and expense, in connection with such Infringement Action, including by promptly supplying or executing all papers and instruments, or requiring its employees to supply or execute such papers and instruments, as may be necessary for purposes of initiating and pursuing such Infringement Action.

12.6.4 **Procedures; Assistance; Expenses**. The Party having the right to initiate any Infringement Action under this Section 12.6 (Enforcement Against Third Party Infringement) will pay all expenses of such Infringement Action, including attorneys' fees and court costs and reimbursement of the other Party's reasonable external costs in rendering assistance requested by the initiating Party. If required under any Applicable Law in order for the initiating Party to initiate or maintain such Infringement Action, or if either Party is unable to initiate or prosecute such Infringement Action solely in its own name or it is otherwise advisable to obtain an effective legal remedy, then, in each case, the other Party will join as a party to such Infringement Action and will execute, and cause its Affiliates to execute, all documents necessary for the initiating Party to initiate litigation to prosecute and maintain such Infringement Action, at the initiating Party's expense. In addition, at the initiating Party's request, the other Party will provide reasonable assistance to the initiating Party in connection with an Infringement Action. The non-initiating Party will have the right to participate and be represented in any such Infringement Action by its own counsel at its own expense.

12.6.5 **Biosimilar Litigation.**

(a) **Receipt of Application; Responsibilities**. If either Party receives a copy of an application submitted to the FDA under subsection (k) of Section 351 of the PHSA (a "**Biosimilar Application**") naming a Product as a reference product or otherwise becomes aware that such a Biosimilar Application has been filed (such as in an instance described in Section 351(l)(9)(C) of the PHSA), then either Party will, within [***] after receipt thereof, similarly notify the other Party so NVS may seek permission to view the application and related confidential information from the filer of the Biosimilar Application under Section 351(l)(1)(B)(iii) of the PHSA. If either Party receives any equivalent or similar certification or notice in any other country in the Territory, either Party will, within [***] of receipt thereof, notify and provide the other Party with copies of such communication. Regardless of the Party that is the "reference product sponsor" for purposes of such Biosimilar Application, NVS will have the sole right to manage and prosecute biosimilar litigation, including: (i) NVS will have the sole right to designate pursuant to Section 351(l)(1)(B)(ii) of the PHSA in-house counsel who will receive confidential access to the Biosimilar Application, with the understanding that a representative of HMI, as patent owner of [***] will have the right to view confidential information related to the [***] disclosed under Section 351(l)(1)(B)(iii); (ii) NVS will have the sole right to list any Patent Rights, including [***] insofar as they Cover the applicable

Product as required or desired pursuant to Applicable Law, to respond to any communications with respect to such lists from the filer of the Biosimilar Application, and to negotiate with the filer of the Biosimilar Application as to whether to utilize a different mechanism for Information exchange than that specified in Section 351(l) of the PHSA; and (iii) NVS will have the sole right to identify Patent Rights or respond to communications under any equivalent or similar listing in any other country in the Territory. However, NVS will reasonably consult with HMI with respect to asserting and enforcing any [***] and will use reasonable efforts to accommodate HMI's timely comments with respect to activities in connection with the assertion and enforcement of such [***]. If required pursuant to Applicable Law, HMI will prepare such lists and make such responses at NVS' direction. HMI will: (A) provide to NVS, within [***] days of NVS' request, all information, including a correct and complete list of [***] Covering any Product, that is [***] to enable NVS to make such lists and communications with respect to the [***]; and (B) cooperate with NVS' reasonable requests in connection therewith, including meeting any submission deadlines, in each case, to the extent required or permitted by Applicable Law. NVS will: (1) reasonably consult with HMI prior to identifying any [***] to a Third Party as contemplated by this Section 12.6.5 (Biosimilar Litigation) and will consider in good faith HMI's timely advice and suggestions with respect thereto; and (2) notify HMI of any such lists or communications promptly after they are made.

(b) **Actions for Infringement; Injunction**. Notwithstanding anything to the contrary in this Section 12.6 (Enforcement Against Third Party Infringement), NVS will have the right to bring an action for infringement of the [***] as required under Section 351(l)(6) of the PHSA following the agreement on a list of patents for litigation under Section 351(l)(4) or exchange of patent lists pursuant to Section 351(l)(5)(B) of such act, or as required following any equivalent or similar certification or notice in any other country. The Parties' rights and obligations with respect to the foregoing legal actions will be as set forth in Section 12.6.2 (NVS' Rights) through Section 12.6.4 (Procedures; Assistance; Expenses); *provided*, that within [***] of reaching agreement on a list of Patent Rights for litigation under Section 351(l)(4) or exchange of patent lists pursuant to Section 351(l)(5)(B), NVS will notify HMI as to whether or not it elects to prosecute such infringement. Either Party will, within [***], notify and provide the other Party with copies of any notice of commercial marketing provided by the filer of a Biosimilar Application pursuant to Section 351(l)(8)(A) of the PHSA, or any equivalent or similar certification or notice in any other country. Thereafter, NVS will have the right to seek an injunction against such commercial marketing as permitted pursuant to Section 351(l)(8)(B) of the PHSA.

12.6.6 **Recoveries**. If either Party obtains any damages, license fees, royalties, or other compensation (including any amount received in settlement of such litigation) from any Third Party in connection with any Competing Infringement, then the amounts will be allocated in all cases as follows:

(a) first, to reimburse each Party for all expenses of such Infringement Action incurred by each Party, including attorneys' fees and disbursements, court costs and other litigation expenses; and

(b) any remaining amounts will be split as follows: (i) [***]% will be paid to the Party initiating or defending such suit or action, and (ii) [***]% will be paid to the non-initiating or non-defending Party.

12.7. Defense of Claims.

12.7.1 **Notice**. If a Party becomes aware of any actual or potential claim alleging that the Research, Development, Manufacture, or Commercialization of any Candidate or Product infringes, misappropriates, or otherwise violates any Intellectual Property Rights of a Third Party (or would if carried out) ("**Third Party Infringement**"), then such Party will notify the other Party as promptly as possible following the receipt of service of process in such action, suit, or proceeding, or the date on which such Party becomes aware that such action, suit, or proceeding has been instituted, and the JSC (or corresponding Subcommittee) (or the Parties directly if the JSC is dissolved during the Term) will meet as soon as possible to discuss the overall strategy for defense of such matter.

12.7.2 **Defense**. Subject to Article 15 (Indemnification; Limitation Of Liability; Insurance): (a) HMI shall have the first right (but not the obligation) to defend any claims of Third Party Infringement alleging that [***] infringes, misappropriates, or otherwise violates the Intellectual Property Rights of any Third Party; and (b) NVS shall have the first right (but not the obligation) to defend any other claims of Third Party Infringement alleging that [***] infringes, misappropriates, or otherwise violates the Intellectual Property Rights of any Third Party.

Article 13. Confidentiality

13.1. Confidential Information.

13.1.1 **General**. Each Party (the "**Receiving Party**") will maintain all Confidential Information disclosed to it or its representatives by or on behalf the other Party (the "**Disclosing Party**") in strict confidence during the Term of this Agreement and for a period of [***] after the expiration or termination of this Agreement; *provided*, that any Confidential Information of either Party that constitutes a trade secret will continue to be subject to the terms of this Article 13 (Confidentiality) in perpetuity, so long as such information remains a trade secret. Each Party will use all such disclosed Confidential Information only to the extent necessary for purposes of this Agreement, including exercising the licenses and rights hereunder and will not disclose such Confidential Information to any Third Party without the prior written consent of the Disclosing Party, except as permitted under this Agreement. Each Party will notify the other Party promptly on discovery of any unauthorized use or disclosure by a Party of the other Party's Confidential Information, including the other Party's trade secrets.

13.1.2 **Confidential Information of Each Party**. All information disclosed prior to the Effective Date pursuant to (a) the Confidentiality Agreement between the Parties dated as of [***], as amended on [***] and (b) the Confidentiality Agreement between the Parties dated as of [***] ((a) and (b), collectively, the "**Confidentiality Agreements**"), by HMI to NVS will be Confidential Information of HMI and by NVS to HMI will be Confidential Information of NVS. The contents of each Interim Report, Success Criteria Report, or Exploratory Research Report that relate solely to HMI Platform Technology will be considered Confidential Information of [***], with

the remainder of the content of all such reports along with all Royalty Reports or reports identifying Development Milestones and Sales Milestones will be considered Confidential Information of [***]. The [***], the non-disclosed terms of this Agreement, and [***] will be the Confidential Information of each Party. The Targets, Candidates, and Products will be Confidential Information of [***]. The [***] (including [***]) will be the Confidential Information of [***] and the [***] (including [***]) will be the Confidential Information of [***].

13.1.3 **Exceptions to Confidentiality**. The obligations of each Receiving Party imposed by Section 13.1.1 (General) will not apply to any Confidential Information disclosed to the Receiving Party by the Disclosing Party that: (a) was known to the Receiving Party without an obligation to keep such information confidential prior to the Effective Date other than as a result of disclosure under any other agreement between the Parties, including the Confidentiality Agreements (as demonstrated by documentary evidence); (b) is or becomes generally available to the public through means other than an unauthorized disclosure by the Receiving Party, its Affiliates, or any agents to whom it or they disclosed such information; (c) was or subsequently is disclosed to the Receiving Party without restriction by a Third Party having a *bona fide* right to disclose such Confidential Information without breaching any obligation to the Disclosing Party; (d) is developed independently by the Receiving Party without benefit of or recourse to any of the Disclosing Party's Confidential Information (as demonstrated by documentary evidence); or (e) is published pursuant to Section 13.1.5 (Publicity). For clarity, (i) specific aspects or details of Confidential Information will not be deemed to be within the public domain or in the possession of the Receiving Party merely because the Confidential Information is embraced by more general information in the public domain or in the possession of the Receiving Party; and (ii) any combination of Confidential Information will not be considered in the public domain or in the possession of the Receiving Party merely because individual elements of such Confidential Information are in the public domain or in the possession of the Receiving Party unless the combination and its principles are in the public domain or in the possession of the Receiving Party.

13.1.4 **Permitted Disclosures**.

(a) **Compliance with Law**. Notwithstanding anything to the contrary set forth in this Article 13 (Confidentiality), each Receiving Party may use and make disclosures of Confidential Information of the Disclosing Party: (i) to its Affiliates, and the Receiving Party's employees, directors, agents, consultants, or advisors to the extent necessary for the potential or actual performance of its obligations or exercise of its licenses and other rights under this Agreement, in each case, who are under an obligation of confidentiality and non-use with respect to such information that is no less stringent than the terms of this Agreement; (ii) to patent offices in any country in which Patent Rights are sought for purposes of prosecuting any applications for any Patent Rights or defending any Patent Rights in interference or opposition actions as contemplated by this Agreement; (iii) to Regulatory Authorities as necessary to pursue Development, Commercialization, Manufacturing, or Marketing Approval of Products; *provided*, that such Confidential Information will be disclosed only to the extent reasonably necessary to do so, and where permitted, subject to confidential treatment; (iv) to Third Parties to the extent a Party is required to do so pursuant to the terms of a Third Party License; *provided*, that such Confidential Information will be disclosed only to the extent reasonably necessary to do so; or

(v) to the extent required to comply with Applicable Law or a court or administrative order, including of the United States Securities and Exchange Commission or similar regulatory agency in other countries, in each case, to the extent applicable to such Party at such time; *provided*, *however*, that the Party who is required to make such disclosure (A) provides the other Party with reasonable prior written notice, (B) coordinates with the other Party with respect to the wording and timing of any such disclosure and affords the other Party an opportunity to oppose or limit, or secure confidential treatment for such required disclosure, (C) if unsuccessful in its efforts pursuant to clause (B), takes all reasonable and lawful actions to obtain confidential treatment for such disclosure, and (D) discloses the minimum amount and scope of the Confidential Information necessary to comply with Applicable Law. Notwithstanding the foregoing, any Confidential Information so disclosed will remain subject to the terms of this Agreement.

(b) **SEC Filings and Other Disclosures**. If either Party concludes that a copy of this Agreement must be filed with the United States Securities and Exchange Commission or a similar regulatory agency in a country other than the United States, such Party will (i) a reasonable time prior to any such filing, provide the other Party with a copy of the Agreement showing any provisions hereof as to which the Party proposes to request confidential treatment, (ii) provide the other Party with an opportunity to comment on any such proposed redactions and to suggest additional redactions, and (iii) take such Party's reasonable comments into consideration before filing such Agreement and use Commercially Reasonable Efforts to have terms identified by such other Party afforded confidential treatment by the applicable regulatory agency.

(c) **Agreement**. Solely with respect to the terms of this Agreement, either Party may disclose the terms of this Agreement, to any *bona fide* actual or prospective acquirers, underwriters, investors, lenders or other financing sources and any *bona fide* actual or prospective licensors, Sublicensees, licensees or strategic partners and to employees, directors, agents, consultants and advisers of such Third Party, who are under an obligation of confidentiality with respect to such information that is no less stringent than the terms of this Agreement, and provided that such Confidential Information will be disclosed only to the extent reasonably necessary to evaluate the proposed transaction or perform its obligations or exercise its rights granted under the applicable agreement.

13.1.5 **Publicity**. Except as otherwise contemplated by this Section 13.1.5 (Publicity), Section 13.3 (Publications and Presentations), and Applicable Law, legal process, or stock exchange rules, neither Party will issue a press or news release or make any similar public announcement related to the execution or terms of this Agreement, the conduct of Research Activities, other Development activities or the Commercialization of Products without the prior written consent of the other Party (solely for the purpose of this Section 13.1.5 (Publicity), consent via e-mail with return receipt will be allowed); [***]. Upon the execution of this Agreement, each Party may issue a press release with respect to this Agreement in a form agreed by the Parties. Thereafter, where a request for a public disclosure is made by a Party with respect to this Agreement, the Parties will agree upon the form of a press release or other public statement, and either Party may make subsequent public disclosure of the contents of press release or other public statement; *provided*, that the disclosing Party will not depart from the agreed-upon form, if any, without the prior written consent of the other Party.

13.2. **No Use of Name**. Subject to the terms of this Agreement, neither Party will use the name or Trademarks of the other Party in any promotional materials or advertising without the prior written consent of the other Party, except as provided under this Agreement or required by Applicable Law, in which case the Party disclosing such name or Trademarks will give advance notice of such use and otherwise comply with Section 13.1.4(a) (Compliance with Law).

13.3. **Publications and Presentations**.

13.3.1 **NVS' Rights to Publish and HMI's Rights to Review**. The Parties recognize the desirability of publishing and publicly disclosing the results of, and scientific information regarding, the activities under this Agreement. NVS will be free to publish and present the results of and information regarding the activities under this Agreement as provided in this Section 13.3.1 (NVS' Rights to Publish and HMI's Rights to Review) in a manner consistent with Applicable Law and industry practices, subject to prior review by HMI for issues of patentability and protection of HMI Confidential Information. Accordingly, prior to publishing or disclosing the results of, or scientific information regarding, any activities under this Agreement. NVS will provide HMI with drafts of proposed abstracts, manuscripts, or summaries of presentations that include such results or information. HMI will respond promptly through its designated representative and in any event no later than [***] after receipt of such proposed publication or presentation or such shorter period as may be agreed to by the Parties. NVS will delay any such proposed publication or presentation for a reasonable period (not to exceed [***] after HMI receives such proposed publication or presentation) to permit HMI to make filings for patent protection and will otherwise remove Confidential Information of HMI identified by HMI in such publication or presentation. [***].

13.3.2 **HMI's Rights to Publish and NVS' Rights to Review**. HMI will be free to publish and present the results of and information regarding any Research during the Research Term as provided in this Section 13.3.2 (HMI's Rights to Publish and NVS' Rights to Review) in a manner consistent with Applicable Law and industry practices, subject to prior review by NVS for issues of patentability and protection of NVS Confidential Information. Accordingly, prior to publishing or disclosing the results of, or scientific information regarding, any such Research, HMI will provide NVS with drafts of proposed abstracts, manuscripts, or summaries of presentations that include such results or information. NVS will respond promptly through its designated representative and in any event no later than [***] after receipt of such proposed publication or presentation or such shorter period as may be agreed to by the Parties. HMI will delay any such proposed publication or presentation for a reasonable period (not to exceed [***] after NVS receives such proposed publication or presentation) to permit NVS to make filings for patent protection and will otherwise remove Confidential Information of NVS identified by NVS in such publication or presentation. [***].

Article 14. Representations, Warranties, and Covenants

14.1. **Mutual Representations and Warranties**. As of the Effective Date, HMI and NVS each hereby represents and warrants to the other as follows:

14.1.1 **Organization**. It is a corporation duly organized, validly existing and in good standing under the laws of the jurisdiction of its organization, and has all requisite power and authority, corporate or otherwise, to execute, deliver and perform this Agreement.

14.1.2 **Authorization**. The execution and delivery of this Agreement and the performance by it of the transactions contemplated hereby have been duly authorized by all necessary corporate action and will not violate (a) such Party's certificate of incorporation or bylaws (or equivalent charter or organizational documents), (b) any agreement, instrument or contractual obligation to which such Party is bound, (c) any requirement of any Applicable Law or regulations or court or administrative under, or (d) any order, writ, judgment, injunction, decree, determination, or award of any court or Governmental Authority presently in effect applicable to such Party.

14.1.3 **No Inconsistent Obligation**. It is not under any obligation, contractual, or otherwise, to any Person that conflicts with or is inconsistent in any respect with the terms of this Agreement or that will impede the diligent and complete fulfillment of its obligations hereunder.

14.1.4 **No Conflicts**. The execution, delivery and performance of this Agreement by such Party does not conflict with such Party's charter documents, bylaws or other organizational documents, any agreement, instrument or understanding, oral or written, to which it is a party or by which it is bound, nor violate Applicable Law or any order, writ, decree, judgment, injunction, determination or award of any Governmental Authority having jurisdiction over it.

14.1.5 **No Litigation**. There is no action or proceeding pending or, to the knowledge of such Party, threatened that could reasonably be expected to impair or delay the ability of such Party to perform its obligations under this Agreement.

14.1.6 **Government Authorizations**. All consents, approvals, and authorizations from all Governmental Authorities or other Third Parties required to be obtained by such Party in connection with this Agreement, including the grant of any licenses, have been obtained.

14.1.7 **Debarment**. Neither such Party, nor any Affiliate of such Party, has been debarred by any Regulatory Authority, including under the Generic Drug Enforcement Act of 1992 (21 U.S.C. §301 et seq.), is under investigation for debarment action by any Regulatory Authority, has been disqualified as an investigator pursuant to 21 C.F.R. §312.70, has a disqualification hearing pending or is currently employing or using any Person that has been so debarred or disqualified by any Regulatory Authority to perform any of such Party's obligations under this Agreement.

14.2. **Additional Representations of HMI as of the Effective Date**. As of the Effective Date, HMI further represents and warrants to NVS, that, except as set forth on Schedule 14.2 (Exceptions to Representations and Warranties):

14.2.1 **HMI Patent Rights**. Schedule 14.2.1 sets forth a complete and accurate list of all HMI Patent Rights in existence, all of which are owned or Controlled by HMI. To the Knowledge of HMI, (a) the issued patents in the HMI Patent Rights are valid and enforceable without any claims, challenges, oppositions,

nullity actions, interferences, inter-partes reexaminations, inter-partes reviews, post-grant reviews, derivation proceedings, or other proceedings pending or threatened and HMI has filed and prosecuted patent applications within the HMI Patent Rights owned by HMI in good faith and complied with all duties of disclosure with respect thereto, (b) HMI has not committed any act, or omitted to commit any act, that may cause the HMI Patent Rights to expire prematurely or be declared invalid or unenforceable, and (c) all application, registration, maintenance and renewal fees in respect of the HMI Patent Rights have been paid and all necessary documents and certificates have been filed with the relevant agencies for the purpose of maintaining the HMI Patent Rights set forth on Schedule 14.2.1.

14.2.2 **HMI Technology Agreements**. Schedule 14.2.2 sets forth a complete and accurate list of all Third Party Licenses pursuant to which HMI Controls any Know-How or Patent Rights that are included within the HMI Licensed Technology.

14.2.3 **HMI Inventions and Assignments**. With respect to any HMI Licensed Technology owned by HMI, (a) HMI and its Affiliates have obtained from all individuals who contributed to the conception or reduction to practice thereof, effective assignments of all ownership rights of such individuals in such HMI Licensed Technology, either pursuant to written agreement or by operation of law, and (b) all of its employees, officers, and consultants have executed agreements or have existing obligations under Applicable Law requiring assignment to HMI or its Affiliates, as applicable, of all inventions made during the course of performance under this Agreement, and no officer or employee of HMI or its Affiliates is subject to any agreement with any other Third Party that requires such officer or employee to assign any interest in any HMI Licensed Technology to any Third Party.

14.2.4 **License to NVS**. HMI has the right and authority to: (a) grant to NVS and its Affiliates the licenses under the HMI Licensed Technology that HMI grants to NVS in accordance with the terms and conditions of this Agreement; and (b) use, disclose, and commercially exploit, and to enable NVS and its Affiliates to use, disclose, and commercially exploit the HMI Licensed Technology in accordance with the terms and conditions of this Agreement.

14.2.5 **Third Party Licenses**. HMI has fully and accurately disclosed to NVS the relevant terms of the COH License and the Caltech License.

14.2.6 **No Third Party Limitations**. HMI has not granted its Affiliates or any Third Party, including any academic organization or agency, rights that would interfere with NVS' rights hereunder, and there are no Third Party Licenses or arrangements other than as set forth in Schedule 14.2.2 to which HMI or any of its Affiliates is a party relating to HMI Licensed Technology that would (a) limit the rights granted to NVS under this Agreement or (b) restrict or result in a restriction on NVS' ability to Research, Develop, Manufacture, use, or Commercialize the Candidates or Products, in accordance with this Agreement.

14.2.7 **Confidentiality**. All employees, officers, and consultants of HMI and its Affiliates have executed agreements or have existing obligations under Applicable Law obligating the individual to maintain as confidential HMI's Confidential Information as well as confidential information of other parties (including of NVS and its

Affiliates) that such individual may receive in its performance under this Agreement, to the extent required to support HMI's obligations under this Agreement, and HMI and its Affiliates have taken commercially reasonable precautions to preserve the confidentiality of HMI Know-How that is not claimed in a published HMI Patent Right or that has not been publicly disclosed.

14.2.8 **No Interference**. Neither HMI nor any Affiliate has been involved in any proceedings or other claims in which such Person alleges any Third Party interference, infringement, misappropriation, or other violation of the HMI Licensed Technology, nor have any such proceedings been threatened in writing by HMI or its Affiliates.

14.2.9 **No HMI Infringement**. There is no pending action or proceeding alleging that the use of the HMI Licensed Technology with respect to the SCD Target or first Ophthalmic Target infringes, misappropriates, or otherwise violates any Intellectual Property Rights of any Third Party, and, to the Knowledge of HMI, there is no pending action or proceeding alleging that the use of the HMI Licensed Technology as otherwise contemplated under this Agreement infringes, misappropriates, or otherwise violates any Intellectual Property Rights of any Third Party.

14.2.10 **No Third Party Infringement**. To the Knowledge of HMI, no Patent Right or trade secret right owned or controlled by a Third Party will be infringed or misappropriated by: the Development, Manufacture, or Commercialization of any Candidates or Products by either Party or its Affiliates or Sublicensees in accordance with this Agreement, nor has HMI or its Affiliates received in writing any notice alleging such infringement or misappropriation.

14.2.11 **No Claims**. There are no claims, judgments, or settlements against or amounts with respect thereto owed by HMI or any of its Affiliates relating to the HMI Licensed Technology.

14.2.12 **No U.S. Government Funding.** Except for the Patent Rights and Know-How licensed to HMI under the COH License or Caltech License, neither HMI nor its Affiliates have entered into a government funding relationship that would result in rights to any Candidate or Product residing in the U.S. Government, National Institutes of Health, National Institute for Drug Abuse or other agency, and the licenses granted hereunder are not subject to overriding obligations to the U.S. Government as set forth in Public Law 96 517 (35 U.S.C. 200 204), as amended, or any similar obligations under the laws of any other country.

14.2.13 **Notices and Consents.** HMI has delivered any and all required notice letters and received any and all necessary consents from any Third Party necessary to effectuate any sublicenses granted to NVS and its Affiliates under HMI Licensed Technology. Upon NVS' request, HMI will provide NVS with written evidence of such notices and consents, including COH's receipt of such notice of the sublicense grant.

14.3. Compliance Covenants. Each of NVS and HMI covenant to the other as follows:

14.3.1 **Compliance with Law**. It will, and will ensure that its Affiliates, comply with all Applicable Law in connection with the performance of its and its Affiliates' activities under this Agreement, including, to the extent applicable, the European Data Protection Directive 95/46/EC, the European General Data Protection Regulation (Regulation (EU) 2016/679), and any other applicable national data protection legislation.

14.3.2 **No Inconsistent Obligations**. It will not, and will ensure that its Affiliates will not, take any action or enter into any agreement with any Third Party that diminishes the rights granted to the other Party under this Agreement.

14.3.3 **Foreign Corrupt Practices Act of 1977**. In performing under this Agreement, it and its Affiliates agree to comply with all applicable anti-corruption laws, including the Foreign Corrupt Practices Act of 1977, as amended from time-to-time; the anti-corruption laws of the Territory; and all laws enacted to implement the Organization for Economic Cooperation and Development Convention on Combating Bribery of Foreign Officials in International Business Transactions.

14.3.4 **No Bribery**. It will not directly or indirectly offer or pay, or authorize such offer or payment of, any money, or transfer anything of value, to improperly seek to influence any: (a) any elected or appointed government official (*e.g.*, a member of a ministry of health); (b) any employee or person acting for or on behalf of a Governmental Authority; (c) any political party officer, employee, or person acting for or on behalf of a political party or candidate for public office; (d) an employee or person acting for or on behalf of a public international organization; or (e) any person otherwise categorized as a government official under local law.

14.3.5 **Export Control**. Neither it nor its Affiliates will export, transfer, or sell any Product to any country or territory except in compliance with Applicable Law.

14.3.6 **Debarment**. It will not engage, in any capacity in connection with this Agreement or any ancillary agreements, any officer, employee, contractor, consultant, agent, representative, or other person who has been debarred by any Regulatory Authority, including under the Generic Drug Enforcement Act of 1992 (21 U.S.C. §301 et seq.), is under investigation for debarment action by any Regulatory Authority, has been disqualified as an investigator pursuant to 21 C.F.R. §312.70, has a disqualification hearing pending or is currently employing or using any Person that has been so debarred or disqualified by any Regulatory Authority to perform any of such Party's obligations under this Agreement. Each Party will inform the other Party in writing promptly if it or any person engaged by it or any of its Affiliates who is performing any obligations under this Agreement or any ancillary agreements is debarred or excluded, or if any action, suit, claim, investigation or legal or administrative proceeding is pending or, to each Party's knowledge, is threatened, pursuant to which a Party, any of its Affiliates or any such person performing obligations hereunder or thereunder may become debarred or excluded.

14.4. Additional Covenants of HMI.

14.4.1 **Conflicting Transactions**. During the Term, HMI will not, and will cause its Affiliates not to, enter into any agreement granting a license or other right under the HMI Licensed Technology that is inconsistent with this Agreement.

14.4.2 **HMI Third-Party License**. HMI will (a) maintain Control of all Patent Rights and Know-How licensed to NVS under each Third Party License to which HMI or its Affiliates is a party; (b) not materially breach or be in material default under any Third Party License to which HMI or its Affiliates is a party under which HMI Controls HMI Licensed Technology [***] for NVS to Research, Develop, Manufacture or Commercialize any Candidates or Products pursuant to this Agreement in a manner that would permit the counterparty thereto to terminate such Third Party License or otherwise diminish the scope or exclusivity of the licenses granted to NVS under the HMI Licensed Technology; and (c) not terminate or breach any Third Party License to which HMI or its Affiliates is a party in a manner that would terminate rights that are sublicensed to NVS or otherwise diminish the scope or exclusivity of the licenses granted to NVS under the HMI Licensed Technology. In the event that HMI receives notice of an alleged material breach by HMI or its Affiliates under any such Third Party License, where termination of such Third Party License or any diminishment of the scope or exclusivity of the licenses granted to NVS under the HMI Licensed Technology is being or could be sought by the counterparty, then HMI will promptly, but in no event less than [***] thereafter, provide written notice thereof to NVS and grant NVS the right (but not the obligation) to cure such alleged breach. HMI will not amend any Third Party License to which HMI or its Affiliates is a party in any manner that [***] affects NVS' exclusive rights to Research, Develop, Manufacture or Commercialize any Candidates or Products pursuant to this Agreement without NVS' prior written consent.

14.4.3 **Caltech License**. HMI will [***] execute the Caltech Side Letter, in a form reasonably acceptable to NVS, within [***] after the Effective Date.

14.5. **Warranty Disclaimer**. EXCEPT AS EXPRESSLY SET FORTH HEREIN, THE INTELLECTUAL PROPERTY RIGHTS, CANDIDATES, AND MATERIALS PROVIDED BY HMI ARE PROVIDED "AS IS" AND WITHOUT WARRANTY. EXCEPT AS EXPRESSLY SET FORTH HEREIN, EACH OF THE PARTIES EXPRESSLY DISCLAIMS ANY AND ALL WARRANTIES OF ANY KIND, EXPRESS OR IMPLIED, INCLUDING THE WARRANTIES OF DESIGN, MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, VALIDITY, OR ENFORCEABILITY OF THEIR RESPECTIVE INTELLECTUAL PROPERTY RIGHTS, AND NONINFRINGEMENT OF THE INTELLECTUAL PROPERTY RIGHTS OF THIRD PARTIES, IN EACH CASE, ARISING FROM A COURSE OF DEALING, USAGE, OR TRADE PRACTICES, IN ALL CASES WITH RESPECT THERETO.

Article 15. Indemnification; Limitation Of Liability; Insurance

15.1. **Indemnification of HMI by NVS**. Subject to Section 15.4 (Conditions to Indemnification), NVS will defend, indemnify, and hold harmless HMI and its Affiliates, and their respective employees, officers and directors ("**HMI Indemnitees**") from and against any and all liability, damage, loss, cost or expense of any nature (including reasonable attorney's fees and litigation expenses) ("**Losses**") incurred or imposed upon the HMI Indemnitees or any one of them in connection with any claims, suits, actions, demands, proceedings, causes of action or judgments resulting from a Third Party claim arising out of or relating to: (a) subject to Section 15.3 (U.S. SCD Product Liability and U.S. SCD Third Party Infringement), the Development or Commercialization of any Candidate or Product by or on behalf of any NVS Indemnitee; (b) subject to Section 15.3 (U.S. SCD Product Liability and U.S. SCD Third Party Infringement) and any supply agreement entered into between the Parties, the Manufacturing of any Candidates

or Products by or on behalf of any NVS Indemnitee; (c) the breach by any NVS Indemnitee of any term of this Agreement; or (d) the negligence or willful misconduct of any NVS Indemnitee, except in each case of ((a) through (d)), to the extent that any such claim results or arises from a matter for which HMI is obligated to indemnify NVS under Section 15.2 (Indemnification of NVS by HMI).

15.2. **Indemnification of NVS by HMI**. Subject to Section 15.4 (Conditions to Indemnification), HMI will defend, indemnify, and hold harmless NVS and its Affiliates, Sublicensees, and their respective employees, officers and directors ("**NVS Indemnitees**") from and against any and all Losses incurred or imposed upon the NVS Indemnitees or any one of them in connection with any claims, suits, actions, demands, proceedings, causes of action or judgments resulting from a Third Party claim arising out of or relating to (a) the conduct of the Research Activities; (b) subject to Section 15.3 (U.S. SCD Product Liability and U.S. SCD Third Party Infringement) and any supply agreement entered into between the Parties, the Manufacture of any Candidates or Products by or on behalf of any HMI Indemnitee; (c) subject to Section 15.3 (U.S. SCD Product Liability and U.S. SCD Third Party Infringement), the Commercialization of U.S. SCD Products by or on behalf of any HMI Indemnitees; (d) the breach by any HMI Indemnitee of any term of this Agreement; or (e) the negligence or willful misconduct of any HMI Indemnitee except, in each case ((a) through (e)), to the extent that any such claim results or arises from a matter for which NVS is obligated to indemnify HMI under Section 15.1 (Indemnification of HMI by NVS).

15.3. **U.S. SCD Product Liability and U.S. SCD Product Third Party Infringement**.

15.3.1 **Product Liability**. Subject to any supply agreements or quality agreements entered into between the Parties, (a) any Losses arising out of Third Party product liability claims arising from [***] will be treated as [***]; (b) any Losses arising out of Third Party product liability claims arising from [***]; and (c) any Losses arising out of Third Party product liability claims arising from [***], regardless of which Party incurs such Losses.

15.3.2 **Third Party Infringement**. Any Losses arising out of or relating to infringement, misappropriation, or other violation of the Intellectual Property Rights of any Third Party ("**Third Party Infringement Losses**") arising from (a) **[***]**; and (b) [***].

15.4. **Conditions to Indemnification**. Any Person seeking indemnification (the "**Indemnitee**") under this Article 15 (Indemnification; Limitation Of Liability; Insurance) will give prompt written notice of the indemnity claim to the indemnifying Party and promptly provide a copy to the indemnifying Party of any complaint, summons, or other written or verbal notice that the Indemnitee receives in connection with any such claim. An Indemnitee's failure to deliver written notice will relieve the indemnifying Party of liability to the Indemnitee under this Article 15 (Indemnification; Limitation Of Liability; Insurance) only to the extent such delay is prejudicial to the indemnifying Party's ability to defend or settle such claim. The indemnifying Party will have the right to assume and control the defense of the indemnification claim at its own expense with counsel selected by the indemnifying Party and reasonably acceptable to the Indemnitee; *provided*, *however*, that an Indemnitee will have the right to retain its own counsel, with the fees and expenses to be paid by the indemnifying Party, if representation of such Indemnitee by the counsel retained by the indemnifying Party would be inappropriate due to actual or potential differing interests between the Indemnitee and any other party represented by such counsel in such proceedings. The indemnifying Party will act reasonably and in good faith with respect to all matters relating to such claim. If the indemnifying Party does not assume the defense of the

indemnification claim as described in this Section 15.4 (Conditions to Indemnification), then the Indemnitee may defend the indemnification claim but will have no obligation to do so. The Indemnitee will not settle or compromise the indemnification claim without the prior written consent of the indemnifying Party, and the indemnifying Party will not settle or compromise the indemnification claim in any manner which would have an adverse effect on the Indemnitee's interests (including any rights under this Agreement or the scope, validity, or enforceability of any Patent Rights, Confidential Information, or other rights licensed to NVS by HMI hereunder), without the prior written consent of the Indemnitee, which consent, in each case (by the indemnifying Party or the Indemnitee, as the case may be), will not be unreasonably withheld, conditioned, or delayed. The Indemnitee will reasonably cooperate with the indemnifying Party at the indemnifying Party's expense and will make available to the indemnifying Party all pertinent information under the control of the Indemnitee, which information will be subject to Article 13 (Confidentiality). The indemnifying Party will not be liable for any settlement or other disposition of the claims by the Indemnitee if such settlement is reached without the written consent of the indemnifying Party pursuant to this Section 15.4 (Conditions to Indemnification).

15.5. **Limited Liability**. NEITHER OF THE PARTIES WILL BE ENTITLED TO RECOVER FROM THE OTHER PARTY ANY SPECIAL, INCIDENTAL, INDIRECT, CONSEQUENTIAL, OR PUNITIVE DAMAGES OR DAMAGES FOR LOSS OF PROFIT OR LOST OPPORTUNITY IN CONNECTION WITH THIS AGREEMENT, ITS PERFORMANCE OR LACK OF PERFORMANCE HEREUNDER, OR ANY LICENSE GRANTED HEREUNDER, EXCEPT TO THE EXTENT THE DAMAGES RESULT FROM (A) A PARTY'S WILLFUL MISCONDUCT OR NEGLIGENCE UNDER THIS AGREEMENT, (B) A BREACH OF THE OBLIGATIONS OF A PARTY UNDER ARTICLE 13 (CONFIDENTIALITY), (C) INFRINGEMENT OF INTELLECTUAL PROPERTY RIGHTS OWNED OR CONTROLLED BY THE OTHER PARTY, OR (D) AMOUNTS REQUIRED TO BE PAID AS PART OF A CLAIM FOR WHICH A PARTY PROVIDES INDEMNIFICATION UNDER Article 15 (INDEMNIFICATION; LIMITED LIABILITY; INSURANCE).

15.6. **Insurance Obligations**. Each Party will maintain during the Term and for a period of at least [***] after the last commercial sale of any Product for which it is responsible hereunder, and at its cost, reasonable insurance with a reputable solvent insurer against liability and other risks associated with its activities contemplated by this Agreement in an amount appropriate for its business and products of the type that are the subject of this Agreement, and for its obligations under this Agreement; *provided*, *however*, that at a minimum, each Party will maintain, in force beginning at least [***] prior to enrollment of the first subject in a Clinical Trial, product liability insurance policy providing coverage of at least [***]. Each Party will furnish to the other Party evidence of such insurance upon request. [***].

15.7. **Acknowledgement**. The Parties each acknowledge and agree that (a) [***], (b) [***], and (c) [***] will not in and of itself constitute a breach or default of any obligation in this Agreement.

Article 16. Term and Termination

16.1. **Term**. This Agreement will commence on the Effective Date and, unless otherwise terminated pursuant to Section 16.2 (Termination), 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 in the Territory (the "**Term**"). On a Product-by-Product and country-by-country basis, effective upon the expiration of the Royalty Term for such Product in such country (but not upon any earlier termination of this Agreement for any reason), the licenses granted to NVS will each become non-exclusive, fully paid-up, royalty-free, irrevocable, and perpetual in such country with respect to such Product.

16.2. **Termination**. This Agreement may be terminated as follows:

16.2.1 **Termination for Convenience by NVS**. NVS may terminate this Agreement on a Target-by-Target basis at will, in its sole discretion, on not less than (a) [***] prior written notice to HMI, following the First Commercial Sale of a Product that Modulates such Target, and (b) [***] prior written notice to HMI, if prior to the First Commercial Sale of a Product that Modulates such Target.

16.2.2 **Termination for Breach**. If a Party commits a material breach of any obligation set forth under this Agreement, then the other Party may terminate this Agreement with respect to the applicable Target that is the subject of such breach, unless such breach is cured within (a) the [***] period after receipt of written notice from the non-breaching Party with respect to any breach of any payment obligation under this Agreement, or (b) the [***] period after receipt of written notice from the non-breaching Party with respect to any other material breach of an obligation set forth under this Agreement; *provided*, that (i) if such breach, by its nature, is curable, but not within the foregoing cure period, then such cure period will be extended for a period of up to [***] (for a total cure period of [***]) if the breaching Party provides a written plan for curing such breach to the non-breaching Party and is using Commercially Reasonable Efforts to cure such breach in accordance with such written plan; and (ii) if the alleged breaching Party disputes in good faith the existence or materiality of any such breach specified in the notice provided by the other Party, and the alleged breaching Party provides notice of such dispute within such [***] period, as applicable, then the Party alleging such breach shall not have the right to terminate this Agreement unless and until the dispute resolution process provided for in Section 17.1 (Dispute Resolution) has been completed (including the tolling and curing period set forth therein).

16.2.3 **Termination for Bankruptcy**. This Agreement may be terminated in its entirety by a Party (the "**Non-Bankrupt Party**") by providing written notice of termination to the other Party upon the filing or institution of bankruptcy, reorganization, liquidation or receivership proceedings, or upon an assignment of a substantial portion of the assets for the benefit of creditors by the other Party (the "**Bankrupt Party**"); *provided*, *however*, that in the event of any involuntary bankruptcy or receivership proceeding such right to terminate will only become effective if the Bankrupt Party consents to the involuntary bankruptcy or receivership or such proceeding is not dismissed within [***] after the filing of such bankruptcy or receivership.

16.2.4 **Termination for Patent Challenge**. If NVS or any of its Affiliates files, assists a Third Party in filing, or joins a Third Party in filing or maintaining, a Patent Challenge of any Patent Right Controlled by HMI that Covers any Candidate or Product, HMI may, in its sole discretion, either (a) terminate this Agreement in its entirety by providing written notice of such termination to NVS or (b) leave the Agreement in effect, but increase each of the Royalty Rates, payable under Section 11.7 (Royalty Payments) by [***] percentage points by providing written notice of such increase to NVS; *provided*, *however*, that no such termination right or Royalty Rate increase right shall apply where (i) such Patent Challenge is brought as a defense in any lawsuit or administrative proceeding first brought by HMI, its Affiliates, or any licensees

for the Patent Rights forming the basis for such claim; or (ii) any Patent Challenge brought by NVS or any of its Affiliates challenging the validity or enforceability of any Patent Rights Controlled by HMI that is not included in the HMI Licensed Technology.

16.3. **Effects of Termination for NVS Breach, Patent Challenge, or for Convenience by NVS**. In the event that (a) HMI terminates this Agreement with respect to a Target for NVS' material breach pursuant to Section 16.2.2 (Termination for Breach), (b) HMI terminates this Agreement for Patent Challenge by NVS or any of its Affiliates pursuant to Section 16.2.4 (Termination for Patent Challenge); or (c) NVS terminates this Agreement with respect to a Target for convenience, then in each case, effective solely as of the effective date of termination, the following provisions will apply with respect to the Terminated Targets and all Candidates and Products that Modulate such Terminated Targets, but excluding, in all cases, any Other Components contained in such Products (the "**Terminated Candidates**" and "**Terminated Products**"), as applicable:

16.3.1 **Termination of Rights and Licenses**. Subject to Section 16.7 (Surviving Provisions), except as expressly set forth in this Agreement, all rights and licenses granted from one Party to the other hereunder will immediately terminate with respect to the Terminated Targets, Terminated Candidates, and Terminated Products, including any sublicenses granted by NVS pursuant to Section 4.3 (Sublicensing Rights); *provided*, *however*, if such termination relates to the Sickle Cell Target and was effected by NVS pursuant to Section 16.2.1 (Termination for Convenience by NVS), HMI's obligation to pay [***] with respect to any In-Vivo SCD Product shall remain payable as provided in Section 11.6.2 ([***]).

16.3.2 **Assignment of Regulatory Submissions**. NVS will (a) [***] assign to HMI all of its rights, title, and interests in and to all Clinical Trial data, Regulatory Submissions, and Regulatory Approvals and Pricing Approvals (where applicable) solely related to any Terminated Targets, Terminated Candidates, and Terminated Products owned or Controlled by NVS or any of its Affiliates or its Sublicensees as of the effective date of termination, and (b) [***] transfer ownership of all such assigned Regulatory Submissions and Regulatory Approvals and Pricing Approvals (where applicable) to HMI, including submitting to each applicable Regulatory Authority a letter or other [***] documentation notifying such Regulatory Authority of the transfer of such ownership of such Regulatory Approval and Pricing Approval (where applicable).

16.3.3 **License Grant to HMI For Termination for NVS Breach or NVS Patent Challenge**. If HMI terminates this Agreement with respect to a Target for NVS' material breach or for a Patent Challenge by NVS or any of its Affiliates, NVS will and hereby does, grant to HMI [***] with the [***] (subject to [***]), to (a) such [***] and [***] and [***] to any [***] or [***] then [***] that are not [***] or that are [***] but the [***] which has [***], in each case, pursuant to [***], (b) [***] respect to those [***] at the time [***] of the [***] such [***], in all cases, [***], in each case ((a) and (b)), to the extent [***], and (c) if, [***] has [***] for the purpose of [***]; *provided*, that with respect to **[***]** clauses (b) and (c), [***] subject to [***] if the [***] following the [***]. [***] pursuant to [***] without the [***] and, as far as [***] and be [***] set forth in [***].

16.3.4 **License Grant to HMI For Termination for Convenience by NVS**. If NVS terminates this Agreement with respect to a Target for convenience, NVS will and hereby does, grant to HMI [***], with the [***] (subject to [***]), to (a) such [***] to any [***] that are [***] or [***] but the [***], in each case, pursuant to [***], (b) [***] with respect to [***] or [***] for which [***] has been [***], such [***] as of [***] and [***], in all cases, [***] in or to [***], in each case ((a) and (b)), to the [***], subject to [***], and [***], and (c) if, as of [***] in the [***] for the purpose of [***] such [***]; *provided*, that with respect to [***] clauses (b) and (c), [***] for such [***], subject to [***] following the [***] on such [***]. If [***] or [***] by **[***]** pursuant to **[***]** of the [***], then [***] and as far as [***] such [***] the terms set forth in [***].

16.3.5 **Ongoing Clinical Trials**.

(a) **Transfer to HMI**. Unless prohibited by any Regulatory Authority or Applicable Law, at HMI's written request, NVS will [***] transfer control of all Clinical Trials involving any Terminated Products being conducted by or on behalf of NVS, an Affiliate, or a Sublicensee as of the effective date of termination to HMI or its Affiliates or a Third Party that is designated in writing by HMI. NVS will [***] continue to conduct such Clinical Trials, [***] to minimize interruption of any such Clinical Trials (including the assignment of all related investigator and other agreements relating to such Clinical Trials); *provided*, that HMI will not have any obligation to continue any Clinical Trial unless required by Applicable Law, accepted pharmaceutical industry norms, or ethical practices. [***]

(b) **NVS Wind-Down**. If HMI does not elect to assume control of any such Clinical Trials, then NVS will, in accordance with accepted pharmaceutical industry norms and ethical practices, wind-down any on-going Clinical Trials of Terminated Products for which it has responsibility hereunder in which Dose Initiation has commenced. [***]

16.3.6 **NVS Knowledge and Inventory Transfer**. NVS will provide to HMI or its designated Affiliate or Third Party copies of all material data, reports, records, and other material sales and marketing related information in NVS' possession and Control to the extent that such data, reports, records, materials or other information relate solely to the Development and Commercialization of such Terminated Candidates and Terminated Products. In connection with such transfer, NVS will, at HMI's option transfer to HMI or its designated Affiliate or Third Party all inventory of Terminated Candidates and Terminated Products and components and works in process held by NVS with respect to the Manufacture of Terminated Candidates and Terminated Products as of the effective date of termination of this Agreement at the cost paid by or on behalf of NVS for such inventory.

16.3.7 **Selected Third Party Agreements**. At HMI's written request, NVS will [***] HMI any Selected Third Party Agreement related solely to any Terminated Candidates or Terminated Products requested by HMI, unless assignment of any such Selected Third Party Agreement is not permitted, in which case NVS (or such Affiliate or Sublicensee, as applicable) will [***] secure the consent of the applicable Third Party to such assignment. If any assignment or such consent cannot be obtained with respect to a Selected Third Party Agreement, then, for a period of up to [***] from the effective date of termination, NVS will, or will cause such Affiliates or Sublicensees, as applicable, to, [***] obtain for HMI [***] practical benefit and burden under such Selected Third Party Agreement by entering into [***] alternative arrangements on terms agreeable to [***].

16.3.8 **Appointment as Exclusive Distributor**. If any Terminated Products are being Commercialized by NVS in any country in the Territory as of the effective date of termination, then, at HMI's election, until the earlier of (a) such time as all Regulatory Approvals and Pricing Approvals (where applicable) with respect to such Terminated Products in such country have been assigned and transferred to HMI, or (b) [***] from the effective date of termination, either (i) NVS will appoint HMI or its designee as its exclusive distributor of such Terminated Products in such country and grant HMI or its designee the right to appoint sub-distributors, to the extent not prohibited by Applicable Law or any written agreement between NVS or any of its Affiliates and a Third Party, or (ii) NVS will have the continued right to sell the Terminated Products in such country from its inventory, and the obligation to continue to Commercialize the Terminated Products in such country in accordance with the terms of this Agreement, and NVS' obligations under this Agreement with respect to all such Terminated Products that NVS sells, including the obligation to remit Royalties to HMI hereunder, will continue in full force and effect during such period.

16.3.9 **Supply of Product**. If NVS is Manufacturing such Terminated Products on the effective date of termination, at HMI's written request, which shall be exercised no later than [***] after the effective date of termination, the Parties will negotiate in good faith a supply agreement under which NVS will supply to HMI such quantities of Terminated Candidates and Terminated Products until the earlier of (a) such time as HMI has established an alternate, validated source of supply for such Terminated Candidates and Terminated Products, and (b) [***] from the anniversary of the effective date of termination of this Agreement. In addition, upon any such termination, any Development Supply Agreements or Commercial Supply Agreements for such Terminated Candidate or Terminated Product shall terminate.

16.3.10 **Responsibility for Costs**. Except as expressly set forth in this Section 16.3 (Effects of Termination for NVS Breach, Patent Challenge, or for Convenience by NVS), if this Agreement is terminated with respect to a Target by NVS for convenience, then within [***] after receipt of an invoice therefor along with reasonable documentation and substantiation of such costs, HMI will reimburse NVS the reasonable costs incurred by NVS in connection with NVS' performance of activities under Section 16.3 (Effects of Termination for NVS Breach, Patent Challenge, or for Convenience by NVS), and if this Agreement is terminated with respect to a Target by HMI for NVS' material breach or by HMI for Patent Challenge, then NVS will bear the costs incurred by NVS in connection with NVS' performance of activities under Section 16.3 (Effects of Termination for NVS Breach, Patent Challenge, or for Convenience by NVS).

16.4. Effects of Termination for Bankruptcy or HMI's Uncured Material Breach. In the event that a Party terminates this agreement pursuant to Section 16.2.3 (Termination for Bankruptcy) or NVS terminates this Agreement with respect to a Target for HMI's material breach then, subject to Section 16.7 (Surviving Provisions), except as expressly set forth in this Agreement, this Agreement and all rights and licenses granted from one Party to the other hereunder will immediately terminate.

16.5. **Special Remedy for HMI's Uncured Material Breach**. In the event that NVS would have the right to terminate this Agreement with respect to a Target for material breach by HMI then, in lieu of exercising such termination right, effective as of the date on which such termination would have taken place: (a) all rights and licenses granted from NVS to HMI with respect to such Target, Product, and Candidate will immediately terminate, including any sublicense granted thereunder; (b) any future milestone payments and future Royalties applicable to Net Sales of such Product will remain applicable in accordance with the terms of this Agreement; and (c) if such Target is the Sickle Cell Target for the In-Vivo Field, then: (i) the licenses granted to HMI pursuant to Section 4.2.2 (Exclusive Commercial License) and Section 10.7.3 (Trademark License) with respect to all U.S. SCD Products shall terminate and revert to NVS, (ii) NVS shall be the Commercializing Party for all U.S. SCD Products; (iii) any SCD with respect to any In-Vivo SCD Product shall be accelerated such that any amounts owed to NVS under [***] shall be paid to NVS within [***] days of the effective date of termination; (iv) all review, comment, discussion, or approval rights granted to HMI under this Agreement with respect to such U.S. SCD Products shall terminate, including rights at the JSC or any Subcommittee and rights with respect to regulatory matters, including Jointly-Agreed Regulatory Submissions; (v) NVS' Development, Manufacturing, and Commercialization reporting obligations (other than Royalty Reports) with respect to such Products shall be reduced to [***] NVS' Development, Manufacturing, and Commercialization activities with respect to such Target provided to HMI through the JSC; and (vi) HMI hereby assigns to NVS all of its right, title, and interest in and to Local Trademarks used by HMI with respect to such In-Vivo SCD Product, including the right to sue and recover for past, present, or future infringement, dilution, or other violation thereof, and all goodwill contained in such Local Trademarks. In addition, NVS shall have the right to [***].

16.6. **Confidential Information**. Upon termination of this Agreement for any reason, the Receiving Party will destroy all written, electronic, or other materials containing Confidential Information of the Disclosing Party provided to it by the Disclosing Party in connection with this Agreement, including all copies thereof, within [***] of such termination and provide certification of such destruction to the Disclosing Party; *provided*, that (a) the Receiving Party may retain one copy in its archives solely for the purpose of monitoring its ongoing confidentiality obligations hereunder, and (b) the Receiving Party will not be obligated to destroy such materials containing Confidential Information of the Disclosing Party that are necessary for the Receiving Party to exercise any other license or right of the Receiving Party that survives such termination of this Agreement; *provided*, that the Receiving Party's use of such Confidential Information of the Disclosing Party will continue to be subject to the requirements and restrictions set forth in Article 13 (Confidentiality).

16.7. **Surviving Provisions**. Subject to the other terms and conditions regarding the termination and survival of obligations under this Agreement in the event of expiration or termination of this Agreement, upon expiration or termination of this Agreement, all provisions of this Agreement will cease to have any effect, except that the following provisions will survive any such expiration or termination for any reason for the period of time specified therein, or if not specified, then they will survive indefinitely: Section 4.1.1(c) (Research License), Section 4.1.4 (Assigned Technology License), Section 4.2.3 (Non-Exclusive NVS Manufacturing Improvements License), Section 7.7 (Pharmacovigilance Agreement) and Section 7.8.2 (Recalls), in each case, where the Commercializing Party for the U.S. SCD Product is not the Manufacturing Party, and until such time that such Manufactured U.S. SCD Product is no longer in the market in the U.S., Section 11.8 (Royalty Reports; Payments), Section 11.9 (Other Payments) and Section 11.11 (Currency of Payment) through Section 11.14 (Withholding Taxes)), in each case, until such time as all payments accruing prior to the effective date of termination of the Agreement have been made, Section 11.10 (Records and Audits) for a period of [***] following the effective date of termination of the Agreement, Section 12.1 (Ownership of Inventions), Article 13 (Confidentiality), Article 15 (Indemnification; Limitation of Liability;

Insurance), Section 16.1 (Term), the last sentence, only upon expiration, Section 16.3 (Effects of Termination for NVS Breach, Patent Challenge, or for Convenience by NVS), Section 16.4 (Effects of Termination for Bankruptcy or HMI's Uncured Material Breach), Section 16.6 (Confidential Information), Section 16.7 (Surviving Provisions), and Article 17 (Miscellaneous). Termination of this Agreement will not relieve either Party of any liability that accrued hereunder prior to the effective date of such termination nor preclude either Party from pursuing all rights and remedies it may have hereunder or at law or in equity with respect to any breach of this Agreement. The remedies provided in this Article 16 (Term and Termination) are not exclusive of any other remedies a Party may have in law or equity.

Article 17. Miscellaneous

17.1. Dispute Resolution.

17.1.1 **Escalation**. In the event of any dispute, claim, controversy or cause of action asserted by a Party against the other Party or by the HMI Indemnitees against NVS or by the NVS Indemnitees against HMI arising out of or related to this Agreement or performance of this Agreement (a "**Claim**"), including any alleged breach of this Agreement or claim for indemnification pursuant to Article 15 (Indemnification; Limitation Of Liability; Insurance), such Party may, by written notice to the other Party, refer such matter to the Parties' respective officers designated below for attempted resolution (each, an "**Executive Officer**"):

For NVS: [***]

For HMI: [***]

17.1.2 **Full Arbitration**. Except as otherwise expressly set forth in this Agreement, if such Executive Officers do not resolve the dispute within [***] after receipt of such request, then, either Party may at any time after such [***] period submit such Claim to be finally settled by arbitration administered in accordance with the procedural rules of the American Arbitration Association (the "**AAA**") in effect at the time of submission, as modified by this Section 17.1.2 (Full Arbitration) (the "**Arbitration**"). The Arbitration will be governed by the Applicable Law of the State of New York. The Arbitration will be heard and determined by 3 arbitrators who are retired judges or attorneys with at least [***] of relevant experience in the pharmaceutical and biotechnology industry, each of whom will be impartial and independent and will not have worked for or on behalf of either Party for at least [***]. Each Party will appoint one arbitrator and the third arbitrator will be selected by the 2 Party-appointed arbitrators, or, failing agreement within [***] following appointment of the second arbitrator, by the AAA. Such Arbitration will take place in New York, New York. The Arbitration award so given will, absent manifest error, be a final and binding determination of the Claim, will be fully enforceable in any court of competent jurisdiction, and will not include any damages expressly prohibited by Section 15.5 (Limited Liability). NVS will pay the fees, costs and expenses for the arbitrator it chooses, HMI will pay the fees, costs and expenses for the arbitrator it chooses, and the Parties will share payment for the third arbitrator. Except in a proceeding to enforce the results of the Arbitration or as otherwise required by Applicable Law or securities exchange, neither Party nor any arbitrator may disclose the existence, content or results of any Arbitration hereunder without the prior written consent of both Parties.

17.1.3 **Expedited Arbitration**. If a Party exercises its rights under this Agreement to refer a dispute to expedited arbitration (an "**Expedited Dispute**"), then the Parties will follow the expedited dispute resolution process in this Section 17.1.3 (Expedited Arbitration) (and not the dispute resolution process in Section 17.1.2 (Full Arbitration)) ("**Expedited Arbitration**"). The Parties agree and acknowledge that any good faith dispute under Expedited Arbitration will not be deemed to be a material breach of this Agreement. The Expedited Dispute will be submitted to fast-track, binding arbitration in accordance with the following:

(a) Prior to referring an Expedited Dispute to arbitration, each Party will provide the other Party with a proposal and written memorandum in support of its position regarding the Expedited Dispute, as well as any documentary evidence it wishes to provide in support thereof (each a "**Brief**"). If the Parties cannot resolve the Expedited Dispute within [***] of exchanging Briefs, the Parties will refer the Expedited Dispute to arbitration.

(b) Arbitration will be conducted in New York, New York under the rules of the AAA for the resolution of commercial disputes in the most expedited manner permitted by such rules. The Parties will appoint a single arbitrator to be selected by mutual agreement. If the Parties are unable to agree on an arbitrator, the Parties will request that the AAA select the arbitrator. The arbitrator will be a professional in business or licensing experienced in the valuation of biopharmaceutical products with at least [***] of experience in the pharmaceutical and life sciences industries, including the conduct of research, development and commercialization collaborations. The cost of the arbitration will be borne equally by the Parties. Except in a proceeding to enforce the results of the arbitration or as otherwise required by Applicable Law, neither NVS nor HMI nor any arbitrator may disclose the existence, content or results of any arbitration hereunder without the prior written agreement of NVS and HMI.

(c) Within [***] after such matter is referred to arbitration, each Party will provide the arbitrator with its Brief, which may be revised from the form provided to the other Party pursuant to paragraph (a) above, and the arbitrator will provide each Party's Brief to the other Party after it receives it from both Parties.

(d) Within [***] after a Party submits its Brief, the other Party will have the right to respond thereto. The response and any material in support thereof will be provided to the arbitrator and the other Party.

(e) The arbitrator will have the right to meet with the Parties as necessary to inform the arbitrator's determination and to perform independent research and analysis. Within [***] of the receipt by the arbitrator of both Parties' responses (or expiration of the [***] period if any Party fails to submit a response), the arbitrator will deliver his/her decision regarding the Expedited Dispute in writing; *provided*, that the arbitrator will select one of the resolutions proposed by the Parties.

17.1.4 [***]. The Parties agree that [***] as well as [***] in which [***], will be [***] set forth in [***] for so long as [***], and the [***] such [***]. In addition, [***] of any [***], including under [***], (a) this [***], (b) the [***], (c) the [***] as to any [***], (d) any [***], and (e) [***] will [***], until the [***] and the [***] of the [***] to be the [***] for the [***]; *provided*, that if such [***] by (i) the [***] will have [***] of the [***] or (ii) the [***], the [***] will [***] and complete such [***] within such [***] or any [***] by such [***] before any such [***]. Further, with respect to [***] of the [***] will have [***] or any [***] by such [***] or [***] by the [***] of such [***].

17.2. **Designation of Affiliates**. Each Party may discharge any obligations and exercise any rights under this Agreement through delegation of its obligations or rights to any of its Affiliates. Each Party hereby guarantees the performance by its Affiliates of such Party's obligations under this Agreement, and will cause its Affiliates to comply with the provisions of this Agreement in connection with such performance. Any breach by a Party's Affiliate of any of such Party's obligations under this Agreement will be a breach by such Party, and the other Party may proceed directly against such Party without any obligation to first proceed against such Party's Affiliate.

17.3. **Injunctive Relief**. Notwithstanding anything to the contrary set forth in this Agreement, the Parties each stipulate and agree that (a) the other Party's Confidential Information includes highly sensitive trade secret information, (b) a breach of Article 13 (Confidentiality) by a Party with respect to such information may cause irrevocable harm for which monetary damages would not provide a sufficient remedy, and (c) in such case of a breach of Article 13 (Confidentiality), the non-breaching Party will be entitled to seek equitable relief (including temporary or permanent restraining orders, specific performance or other injunctive relief) from any court of competent jurisdiction. In addition, and notwithstanding anything to the contrary set forth in this Agreement, in the event of any other actual or threatened breach hereunder, the aggrieved Party may seek equitable relief (including temporary or permanent restraining orders, specific performance or other injunctive relief) from any court of competent jurisdiction without first submitting to the dispute resolution procedures set forth in Section 17.1 (Dispute Resolution).

17.4. **Governing Law**. This Agreement will be governed by and construed in accordance with the laws of the State of New York without taking into consideration any choice of law principles that would lead to the application of the laws of another jurisdiction.

17.5. **Waiver of Jury Trial**. TO THE EXTENT NOT PROHIBITED BY APPLICABLE LAW THAT CANNOT BE WAIVED, THE PARTIES HEREBY WAIVE, AND COVENANT THAT THEY WILL NOT ASSERT (WHETHER AS PLAINTIFF, DEFENDANT OR OTHERWISE), ANY RIGHT TO TRIAL BY JURY IN ANY ACTION ARISING IN WHOLE OR IN PART UNDER OR IN CONNECTION WITH THIS AGREEMENT, WHETHER NOW EXISTING OR HEREAFTER ARISING, AND WHETHER SOUNDING IN CONTRACT, TORT, OR OTHERWISE. THE PARTIES AGREE THAT ANY OF THEM MAY FILE A COPY OF THIS PARAGRAPH WITH ANY COURT AS WRITTEN EVIDENCE OF THE KNOWING, VOLUNTARY AND BARGAINED-FOR AGREEMENT AMONG THE PARTIES IRREVOCABLY TO WAIVE ITS RIGHT TO TRIAL BY JURY IN ANY PROCEEDING WHATSOEVER BETWEEN THEM RELATING TO THIS AGREEMENT WILL INSTEAD BE TRIED IN A COURT OF COMPETENT JURISDICTION BY A JUDGE SITTING WITHOUT A JURY.

17.6. **Cumulative Remedies**. The rights and remedies of the Parties under this Agreement are cumulative and not exclusive and, accordingly, are in addition to and not in lieu of any other rights and remedies of the Parties at law or in equity.

17.7. **Notices**. Any notice or report required or permitted to be given or made under this Agreement by either Party to the other will be in writing and delivered to the other Party at its address indicated below or to such other address as the addressee will have theretofore furnished in writing to the addressor by hand, courier or by registered or certified airmail (postage prepaid), in writing, by registered or certified airmail (postage prepaid):

If to NVS: Novartis Institutes for BioMedical Research, Inc.
250 Massachusetts Avenue
Cambridge, MA 02139
Attention: General Counsel

If to HMI: Homology Medicines, Inc.
45 Wiggins Avenue
Bedford, MA 01730
Attention: Chief Operating Officer

Copy to (which copy will not constitute notice):

Homology Medicines, Inc.
45 Wiggins Avenue
Bedford, MA 01730
Attention: Vice President, Intellectual Property

Copy to (which copy will not constitute notice):

Ropes & Gray LLP
800 Boylston Street, Prudential Tower
Boston, MA 02199
Attention: David M. McIntosh

All notices will be deemed effective: (a) if by courier, on the Business Day of delivery as evidenced by the courier's receipt (or if delivered or sent on a non-Business Day, then on the next Business Day); or (b) if sent by registered or certified airmail, on the Business Day of receipt as evidenced on the return receipt.

17.8. **Amendment; Waiver**. This Agreement may be amended, modified, superseded or cancelled only by a written agreement between the Parties, and any of the terms of this Agreement may be waived only by a written instrument executed by each Party or, in the case of waiver, by the Party or Parties waiving compliance. The delay or failure of either Party at any time or times to require performance of any provisions will in no manner affect the rights at a later time to enforce the same. No waiver by either Party of any condition or of the breach of any term contained in this Agreement, whether by conduct, or otherwise, in any one or more instances, will be deemed to be, or considered as, a further or continuing waiver of any such condition or of the breach of such term or any other term of this Agreement.

17.9. **Assignment and Successors**. Neither Party may assign or transfer this Agreement and the licenses granted under this Agreement without the other Party's prior written consent *unless* such assignment is to (a) a Third Party successor or purchaser of all or substantially all of the assets or businesses to which this Agreement relates whether pursuant to a sale of assets, merger, or other transaction, in which case the assigning Party will provide prior written notice to the other Party and need not obtain the other Party's consent, or (b) an Affiliate of such Party, in which case the

assigning Party will provide prior written notice to the other Party and need not obtain the other Party's consent; *provided*, that the assigning Party remains fully liable for the performance of its obligations hereunder by such assignee. [***] Any other assignment of this Agreement by a Party requires the prior written consent of the other Party. An assignment to an Affiliate will terminate, and all rights so assigned will revert to the assigning Party, if and when such Affiliate ceases to be an Affiliate of the assigning Party. For clarity, any assignment in violation of this Section 17.9 (Assignment and Successors) will be null, void, and of no legal effect. This Agreement will be binding upon and inure to the benefit of the Parties and their respective legal representatives, successors and permitted assigns.

17.10. **Force Majeure**. Neither NVS nor HMI will be liable for failure of or delay in performing obligations set forth in this Agreement, and neither will be in breach of its obligations, to the extent such failure or delay is due to a Force Majeure; *provided*, *however*, that a Force Majeure will not excuse any Party from any undisputed payment obligations to the other Party under this Agreement. In event of such Force Majeure, the Party affected will use reasonable efforts to avoid or remove such causes of nonperformance, and will continue to perform hereunder with reasonable dispatch whenever such causes are removed. The Party invoking such Force Majeure rights of this Section 17.10 (Force Majeure) must promptly notify the other Party by courier or overnight dispatch (*e.g.*, Federal Express) within a period of [***] of both the first and last day of the Force Majeure.

17.11. **Interpretation**. The Parties acknowledge and agree that: (a) each Party and its counsel reviewed and negotiated the terms and provisions of this Agreement and have contributed to its revision; (b) the rule of construction to the effect that any ambiguities are resolved against the drafting Party will not be employed in the interpretation of this Agreement; and (c) the terms and provisions of this Agreement will be construed fairly as to each Party and not in a favor of or against either Party, regardless of which Party was generally responsible for the preparation of this Agreement. In addition, except as otherwise explicitly specified to the contrary, (i) references to a section, schedule or exhibit means a section of, or schedule or exhibit to this Agreement, unless another agreement is specified, (ii) the word "including" (in its various forms) means "including without limitation," (iii) the words "shall" and "will" have the same meaning, (iv) references to a particular statute or regulation include all rules and regulations thereunder and any predecessor or successor statute, rules or regulations, in each case as amended or otherwise modified from time-to-time, (v) words in the singular will be held to include the plural and vice versa, and words of one gender will be held to include the other gender as the context requires, (vi) references to a particular Person include such Person's successors and assigns to the extent not prohibited by this Agreement, (vii) references to "days" will mean calendar days, unless otherwise specified, (viii) the word "or" will not be exclusive, unless the context otherwise requires, (ix) references to "written" or "in writing" include in electronic form, (x) the titles and headings contained in this Agreement are for reference purposes only and will not affect in any way the meaning or interpretation of this Agreement, (xi) the terms "hereof," "hereby," "hereto," and derivative or similar words refer to this entire Agreement, including any schedules or exhibits hereto, and (xii) unless otherwise specified, "$" is in reference to United States Dollars.

17.12. **Integration**. This Agreement and the COH Side Letter, together with all exhibits and schedules attached hereto, sets forth the entire agreement with respect to the subject matter hereof and thereof and supersedes all other agreements and understandings between the Parties with respect to such subject matter, including the Confidentiality Agreements.

17.13. **Severability**. Each Party hereby agrees that it does not intend to violate any public policy, statutory or common laws, rules, regulations, treaty, or decision of any government agency or executive body thereof of any country or community or association of countries. Should one or more provisions of this Agreement be or become invalid, the Parties will substitute, by mutual consent, valid provisions for such invalid provisions which valid provisions in their economic effect are sufficiently similar to the invalid provisions such that it can be reasonably assumed that the Parties would have entered into this Agreement with such valid provisions. In case such valid provisions cannot be agreed upon, the invalidity of one or several provisions of this Agreement will not affect the validity of this Agreement as a whole, unless the invalid provisions are of such essential importance to this Agreement such that it is to be reasonably assumed that the Parties would not have entered into this Agreement without the invalid provisions.

17.14. **Further Assurances**. Each of HMI and NVS agrees to duly execute and deliver, or cause to be duly executed and delivered, such further instruments and do and cause to be done such further acts and things, including, the filing of such additional assignments, agreements, documents and instruments, as the other Party may at any time and from time-to-time reasonably request in connection with this Agreement or to carry out more effectively the provisions and purposes of, or to better assure and confirm unto such other Party its rights and remedies under, this Agreement.

17.15. **Rights in Bankruptcy**. All licenses and rights to licenses granted under or pursuant to this Agreement by the Bankrupt Party to the Non-Bankrupt Party are, and will otherwise be deemed to be, for purposes of Section 365(n) of the United States Bankruptcy Code (the "**Bankruptcy Code**"), licenses of rights to "intellectual property" as defined under Section 101(35A) of the Bankruptcy Code. The Parties agree that the Non-Bankrupt Party, as a licensee of such rights under this Agreement, will retain and may fully exercise all of its rights and elections under the Bankruptcy Code. The Parties further agree that upon commencement of a bankruptcy proceeding by or against the Bankrupt Party under the Bankruptcy Code, the Non-Bankrupt Party will be entitled to a complete duplicate of, or complete access to (as the Non-Bankrupt Party deems appropriate), all such intellectual property and all embodiments of such intellectual property. Such intellectual property and all embodiments of such intellectual property will be promptly delivered to the Non-Bankrupt Party (a) upon any such commencement of a bankruptcy proceeding and upon written request by the Non-Bankrupt Party, unless the Bankrupt Party elects to continue to perform all of its obligations under this Agreement, or (b) if not delivered under (a) above, upon the rejection of this Agreement by or on behalf of the Bankrupt Party and upon written request by the Non-Bankrupt Party. The Bankrupt Party (in any capacity, including debtor-in-possession) and its successors and assigns (including any trustee) agrees not to interfere with the exercise by the Non-Bankrupt Party or its Affiliates of its rights and licenses to such intellectual property and such embodiments of intellectual property in accordance with this Agreement, and agrees to assist the Non-Bankrupt Party and its Affiliates in obtaining such intellectual property and such embodiments of intellectual property in the possession or control of Third Parties as reasonably necessary or desirable for the Non-Bankrupt Party to exercise such rights and licenses in accordance with this Agreement. The foregoing provisions are without prejudice to any rights the Non-Bankrupt Party may have arising under the Bankruptcy Code or other Applicable Law.

17.16. **Counterparts**. This Agreement may be executed simultaneously in any number of counterparts by digital or telephonic facsimile transmission, each of which will be an original and both of which, together, will constitute a single agreement.

[Remainder of page intentionally left blank.]

Confidential Portions of this Exhibit marked as [***] have been omitted pursuant to a request for confidential treatment and have been filed separately with the Securities and Exchange Commission.

IN WITNESS WHEREOF, the Parties have caused this Agreement to be executed by their duly authorized representatives.

HOMOLOGY MEDICINES, INC.

By: /s/ Arthur Tzianabos
Name: Arthur Tzianabos
Title: President & Chief Executive Officer

NOVARTIS INSTITUTES FOR BIOMEDICAL RESEARCH, INC.

By: /s/ Scott A. Brown
Name: Scott A. Brown
Title: VP, General Counsel

[Signature Page to Collaboration and License Agreement]

Exhibit A

Form of Invoice

[***]

Confidential Portions of this Exhibit marked as [***] have been omitted pursuant to a request for confidential treatment and have been filed separately with the Securities and Exchange Commission.

Schedule 1.130

HMI Platform Patent Rights

[***]

Confidential Portions of this Exhibit marked as [***] have been omitted pursuant to a request for confidential treatment and have been filed separately with the Securities and Exchange Commission.

Schedule 1.165

Knowledge of HMI

[***]

Schedule 3.4.1

General Research Plan

1. [***]

Schedule 4.5

Third Party License Terms

[***]

Confidential Portions of this Exhibit marked as [***] have been omitted pursuant to a request for confidential treatment and have been filed separately with the Securities and Exchange Commission.

Schedule 14.2

Exceptions to Representations and Warranties

[***]

Confidential Portions of this Exhibit marked as [***] have been omitted pursuant to a request for confidential treatment and have been filed separately with the Securities and Exchange Commission.

Schedule 14.2.1

HMI Patent Rights

[***]

Schedule 14.2.2

Third Party Licenses of HMI

The COH License

The CalTech License

Confidential Portions of this Exhibit marked as [***] have been omitted pursuant to a request for confidential treatment and have been filed separately with the Securities and Exchange Commission.

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the use in this Amendment No. 2 to Registration Statement No. 333-223409 on Form S-1 of our report dated February 23, 2018 (March 19, 2018 as to the effects of the reverse stock split and other matters described in Note 17) relating to the financial statements of Homology Medicines, Inc. appearing in the Prospectus, which is part of this Registration Statement.

We also consent to the reference to us under the heading “Experts” in such Prospectus.

/s/ DELOITTE & TOUCHE LLP

Boston, Massachusetts
March 23, 2018