Filed Pursuant to Rule 424(b)(3)
Registration No. 333-276093

Prospectus Supplement No. 1
(To Proxy Statement/Prospectus dated February 14, 2024)

Homology Medicines, Inc.

This prospectus supplement updates, amends and supplements the proxy statement/prospectus dated February 14, 2024 (the "Proxy Statement/Prospectus"), relating to the proposed merger of Homology Medicines, Inc., a Delaware corporation ("Homology"), and Q32 Bio Inc., a Delaware corporation ("Q32"), pursuant to an Agreement and Plan of Merger, entered into on November 16, 2023, pursuant to which Kenobi Merger Sub, Inc., a direct, wholly owned subsidiary of Homology, will merge with and into Q32, with Q32 surviving as a direct, wholly owned subsidiary of Homology, and the surviving corporation of the merger. The Proxy Statement/Prospectus forms a part of our Registration Statement on Form S-4 (Registration No. 333-276093).

This prospectus supplement is being filed to update, amend and supplement the Proxy Statement/Prospectus with the information contained in our Annual Report on Form 10-K filed with the SEC on March 12, 2024, which is set forth below.

This prospectus supplement is not complete without the Proxy Statement/Prospectus. This prospectus supplement should be read in conjunction with the Proxy Statement/Prospectus, which is to be delivered with this prospectus supplement, and is qualified by reference thereto, except to the extent that the information in this prospectus supplement updates or supersedes the information contained in the Proxy Statement/Prospectus. Please keep this prospectus supplement with your Proxy Statement/Prospectus for future reference.

Our common stock is listed on the Nasdaq Global Select Market under the symbol "FIXX". On March 12, 2024, the closing sale price of our common stock was $0.898 per share.

INVESTING IN OUR SECURITIES INVOLVES RISKS THAT ARE DESCRIBED IN THE "RISK FACTORS" SECTION BEGINNING ON PAGE 30 OF THE PROXY STATEMENT/PROSPECTUS.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus supplement or the Proxy Statement/Prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus supplement is March 13, 2024.

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

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2023

OR

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

For the transition period from to

Commission File Number: 001-38433

Homology Medicines, Inc.
(Exact name of Registrant as specified in its Charter)

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

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

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

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

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

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES ☐ NO ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. YES ☐ NO ☒

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

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

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

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

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

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

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

The aggregate market value of the voting and non-voting stock held by non-affiliates of the registrant, as of June 30, 2023, the last business day of the registrant's most recently completed second fiscal quarter, was approximately $45.8 million. Solely for purposes of this disclosure, shares of common stock held by executive officers, directors and certain stockholders of the registrant as of such date have been excluded because such holders may be deemed to be affiliates.

As of March 1, 2024, there were 58,133,540 shares of the registrant's common stock, par value $0.0001 per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Certain portions of the information required to be furnished pursuant to Part III of this Annual Report on Form 10-K will be set forth in, and incorporated by reference from, the registrant's definitive proxy statement for the annual meeting of stockholders or an amendment to this Annual Report on Form 10-K which will be filed with the Securities and Exchange Commission no later than 120 days after the end of the fiscal year ended December 31, 2023.

Auditor Firm Id:	34	Auditor Name:	Deloitte & Touche LLP	Auditor Location:	Boston, Massachusetts, USA

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements. We intend such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. All statements other than statements of historical fact contained in this Annual Report on Form 10-K, including, without limitation, statements regarding our future results of operations and financial position, the anticipated impact of the COVID-19 pandemic and the current economic slowdown on our business, the anticipated use of cash and business strategy, the potential, safety, efficacy, and regulatory and clinical progress of our product candidates, prospective products, product approvals, research and development costs, the anticipated timing and likelihood of success of clinical trials, the expected timing of the release of clinical trial data, the timing and expectations surrounding regulatory communications, our relationship with third-parties, our intent to engage in future strategic partnerships, and the plans and objectives of management for future operations and future results of anticipated products, are forward-looking statements. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplate,” “believe,” “estimate,” “predict,” “potential,” or “continue” or the negative of these terms or other similar expressions, though not all forward-looking statements use these words or expressions. The forward-looking statements in this Annual Report on Form 10-K 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 Annual Report on Form 10-K and are subject to a number of important factors that could cause actual results to differ materially from those in the forward-looking statements, including the factors described under “Summary Risk Factors” below and in the sections in Item 1A. "Risk Factors" of Part I and Items 7 and 7A. "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Quantitative and Qualitative Disclosures About Market Risk," respectively, of Part II of this Annual Report on Form 10-K.

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

You should read this Annual Report on Form 10-K and the documents that we reference in this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances, or otherwise. Unless the context requires otherwise, we use the terms “Homology,” “the Company,” “we,” “us,” “our” and similar designations in this Annual Report on Form 10-K to refer to Homology Medicines, Inc. and its wholly-owned subsidiary.

Summary Risk Factors

Our business is subject to numerous risks and uncertainties, including those described in Part I, Item 1A. "Risk Factors" in this Annual Report on Form 10-K. You should carefully consider these risks and uncertainties when investing in our common stock. The principal risks and uncertainties affecting our business include the following:

- 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 will require additional capital to fund our operations, and if we fail to obtain necessary financing, we may not be able to continue our operations for more than twelve months after the issuance date of our consolidated financial statements included elsewhere in this Annual Report on Form 10-K.
- Any financial or strategic option we pursue may not be successful. Moreover, our decision to discontinue further program development efforts may not result in the anticipated savings for the Company and may adversely affect our business.
- 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.
- Should we resume development of our product candidates, we would be heavily dependent on the success of our product candidates, and if none of our candidates receives regulatory approval or is not successfully commercialized, our business may be harmed.
- Should we resume development of our product candidates, 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. 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, prior to our initiated Phase 1 pheEDIT clinical trial. In addition, there have been a limited number of gene therapy products approved in the United States or in Europe and none of these products have utilized our AAVHSC platform.
- The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming and inherently unpredictable.
- Our product candidates have caused and may in the future 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.
- Adverse public perception of genetic medicine, and gene editing in particular, may negatively impact the length of time required to advance our product candidates through clinical trials, should we resume development of our product candidates, including the pace at which we advance patient enrollment, and potential regulatory approval of, or demand for, our potential products.
- We have historically contracted with third parties, including Oxford Biomedica (US) LLC, for the manufacture of certain materials for our research programs, preclinical and clinical studies. This reliance on third parties increases the risk that we will not have sufficient quantities of such materials, product candidates, or any medicines that we may develop and commercialize, or that such supply will not be available to us at an acceptable cost or in compliance with regulatory requirements, which could delay, prevent, or impair our development or commercialization efforts.
- Our contract manufacturers, including Oxford Biomedica (US) LLC, are subject to significant regulation with respect to manufacturing our former product candidates. The manufacturing facilities on which we historically and may in the future rely may not meet or continue to meet regulatory requirements, as applicable and as imposed to date, and have limited capacity.
- Even if we obtain FDA approval for our product candidates in the United States, we may never obtain approval for or commercialize them in any other jurisdiction, which would limit our ability to realize their full market potential.
- We may collaborate with third parties for the development and commercialization of our product candidates in the future, but there are no assurances that we will succeed in establishing and maintaining such collaborative relationships, which may significantly limit our ability to develop and commercialize our product candidates successfully, if at all.
- 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.
- Our recent reduction in force undertaken to significantly reduce our ongoing operating expenses may not result in our intended outcomes and may yield unintended consequences and additional costs.

PART I

Item 1. Business.

Overview

We are a clinical-stage genetic medicines company historically focused on transforming the lives of patients suffering from rare genetic diseases with significant unmet medical needs by addressing the underlying cause of the disease. Our proprietary platform is designed to utilize our human hematopoietic stem cell-derived adeno-associated virus vectors, or AAVHSCs, to precisely and efficiently deliver single administration genetic medicines *in vivo* through a nuclease-free gene editing modality, gene therapy, or gene therapy to express antibodies platform, or GTx-mAb, which is designed to produce antibodies throughout the body.

In July 2023, we completed a review of our business and our Board of Directors approved a plan to explore, review and evaluate a range of potential strategic options available to us, including, without limitation, an acquisition, merger, reverse merger, sale of assets, strategic partnerships or other transactions. Based on the financing environment and the anticipated clinical development timeline for our lead program, HMI-103, we stopped further development of our programs and reduced our workforce by 86% to significantly reduce our ongoing operating costs as we evaluated strategic alternatives.

Agreement and Plan of Merger

After a comprehensive review of strategic alternatives, on November 16, 2023, we entered into an Agreement and Plan of Merger, or the Merger Agreement, with Q32 Bio Inc., a Delaware corporation, or Q32, and Kenobi Merger Sub, Inc., a Delaware corporation and our direct, wholly owned subsidiary, or Merger Sub, pursuant to which, among other matters, and subject to the satisfaction or waiver of the conditions set forth in the Merger Agreement, Merger Sub will merge with and into Q32, with Q32 continuing as our wholly owned subsidiary and the surviving corporation of the merger, or the Merger. Our future operations are highly dependent on the success of the Merger and there can be no assurance that the Merger will be successfully consummated. If the Merger is completed, the business of Q32 will continue as the business of the combined company.

Merger Consideration

Subject to the terms and conditions of the Merger Agreement, (i) immediately prior to the effective time of the Merger, or the Effective Time, all Q32 preferred stock will be converted into Q32 common stock pursuant to the organizational documents of Q32, or the Q32 Preferred Stock Conversion, and (ii) at the Effective Time, (a) each outstanding share of Q32 common stock (excluding Q32 common stock issued in the Concurrent Financing, as described below) will be converted into the right to receive a number of shares of our common stock, or the Company Common Stock, calculated in accordance with the Merger Agreement, (b) each outstanding Q32 stock option and warrant that has not previously been exercised prior to the closing of the Merger will be assumed by us and become an option or warrant, as applicable, to purchase a number of shares of Company Common Stock and (c) the Q32 common stock issued in the Concurrent Financing will be converted into the right to receive a number of shares of Company Common Stock calculated in accordance with the Merger Agreement. The shares of Company Common Stock that will be issued to stockholders of Q32 will be calculated using a formula in the Merger Agreement based on the equity value of each of Q32 and us. Q32 has been ascribed an aggregate equity value of $195 million and our equity value is expected to be approximately $80 million subject to adjustment based on the amount of our net cash at closing of the Merger.

Concurrent Financing

Pursuant to the Merger Agreement, immediately prior to the Effective Time, Q32 will consummate a financing through the sale of its common stock for aggregate gross proceeds of $42 million based on the same aggregate equity value of Q32 used in the Merger, or the Concurrent Financing. On November 16, 2023, Q32 entered into subscription agreements with certain accredited investors, or the Investors, for the Concurrent Financing with expected gross proceeds to Q32 of $42 million. In connection with the Concurrent Financing, at the closing of the Merger, Q32 will enter into a registration rights agreement with the Investors providing for the registration under the Securities Act of 1933, as amended, or the Securities Act, of the shares of common stock sold in the Concurrent Financing. The consummation of the transactions contemplated by the subscription agreements is conditioned on the satisfaction or waiver of the conditions set forth in the Merger Agreement and in the subscription agreements. Shares of Q32 common stock issued pursuant to the Concurrent Financing will be converted into shares of Company Common Stock in the Merger in accordance with the Merger Agreement.

Contingent Value Rights Agreement

At the Effective Time, if any Legacy Assets (as defined below) have not been disposed of in a Legacy Asset Disposition (as defined below) or if additional consideration may be payable for the Legacy Assets (as defined below) after closing of the Merger, the Company and Equiniti Trust Company, LLC, a New York limited liability company, as the initial rights agent, or the Rights Agent, will enter into a Contingent Value Rights Agreement, or the CVR Agreement, pursuant to which our common stockholders of record as of the close of business on the last business day prior to the day on which the Effective Time occurs will receive one contingent value right (each, a "CVR") for each outstanding share of Company Common Stock held by such stockholder on such date.

Each CVR will represent the contractual right to receive payments from us upon the actual receipt by us or our subsidiaries of certain contingent proceeds derived from any cash consideration that is paid to us or our subsidiaries as a result of the sale, transfer, license, assignment or other divestiture, disposition or commercialization of any of our assets, rights and interests relating to our HMI-103, HMI-204, Capsids and AAVHSC Platform, including any equity interests held directly or indirectly by us in Oxford Biomedica (US) LLC (f/k/a Oxford Biomedica Solutions LLC and Roadrunner Solutions LLC), or OXB (US), pursuant to that certain Equity Securities Purchase Agreement, dated as of January 28, 2022, by and between the Company and OXB Solutions, or the Legacy Assets, and such disposition, or a Legacy Asset Disposition, net of certain tax, transaction costs and certain other expenses.

The contingent payments under the CVR Agreement, if they become payable, will become payable to the Rights Agent for subsequent distribution to the holders of the CVRs. There can be no assurance that any holders of CVRs will receive payments with respect thereto. The right to the contingent payments contemplated by the CVR Agreement is a contractual right only and will not be transferable, except in the limited circumstances specified in the CVR Agreement. The CVRs will not be evidenced by a certificate or any other instrument and will not be registered with the Securities and Exchange Commission, or SEC. The CVRs will not have any voting or dividend rights and will not represent any equity or ownership interest in the Company or any of its affiliates. No interest will accrue on any amounts payable in respect of the CVRs.

Former Clinical Programs

Our former clinical programs include: HMI-103, an investigational gene editing candidate for the treatment of patients with phenylketonuria, or PKU; HMI-203, an investigational gene therapy candidate for the treatment of patients with mucopolysaccharidosis type II (MPS II), or Hunter syndrome; and HMI-102, an investigational gene therapy candidate for the treatment of adult patients with PKU. Our former preclinical programs include: HMI-104, a GTx-mAb gene therapy candidate for the treatment of patients with paroxysmal nocturnal hemoglobinuria, or PNH, and HMI-204, a gene therapy candidate for metachromatic leukodystrophy, or MLD. We are currently exploring strategic alternatives for HMI-103 (Adult/Pediatric PKU), HMI-204 (MLD) and our capsids and AAVHSC platform, including the sale of these programs.

In August 2023, we withdrew our Clinical Trial Application, or CTA, for HMI-203 in Canada. In September 2023, we withdrew our IND for HMI-102, which the FDA formally acknowledged in November 2023. In December 2023, we withdrew our IND for HMI-203 and in March 2024, we withdrew our IND for HMI-103. All clinical trial sites have been notified that all studies we had been conducting for our programs have been terminated; sites have been duly notified of their responsibilities. We have also withdrawn all orphan drug designations for our programs in both the United States and the EU.

In September 2023, we inactivated the pheEDIT Phase 1 gene editing clinical trial evaluating HMI-103 in adults with classical PKU (NCT05222178). In October 2023, we reported clinical data from the first dose cohort in the pheEDIT trial. As of the data cut-off date of September 14, 2023, HMI-103 was generally well-tolerated in all three participants with no serious adverse events, and the majority of treatment-related adverse events were mild and transient. All liver function tests remained in the normal range during the prophylactic immunosuppression regimen incorporating the T-cell inhibitor tacrolimus in combination with corticosteroid. Participant 1 experienced a reduction in plasma phenylalanine, or Phe, levels to below the U.S. American College of Medical Genetics and Genomics PKU treatment guideline threshold of <360 μmol/L, and the majority of Phe levels were below 360 mmol/L through 39 weeks post-dose, including after the initiation of dietary protein supplementation. Participant 2 experienced a meaningful plasma Phe reduction of 50% at 23 weeks post-dose. Participant 3 experienced a meaningful plasma Phe reduction of 60% at 14 weeks post-dose.

In August 2023, we terminated both the pheNIX Phase 1/2 gene therapy clinical trial evaluating HMI-102 in adults with classical PKU and the juMPStart Phase 1 gene therapy clinical trial evaluating HMI-203 in adults with Hunter Syndrome. INDs for both the pheNIX Phase 1/2 and juMPStart Phase 1 clinical trials have been withdrawn.

Earlier-Stage Product Candidates

We completed IND-enabling studies with HMI-202, an investigational gene therapy for the treatment of patients with MLD. Applying the learnings from these IND-enabling studies, in August 2022, we announced the details of HMI-204, an optimized, *in vivo*, one-time gene therapy product candidate for the treatment of MLD. Following a single I.V. administration in the MLD murine model, this optimized candidate, which uses one of our proprietary AAVHSC capsids, crossed the blood-brain-barrier to the CNS and reached key peripheral organs involved in MLD. This resulted in expression of human ARSA, or hARSA, levels in multiple brain regions and cell types above the minimum level of enzyme needed to correct the MLD disease phenotype, hARSA activity levels in the brain predictive of functional assay improvements and hARSA activity in the serum. Additionally, these optimizations led to significant improvements in vector yield and superior packaging for the product candidate.

HMI-104 was a candidate for PNH from our GTx-mAb platform. This platform represents an additional way that we could potentially leverage our AAVHSCs in an effort to deliver one-time *in vivo* gene therapy to express and secrete antibodies from the liver, which we believe may allow us to target diseases with larger patient populations. In support of this program, we generated and presented preclinical data targeting complement protein 5, demonstrating preclinical proof-of-concept in PNH. A single I.V. dose of an AAVHSC GTx-mAb showed expression of full-length antibodies from the liver consistent with levels associated with anti-C5 therapeutics, sustained and robust Immunoglobulin G, or IgG, expression *in vivo* in a humanized murine liver model and a murine NOD-SCID model, and *in vivo* vector-expressed C5 mAb had potent functional activity as shown by an *ex vivo* hemolysis assay. Additionally, we observed sustained expression of C5 mAb in the presence of murine and human neonatal fragment crystallizable (Fc) receptor, or FcRn. We completed IND-enabling studies with HMI-104.

Oxford Biomedica (US) LLC Transaction

On March 10, 2022, we closed a transaction with OXB (US), Oxford Biomedica (US), Inc., or OXB, and Oxford Biomedica plc, or OXB Parent, and collectively with OXB, Oxford, pursuant to the Equity Securities Purchase Agreement, or the Purchase Agreement, dated as of January 28, 2022, by and among Homology, OXB (US) LLC and Oxford, whereby, among other things, we and Oxford agreed to collaborate to operate OXB (US) LLC, which provides AAV vector process development and manufacturing services to biotechnology companies, which we refer to as the Oxford Biomedica (US) LLC Transaction, or the OXB (US) LLC Transaction. OXB (US) LLC incorporates our proven 'plug and play' process development and manufacturing platform, as well as our experienced team and high-quality GMP vector production capabilities that we built and operated since 2019.

Pursuant to the terms of the Purchase Agreement and a contribution agreement, or the Contribution Agreement, entered into between us and OXB (US) LLC prior to the closing of the OXB (US) LLC Transaction, or the Closing, we agreed to assign and transfer to OXB (US) LLC all of our assets that are primarily used in the manufacturing of AAV vectors for use in gene therapy or gene editing products, but excluding certain assets related to manufacturing or testing of our proprietary AAV vectors, or collectively, the Transferred Assets, in exchange for 175,000 common equity units in OXB (US) LLC, or Units, and OXB (US) LLC assumed from us, and agreed to pay, perform and discharge when due, all of our duties, obligations, liabilities, interests and commitments of any kind under, arising out of or relating to the Transferred Assets.

Effective as of the Closing, we sold to OXB, and OXB purchased from us, 130,000 Units, or the Transferred Units, in exchange for $130.0 million. In connection with the Closing, OXB contributed $50.0 million in cash to OXB (US) LLC in exchange for an additional 50,000 Units. Immediately following the Closing, (i) OXB owned 180,000 Units, representing 80 percent (80%) of the fully diluted equity interests in OXB (US) LLC, and (ii) we owned 45,000 Units, representing 20 percent (20%) of the fully diluted equity interests in OXB (US) LLC.

Pursuant to the Amended and Restated Limited Liability Company Agreement of OXB (US) LLC, or the OXB (US) LLC Operating Agreement, which was executed in connection with the Closing, at any time following the three-year anniversary of the Closing, (i) OXB will have an option to cause us to sell and transfer to OXB, and (ii) we will have an option to cause OXB to purchase from us, in each case all of our equity ownership interest in OXB (US) LLC at a price equal to 5.5 times the revenue for the immediately preceding 12-month period, subject to a maximum amount of $74.1 million. Pursuant to the terms of the OXB (US) LLC Operating Agreement, we are entitled to designate one director on the board of directors of OXB (US) LLC, currently Paul Alloway, Ph.D., our President and Chief Operating Officer.

Concurrently with the Closing, we entered into certain ancillary agreements with OXB (US) LLC including a license and patent management agreement whereby OXB (US) LLC granted certain licenses to us, a supply agreement, or the Supply Agreement, for a term of three years which includes certain annual minimum purchase commitments, a lease assignment pursuant to which we assigned all of our right, title and interest in, to and under our facility lease to OXB (US) LLC, a sublease agreement whereby OXB (US) LLC subleased certain premises in its facility to us, as well as several additional ancillary agreements.

Corporate Headquarters Lease

In November 2021, we entered into an amendment of our December 2017 lease agreement, or the Lease Amendment, for our corporate headquarters in Bedford, Massachusetts. The Lease Amendment increased the space under the lease by approximately 23,011 square feet, or the Expansion Premises, and extended the expiration date of the existing premises under the lease from February 2027 to June 2030. The term with respect to the Expansion Premises commenced on May 1, 2022 and continues for a period of ten years and five months. The term of the Expansion Premises and the existing premises are not coterminous. Annual base rent for the existing premises under the Lease Amendment is approximately $4.7 million beginning on March 1, 2027, and increases by three percent annually; annual base rent for the Expansion Premises is approximately $1.4 million per year and increases by three percent annually. The Lease Amendment allows for tenant improvement allowances not to exceed $6.3 million in the aggregate. Under the terms of the agreement with Oxford, our lease for our corporate headquarters, including the Expansion Premises, has been assigned to OXB (US) LLC with Homology subleasing a portion of lab and office space back from OXB (US) LLC until December 31, 2024. Effective October 1, 2023, we were released from being primary obligor under such lease, See Note 10 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for additional information regarding our lease agreement.

License Agreements

In April 2016, we entered into an exclusive license agreement with City of Hope, or COH, pursuant to which COH granted us an exclusive, sublicensable, worldwide license, or the COH 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. On August 6, 2021, we received notice from COH that we did not accomplish at least one of the partnering milestones by the applicable deadline, as set forth in the COH License. This notice does not affect our exclusive license in the field of mammalian therapeutics, including all human therapeutics, associated diagnostics, and target validation, or the Mammalian Therapeutic Field, where we retain exclusive rights. Instead, the notice served as written notice that the exclusive license granted pursuant to the COH License in all fields except the Mammalian Therapeutic Field converted from exclusive to non-exclusive effective as of September 20, 2021, which was forty-five days from the receipt of notice. In connection with the conversion, any royalty obligations and sublicensee fees relating to fields outside of the Mammalian Therapeutic Field shall be reduced by a certain percentage. This change to our exclusive worldwide license with COH does not impact any of our former therapeutic product development candidates, including HMI-102, HMI-103, HMI-203, HMI-204 and HMI-104.

Financial Overview

Since our inception in 2015 through December 31, 2023, we have raised approximately $721 million in aggregate net proceeds through our initial public offering, or IPO, in April 2018, follow-on public offerings of common stock in April 2019 and April 2021, proceeds from the sale of common stock under an “at-the-market” sales agreement, equity investments from pharmaceutical companies, preferred stock financings and our agreement with Oxford. Included in our net proceeds is a $130.0 million up-front cash payment from our agreement with Oxford, $50.0 million from a former collaboration partner, comprised of an up-front payment of $35.0 million and a $15.0 million equity investment, and a $60.0 million equity investment from Pfizer Inc., or Pfizer, through a private placement transaction. Should we resume development of one or more of our product candidates, we will require additional capital in order to advance our product candidates through clinical development and commercialization.

Our Opportunity in Genetic Medicines

We were historically focused on monogenic diseases where the genetic abnormality is known to occur in a single gene. The majority of monogenic diseases harbor thousands of individual mutations within the diseased gene, each resulting in a loss of function. Adding a functional gene to the cell where there is a missing or mutated gene (gene therapy), replacing an entire diseased gene with a whole functional gene (gene editing), or expressing an antibody to address the underlying genetic disease mechanism (GTx-mAb), are the optimal therapeutic approaches 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 integration in rapidly dividing cells.

The current focus of most nuclease-based gene editing companies 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 requires knock-down or inactivation. Our HR-driven gene editing approach aims to achieve functional gene integration into the patient’s genome and potentially address the majority of monogenic diseases by replacing an entire diseased gene with a whole functional gene. Our gene therapy approach, on the other hand, seeks to introduce a functional copy of a defective gene 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.

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 1990s, researchers discovered that certain 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. Despite high potential for error, the majority of nuclease-based gene editing approaches primarily utilize the NHEJ pathway.

We believe the major limitation of nuclease-based gene editing 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 replace 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 carries the risk of unwanted mutations from NHEJ including insertions and deletions or opposite orientation insertion of the template DNA, and also requires the separate delivery of both the nuclease and the DNA template to the same location at the same time.

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

Our Platform & Approach

In developing a genetic medicine product candidate, our strategy was to choose the AAVHSC that reaches the area(s) of the body needed to address the specific disease we were targeting. We then designed the product candidate to precisely and efficiently deliver genetic medicines following a one-time I.V. infusion (*in vivo*) using a gene therapy, nuclease-free gene editing, or GTx-mAb modality. Refer to Figure 1 below for a graphical depiction of our platform.

Modality (*in vivo*)	GENE THERAPY	GTx-mAb	NUCLEASE-FREE GENE EDITING
Target	Slowly or Non-Dividing Cells	Slowly or Non-Dividing Cells	Dividing Cells
Method	Gene Transfer to Express Therapeutic Proteins *Does not integrate into DNA*	Gene Therapy to Produce Antibodies Throughout the Body	Gene Integration to Replace Entire Diseased Gene with Whole Functional Gene

Figure 1. Our Genetic Medicines Platform.

Our novel AAVHSCs are packaged with either a gene therapy or a gene editing construct. Our gene therapy construct includes a functional copy of the gene and a promoter 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. Our 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, enable correction of the diseased gene in the genome by replacement with a whole functional copy. Our GTx-mAb platform is an extension of our gene therapy approach. It is designed to utilize AAVHSCs to deliver therapeutic DNA for heavy chain and light chain antibody proteins that can be delivered to the liver where they form fully functional, full-length Immunoglobulin G (IgG) antibodies and are secreted throughout the body.

While others are working on identifying and testing ways to mitigate the inherent risk in working with nucleases for gene editing, 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 integration, which we believe is capable of providing potential cures for a wide range of rare genetic diseases. Refer to Figure 2 below for a graphical depiction of how our AAVHSCs are designed to enable each therapeutic modality.

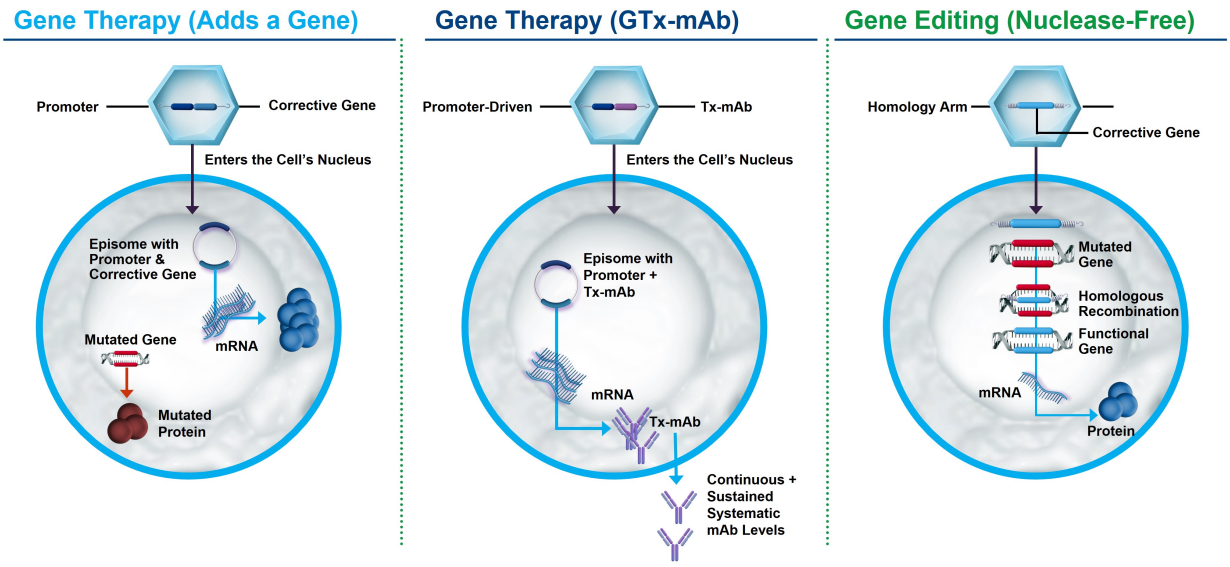


Figure 2. How our AAVHSCs are designed to enable each therapeutic modality.

We believe our approach has several key advantages, including:

- ***Our proprietary AAVHSC platform enables a nuclease-free gene editing modality, gene therapy, or GTx-mAb.*** Our platform provides us the flexibility to deliver genetic medicines through the best suited modality 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 AAVHSCs are naturally occurring as they were originally isolated from normal human CD34 cells and have the potential to result in an improved safety profile.
- ***Ability to perform nuclease-free gene editing mediated by HR with gene integration efficiencies that achieve therapeutic ranges.*** Our family 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 integration efficiencies that we believe 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, which is only potentially useful for the minority of monogenic diseases, they have shown limited published evidence of gene integration 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 also known as gene integration, 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 integration 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 family of AAVHSCs has demonstrated unique biodistribution properties across the serotypes and the ability to target a wide variety of tissues including the liver, CNS, including the ability to cross the blood-brain-barrier, PNS, muscle, bone marrow, eye and heart, enabling us to potentially address a broad range of monogenic diseases. The diversity of our AAVHSC library of capsids can also be expanded through targeted shuffling of the capsid sequences.
- **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 therapeutic candidates relative to existing nuclease-based gene editing approaches.

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

Our Former Pipeline Strategy

We initially pursued monogenic diseases where we knew exactly what we were seeking to correct and exactly which gene to insert into patients' cells, including delivery via our GTx-mAb platform to express and secrete antibodies from the liver. We prioritized monogenic diseases with significant unmet medical needs, validated regulatory pathways, well-accepted biomarkers and significant commercial opportunities. We were formerly focused on developing product candidates to treat monogenic diseases in the liver, CNS and peripheral tissues, bone marrow, and the eye, given that our AAVHSCs naturally show a high degree of tropism or ability to enter cells in these organs and organ systems. These tissues are affected in many rare genetic diseases.

Our initial focus areas included 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 were 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 believe we have validated our AAVHSC platform in the liver based on the results observed in the dose-escalation portion of our Phase 1/2 trial with HMI-102, and in the first dose cohort of our Phase 1 trial with HMI-103. We have completed a comprehensive *in vivo* biodistribution study in NHPs in which all 11 of the AAVHSCs tested crossed the blood-brain-barrier and the blood-nerve-barrier.

Our Genetic Medicines Platform

Our proprietary genetic medicines platform is built on our novel AAVHSCs, which allow us to choose the best suited modality from either a gene therapy, nuclease-free gene editing, or GTx-mAb modality 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. The unique characteristics of our platform enable nuclease-free gene editing, specifically gene integration, and broad, systemic tissue distribution. 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 system simplifies the manufacturing and delivery of our therapeutics. We believe our gene editing approach has the potential to be curative 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 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 for more efficient and safer therapeutics for a wide range of genetic diseases.

Homologous Recombination—A Powerful Basis for Gene Editing

Our technology is based on the natural DNA repair process of HR and is designed to enable precise and efficient gene integration without an exogenous nuclease.

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 (refer to Figure 3 below). 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 integration 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. Based on the packaging size of our AAVHSCs, we believe our capsids are capable of accommodating and delivering up to approximately 85% of the genes in the human genome and thus have the ability to address a significant majority of genetic disorders. 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 30 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. 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 at the right place at the same time, 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.

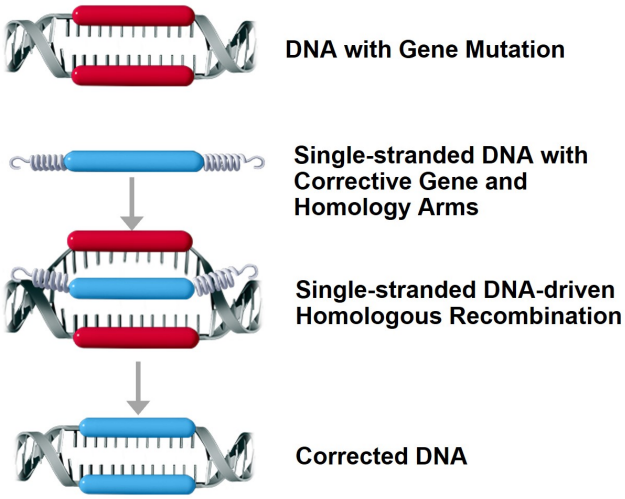


Figure 3. Schematic of homologous recombination.

Our Proprietary AAVHSCs

Our genetic medicines platform is based on a family of 15 proprietary AAVHSCs which we can deploy with a gene therapy, gene editing or GTx-mAb construct. We have the opportunity to expand on this family through capsid shuffling. Both applications rely on the 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 integration with higher efficiency relative to that indicated in published data for other AAV-based gene editing approaches. 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 factors such 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 In Vivo *Nuclease-free Gene Editing Mediated by HR*

To demonstrate the utility of AAVHSC-mediated gene editing *in vivo*, we conducted a series of initial experiments utilizing AAVHSC15.

We obtained initial preclinical proof-of-concept for *in vivo* editing efficiency and tissue-specific expression through the design of a promoter-less luciferase construct targeting the murine Factor 8, or *F8*, locus using AAVHSC15. *F8* is a locus in the murine genome that is known to have a strong promoter but is expressed only in the liver.

AAVHSC15 packaging the promoter-less F8 targeting cassette (AAVHSC15-mF8-Luc) was administered by a single intravenous injection to albino-B6 mice and high levels of luciferase expression in livers were observed. Bioluminescence increased within a week post-dosing, reached a maximum within 1-2 months and remained significantly above that observed in vehicle-treated mice until the end of the study at 470 days post-dosing (*= $P<0.0001$ vs vehicle). *Ex vivo* imaging of tissues harvested on Day 470 showed highest luciferase expression within liver (*=$p<0.008$ vs vehicle), greater than 100-fold higher than other tissues assessed (**=$P<0.0001$ vs other tissues), which demonstrated specificity of tissue targeting by

AAVHSC15-mF8-Luc. At 470 days post-dosing, vector genome levels within livers of treated mice were on average 4.7 ± 2.7 vector genomes/allele.

To molecularly characterize AAVHSC15-mF8-Luc-mediated genome editing, a ddPCR-based quantitative F8 editing assay was established. A combination of an F8 locus-specific primer and probe and editing vector specific primer and probe in the FAM and HEX channel, respectively, were used to calculate the fraction of *F8* loci that had an inserted luciferase transgene. Genomic DNA was isolated from livers of treated mice at termination of the study at 470 days post-dosing. Mice treated with AAVHSC15-mF8-Luc at this initial low dose of 5e12 vg/kg showed a statistically significant increase in genome editing efficiencies with up to 2.8% of alleles edited (mean 0.8% of alleles edited with a range of editing efficiencies 0.2-2.8%; $p<0.03$ vs. vehicle). These data demonstrate that AAVHSC15 mediated long-term *in vivo* editing of the targeted locus within the liver of mice at this dose.

To assess whether expression from AAVHSC15-mF8-Luc was episomal, an AAVHSC15-Luc editing vector was prepared with the splice acceptor sequences removed (designated AAVHSC15-Δ2AmF8-Luc) but maintained an intact Met initiator codon. Relative to an IV injection of vehicle alone, injection of AAVHSC15-mF8-Luc increased luciferase expression at Days 3, 7, and 14 post-dosing, similar to the results described above. By contrast, luciferase expression was reduced >95% for mice that received an identical dose of AAVHSC15-Δ2AmF8-Luc.

Ability to Introduce Entire Gene into the Genome Mediated via HR

This preliminary proof-of-principle described above provided data confirming the ability to edit the genome via nuclease free HR. Expanding on these initial data led to the discovery and development of a therapeutic program for PKU focused on the targeted integration of a full-length *PAH* cDNA into the human *PAH* locus.

We have successfully inserted full-length cDNA encoding PAH *in vivo* reaching levels of efficiency required for therapeutic efficacy. The preclinical data that supports HMI-103 is described in detail below in the Our Former Product Candidates section.

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 integration 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 technologies, 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 did not detect any co-incident random mutations at or above our lower limit of detection (0.5%) or inverted terminal repeat, or ITR, sequences at the site of integration.

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 testing integration into the human AAVS1 locus, we estimate that 99.967% of insertions (>2.2 million reads) are at the targeted site and that the balance is within expected background of the assay. We have expanded on this assay to characterize the on-target precision of integration at the *PAH* locus in support of HMI-103. In a humanized *in vivo* liver model, HMI-103 showed precise on-target integration and no off-target edits. These data were peer-reviewed and published in *PLOS ONE* in 2020 and are described below.

Ability to Target Multiple Tissues

In preclinical studies, intravenous administration of our family of AAVHSCs has demonstrated the ability to target a wide variety of tissues including the liver, CNS, PNS, muscle, bone marrow, eye and heart (refer to Figure 4 below). Specifically, we have generated evidence of our AAVHSCs' ability to target a number of tissues including:

- neurons throughout the brain, spinal cord, and dorsal root ganglion by crossing the blood-brain-barrier and the blood-nerve-barrier;
- 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, including photoreceptors, retinal pigment epithelial cells and horizontal 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.

We generated preclinical data showing that AAVHSC16, one of the capsids in our family of 15 naturally occurring AAVHSCs, demonstrated low levels of tropism to the liver and no elevations in liver enzymes while maintaining robust distribution to the CNS and peripheral organs following a single I.V. administration (refer to Figure 5 below). We believe the unique properties of AAVHSC16 make it an attractive capsid for development in new disease indications with our genetic medicines platform. The data were peer-reviewed and published in the journal *Molecular Therapy - Methods & Clinical Development*.

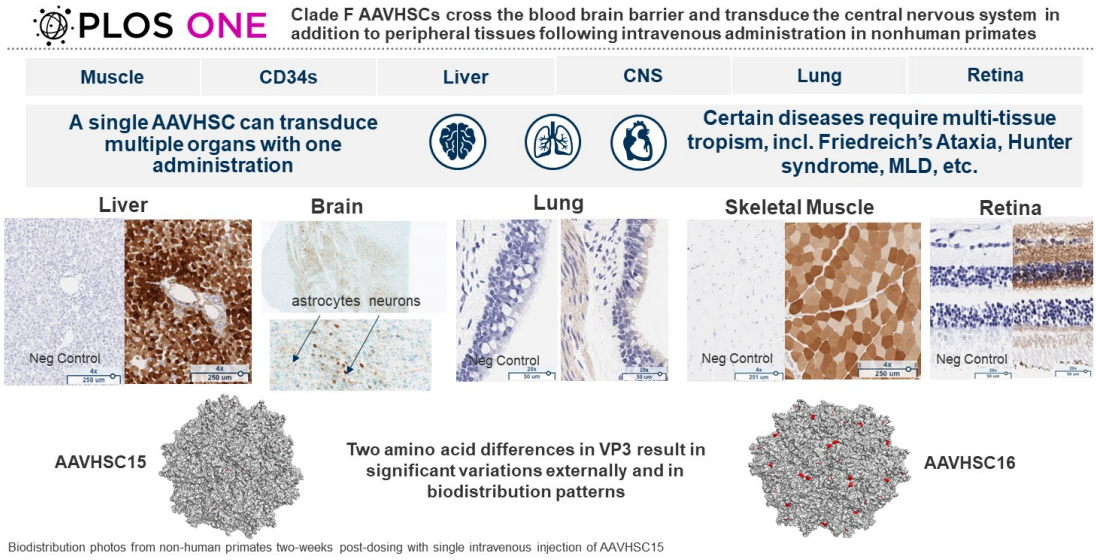


Figure 4. Our family of AAVHSCs has demonstrated the ability to target a wide variety of tissues.

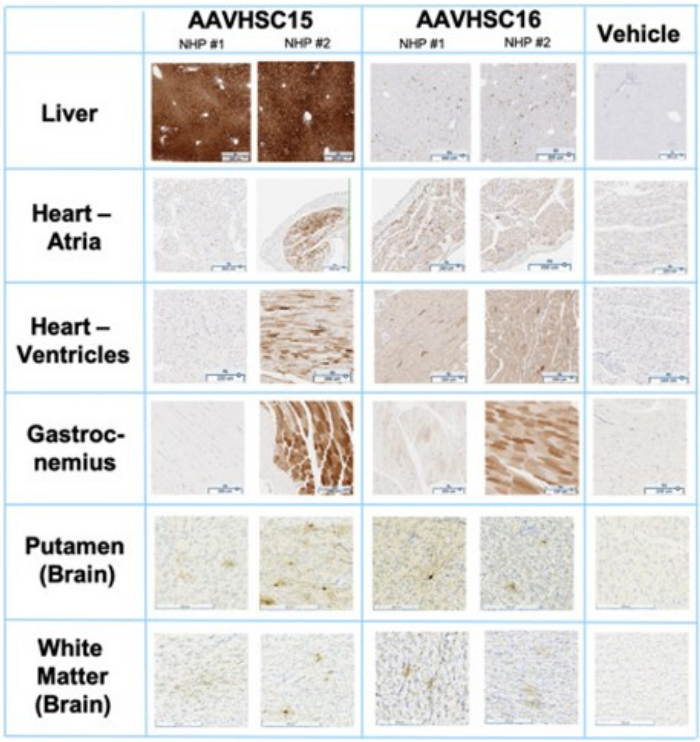


Figure 5. AAVHSC16 has reduced *in vivo* liver tropism in NHPs while exhibiting robust distribution to other peripheral organs and the CNS.

In vivo *Administration with a Single Component Delivery System*

Our platform is designed to perform gene integration at higher efficiency without the use of a nuclease, enabling us to deliver genetic medicines *in vivo* using a single vector system (refer to Figure 6 below). 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 integrate DNA with no need for additional exogenous nucleases, template DNA or editing machinery.

We believe our ability to perform gene integration at efficiencies that are 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* therapeutic approaches resulting in reduced manufacturing costs;
- improved delivery of therapeutics 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 mobilization and myeloablation, a common requirement for many *ex vivo* gene editing therapies; and
- improved safety profile, as compared to an *ex vivo* therapy.

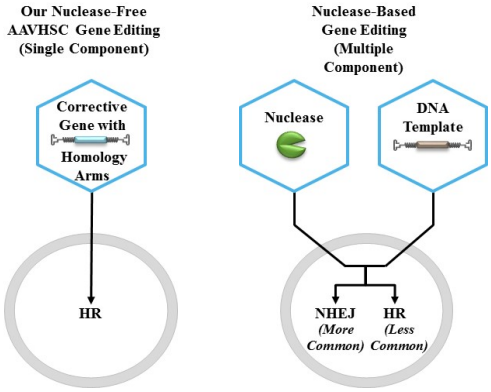


Figure 6. Our nuclease-free AAVHSC single component gene editing construct vs. nuclease-based multiple component gene editing construct for gene editing applications.

Ability to Target a Broad Range of Patients Given Low Frequency of Pre-Existing Neutralizing Antibodies

A potential concern for all AAV vectors is the presence of pre-existing 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. These findings were published in *Human Gene Therapy Clinical Development* in March 2018.

Our Former Product Candidates

HMI-103 Gene Editing Candidate for the Treatment of Adult Patients with PKU

Our lead gene editing program, HMI-103, was a one-time, *in vivo*, nuclease-free gene editing candidate for the treatment of classical PKU. HMI-103 was designed to harness the body's natural DNA repair process of homologous recombination to replace the disease-causing gene with a functional gene and liver-specific promoter and to maximize PAH expression in all transduced liver cells through episomal expression.

PKU Disease Overview

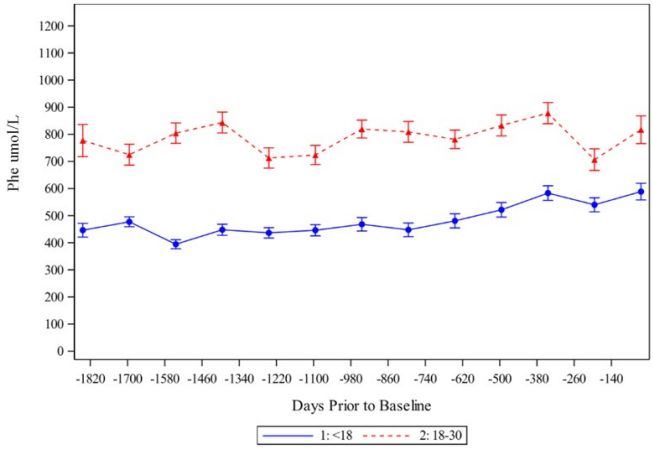
PKU is an inborn error of metabolism that results from mutations in the *PAH* gene. PAH is an enzyme that is normally expressed in the liver and is necessary to metabolize dietary phenylalanine, or Phe, to the amino acid tyrosine, or Tyr. Tyr is a product of Phe metabolism and a precursor to neurotransmitters, and its increase indicates increased enzymatic activity. PKU results from mutations in *PAH* that render its enzymatic activity deficient. If it is not metabolized by PAH, Phe builds up throughout the body, including 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 Tyr. Excessive blood Phe and low levels of Tyr 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 validated 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 350 cases per year with an overall prevalence of 16,500. It has also been estimated that the prevalence of PKU in the European Union is 25,000. Worldwide, the estimated prevalence is 50,000 with 1,000 to 1,500 new cases annually.

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 within the recommended range is not achievable 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 with diet. In a retrospective study of PKU patients, peer-reviewed and published in the journal of *Molecular Genetics & Metabolism*, 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 Phe-restricted 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.

We conducted a five-year retrospective chart review of PKU patients, which confirmed key elements of our PKU programs. Consistent findings from two PKU academic centers of excellence in the U.S. in 152 PKU patients showed that actively monitored patients, including those on restrictive low Phe diet, had Phe levels well-above the recommended threshold of 360 umol/L, based on current U.S. treatment guidelines, underscoring the need for treatments that restore the normal biochemical pathway (refer to Figure 7 below). Furthermore, we confirmed that Phe continues to be higher, even on standard of care, in the classical PKU population, defined as patients with Phe levels greater than 1200 umol/L (66% of the study population) without treatment, and was significantly elevated in the adult population compared to those patients who were less than 18 years of age. These findings were published in *Molecular Genetics and Metabolism* in December 2019.



	Combined Sites
# Patients	152
% Female / Male	51% / 49%
% Classical PKU	66%
≥18	57%

Figure 7. Retrospective five-year chart review demonstrates actively monitored adult classical PKU patients across two academic centers have Phe levels >700 umol/L.

Current Treatments

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

Saproterin dihydrochloride, or Kuvan(R), is an FDA-approved therapy to reduce elevations in serum Phe. Kuvan is a synthetic version of BH4, a cofactor that is required for PAH activity. Treatment with BH4 can activate residual PAH enzyme activity, improve the normal oxidative metabolism of Phe, and decrease Phe levels in some patients; however, clinical data suggests that Kuvan 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. While this approach can increase residual PAH activity, it does not fully correct the underlying genetic disorder (PAH deficiency). Worldwide sales of Kuvan were approximately $180.8 million in 2023. Generic versions of Kuvan are available in several countries around the world, including multiple generic versions in the U.S.

Pegvaliase, or Palynziq(R), is a pegylated plant-derived enzyme called phenylalanine ammonia lyase that was approved in the U.S. by the FDA in 2018 and in Europe by the EC in 2019. Similar to Kuvan, this approach does not correct the underlying genetic disorder (PAH deficiency) and will not reconstitute the natural pathway. We believe Palynziq to have certain limitations including that it must be administered via daily injections and its label contains a black box warning that it can cause severe allergic reaction (anaphylaxis) that may be life-threatening and can happen at any time during treatment with Palynziq. The label states that patients must carry auto-injectable epinephrine with them at all times during Palynziq treatment. Patients in its Phase 3 trials did not meet the secondary efficacy endpoints for cognitive benefit. Worldwide sales of Palynziq were approximately $303.9 million in 2023.

Our Gene Editing Approach to PKU

The goal of our gene integration approach 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 Tyr levels, the product of PAH-driven Phe metabolism. We believe the gene integration approach would be optimal for newborn and pediatric patients due to the higher rate of dividing cells as the child grows. 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 has the potential to normalize not only Phe levels, but also Tyr levels, the product of the Phe metabolism 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 editing treatment 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 and potentially represent a curative therapy.

The gene editing vector transgene is flanked by left and right homology arms, containing sequences that are identical and specific to the genomic target. The arms were designed to integrate by non-nuclease-based, AAV-mediated HR into the target human PAH locus. This therapy aims to correct the genetic defect within the treated liver cells then directing the expression of the PAH protein. HR-based integration via AAVHSCs is highly precise, without the introduction of insertions, deletions or viral ITRs. The corrected copy of the PAH gene would be retained as cells divide into daughter cells as the liver grows. Screening for PKU of all newborns in the United States allows for the identification of affected individuals before serious neurological complications develop. We believe our HR approach possesses the efficacy and durability characteristics that would be appropriate to treat PKU in newly identified patients.

Preclinical Studies with HMI-103

We have conducted *in vivo* experiments showing the integration of a human PAH cDNA into the human PAH gene locus using a humanized liver mouse model. In this model, human hepatocytes constitute the majority of the liver cells, providing an *in vivo* model to test human-specific editing constructs. Injection of the HMI-103 gene editing candidate in this model resulted in the insertion of a codon-optimized human *PAH* cDNA into the human *PAH* locus and mRNA expression of the *PAH* cDNA. The *in vivo* integration rate at the target locus, shown in Figure 8, was calculated at a frequency of 6%. This level of editing has been shown to be sufficient to normalize Phe levels in the murine model. A second assay was also performed on DNA that was specific for human and murine hepatocytes obtained from this study. The assay provides an orthogonal approach for characterizing the frequency of targeted integration and enables testing the species-selectivity of the targeted integration. The results of this assay showed integration only in the human hepatocytes and not in the murine hepatocytes, demonstrating selectivity for the human locus. Figure 9 below shows data following I.V. administration of the murine surrogate, or the murine version of HMI-103. The human construct is designed with human-specific homology arms, so a murine surrogate is necessary for testing in the PKU murine model. As depicted, we observed that *PAH* gene integration was durable out to 43 weeks (end of study) and resulted in marked and durable serum Phe reduction.

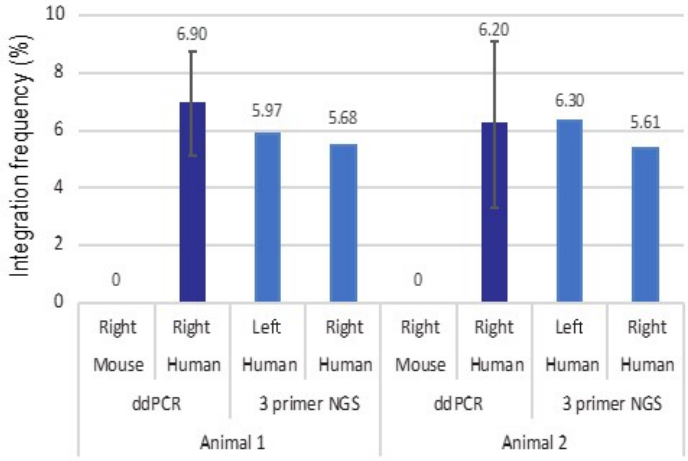


Figure 8. Human-specific AAVHSC *PAH* gene editing candidate resulted in a targeted integration rate of 6%, as measured by NGS in an *in vivo* humanized liver murine model.

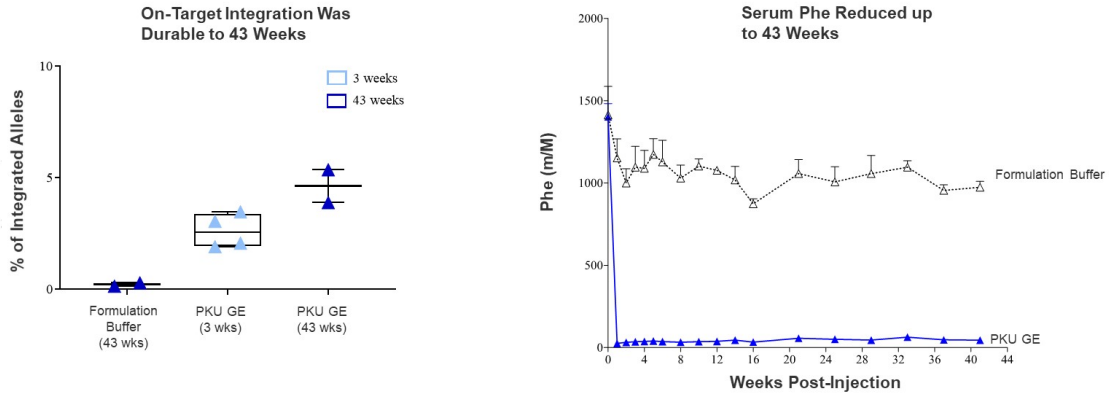


Figure 9. I.V. administration of murine surrogate (with murine homology arms) of HMI-103 showed durable gene integration in the Pah^{enu2} model of PKU.

The fidelity of the integration of the cDNA into the target locus was evaluated by NGS sequencing. There were no *de novo* mutations detected in either homology arm target site. We also evaluated the samples for the presence of ITRs. Viral ITRs are non-homologous sequences that lie beyond the extent of the recombination event and thus should not be integrated into the target site. The integrated alleles were free of ITR sequence, consistent with HR as the main mechanism for integration. Together, these data showed that the targeted integration of the human *PAH* cDNA into the human *PAH* locus displayed sequence fidelity with no evidence of mutations. A genome wide integration assay using long read NGS was developed to assess for off-target HR-mediated integration in human hepatocytes. No off-target HR-mediated integration sites were detected above the limit of detection.

The potency of HMI-103 was compared to non-integrating gene therapy vector HMI-102. In a dose-range finding study, the murine surrogate of HMI-103 and gene therapy vector HMI-102 were administered via one-time I.V. infusions to the *Pah*^{enu2} model, and the murine surrogate of HMI-103 was ten times more potent than HMI-102, which was consistent across all time points tested.

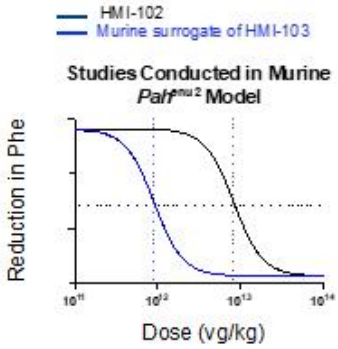


Figure 10. HMI-103 was ten times more potent than non-integrating gene therapy construct HMI-102 in the *Pah*^{enu2} model of PKU. The analysis compared the dose at which fifty percent Phe reduction was achieved in the model.

In 2023, we presented preclinical data at WORLDSymposium™, which supported the immunosuppression regimen that was incorporated in our former clinical trials. In NHPs, our data demonstrated that modulating T-cell activity using tacrolimus

together with dexamethasone was important in reducing B-and T-cell activity, neutralizing antibody, or nAb, formation, and maintaining transgene expression following rAAV administration in NHPs.

pheEDIT Phase 1 Clinical Trial with HMI-103

In September 2023, we inactivated our pheEDIT Phase 1 gene editing clinical trial evaluating HMI-103 in adults with classical PKU (NCT05222178).

The pheEDIT clinical trial was an open-label, dose escalation study evaluating the safety and efficacy of a single I.V. administration of HMI-103 in patients ages 18-55 years old who were diagnosed with classical PKU due to phenylalanine hydroxylase, or PAH, deficiency. In addition to safety endpoints, the trial measured serum Phe changes. The trial incorporated an immunosuppressive regimen that included a T-cell inhibitor used in combination with a steroid-sparing regimen. Patients were dosed following requisite Institutional Biosafety Committee and Institutional Review Board approvals at the clinical sites, and completion of an 82-day screening/run-in period to account for and more closely understand day-to-day Phe fluctuations of participants.

In October 2023, we reported clinical data from the first dose cohort in the pheEDIT trial. As of the data cut-off date of September 14, 2023, HMI-103 was generally well-tolerated in all three participants with no serious adverse events, and the majority of treatment-related adverse events were mild and transient. All liver function tests remained in the normal range during the prophylactic immunosuppression regimen incorporating the T-cell inhibitor tacrolimus in combination with corticosteroid. Participant 1 experienced a reduction in plasma phenylalanine, or Phe, levels to below the U.S. American College of Medical Genetics and Genomics PKU treatment guideline threshold of <360 µmol/L, and the majority of Phe levels were below 360 µmol/L through 39 weeks post-dose, including after the initiation of dietary protein supplementation. Participant 2 experienced a meaningful plasma Phe reduction of 50% at 23 weeks post-dose. Participant 3 experienced a meaningful plasma Phe reduction of 60% at 14 weeks post-dose.

HMI-102 Investigational Gene Therapy for the Treatment of Adult Patients with PKU

HMI-102 was an AAVHSC vector gene therapy candidate designed to treat PAH deficiency, the underlying genetic cause of PKU. HMI-102 consisted 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 tropism for the liver, the normal site for PAH protein expression.

pheNIX Phase 1/2 Clinical Trial with HMI-102

In August 2023, we terminated the pheNIX Phase 1/2 gene therapy clinical trial evaluating HMI-102 in adults with classical PKU. In September 2023, we withdrew our IND for the pheNIX Phase 1/2 clinical trial.

The pheNIX clinical trial was designed to evaluate the safety and efficacy of the investigational gene therapy in a randomized, concurrently controlled, dose-escalation study in adult patients aged 18–55 years old with classical PKU. The dose-escalation phase of the trial was designed to evaluate safety and efficacy of ascending doses of HMI-102 to enable the selection of a dose for the randomized, concurrently controlled Phase 2 portion of the trial. We enrolled six patients in the dose-escalation phase across three dose cohorts.

In November 2020, we reported positive clinical data from the dose-escalation phase of the trial. Safety data from the six patients as of the cutoff date of October 19, 2020, showed HMI-102 was generally well-tolerated, and there were no treatment-related serious adverse events. There were no clinically significant changes in electrocardiogram or vital signs, no clinical signs of complement activation and no adverse events related to bilirubin. Alanine aminotransferase, or ALT, elevations, which are common in AAV-based gene therapy trials, were asymptomatic and managed with increased steroids when necessary and all ALT elevations were resolved. Efficacy data showed significant plasma Phe reductions in Cohorts 2 and 3, compared to Cohort 1 ($P<0.004$ post-hoc comparison using repeated measures MANOVA, or multivariate analysis of variance,/regression analysis), with two patients achieving target Phe levels per treatment guidelines, even while self-liberalizing diet. Compared to baseline, patients in Cohorts 2 and 3 also displayed Tyr increases and Phe-to-Tyr ratio decreases consistent with PAH enzymatic activity.

Based on the safety and efficacy results observed in the dose-escalation phase as of the cutoff date, in early 2021 we advanced to the Phase 2 randomized, concurrently controlled, expansion phase of the pheNIX trial. We selected two doses for the expansion phase: 6E13 vg/kg and 8E13 vg/kg. In October 2021, we announced that as of September 30, 2021, both doses in the expansion phase of the trial were generally well-tolerated and showed evidence of biological activity, including clinically meaningful reductions in Phe levels, increases in Tyr and reductions in the Phe-to-Tyr ratio.

On February 18, 2022, we announced that our pheNIX gene therapy trial was placed on clinical hold due to the need to modify risk-mitigation measures in the study in response to observations of elevated liver function tests, or LFTs. On March 17, 2022, we received the official clinical hold letter from the FDA requesting information on elevated LFTs observed in some patients in the trial and modified clinical risk-mitigation measures. In patients who experienced elevated LFTs, all have resolved and no hospitalizations were required. We responded to the FDA regarding the clinical hold and included in our response was a protocol amendment designed to address the FDA's requests and reduce the risk of observing further elevated LFTs in the trial, including among other things, a new, more targeted immunosuppressive regimen that utilized a T-cell inhibitor and a shorter duration and earlier tapering of steroids. The use of T-cell inhibitors has been shown to be effective in dampening the anticipated immune response to AAV capsids in the clinical setting. This proposed immunosuppressive regimen was incorporated into our pheEDIT clinical trial for the treatment of patients with PKU. On June 13, 2022, we announced that the FDA lifted the clinical hold, with the FDA noting in its response that we satisfactorily addressed all clinical hold issues identified in the March 17, 2022 letter.

On August 15, 2022, we paused the enrollment of our Phase 1/2 pheNIX clinical trial with HMI-102, in order to focus resources and efforts on our Phase 1 pheEDIT clinical trial evaluating *in vivo* gene editing candidate HMI-103 for PKU. In August 2023, we terminated our pheNIX Phase 1/2 gene therapy clinical trial evaluating HMI-102 in adults with classical PKU and in September 2023, we withdrew our IND for the pheNIX clinical trial.

HMI-203 Investigational Gene Therapy for the Treatment of Adult Patients with MPS II (Hunter Syndrome)

HMI-203 was a one-time gene therapy candidate for the treatment of patients with Hunter syndrome. HMI-203 was designed to use one of our AAVHSC vectors to deliver functional copies of the *IDS* gene to multiple target organs, including the PNS and CNS, following a single I.V. administration, where there are missing or mutated copies of the gene.

Hunter Syndrome Disease Overview

Hunter syndrome is a rare, X-linked lysosomal storage disorder caused by mutations in the iduronate-2-sulfatase, or *IDS*, gene, which is responsible for producing the I2S enzyme that breaks down large sugar molecules, or cellular waste, called glycosaminoglycans, or GAGs. Severe Hunter syndrome results in toxic lysosomal accumulation of GAGs that causes progressive debilitation and decline in intellectual function. Hunter syndrome occurs in approximately 1 in 100,000 to 1 in 170,000 males, and the severe form leads to life expectancy of 10 to 20 years. In August 2022, the Department of Health and Human Services approved the addition of MPS II as a condition to the recommended uniform screening panel for newborns.

Current Treatments

The standard of care for treating Hunter syndrome is enzyme replacement therapy, or ERT, which can delay some complications but does not treat CNS manifestations of Hunter syndrome given that the enzyme cannot cross the blood-brain-barrier. In 2006, the recombinant form of human I2S (Elaprase), an ERT for the treatment of Hunter syndrome was approved by the FDA and subsequently approved for use internationally. In January 2021, the recombinant form of idursulfase-beta (Hunterase), an ERT for the treatment of Hunter syndrome received manufacturing and marketing approval in Japan and in March 2021, pabinafusp alfa, a recombinant iduronate-2-sulfatase ERT that delivers therapeutics across the blood-brain barrier was approved by the Ministry of Health, Labour and Welfare in Japan and has been marketed since May 2021 under the brand name “IZCARGO® I.V. Infusion 10mg.” However, specific treatment to address the neurological manifestations of Hunter syndrome and prevent or stabilize cognitive decline remains a significant unmet medical need outside of Japan.

Preclinical Studies with HMI-203

In preclinical studies, a single I.V. administration of HMI-203 led to robust biodistribution and sustained human I2S (hI2S) enzyme expression, which resulted in significant reductions in key Hunter syndrome biomarkers of heparan sulfate GAGs and lysosomal-associated membrane protein 1 (LAMP-1) in the brain, liver, heart, spleen, lungs and kidneys compared with the vehicle. Significant reductions in heparan sulfate GAGs in the cerebrospinal fluid (CSF) compared with vehicle were also observed, as well as ameliorated paw deformities, as shown by significant changes in measurements of ankle depth, paw width, paw depth and ankle width compared with vehicle. Finally, HMI-203 administration led to uptake of hI2S from the serum of the HMI-203-treated model in human cell lines, which demonstrated the potential for cell cross-correction. These data were presented at WORLD*Symposium*™ in 2021 and 2022 (refer to Figure 11 below).

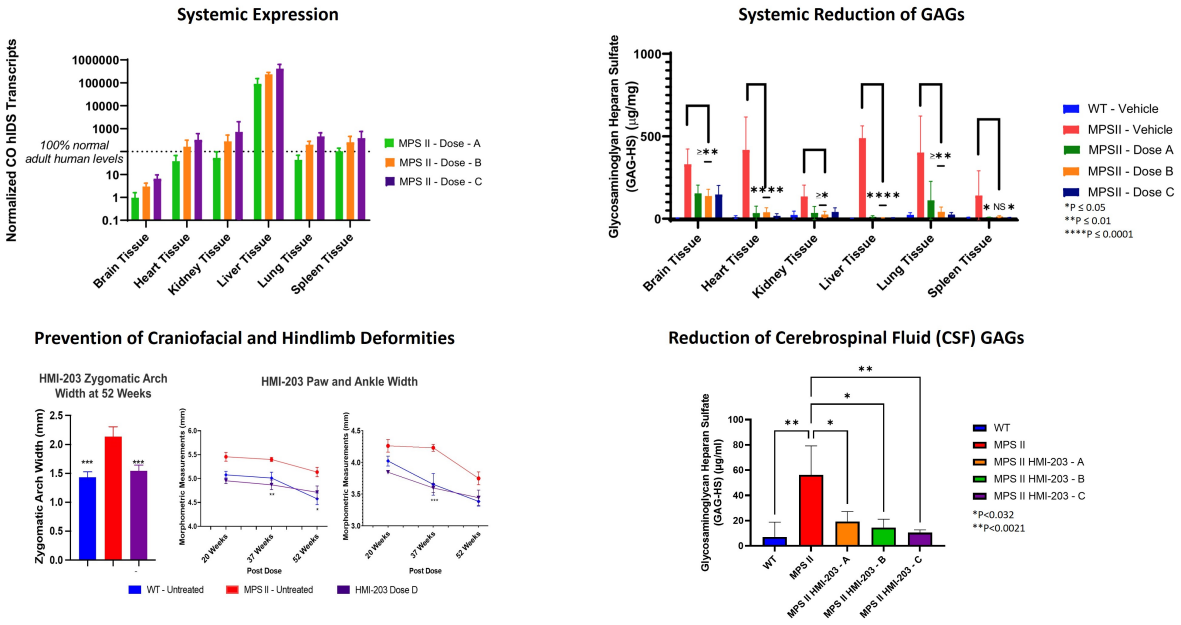


Figure 11. Single IV administration of HMI-203 demonstrated systemic expression, reduction of GAGs, and correction of phenotype in murine model.

juMPStart Phase 1 Clinical Trial with HMI-203

In August 2023, Homology terminated its juMPStart Phase 1 gene therapy clinical trial evaluating HMI-203 in adults with Hunter Syndrome and in December 2023, withdrew its IND for the juMPStart clinical trial.

The juMPStart clinical trial was an open-label, dose-escalation study evaluating the safety and efficacy of a single I.V. administration of HMI-203, expected to enroll up to nine male patients in up to three dose cohorts, ages 18-45 years old, who had been diagnosed with Hunter syndrome and were receiving enzyme replacement therapy. In addition to safety endpoints, the trial was designed to measure plasma I2S activity, urinary GAG levels and other peripheral disease manifestations. Qualitative data on unmet medical needs from ERT-treated adult MPS II patients and/or their caregivers helped inform our trial design. Patients and caregivers reported that weekly ERT infusions, surgeries and supportive therapies inadequately address range of motion and mobility, pain, and hearing loss, that there are burdens associated with ERT and other therapies, including frequency and duration of treatment, and painful and extended recoveries, that there is a high degree of anxiety regarding prognosis, longevity, need for more invasive surgeries, and financial challenges and that the expectations for a potential one-time gene therapy include the ability to maintain their current quality of life with ERT independence. Also, key opinion leaders surveyed supported our planned design for the juMPStart clinical trial, including our plan to discontinue ERT.

HMI-204 for Treatment of Adult Patients with MLD

We completed IND-enabling studies with HMI-202, an investigational gene therapy for the treatment of patients with MLD. Applying the learnings from these IND-enabling studies, in August 2022, we announced the details of HMI-204, an optimized, *in vivo*, one-time gene therapy product candidate for the treatment of MLD. We are no longer developing HMI-204.

MLD is a lysosomal storage disease caused by mutation of a gene called arylsulfatase A, or *ARSA*. The protein ARSA is required for the breakdown of cellular metabolic products that in MLD accumulate in all cells of the body. Cells responsible for the production of myelin are especially sensitive to the toxic build-up of these cellular metabolic products, leading to progressive serious neurological deterioration. The late infantile form of MLD, which is the most common form, includes rapidly progressive motor and cognitive decline and loss of vision. The majority of these patients do not survive past the first decade of life.

In Europe, Libmeldy (autologous CD34+ cells encoding the ARSA gene), a lentiviral vector-based gene therapy for the treatment of MLD, became the first therapy approved for eligible patients with early-onset MLD in December 2020 following receipt of full (standard) market authorization by the EC. This treatment is not currently approved in the United States. While

efficacious in late infantile and early juvenile children (with no or very early onset of symptoms), it has significant drawbacks, including myeloablation, the use of immunosuppression therapy, delayed onset of ARSA expression post-engraftment, conditioning regimens, and the risk of death from stem cell transplantation.

At WORLD*Symposium*™ in 2023, we reported the outcome of the optimization of HMI-202 resulting in the nomination of HMI-204. The design optimization focused on achieving near-normal (or higher) ARSA expression in all disease-relevant tissues, in addition to overall manufacturing improvements. HMI-204 is a single-stranded codon-optimized *ARSA* sequence driven by a ubiquitous promoter (AAVHSCco*ARSA*). Following a single intravenous administration, HMI-204 resulted in broad and targeted systemic biodistribution and robust expression in the central nervous system, consistent with our previously reported crossing of the blood-brain barrier in the *Arsa* knockout murine model of MLD.

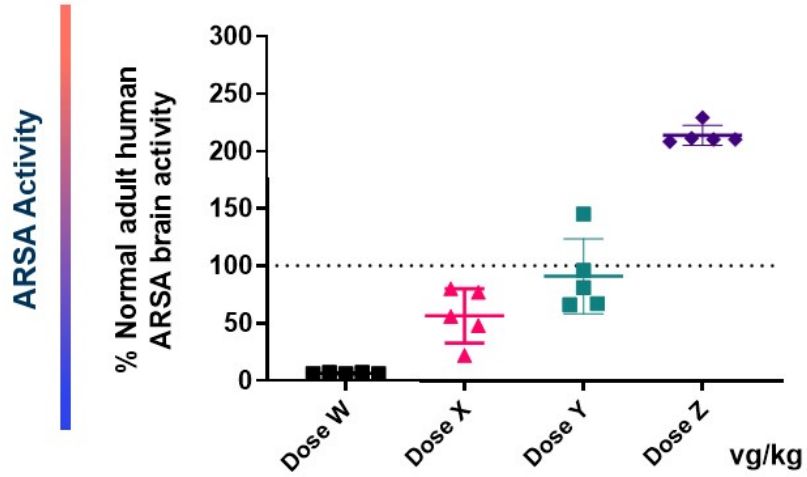


Figure 12. Single administration of HMI-204 crossed the blood-brain barrier and resulted in a dose-response in ARSA activity in the brain of Arsa KO mice, as assessed 12 weeks post dosing. HMI-204 achieved levels of ARSA expression (doses X, Y and Z) predicted to lead to a direct motor benefit in the rotarod assay, as previously demonstrated with HMI-202.

In the brain of HMI-204-treated adult Arsa knockout mice, ARSA cellular expression patterns were nearly identical to that of murine Arsa distribution in wildtype age-matched littermates, as previously demonstrated with HMI-202. Moreover, the optimized HMI-204 construct showed lowered expression in the heart (as compared with HMI-202), while maintaining strong liver expression, as demonstrated by anti-ARSA immunohistochemistry (refer to Figure 13 below). Lastly, an overall improvement in HMI-204 productivity was achieved (refer to Figure 14 below).

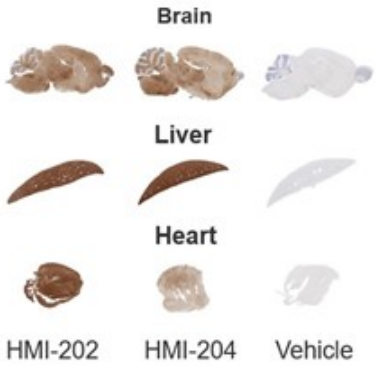


Figure 13. In *Arsa* KO mice, HMI-204 maintained a robust and broad distribution of ARSA across the entire axis of the brain and liver while lowering its expression in heart tissue, as compared with the anti-ARSA biodistribution achieved with HMI-202.

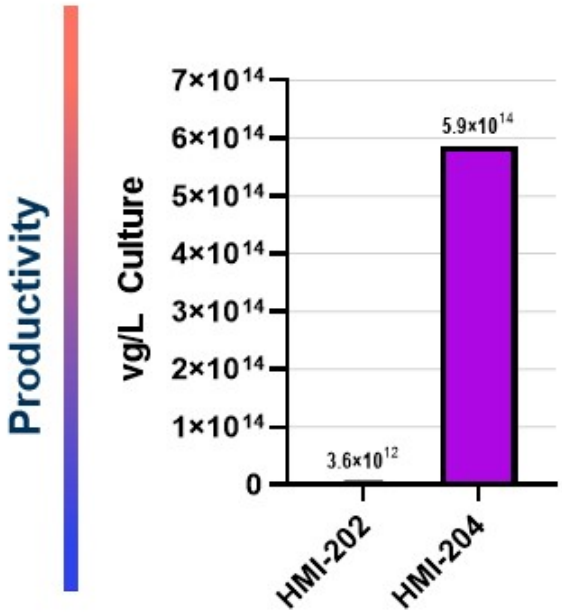


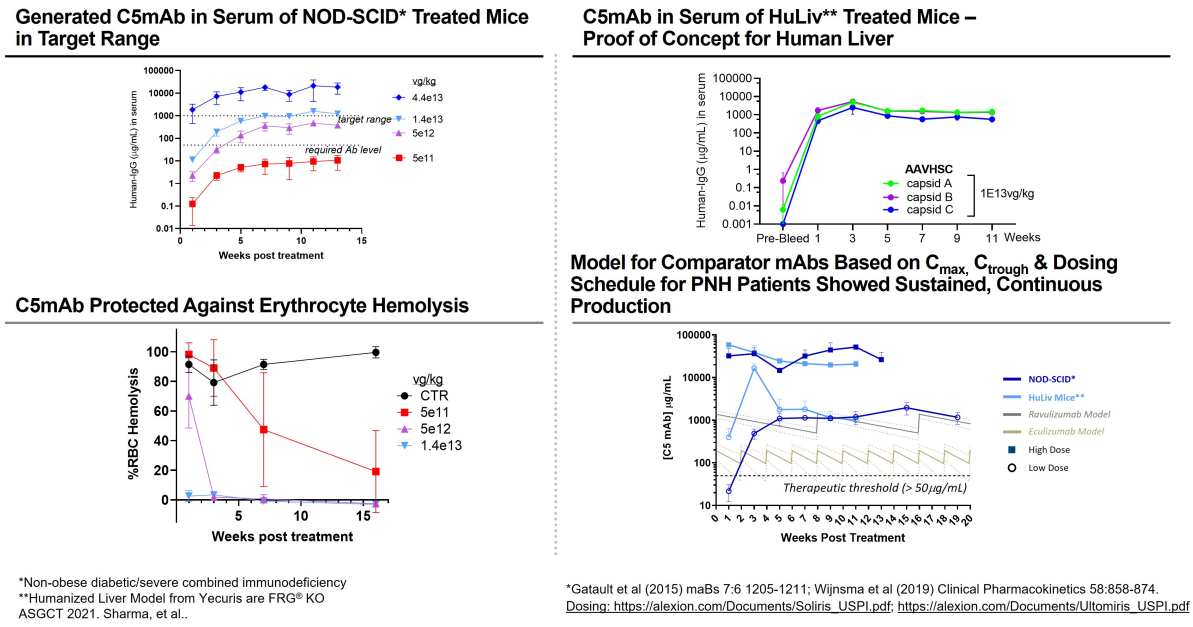
Figure 14. Outcome of HMI-204 packaging productivity achieved leading to an ~120% improvement in vector genome yields compared with historical HMI-202 data.

HMI-104 for the Treatment of Adult Patients with PNH

In August 2021, we named a clinical development candidate for PNH, HMI-104, from our GTx-mAb platform. Homology is no longer developing HMI-104.

PNH is a rare, acquired, life-threatening blood disease caused by mutations in the PIGA gene that result in intravascular hemolysis, or red blood cell destruction, mediated by uncontrolled activation of the complement system. PNH results in thromboses, recurrent pain, severe anemia, kidney disease and impaired quality of life, among other outcomes.

Our GTx-mAb platform represents an additional way that we could potentially leverage our AAVHSCs to deliver one-time *in vivo* gene therapy to express and secrete antibodies from the liver, which we believe may allow us to target diseases with larger patient populations. In support of this program, we generated and presented preclinical data targeting complement protein 5, demonstrating preclinical proof-of-concept in PNH. A single I.V. dose of an AAVHSC GTx-mAb showed expression of full-length antibodies from the liver consistent with anti-C5 therapeutics levels, sustained and robust Immunoglobulin G, or IgG, expression *in vivo* in a humanized murine liver model and a murine NOD-SCID model, and *in vivo* vector-expressed C5 mAb had potent functional activity as shown by an *ex vivo* hemolysis assay. Additionally, we observed sustained expression of C5 mAb in the presence of murine and human FcRn. We completed IND enabling studies with HMI-104.



*Non-obese diabetic/severe combined immunodeficiency
**Humanized Liver Model from Yecuris are FRG® KO
ASGCT 2021. Sharma, et al..

*Gatault et al (2015) maBs 7:6 1205-1211; Wijnsma et al (2019) Clinical Pharmacokinetics 58:858-874.
Dosing: https://alexion.com/Documents/Soliris_USPI.pdf; https://alexion.com/Documents/Ultomiris_USPI.pdf

Figure 15. Preclinical C5 Data Demonstrated Potential when Administered as a Sustained, Low Dose, One-Time Treatment.

Manufacturing

In 2022, we established OXB (US) LLC, an AAV manufacturing and innovation business which incorporated our process development and manufacturing platform and process that supports both gene therapy, gene editing and our GTx-mAb platform, and is scalable from preclinical to GMP. Our process development and manufacturing strategy leveraged a single platform for gene therapy, gene editing and our GTx-mAb platform that is scalable and facilitates rapid development to the clinic. We leveraged our manufacturing platform across our entire pipeline, from our research programs to our preclinical and clinical programs. Our platform was designed from its inception to be our commercial process, allowing us to rapidly transition from research into the clinic and eventually to commercialization. Prior to the transaction with Oxford, our manufacturing platform was scaled and tested across more than 450 different constructs with more than 550 unique lots of vector successfully executed. OXB (US) LLC announced that its platform has produced high-quality titers of E15 vg/L and achieved over 90% fully intact vector. Our manufacturing platform has been scaled to 2000L in non-GMP and 500L in GMP.

Our manufacturing strategy utilized mammalian cells for our AAVHSC vector-based product candidates. All of our former programs utilized HEK293 transfection in a serum-free suspension bioreactor process. HEK293 is a well-characterized and commonly used system for many clinical-stage AAV vector products. Additionally, HEK293 cells are familiar to regulatory authorities, and commercial raw materials and reagents are readily available. Our purification leveraged chromatography-based operations to provide high quality vector and ensure robust commercial-scale operations. In addition to our process development, we also internally developed 45 analytical methods to test, monitor, and characterize our products.

Oxford Biomedica (US) LLC Transaction

On March 10, 2022, we closed a transaction with OXB (US) LLC, OXB and OXB Parent pursuant to the Purchase Agreement, dated as of January 28, 2022, by and among Homology, OXB (US) LLC and Oxford, whereby, among other things, we and Oxford agreed to collaborate to operate OXB (US) LLC, which provides AAV vector process development and manufacturing services to biotechnology companies, which we refer to as the Oxford Biomedica (US) LLC Transaction, or the OXB (US) LLC Transaction. OXB (US) LLC incorporates our proven 'plug and play' process development and manufacturing platform, as well as our experienced team and high-quality GMP vector production capabilities that we built and operated since 2019.

Pursuant to the terms of the Purchase Agreement and a contribution agreement, or the Contribution Agreement, entered into between us and OXB (US) LLC prior to the closing of the OXB (US) LLC Transaction, or the Closing, we agreed to assign and transfer to OXB (US) LLC all of our assets that are primarily used in the manufacturing of AAV vectors for use in

gene therapy or gene editing products, but excluding certain assets related to manufacturing or testing of our proprietary AAV vectors, or collectively, the Transferred Assets, in exchange for 175,000 common equity units in OXB (US) LLC, or Units, and OXB (US) LLC assumed from us, and agreed to pay, perform and discharge when due, all of our duties, obligations, liabilities, interests and commitments of any kind under, arising out of or relating to the Transferred Assets.

Effective as of the Closing, we sold to OXB, and OXB purchased from us, 130,000 Units, or the Transferred Units, in exchange for $130.0 million. In connection with the Closing, OXB contributed $50.0 million in cash to OXB (US) LLC in exchange for an additional 50,000 Units. Immediately following the Closing, (i) OXB owned 180,000 Units, representing 80 percent (80%) of the fully diluted equity interests in OXB (US) LLC, and (ii) we owned 45,000 Units, representing 20 percent (20%) of the fully diluted equity interests in OXB (US) LLC.

Pursuant to the Amended and Restated Limited Liability Company Agreement of OXB (US) LLC, or the OXB (US) LLC Operating Agreement, which was executed in connection with the Closing, at any time following the three-year anniversary of the Closing, (i) OXB will have an option to cause us to sell and transfer to OXB, and (ii) we will have an option to cause OXB to purchase from us, in each case all of our equity ownership interest in OXB (US) LLC at a price equal to 5.5 times the revenue for the immediately preceding 12-month period, subject to a specified maximum amount. Pursuant to the terms of the OXB (US) LLC Operating Agreement, we are entitled to designate one director on the board of directors of OXB (US) LLC, currently Paul Alloway, Ph.D., our President and Chief Operating Officer.

Concurrently with the Closing, we entered into certain ancillary agreements with OXB (US) LLC including a license and patent management agreement whereby OXB (US) LLC granted certain licenses to us, a supply agreement for a term of three years which includes certain annual minimum purchase commitments, a lease assignment pursuant to which we assigned all of our right, title and interest in, to and under our facility lease to OXB (US) LLC, a sublease agreement whereby OXB (US) LLC subleased certain premises in its facility to us, as well as several additional ancillary agreements.

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 have requested withdrawal or discontinuation of each of our previously open INDs. Should we resume development of our product candidates, we will 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 would 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 would 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* through a nuclease-free gene editing modality, gene therapy, or GTx-mAb, which is designed to produce antibodies throughout the body. If we were to resume development of one or more of our product candidates and any of those product candidates were approved for the indications for which our clinical trials were originally designed, they may compete with other products currently under development, including gene therapy and gene editing products or other types of therapies, such as small molecule, antibody or protein therapies. If we were to resume development of our HMI-103 product candidate and it were to be approved, it may compete with therapies from American Gene Technologies, BioMarin, Generation Bio, Moderna, Nestlé Health Science, PTC Therapeutics, Jnana Therapeutics, Poseida Therapeutics and Synlogic. However, we believe that only gene therapy or gene editing approaches have the potential to restore the normal Phe biochemical pathway with a single administration.

There are a number of companies developing nuclease-based gene editing technologies using CRISPR/Cas9, TALENs, meganucleases, Mega-TALs and ZFNs, including Beam Therapeutics, bluebird bio, Caribou Biosciences, Cellectis, CRISPR Therapeutics, Editas Medicine, Intellia Therapeutics, Precision BioSciences and Sangamo Therapeutics and non-nuclease-based technology, including LogicBio Therapeutics, a wholly-owned subsidiary of Alexion.

If we were to resume development of our Hunter syndrome HMI-203 product candidate and if it were to be approved, it may compete with approved products such as IZCARGO(R), a blood-brain-barrier-penetrating recombinant iduronate-2-sulfatase approved in Japan, Elaprase®, an enzyme replacement therapy, or ERT, from Takeda, and Hunterase ICV Injection, an ERT from GC Pharma, as well as investigational product candidates from Avrobio, Denali Therapeutics and REGENXBIO.

However, we believe that only an I.V. gene therapy approach with the ability to cross the blood-brain-barrier has the potential to treat the peripheral and neurological manifestations.

If we were to resume development of our MLD HMI-204 product candidate and if it were to be approved, it may compete with approved products such as Libmeldy, a lentiviral vector-based *ex vivo* gene therapy from Orchard Therapeutics, which is approved in the EU and a select group of additional countries for the treatment of MLD in pre-symptomatic and early symptomatic patients, as well as investigational product candidates from Takeda and Passage Bio. We believe that our optimized *in vivo* gene therapy approach for MLD could be used early in the disease progression with the potential for earlier protein expression, potentially offering advantages over Orchard Therapeutics' *ex vivo* approach, as well as advantages over chronic, intrathecal ERTs, such as Takeda's approach.

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. We have paused development of each of our product candidates. 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 competitors may also 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 in the future. 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 have relied 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 development candidates. Our success has depended in large part on our ability to secure and maintain patent protection in the United States and other countries with respect to our former and any future product development 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, 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 development candidates in the future. For more information regarding these competitive risks, see Item 1A. "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 collaborating with our licensors to file, U.S. and foreign patent applications related to our proprietary technology, inventions, and improvements and trademarks that are important to the development and implementation of our business. We require employees who are inventors on any company-owned patent applications to assign the rights to us. Also, we use other forms of protection, particularly where we do not believe patent protection is appropriate or obtainable. We rely on trade secrets, technical know-how, and continuing innovation to develop and maintain our competitive advantage. In addition, we 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.

Our patent portfolio includes a combination of issued patents and pending patent applications that are licensed from third parties. We are exploring strategic alternatives for certain of our programs and the related intellectual property, and we are in the process of abandoning non-core intellectual property.

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 Biologics License Application, or BLA. Similarly, certain foreign jurisdictions also have mechanisms for extending patent term and, to the extent we have granted patents that are eligible, we may decide to apply for patent term extensions in those jurisdictions.

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.

Licensed Intellectual Property

Certain of our issued patents and pending patent applications are exclusively licensed to us from COH.

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 thirteen granted patents in the United States, seven foreign granted patents, and 15 pending applications in the United States, Europe, Canada, Australia and other selected countries in Latin America and Asia. The first family of issued patents and patent applications relates to our novel AAV vectors and their use in cellular transduction. The ten issued U.S. patents in this family are expected to expire in 2031 and may be extended by up to five years in the United States via patent term extension depending on the regulatory pathway of the products covered by such patents. The second family includes three issued U.S. patents relating to our AAV vectors and their use in genome editing. The issued patents in this family are expected to expire in 2035 and may be extended by up to five years in the United States and in certain other countries via patent term extension depending on the regulatory pathway of the products covered by such patents.

Trademarks

Our trademarks Homology Medicines, HMI, the H logo, the HOMOLOGY MEDICINES, INC. logo and AMENDR, are pending or registered in the United States and/or certain international countries. In connection with the anticipated Merger, we are in the process of abandoning our trademarks.

Strategic Collaborations

City of Hope License Agreement

In April 2016, we entered into an exclusive 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.

On August 6, 2021, we received notice from COH that we did not accomplish at least one of the partnering milestones by the applicable deadline, as set forth in the COH License. This notice does not affect our exclusive license in the field of mammalian therapeutics, including all human therapeutics, associated diagnostics, and target validation, or the Mammalian Therapeutic Field, where we retain exclusive rights. Instead, the notice served as written notice that the exclusive license granted pursuant to the COH License in all fields except the Mammalian Therapeutic Field converted from exclusive to non-exclusive effective as of September 20, 2021, which was forty-five days from the receipt of notice. In connection with the conversion, any royalty obligations and sublicensee fees relating to fields outside of the Mammalian Therapeutic Field shall be reduced by a certain percentage. This change to our exclusive worldwide license with COH does not impact any of our former therapeutic product candidates, including HMI-102, HMI-103, HMI-203, HMI-204 and HMI-104.

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. 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 integration product candidates.

FDA Approval Process

If we resume development of our product candidates, 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 FDCA, and the Public Health Service Act, or PHS Act, and other federal, state, local and foreign statutes and regulations. Both the FDCA 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.

We, along with third-party contractors, will be required to navigate the various preclinical, clinical and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval or licensure of our product candidates. 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.

U.S. Biological Products Development Process

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 preclinical laboratory tests, animal studies and formulation studies in accordance with applicable regulations, including good laboratory practices, or GLP, requirements;
- submission to the FDA of an IND, 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 good clinical practice, or GCP, requirements and any additional requirements needed 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;
- preparation and submission to the FDA of a BLA for marketing approval that includes substantive evidence of safety, purity and potency from results of nonclinical testing and clinical trials;
- a determination by the FDA within 60 days of its receipt of a BLA to file the application for review;
- completion of an FDA Advisory Committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the biological product is produced to assess compliance with GMP 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 candidate, 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 GLP.

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 an IND. An IND is a request for authorization from the FDA to administer an investigational new drug to humans. 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.

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

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 IRB or ethics committee 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. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board or a data monitoring committee, which provides guidance for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries.

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. The biological product candidate is further evaluated for dosage, clinical efficacy, potency, and safety in an expanded patient population, generally 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 some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so-called Phase 4 studies may also be made a condition to approval of the BLA.

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 and nonclinical studies performed since the last progress report, among other information, must be submitted to the FDA. Written IND safety reports must be promptly submitted to the FDA 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. 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.

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 GMP 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 sponsor or FDA may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug or biologic is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. Unless otherwise required by regulation, PREA does not apply to any biological product for an indication for which orphan designation has been granted.

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 marketed 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 the submitted BLA 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. For example, the FDA may give a priority review to BLAs submitted for biological products that are designed to treat a serious or life-threatening disease or condition, and if approved, would offer a significant improvement in safety or efficacy compared to marketed products. 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, pure and potent, or effective, for its intended use, and whether the product is being manufactured in accordance with GMP 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.

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 GMP requirements and are 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 GCP.

After the FDA evaluates a BLA, conducts inspections of manufacturing facilities where the investigational product and/or its drug substance will be produced and conducts inspections at select clinical sites, the FDA may issue an approval letter or a Complete Response Letter, or CRL. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A CRL will describe all of the deficiencies that the FDA has identified in the BLA, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the CRL without first conducting required inspections, testing submitted product lots, and/or reviewing proposed labeling. In issuing the CRL, the FDA may recommend actions that the applicant might take to place the BLA in condition for approval, including requests for additional information or clarification. The FDA may delay or refuse approval of a BLA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product.

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 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.

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 disease or condition 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 disease or condition 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 disease or condition for which the orphan product has exclusivity or obtain approval for the same product but for a different disease or condition for which the orphan product has exclusivity. Orphan product exclusivity also could block the approval of a product for seven years if a competitor obtains approval of the same biological product as defined by the FDA or if such product candidate is determined to be contained within the competitor's product for the same condition or disease. If a drug or biological product designated as an orphan product receives marketing approval for a disease or condition 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.

Rare Pediatric Disease Priority Review Voucher Program

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

For purposes of this program, a “rare pediatric disease” is a (a) serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years, including age groups often called neonates, infants, children, and adolescents; and (b) rare diseases or conditions within the meaning of the Orphan Drug Act. Congress has only authorized the Rare Pediatric Disease Priority Review Voucher program until September 30, 2024. Consequently, sponsors of marketing applications approved after that date will not receive the voucher unless Congress reauthorizes the Rare Pediatric Disease Priority Review Voucher program before that time. However, even if the program is not reauthorized, if a drug candidate receives Rare Pediatric Disease Designation before October 1, 2024, the sponsor of the marketing application for such drug will be eligible to receive a voucher if the application for the designated drug is approved by the FDA before October 1, 2026.

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, 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 candidate and the specific indication for which it is being studied. The sponsor of a biologic product candidate 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. With regard 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.

A biological product candidate intended to treat a serious or life-threatening disease or condition may also be eligible for Breakthrough Therapy designation to expedite its development and review. A biologic can receive Breakthrough Therapy designation if preliminary clinical evidence indicates that the biologic, alone or in combination with one or more other drugs or biologics, 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 Fast Track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product candidate, including involvement of senior managers.

Any product candidate submitted to the FDA for marketing, including a product candidate with a Fast Track designation or Breakthrough Therapy designation, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. A BLA is eligible for priority review if the biological product candidate has the potential to treat a serious or life-threatening condition and, if approved, would provide 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 candidate may be eligible for accelerated approval. Biological product candidates 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 such product candidates be approved on the FDA's determination that the product candidate 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 receiving accelerated approval perform adequate and well-controlled confirmatory clinical studies to verify and describe the predicted clinical benefit and, under FDORA, the FDA may require, as appropriate, that such trials be underway prior to approval or within a specific time period after the date of approval for a product granted accelerated approval. Failure to conduct required confirmatory trials in a timely manner, or to verify a clinical benefit during such confirmatory trials, will allow the FDA to withdraw the approved biologic product from the market on an expedited basis. In addition, the FDA generally requires, unless otherwise informed by the agency, pre-approval of promotional materials for products approved under the accelerated approval pathway, which could adversely impact the timing of the commercial launch of the product.

Moreover in 2017, the FDA established the Regenerative Medicine Advanced Therapy, or RMAT, designation as part of its implementation of the 21st Century Cures Act. An investigational drug is eligible for RMAT designation if: (1) it meets the definition of a regenerative medicine therapy, which is defined as a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, with limited exceptions; (2) it is intended to treat, modify, reverse, or cure a serious disease or condition; and (3) preliminary clinical evidence indicates that the investigational drug has the potential to address unmet medical needs for such disease or condition. In a February 2019 final guidance, the FDA also stated that certain gene therapies that lead to a sustained effect on cells or tissues may meet the

definition of a regenerative medicine therapy. RMAT designation provides potential benefits that include more frequent meetings with FDA to discuss the development plan for the product candidate, and eligibility for rolling review of BLAs and priority review. Product candidates granted RMAT designation may also be eligible for accelerated approval if the relevant statutory conditions are met.

Fast Track designation, priority review, RMAT designation 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 meet 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 GMP requirements, record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. 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 GMP requirements and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain GMP 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.

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 closely regulates the marketing, labeling, advertising and promotion of biologics. A company can make only those claims relating to safety and efficacy, purity and potency that are consistent with the provisions of the FDA-approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products.

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.

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.

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.

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.

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 and transparency laws and regulations regarding drug pricing and payments and other transfers of value made to physician and other licensed healthcare professionals. 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. See section entitled *"Risk Factors—Risks Related to Healthcare Laws and Other Legal Compliance Matters—Homology's 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 Homology to penalties."*

Moreover, analogous state and foreign laws and regulations may be broader in scope than the provisions described above and may apply regardless of payor. These laws and regulations may differ from one another in significant ways, thus further complicating compliance efforts. For instance, in the European Union, or EU, many EU member states have adopted specific anti-gift statutes that further limit commercial practices for medicinal products, in particular vis-à-vis healthcare professionals and organizations. Additionally, there has been a recent trend of increased regulation of payments and transfers of value provided to healthcare professionals or entities and many EU member states have adopted national "Sunshine Acts" which impose reporting and transparency requirements (often on an annual basis), similar to the requirements in the United States, on pharmaceutical companies. Certain countries also mandate implementation of commercial compliance programs, or require disclosure of marketing expenditures and pricing information. Violation of any of such laws or any other governmental regulations that apply may result in penalties, including, without limitation, significant administrative, civil and criminal penalties, damages, fines, disgorgement, additional reporting obligations and oversight if a manufacturer becomes subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, the curtailment or restructuring of operations, exclusion from participation in governmental healthcare programs and 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. Moreover, for drugs and biologics administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such products. 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. See section entitled *"Risk Factors—Risks Related to Healthcare Laws and Other Legal Compliance Matters—The successful commercialization of Homology's 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 Homology's product candidates, if approved, could limit Homology's ability to market those products and decrease its ability to generate revenue."*

In addition, in many countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country. In the EU, governments influence the price of products through their pricing and reimbursement rules and control of national healthcare systems that fund a large part of the cost of those products to consumers. Member states are free to restrict the range of pharmaceutical products for which their national health insurance systems provide reimbursement, and to control the prices and reimbursement levels of pharmaceutical products for human use. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed to by the government. Member states may approve a specific price or level of reimbursement for the pharmaceutical product, or alternatively adopt a system of direct or indirect controls on the profitability of the company responsible for placing the pharmaceutical product on the market, including volume-based arrangements, caps and reference pricing mechanisms. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular product to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. The downward pressure on healthcare costs in general, particularly prescription products, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross border imports from low priced markets exert a commercial pressure on pricing within a country.

Healthcare Reform

The United States and several other jurisdictions are considering, or have already enacted, a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell any of our product candidates profitably, if approved. Among policy-makers and payers in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access to healthcare. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. There have been, and likely will continue to be, legislative and regulatory proposals at the federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. See section entitled "*Risk Factors – Risks Related to Healthcare Laws and Other Legal Compliance Matters – If Homology resumes development of its product candidates, enacted and future healthcare legislation*

could increase the difficulty and cost for Homology to obtain marketing approval of and commercialize its product candidates and may affect the prices Homology may set."

The continuing efforts of the government, insurance companies, managed care organizations and other payers of healthcare services to contain or reduce costs of healthcare may adversely affect:

- the demand for any of our product candidates, if approved;
- the ability to set a price that we believe is fair for any of our product candidates, if approved;
- our ability to generate revenues and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical and biologic products. We cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

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. There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs.

Similar political, economic and regulatory developments are occurring in the EU and may affect the ability of pharmaceutical companies to profitably commercialize their products. 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. 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 restrict or regulate post-approval activities and affect the ability of pharmaceutical companies to commercialize their products. In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

On December 13, 2021, Regulation No 2021/2282 on Health Technology Assessment, or HTA, amending Directive 2011/24/EU, was adopted in the EU. While the regulation entered into force in January 2022, it will only begin to apply from January 2025 onwards, with preparatory and implementation-related steps to take place in the interim. Once the regulation becomes applicable, it will have a phased implementation depending on the concerned products. This regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products, and providing the basis for cooperation at the EU level for joint clinical assessments in these areas. The regulation will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement.

We expect that the healthcare reform measures that have been adopted and may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product and

could seriously harm our future revenues. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products.

Data Privacy and Security Laws

Numerous state, federal and foreign laws, including consumer protection laws and regulations, govern the collection, dissemination, use, access to, confidentiality and security of personal information, including health-related information. In the United States, numerous laws and regulations, including data breach notification laws, health information privacy and security laws, and consumer protection laws and regulations that govern the collection, use, disclosure, and protection of health-related and other personal information and could apply to our operations or the operations of our partners. In addition, certain foreign laws govern the privacy and security of personal data, including health-related data. Failure to comply with these laws, where applicable, can result in the imposition of significant civil and/or criminal penalties and private litigation. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

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 may be subject to a variety of regulations in other jurisdictions, for instance in the European Union, or EU, governing, among other things, clinical trials, marketing authorizations, post-marketing authorization requirements 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.

In addition, 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. 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 trials or marketing of the product in those countries. The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. Failure to comply with applicable foreign regulatory requirements, may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Non-clinical Studies and Clinical Trials

Similarly to the United States, the various phases of non-clinical and clinical research in the EU are subject to significant regulatory controls.

Non-clinical studies are performed to demonstrate the health or environmental safety of new chemical or biological substances. Non-clinical (pharmaco-toxicological) studies of medicinal products must be conducted in compliance with the principles of good laboratory practice, or GLP, as set forth in EU Directive 2004/10/EC (unless otherwise justified for certain particular medicinal products – e.g., radio-pharmaceutical precursors for radio-labelling purposes). Such GLP standards reflect the Organization for Economic Co-operation and Development requirements.

Clinical trials of medicinal products in the EU must be conducted in accordance with EU and national regulations and the International Conference on Harmonization, or ICH, guidelines on Good Clinical Practices, or GCP, as well as the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. Additional GCP guidelines from the EC, focusing in particular on traceability, apply to clinical trials of advanced therapy medicinal products, or ATMPs. If the sponsor of the clinical trial is not established within the EU, it must appoint an EU entity to act as its legal

representative. The sponsor must take out a clinical trial insurance policy, and in most EU member states, the sponsor is liable to provide 'no fault' compensation to any study subject injured in the clinical trial.

The regulatory landscape related to clinical trials in the EU has been subject to recent changes. The EU Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repealed the EU Clinical Trials Directive, became applicable on January 31, 2022. Unlike directives, the CTR is directly applicable in all EU member states without the need for member states to further implement it into national law. The CTR notably harmonizes the assessment and supervision processes for clinical trials throughout the EU via a Clinical Trials Information System, which contains a centralized EU portal and database.

While the Clinical Trials Directive required a separate clinical trial application, or CTA, to be submitted in each member state in which the clinical trial was to take place, to both the competent national health authority and an independent ethics committee, much like the FDA and IRB respectively, the CTR introduces a centralized process and only requires the submission of a single application for multi-center trials. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The CTA must include, among other things, a copy of the trial protocol and an investigational medicinal product dossier containing information about the manufacture and quality of the medicinal product under investigation. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed.

The CTR provides for a three-year transition period. Clinical trials for which an application was submitted (i) prior to January 31, 2022 under the Clinical Trials Directive, or (ii) between January 31, 2022 and January 31, 2023 and for which the sponsor has opted for the application of the Clinical Trials Directive remain governed by said Clinical Trials Directive until January 31, 2025. After this date, all clinical trials (including those which are ongoing) will become subject to the provisions of the CTR.

Medicines used in clinical trials must be manufactured in accordance with Good Manufacturing Practice, or GMP. Other national and EU-wide regulatory requirements may also apply.

During the development of a medicinal product, the European Medicines Agency, or EMA, and national regulators provide the opportunity for dialogue and guidance on the development program. At the EMA level, this is usually done in the form of scientific advice, which is given by the Scientific Advice Working Party of the Committee for Medicinal Products for Human Use, or CHMP. A fee is incurred with each scientific advice procedure. Advice from the EMA is typically provided based on questions concerning, for example, quality (chemistry, manufacturing and controls testing), nonclinical testing and clinical trials, and pharmacovigilance plans and risk-management programs. Advice is not legally binding with regard to any future marketing authorization application of the product concerned.

Marketing Authorization

In order to market our product candidates in the EU and many other foreign jurisdictions, we must obtain separate regulatory approvals. In the EU, medicinal products can only be placed on the market after obtaining a marketing authorization, or MA. The process for obtaining an MA in the EU depends, among other things, on the nature of the medicinal product. There are two types of MAs.

"Centralized MAs" are issued by the EC through the centralized procedure, based on the opinion of the EMA's CHMP, and are valid across the entire territory of the EU. The centralized procedure is compulsory for certain types of product candidates such as: (i) medicinal products derived from biotechnology processes, such as genetic engineering, (ii) medicinal products containing a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative diseases, autoimmune and other immune dysfunctions and viral diseases, (iii) designated orphan medicines and (iv) ATMPs (i.e. gene therapy, somatic cell therapy or tissue-engineered medicines). The centralized procedure is optional for product candidates containing a new active substance not yet authorized in the EU, or for product candidates that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU. It is very likely that the centralized procedure would apply to the products we are developing.

The Committee for Advanced Therapies, or CAT, is responsible in conjunction with the CHMP for the evaluation of ATMPs. The CAT is primarily responsible for the scientific evaluation of ATMPs and prepares a draft opinion on the quality, safety and efficacy of each ATMP for which a marketing authorization application, or MAA, is submitted. The CAT's opinion is then considered by the CHMP when giving its final recommendation regarding the authorization of a product in view of the balance of benefits and risks identified. Although the CAT's draft opinion is submitted to the CHMP for final approval, the CHMP may depart from the draft opinion, if it provides detailed scientific justification. The CHMP and CAT are also responsible for providing guidelines on ATMPs and have published numerous guidelines, including specific guidelines on gene

therapies and cell therapies. These guidelines provide additional guidance on the factors that the EMA will consider in relation to the development and evaluation of ATMPs and include, among other things, the preclinical studies required to characterize ATMPs; the manufacturing and control information that should be submitted in an MAA; and post-approval measures required to monitor patients and evaluate the long term efficacy and potential adverse reactions of ATMPs.

Under the centralized procedure, the maximum timeframe for the evaluation of an MAA by the EMA is 210 days. This excludes so-called clock stops, during which additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. At the end of the review period, the CHMP provides an opinion to the EC. If this opinion is favorable, the EC may then adopt a decision to grant an MA.

In exceptional cases, the CHMP might perform an accelerated review of a MAA in no more than 150 days (not including clock stops). Innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the PRIME scheme, which provides incentives similar to the breakthrough therapy designation in the U.S. PRIME is a voluntary scheme aimed at enhancing the EMA's support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated MAA assessment once a dossier has been submitted, but this is not guaranteed. Importantly, a dedicated contact and rapporteur from the CHMP is appointed early in the PRIME scheme facilitating increased understanding of the product at the EMA's committee level. An initial meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

"National MAs" are issued by the competent authorities of the EU member states, only cover their respective territory, and are available for products not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in an EU member state, this national MA can be recognized in another member state through the mutual recognition procedure. If the product has not received a national MA in any member state at the time of application, it can be approved simultaneously in various member state through the decentralized procedure. Under the decentralized procedure an identical dossier is submitted to the national competent authority of each of the member states in which the MA is sought, one of which is selected by the applicant as the reference member state.

Under the above described procedures, in order to grant the MA, the EMA or the competent authorities of the EU member states make an assessment of the risk benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy. MAs have an initial duration of five years. After these five years, the authorization may be renewed on the basis of a reevaluation of the risk-benefit balance. Once renewed, the MA is valid for an unlimited period unless the EC or the national competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal period.

Moreover, in the EU, a "conditional" MA may be granted in cases where all the required safety and efficacy data are not yet available. The conditional MA is subject to conditions to be fulfilled for generating the missing data or ensuring increased safety measures. It is valid for one year and has to be renewed annually until fulfillment of all the conditions. Once the pending studies are provided, it can become a "standard" MA. However, if the conditions are not fulfilled within the timeframe set by the EMA, the MA ceases to be renewed. Furthermore, an MA may also be granted "under exceptional circumstances" when the applicant can show that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use even after the product has been authorized and subject to specific procedures being introduced. This may arise in particular when the intended indications are very rare and, in the present state of scientific knowledge, it is not possible to provide comprehensive information, or when generating data may be contrary to generally accepted ethical principles. This MA is close to the conditional MA as it is reserved to medicinal products to be approved for severe diseases or unmet medical needs and the applicant does not hold the complete data set legally required for the grant of an MA. However, unlike the conditional MA, the applicant does not have to provide the missing data and will never have to. Although the MA "under exceptional circumstances" is granted definitively, the risk-benefit balance of the medicinal product is reviewed annually and the MA is withdrawn if the risk-benefit ratio is no longer favorable.

Advanced Therapy Classification

The EMA offers sponsors who are developing ATMPs (i.e., gene therapy, somatic cell therapy or tissue engineered medicines) a variety of benefits similar to those associated with the PRIME scheme, including scientific and regulatory guidance, additional opportunities for dialogue with regulators, and pre-submission review and certification of the chemistry, manufacturing and controls, and nonclinical data proposed for submission in a forthcoming MAA for micro-,small-, or

medium-sized enterprises. Companies can consult the EMA to determine whether a medicine they are developing is an ATMP through the ATMP classification procedure.

Data and Marketing Exclusivity

The EU also provides opportunities for data and market exclusivity. Upon receiving an MA, reference products generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, the data exclusivity period prevents generic or biosimilar applicants from relying on the preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar MA in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until 10 years have elapsed from the grant of the initial MA for the reference product in the EU. The overall ten-year market exclusivity period may be extended to a maximum of eleven years if, during the first eight years of those ten years, the MA holder obtains an authorization for one or more therapeutic indications, which, during the scientific evaluation prior to their authorization, are held to bring significant clinical benefit over existing therapies. However, there is no guarantee that a product will be considered by the EU regulatory authorities to be a new chemical or biological entity, and products may not qualify for data exclusivity.

There is a special regime for biosimilars, or biological medicinal products that are similar to a reference medicinal product but that do not meet the definition of a generic medicinal product, for example, because of differences in raw materials or manufacturing processes. For such products, the results of appropriate preclinical or clinical trials must be provided, and guidelines from the EMA detail the type and quantity of supplementary data to be provided for different types of biological product. There are no such guidelines for complex biological products, such as gene or cell therapy medicinal products, and so it is unlikely that biosimilars of those products will currently be approved in the EU. However, guidance from the EMA states that they will be considered in the future in light of the scientific knowledge and regulatory experience gained at the time.

Orphan Medicinal Products

The criteria for designating an "orphan medicinal product" in the EU are similar in principle to those in the United States. A medicinal product may be designated as orphan if its sponsor can establish that: (1) the product 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 EU when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify the necessary investment in its development; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or if such a method exists, the product will be of significant benefit to those affected by the condition.

The application for orphan designation must be submitted before the MAA. An EU orphan designation entitles a party to incentives such as reduction of fees or fee waivers, protocol assistance, and access to the centralized procedure. Upon grant of an MA, orphan medicinal products are entitled to ten years of market exclusivity for the approved therapeutic indication. During the ten-year market exclusivity period, the regulatory authorities cannot accept an MAA, or grant an MA, or accept an application to extend an MA, for the same indication, in respect of a similar medicinal product. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed pediatric investigation plan, or PIP. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The 10-year orphan market exclusivity period 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 which it received orphan designation, for example, where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity or where the prevalence of the condition has increased above the threshold. Additionally, an MA may be granted to a similar product for the same indication at any time if (1) the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior to the authorized orphan product; (2) the MA holder for the authorized orphan product consents to a second orphan medicinal product application; or (3) the MA holder for the authorized orphan product cannot supply enough orphan medicinal product.

Pediatric Development

In the EU, MAAs for new medicinal products have to include the results of trials conducted in the pediatric population, in compliance with a PIP agreed with the EMA's Pediatric Committee, or PDCO. The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which an MA is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the

PDCO when these data are not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Once the MA is obtained in all member states and study results are included in the product information, even when negative, the product is eligible for a six-month supplementary protection certificate, or SPC, extension (provided an application for such extension is made at the same time as filing the SPC application for the product, or at any point up to two years before the SPC expires) or, in the case of orphan pharmaceutical products, a two year extension of the orphan market exclusivity is granted (as described above).

Post-Approval Requirements

Similar to the United States, both MA holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA, the EC and/or the competent regulatory authorities of the member states. The holder of an MA must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance, or QPPV, who is responsible for the establishment and maintenance of that system, and oversees the safety profiles of medicinal products and any emerging safety concerns. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports, or PSURs.

All new MAAs must include a risk management plan, or RMP, describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the MA. Such risk-minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical trials or post-authorization safety studies.

The advertising and promotion of medicinal products is also subject to laws concerning promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. All advertising and promotional activities for the product must be consistent with the approved summary of product characteristics, and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription medicines is also prohibited in the EU. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each member state and can differ from one country to another.

Failure to comply with EU and member state laws that apply to the conduct of clinical trials, manufacturing approval, MA of medicinal products and marketing of such products, both before and after grant of the MA, manufacturing of pharmaceutical products, statutory health insurance, bribery and anti-corruption or with other applicable regulatory requirements may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials, or to grant an MA, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the MA, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

The aforementioned EU rules are generally applicable in the European Economic Area, or EEA, which consists of the 27 EU member states plus Norway, Liechtenstein and Iceland.

UK-specific requirements

Since the end of the Brexit transition period on January 1, 2021, Great Britain (England, Scotland and Wales) has not been directly subject to EU laws, however under the terms of the Ireland/Northern Ireland Protocol, EU laws generally apply to Northern Ireland. The EU laws that have been transposed into United Kingdom law through secondary legislation remain applicable in Great Britain. However, under the Retained EU Law (Revocation and Reform) Bill 2022, which is currently before the UK parliament, any retained EU law not expressly preserved and "assimilated" into domestic law or extended by ministerial regulations (to no later than June 23, 2026) will automatically expire and be revoked by December 31, 2023. Legislation which came into force after the expiry of the Brexit transition period, such as the EU CTR, is not applicable in Great Britain, or GB.

Under the Medicines and Medical Devices Act 2021, the Secretary of State or an 'appropriate authority' has delegated powers to amend or supplement existing regulations in the area of medicinal products and medical devices. This allows new rules to be introduced in the future by way of secondary legislation, which aims to allow flexibility in addressing regulatory gaps and future changes in the fields of human medicines, clinical trials and medical devices.

Since January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or MHRA, has been the UK's standalone medicines and medical devices regulator. As a result of the Northern Ireland Protocol, Northern Ireland will continue to follow the EU regulatory regime, but its national competent authority will remain the MHRA.

The MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicines that will benefit patients, including a 150-day assessment and a rolling review procedure. All existing EU MAs for centrally authorized products were automatically converted or grandfathered into UK MAs, effective in GB (only), free of charge on January 1, 2021, unless the MA holder opted-out. In order to use the centralized procedure to obtain an MA that will be valid throughout the EEA, companies must be established in the EEA. Therefore since Brexit, companies established in the UK can no longer use the EU centralized procedure and instead an EEA entity must hold any centralized MAs. Until January 1, 2024, the MHRA may rely on a decision taken by the EC on the approval of a new MA in the centralized procedure in order to more quickly grant a new GB MA. A new international recognition framework will be put in place from January 1, 2024, whereby the MHRA will have regard to decisions on the approval of MAs made by the EMA and certain other regulators when determining an application for a new GB MA.

There is now no pre-MA orphan designation in GB. Instead, the MHRA reviews applications for orphan designation in parallel to the corresponding MA application. The criteria are essentially the same, but have been tailored for the market, i.e., the prevalence of the condition in GB, rather than the EU, must not be more than five in 10,000. Should an orphan designation be granted, the period or market exclusivity will be set from the date of first approval of the product in GB.

The UK regulatory framework in relation to clinical trials is derived from the previous EU Clinical Trials Directive (as implemented into UK law, through secondary legislation). On January 17, 2022, the MHRA launched an eight-week consultation on reframing the UK legislation for clinical trials. The consultation closed on March 14, 2022 and aims to streamline clinical trials approvals, enable innovation, enhance clinical trials transparency, enable greater risk proportionality, and promote patient and public involvement in clinical trials. The outcome of the consultation is being closely watched and will determine whether the UK chooses to align with the CTR or diverge from it to maintain regulatory flexibility.

On February 27, 2023, the UK government and the EC announced a political agreement in principle to replace the Northern Ireland Protocol with a new set of arrangements, known as the Windsor Framework. This new framework fundamentally changes the existing system under the Northern Ireland Protocol, including with respect to the regulation of medicinal products in the UK. In particular, the MHRA will be responsible for approving all medicinal products destined for the UK market (i.e., GB and Northern Ireland), and the EMA will no longer have any role in approving medicinal products destined for Northern Ireland. A single UK-wide MA will be granted by the MHRA for all medicinal products to be sold in the UK, enabling products to be sold in a single pack and under a single authorization throughout the UK. The Windsor Framework was approved by the European Union-United Kingdom Joint Committee on March 24, 2023, so the UK government and the EU will enact legislative measures to bring it into law. On June 9, 2023, the MHRA announced that the medicines aspects of the Windsor Framework will apply from January 1, 2025.

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 and Human Capital

As of December 31, 2023, we had 7 full-time employees, including one employee with an M.D. or Ph.D. degree. None of our employees is represented by a labor union or covered by a collective bargaining agreement. We consider our relationships with our employees to be good.

Corporate Information

We were incorporated in Delaware in March 2015. Our principal executive offices are located at One Patriots Park, Bedford, MA 01730 and our telephone number is (781) 327-2633. Our website address is *www.homologymedicines.com*. Information contained on or accessible through our website is not a part of this Annual Report on Form 10-K, and the inclusion of our website address in this Annual Report on Form 10-K is an inactive textual reference only.

Available Information

We file electronically with the Securities and Exchange Commission, or SEC, our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, proxy statements and other information. Our SEC filings are available to the public over the Internet at the SEC's website at *http://www.sec.gov*. We make available on our website at *www.homologymedicines.com*, under “Investors,” free of charge, copies of these reports as soon as reasonably practicable after filing or furnishing these reports with the SEC. The information contained in the websites referenced in this Annual Report on Form 10-K is not incorporated by reference into this Annual Report on Form 10-K.

Item 1A. Risk Factors.

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

Risks Related to the Merger

The Merger may not be completed and the Merger Agreement may be terminated in accordance with its terms.

The Merger is subject to a number of conditions that must be satisfied or waived, in each case, prior to the completion of the Merger, as specified in the Merger Agreement. These conditions to the completion of the Merger, some of which are beyond our control, may not be satisfied or waived in a timely manner or at all, and, accordingly, the Merger may be delayed or not completed.

If the Merger is not completed, we are subject to the following risks:

- if the Merger Agreement is terminated under specified circumstances, we may be required to pay Q32 a termination fee of $2.4 million;
- the price of our common stock may decline and could fluctuate significantly; and
- costs related to the Merger, such as financial advisor, legal and accounting fees, which we estimate will total approximately $5.6 million, which must be paid even if the Merger is not completed.

If the Merger Agreement is terminated and our board of directors determines to seek another business combination, there can be no assurance that we will be able to find a partner with whom a business combination would yield greater benefits than the benefits to be provided under the Merger Agreement.

If we and Q32 complete the Merger, the combined company will need to raise additional capital by issuing equity securities or additional debt or through licensing arrangements, which may cause significant dilution to the combined company's stockholders or restrict the combined company's operations.

Additional financing may not be available to the combined company when it is needed or may not be available on favorable terms. To the extent that the combined company raises additional capital by issuing equity securities, such financing will cause additional dilution to all securityholders of the combined company, including our pre-Merger stockholders and Q32's former securityholders. It is also possible that the terms of any new equity securities may have preferences over the combined company's common stock. Any debt financing the combined company enters into may involve covenants that restrict its operations. These restrictive covenants may include limitations on additional borrowing and specific restrictions on the use of the combined company's assets, as well as prohibitions on its ability to create liens, pay dividends, redeem its stock or make investments. In addition, if the combined company raises additional funds through licensing arrangements, it may be necessary to grant licenses on terms that are not favorable to the combined company.

Our stockholders may not realize a benefit from the Merger commensurate with the ownership dilution they will experience in connection with the Merger.

If the combined company is unable to realize the full strategic and financial benefits currently anticipated from the Merger, our stockholders will have experienced substantial dilution of their ownership interests without receiving any commensurate benefit, or only receiving part of the commensurate benefit to the extent the combined company is able to realize only part of the strategic and financial benefits currently anticipated from the Merger.

Certain provisions of the Merger Agreement may discourage third parties from submitting competing proposals, including proposals that may be superior to the transactions contemplated by the Merger Agreement.

The terms of the Merger Agreement prohibit us from soliciting competing proposals or cooperating with persons making unsolicited takeover proposals, except in limited circumstances. In addition, if we terminate the Merger Agreement under specified circumstances, we may be required to pay Q32 a termination fee of $2.4 million. This termination fee may discourage

third parties from submitting competing proposals to us or our stockholders, and may cause our board of directors to be less inclined to recommend a competing proposal.

Because the lack of a public market for Q32's stock makes it difficult to evaluate the fair market value of Q32's stock, we may pay more than the fair market value of Q32's stock and/or the stockholders of Q32 may receive consideration in the Merger that is less than the fair market value of Q32's stock.

The outstanding Q32 common stock is privately held and is not traded in any public market. The lack of a public market makes it difficult to determine the fair market value of Q32's stock. Because the percentage of our equity to be issued to Q32 stockholders was determined based on negotiations between the parties, it is possible that the value of our common stock to be received by Q32 stockholders will be less than the fair market value of Q32's stock, or we may pay more than the aggregate fair market value for Q32's stock.

Stockholders could file lawsuits relating to the Merger.

As of the date of this Annual Report on Form 10-K, there are no pending lawsuits challenging the Merger. However, potential plaintiffs may file lawsuits challenging the Merger. The outcome of any future litigation is uncertain. Such litigation, if not resolved, could prevent or delay consummation of the Merger and result in substantial costs to us, Q32, or the combined company, including any costs associated with the indemnification of directors and officers. One of the closing conditions is the absence of any order or legal requirement that restrains, enjoins, or otherwise prevents the consummation of the Merger. Therefore, if a plaintiff were successful in obtaining an injunction prohibiting the consummation of the Merger on the agreed-upon terms, then such injunction may prevent the Merger from being consummated, or from being consummated within the expected time frame.

Risks Related to Our Financial Position and Need for Additional Capital

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

We are a clinical-stage genetic medicines company with a limited operating history. Since inception, we have incurred significant operating losses. Our net losses for the year ended December 31, 2023 was $113.0 million. As of December 31, 2023 and December 31, 2022, we had an accumulated deficit of $542.1 million and $429.1 million, respectively. On March 10, 2022, we closed our transaction with OXB (US) LLC and recorded a gain of $131.2 million on the sale of our manufacturing business which resulted in which resulted in net income of $92.1 million for the three months ended March 31, 2022 (see Note 6 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for additional information regarding the OXB (US) LLC Transaction). Our net loss for the year ended December 31, 2022 was $5.0 million. In addition, we have not commercialized any products and have never generated any revenue from product sales. We have historically devoted most of our financial resources to research and development, including our preclinical development activities.

In July 2023, we completed a review of our business and our board of directors approved a plan to explore, review and evaluate a range of potential strategic options available to us, including, without limitation, an acquisition, merger, reverse merger, sale of assets, strategic partnerships or other transactions. Based on the financing environment and our anticipated clinical development timeline, we stopped further development of our programs and reduced our workforce by 86% to significantly reduce our ongoing operating costs as we evaluate strategic alternatives.

We have incurred and expect to continue to incur costs and expenditures in connection with the process of evaluating our strategic alternatives and will continue to incur costs associated with operating as a public company. The process of continuing to evaluate strategic transactions may be costly, time-consuming and complex, and we may incur significant costs related to these processes, such as legal, accounting and advisory fees and expenses and other related charges. A considerable portion of these costs will be incurred regardless of whether any particular course of action is implemented or transaction is completed. Any such expenses will decrease the remaining cash available for use in our business.

Should we resume development of our product candidates, we would 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 U.S. Food and Drug Administration, or FDA, or foreign regulatory authorities 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 medicines product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be

able to begin generating revenue from the commercialization of products or achieve or maintain profitability. Our expenses will also increase substantially if and as we:

- continue our current research programs and our preclinical development of product candidates from our current research programs;
- seek to identify, assess, acquire and/or develop additional research programs and additional product candidates;
- initiate preclinical testing and clinical trials for any product candidates we identify and develop;
- establish a sales, marketing and distribution infrastructure to commercialize any product candidates for which we may obtain marketing approval;
- maintain, expand and protect our intellectual property portfolio;
- further develop our genetic medicines platform;
- hire additional clinical, scientific and commercial personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts, as well as to support our operations as a public reporting company;
- acquire or in-license other commercial products, product candidates and technologies;
- make royalty, milestone or other payments under current and any future in-license agreements; and
- further expand our Good Manufacturing Practices, or GMP, manufacturing capacity.

Furthermore, should we resume development of our product candidates, our ability to successfully develop, commercialize and license our products and generate product revenue would be 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.

Any financial or strategic option we pursue may not be successful.

In July 2023, our board of directors approved a process to explore, review and evaluate a range of potential strategic options available to us, including, without limitation, an acquisition, merger, reverse merger, sale of assets, strategic partnerships or other transactions. The process of continuing to evaluate these strategic options has been and may continue to be costly, time-consuming and complex and we may incur significant costs related to this continued evaluation, such as legal, accounting and advisory fees and expenses and other related charges. There can be no assurance that the proposed Merger with Q32 will be completed, and we can provide no assurance that any other strategic alternative we may pursue will have a positive impact on our results of operations or financial condition.

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

Until such time, if ever, as we can generate substantial revenue, we may finance our cash needs through a combination of equity offerings, debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements. As of December 31, 2023, we do not 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 believes that we have sufficient funds for our current or future operating plans.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, including under our effective Registration Statement on Form S-3, the ownership interests of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raises 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, should we resume development of our product candidates, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our decision to discontinue further program development efforts may not result in the anticipated savings for the Company and may adversely affect our business.

In connection with our decision to pursue strategic alternatives and reduce our ongoing operating expenses, in July 2023 we decided to stop further program developments. Based on the anticipated clinical development timeline of HMI-103 and the financing environment, we believe this decision to discontinue further program development efforts will significantly reduce our ongoing operating costs. We may not realize, in full or in part, the anticipated benefits and savings in operating expenses from this decision due to unforeseen difficulties, delays or other unexpected costs. For instance, this decision to stop further program developments may include higher than expected costs associated with winding down our clinical programs. Moreover, if we are unable to realize the expected cost savings, our financial condition could be adversely affected, and it may be more difficult to complete the proposed Merger with Q32 or any other potential strategic transaction.

We will require additional capital to fund our operations, and if we fail to obtain necessary financing, we may not be able to continue our operations for more than twelve months after the issuance date of our consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

We will require additional capital, which we may raise through equity offerings, debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or other sources to enable us to complete the development and potential commercialization of our product candidates and any future product candidates, should we resume such activities. 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.

Based upon our current projections, we believe that our existing cash, cash equivalents, and short-term investments will enable us to fund our operations for at least one year from the issuance date of our consolidated financial statements for the year ended December 31, 2023 included elsewhere in this Annual Report on Form 10-K. However, due to considerations of certain qualitative factors, including the discontinuation of all clinical trials and research activities, as well as our significant reduction in force of all but a few custodial employees, our management has concluded that there is substantial doubt regarding our ability to continue as a going concern for more than twelve months after the issuance date of our consolidated financial statements included elsewhere in this Annual Report on Form 10-K. Beyond that, we will need to raise additional capital in order to fund operating expenses and capital expenditure requirements. 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. In addition, our resource requirements could materially change depending on the outcome of our ongoing strategic alternative review process. As a result, we are unable to estimate the exact amount of our working capital requirements. 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. Should we resume development of our product candidates our future funding requirements, both near and long-term, would depend on many factors, including, but not limited to:

- the initiation, progress, timing, costs and results of our planned clinical trials for our 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 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 our product candidates in regions where we choose to commercialize our products; and
- the initiation, progress, timing and results of our commercialization of our product candidates, if approved for commercial sale.

We maintain the majority of our cash and cash equivalents in accounts with major U.S. and multi- national financial institutions, and our deposits at these institutions exceed insured limits. Market conditions can impact the viability of these institutions. In the event of failure of any of the financial institutions where we maintains our cash and cash equivalents, there can be no assurance that we would be able to access uninsured funds in a timely manner or at all. Any inability to access or delay in accessing these funds could adversely affect our business and financial position.

We cannot be certain that additional funding will be available on acceptable terms, or at all. For example, the trading prices for our and other biopharmaceutical companies' stock have been highly volatile as a result of macroeconomic conditions, developments in the industry and the COVID-19 pandemic. As a result, we may face difficulties raising capital through sales of our common stock and any such sales may be on unfavorable terms. 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 or product candidates or potentially discontinue operations.

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, should we resume development of our product candidates, 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.

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.

Should we resume development of our product candidates, we would be heavily dependent on the success of our product candidates, and if none of our candidates receives regulatory approval or is not successfully commercialized, our business may be harmed.

We have historically invested a significant portion of our efforts and financial resources in the development of our product candidates. 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 our product candidates. We currently have no products that are approved for commercial sale and may never be able to develop marketable products, and we have stopped development activities. Should we resume development of our product candidates, we expect that a substantial portion of our efforts and expenditures over the next few years will be devoted to development of these candidates, which would require additional clinical development, management of clinical and manufacturing activities, regulatory approval in multiple

jurisdictions, securing manufacturing supply, building of a commercial organization, substantial investment and significant marketing efforts before we can generate any revenues from any commercial sales. Accordingly, our business has historically depended heavily on the successful development, regulatory approval and commercialization of our product candidates, which may never occur. Therefore, we cannot be certain that any of our product candidates would be successful in future clinical trials, receive regulatory approval or be successfully commercialized even if we receive regulatory approval.

Even if we receive approval to market any product candidate from the FDA or other regulatory authorities, we cannot be certain that our product candidates 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 any product candidate 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.

If any of our product candidates 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.

Historically, part of our strategy involved, and to the extent such activities are resumed in the future may involve, 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 may be too complex and difficult to navigate successfully or economically.

In addition, should we resume development of our product candidates, 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 may be required to make significant payments in connection with our license agreement with the City of Hope.

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

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

Should we resume development of our product candidates, 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. 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, prior to our initiated Phase 1 pheEDIT clinical trial. In addition, there have been a limited number of gene therapy products approved in the United States or in Europe and none of these products have utilized our AAVHSC platform.

We have historically 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. There have been a limited number of clinical trials of gene editing technologies, and, prior to our Phase 1 pheEDIT clinical trial, none of these clinical trials involved product candidates that utilize our novel gene correction editing technology. Moreover, there have been a limited number of gene therapy products approved in the United States or in Europe and none of these products have utilized our AAVHSC platform. In addition, because our programs, prior to our pausing of further product development, were all in the research, preclinical or early-clinical stage, we have not been able to fully assess safety in humans, and there may be long-term effects from treatment with any of our future product candidates that we cannot predict at this time. Any gene correction editing product candidates we may develop will act at the level of DNA, and, because animal DNA differs from human DNA, it will be difficult for us to test our future product candidates in animal models for either safety or efficacy. Also, animal models may not exist for some of the diseases we expect to pursue, should we resume development of our product candidates. Our genetic medicines platform is based on a family of 15 proprietary AAVHSCs which we can deploy through a nuclease-free gene editing modality, gene therapy, or GTx-mAb, which is designed to produce antibodies throughout the body. All applications rely on the 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. Should we resume development of our product candidates, 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, studies conducted by a third party in non-human primates, or NHPs, suggest that intravenous delivery of certain AAV vectors at very high doses may result in severe toxicity of the dorsal root ganglion, or DRG. To date, we have not observed the severe DRG toxicities described in these publications after intravenous administration in NHPs with our naturally occurring AAVHSC vectors, and we have not seen these toxicities in our product candidates. However, we cannot be certain that we will be able to avoid triggering toxicities in our future preclinical or clinical studies we may conduct with our product candidates. 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, should we resume development of our product candidates, or commercializing any product candidates we may develop on a timely or profitable basis, if at all.

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

Regulatory requirements governing products created with genome editing technology or involving gene therapy treatment have changed frequently and will likely continue to change in the future. Approvals by one regulatory authority may

not be indicative of what any other regulatory authority may require for approval, and there is substantial, and sometimes uncoordinated, overlap in those responsible for regulation of gene therapy products, cell therapy products and other products created with genome editing technology. For example, the FDA maintains the Office of Therapeutic Products within its Center for Biologics Evaluation and Research, or CBER, with responsibility for the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. Should we resume development of our product candidates, these and other regulatory review agencies, committees and advisory groups and any requirements and guidelines they promulgate may lengthen the regulatory review process, require us to perform additional preclinical studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates or lead to significant post-approval limitations or restrictions.

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

In the European Union, or EU, the European Medicines Agency, or EMA, has a Committee for Advanced Therapies, or CAT, that, in conjunction with the Committee for Medicinal Products for Human Use, or CHMP, is responsible for assessing the quality, safety and efficacy of advanced therapy medicinal products, or ATMPs. ATMPs include gene therapy medicines, somatic-cell therapy medicines and tissue-engineered medicines. The role of the CAT is to prepare a draft opinion on an application for marketing authorization for a gene therapy medicinal candidate that is submitted to the EMA. The CAT's opinion is considered by the CHMP when giving its final recommendation regarding the authorization of a product in view of the balance of benefits and risks identified. Although the CAT's draft opinion is submitted to the CHMP for final approval, the CHMP may depart from the draft opinion, if it provides detailed scientific justification. In the EU, the development and evaluation of a gene therapy medicinal product must be considered in the context of the relevant EU guidelines. The CHMP and CAT are also responsible for providing guidelines on ATMPs and have published numerous guidelines, including specific guidelines on gene therapies and cell therapies. These guidelines provide additional guidance on the factors that the EMA will consider in relation to the development and evaluation of ATMPs and include, among other things, the preclinical studies required to characterize ATMPs; the manufacturing and control information that should be submitted in a marketing authorization application; and post-approval measures required to monitor patients and evaluate the long term efficacy and potential adverse reactions of ATMPs. Although these guidelines are not legally binding, we believe that our compliance with them is likely necessary to gain and maintain approval for any of our product candidates. In addition, the EMA may issue new guidelines concerning the development and marketing authorization for gene therapy medicinal products and require that we comply with these new guidelines. Similarly complex regulatory environments exist in other jurisdictions in which we might consider seeking regulatory approvals for our product candidates, further complicating the regulatory landscape. As a result, the procedures and standards applied to gene therapy products and cell therapy products may be applied to any of our gene therapy or genome editing product candidates, but that remains uncertain at this point.

The clinical trial requirements of the FDA, the EMA and other regulatory authorities and the criteria these regulators use to evaluate the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for product candidates created with novel genome editing technology such as ours can be more lengthy, rigorous and expensive than the process for other better known or more extensively studied product candidates and technologies. To the extent we resume our activities developing novel treatments for diseases in which there is little clinical experience with new endpoints and methodologies, there is heightened risk that the FDA, the EMA or comparable regulatory authorities may not consider the clinical trial endpoints to provide clinically meaningful results, and the resulting clinical data and results may be more difficult to analyze. This may be a particularly significant risk for many of the genetically defined diseases for which we may develop product candidates alone or with collaborators due to small patient populations for those diseases, and designing and executing a rigorous clinical trial with appropriate statistical power is more difficult than with diseases that have larger patient populations. Regulatory authorities administering existing or future regulations or legislation may not allow production and marketing of products utilizing genome editing technology in a timely manner or under technically or commercially feasible conditions. Even if our product candidates obtain required regulatory approvals, such approvals may later be withdrawn as a result of changes in statute or regulations or the interpretation of new available data by applicable regulatory agencies.

Changes in applicable regulatory guidelines may lengthen the regulatory review process for our product candidates, require additional studies or trials, increase development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of such product candidates, or lead to significant post-approval limitations or restrictions. Additionally, adverse developments in clinical trials conducted by others of gene therapy products or products created using genome editing technology, or adverse public perception of the field of genome editing, may cause the FDA and

other regulatory authorities to revise the requirements for approval of any product candidates we may develop or limit the use of products utilizing genome editing technologies, either of which could materially harm our business. Furthermore, regulatory action or private litigation could result in expenses, delays or other impediments to our research programs or the development or commercialization of current or future product candidates.

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

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

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. Should we resume development of our product candidates, 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 medicines 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 current and future clinical trials are completed as planned, we cannot be certain that their results will establish the safety, purity, potency and/or effectiveness of any of our product candidates to the satisfaction of the FDA or other regulatory authorities, even if we believe that such trials were successful.

To date, we have not completed any clinical trials for our product candidates. Should we resume development of our product candidates, we may experience delays in conducting any clinical trials and we do not know whether planned clinical trials will begin on time, need to be redesigned, recruit and enroll patients on time or be completed on schedule, or at all. Clinical trials can be delayed or terminated for a variety of reasons, including delays or failures related to:

- the FDA or comparable foreign regulatory authorities disagreeing as to the design or implementation of our clinical studies;
- obtaining regulatory approval to commence a trial;
- reaching an agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining institutional review board, or IRB, and ethics committee approval or positive opinion 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.

Should we resume development of our product candidates, we may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates or significantly increase the cost of such trials, including:

- we may receive feedback from regulatory authorities that requires us to modify the design of our clinical trials;
- clinical trials of our product candidates may produce negative safety and/or efficacy data or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon development programs;

- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we or our investigators might have to suspend or terminate clinical trials of our product candidates for various reasons, including non-compliance with regulatory requirements, a finding that our product candidates have undesirable side effects or other unexpected characteristics, or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate, and we may not have funds to cover the costs;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;
- regulators may revise the requirements for approving our product candidates, or such requirements may not be as we anticipate; and
- any future collaborators that conduct clinical trials may face any of the above issues, and may conduct clinical trials in ways they view as advantageous to them but that are suboptimal for us.

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

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

We could encounter further 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 Monitoring Committee, or DMC, 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."

To the extent we were to resume such activities, all of our product candidates would require extensive clinical testing before we would be prepared to submit a BLA or similar applications seeking regulatory approval. We cannot predict with any certainty if or when we might complete the development of any of our product candidate and submit a BLA or similar applications or whether any such BLA or similar applications will be approved by the FDA or comparable foreign authorities. We may seek feedback from the FDA or other regulatory authorities on our clinical development program, and the FDA or such regulatory authorities may not provide such feedback on a timely basis, or such feedback may not be favorable, which could further delay our development programs.

If we experience delays in the commencement or completion of our clinical trials, or if we terminate a clinical trial prior to completion, the commercial prospects of our product candidates could be harmed, and our ability to generate revenues from

our product candidates 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.

In addition, the FDA's and other regulatory authorities' policies with respect to clinical trials may change and additional government regulations may be enacted. For instance, the regulatory landscape related to clinical trials in the EU recently evolved. The EU Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the Clinical Trials Directive required a separate clinical trial application, or CTA, to be submitted in each member state in which the clinical trial takes place, to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application for multi-center trials. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed. The CTR provides for a three-year transition period. Clinical trials for which an application was submitted (i) prior to January 31, 2022 under the Clinical Trials Directive, or (ii) between January 31, 2022 and January 31, 2023 and for which the sponsor has opted for the application of the EU Clinical Trials Directive remain governed by said Clinical TrialDirective until January 31, 2025. After this date, all clinical trials (including those which are ongoing) will become subject to the provisions of the CTR. Compliance with the CTR requirements by us and our third-party service providers, such as clinical research organizations, or CROs, may impact our developments plans.

It is currently unclear to what extent the United Kingdom, or UK, will seek to align its regulations with the EU. The UK regulatory framework in relation to clinical trials is derived from existing EU legislation (as implemented into UK law, through secondary legislation). On January 17, 2022, the UK Medicines and Healthcare Regulatory Agency, or MHRA, launched an eight-week consultation on reframing the UK legislation for clinical trials, with the aim to streamline clinical trials approvals, enable innovation, enhance clinical trials transparency, enable greater risk proportionality, and promote patient and public involvement in clinical trials. The UK Government published its response to the consultation is on March 21, 2023 confirming that it would bring forward changes to the legislation. These resulting legislative amendments will be closely watched and will determine how closely the UK regulations are aligned with the CTR. Under the terms of the Protocol on Ireland/Northern Ireland, provisions of the CTR which relate to the manufacture and import of investigational medicinal products and auxiliary medicinal products apply in Northern Ireland. On February 27, 2023, the UK Government and the European Commission reached a political agreement on the "Windsor Framework" which will revise the Protocol on Ireland/Northern Ireland in order to address some of the perceived shortcomings in its operation. Once implemented, this may have further impact on the application of the CTR in Northern Ireland. A decision by the UK Government not to closely align any new legislation with the new approach adopted in the EU may have an effect on the cost of conducting clinical trials in the UK as opposed to other countries.

If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may also be adversely impacted.

Adverse public perception of genetic medicine, and gene editing in particular, may negatively impact the length of time required to advance our product candidates through clinical trials should we resume development of our product candidates, including the pace at which we advance patient enrollment, and potential regulatory approval of, or demand for, our potential products.

Some of our therapeutic candidates involved editing the human genome. If we resume the development of our product candidates in the future, the clinical and commercial success of such potential products would depend in part on public acceptance of the use of gene editing and gene therapy for the prevention or treatment of human diseases. Public attitudes may be influenced by claims that gene therapy and gene editing are unsafe, unethical, or immoral, and, consequently, our products may not gain the acceptance of the public or the medical community. Adverse public attitudes may adversely impact our ability to enroll clinical trials. Moreover, our success will depend upon physicians prescribing, and their patients being willing to receive, treatments that involve the use of product candidates we may develop in lieu of, or in addition to, existing treatments with which they are already familiar and for which greater clinical data may be available.

In addition, gene editing technology is subject to public debate and heightened regulatory scrutiny due to ethical concerns relating to the application of gene editing technology to human embryos or the human germline. For example, in April 2015,

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

Although we do not use our technologies to edit human embryos or the human germline, should we resume development of our product candidates, 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 from 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.

Should we resume development of our product candidates, 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 and rolling review of a BLA, if the relevant criteria are met.

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

On May 1, 2019, we received Fast Track Designation for HMI-102 for the prevention or treatment of neurocognitive defects due to phenylalanine hydroxylase deficiency through normalization of circulating phenylalanine levels, and on October 25, 2021, we received Fast Track Designation for HMI-103 for the treatment of neurocognitive and neuropsychiatric manifestations of PKU secondary to phenylalanine hydroxylase deficiency. Should resume development of our product candidates, we may seek such designation for some or all of our other product candidates. If a drug or biologic, in our case, is intended for the treatment of a serious or life-threatening condition and the biologic demonstrates the potential to address unmet medical needs for this condition, the biologic sponsor may also apply for FDA Fast Track Designation. The sponsor of a Fast Track product candidate has opportunities for more frequent interactions with the applicable FDA review team during

product development and, once a BLA is submitted, the product candidate may be eligible for priority review. A Fast Track product candidate may also be eligible for rolling review, where the FDA may consider for review sections of the BLA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the BLA, the FDA agrees to accept sections of the BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the BLA. 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.

In the future, we may seek EMA PRIME designation or apply for other expedited regulatory pathways, designations, schemes or tools in the EU or UK for one or more of our product candidates, which we may not receive. Such designations may not lead to a faster development or regulatory review or approval process and do not increase the likelihood that our product candidates will receive marketing authorization.

In the future, we may seek EMA PRIME (Priority Medicines) designation or other designations, schemes or tools for one or more of our product candidates. In the EU, innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the PRIME scheme, which provides incentives similar to the Breakthrough Therapy and Fast-Track designation in the United States. PRIME is a voluntary scheme aimed at enhancing the EMA's support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. The benefits of a PRIME designation include the appointment of a rapporteur before submission of a marketing authorization application, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review earlier in the application process.

Even if we believe one of our product candidates is eligible for PRIME, the EMA may disagree and instead determine not to make such designation. The EMA PRIME scheme or other schemes, designations, or tools, even if obtained or used for any of our product candidates may not lead to a faster development, regulatory review or approval process compared to therapies considered for approval under conventional procedures and do not assure ultimate approval. In addition, even if one or more of our product candidates is eligible to the PRIME scheme, the EMA may later decide that such product candidates no longer meet the conditions for qualification or decide that the time period for review or approval will not be shortened. Product developers that benefit from PRIME designation may be eligible for accelerated assessment (in 150 days instead of 210 days), which may be granted for medicinal products of major interest from a public health perspective or that target an unmet medical need, but this is not guaranteed.

We may equally pursue some of the post-Brexit MHRA procedures to prioritize access to new medicines that will benefit patients, such as a 150-day assessment, a rolling review procedure and an innovative licensing and access pathway, or ILAP. ILAP aims to accelerate the time to market and to facilitate patient access to medicines, including new chemical entities, biological medicines, new indications and repurposed medicines. To benefit from ILAP, we must first apply to the MHRA for an innovation passport. An innovation passport allows for enhanced engagement with the MHRA and its partner agencies. Once an innovation passport has been granted, the next step in the pathway is the preparation of a target development profile, or TDP, document by the MHRA and its partner agencies. The TDP sets out the regulatory and development milestones, identifies potential pitfalls and creates a roadmap to achieving early patient access in the UK. Product developers that benefit from ILAP will be provided with advice on clinical trial design to ensure optimal data generation for both regulatory approval and health technology appraisal.

The competent regulatory authorities in the EU and the UK have broad discretion whether to grant access to the aforementioned schemes and designations, and even if we were to be eligible for some of these procedures, we may not experience a faster development process, review or authorization compared to conventional procedures. Moreover, the removal or threat of removal of such designation may create uncertainty or delay in the clinical development of our product candidates and threaten the commercialization prospects of our product candidates, if approved. Such an occurrence could materially impact our business, financial condition and results of operations.

Should we resume development of our product candidates, we may attempt to secure approval from the FDA or comparable foreign regulatory authorities through the use of accelerated approval pathways or similar expedited approval pathways outside the United States. If we are unable to obtain such approval, we may be required to conduct additional clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals. Even if we receive accelerated approval from the FDA or similar expedited approval pathways by foreign regulatory authorities, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA or foreign regulatory authorities may seek to withdraw accelerated approval or similar expedited approval.

To the extent we resume development of our product candidates, we may in the future seek an accelerated approval for our one or more of our product candidates. Under the accelerated approval program, the FDA may grant accelerated approval to a product candidate designed to treat a serious or life-threatening condition that provides meaningful therapeutic benefit over available therapies upon a determination that the product candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit.

The accelerated approval pathway may be used in cases in which the advantage of a drug or biologic over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is usually contingent on the sponsor's agreement to conduct, in a diligent manner, confirmatory studies to verity and describe the drug or biologic's predicted clinical benefit. Under the Food and Drug Omnibus Reform Act of 2022, or FDORA, the FDA is permitted to require, as appropriate, that a post-approval confirmatory study or studies be underway prior to approval or within a specified time period after the date of accelerated approval was granted. FDORA also requires sponsors to send updates to the FDA every 180 days on the status of such studies, including progress toward enrollment targets, and the FDA must promptly post this information publicly. FDORA also gives the FDA increased authority to withdraw approval of a drug or biologic granted accelerated approval on an expedited basis, if the sponsor fails to conduct such studies in a timely manner, send the necessary updates to the FDA, or if confirmatory studies fail to confirm such clinical benefit.

In the EU, a "conditional" marketing authorization may be granted in cases where all the required safety and efficacy data are not yet available. A conditional marketing authorization is subject to conditions to be fulfilled for generating missing data or ensuring increased safety measures. A conditional marketing authorization is valid for one year and has to be renewed annually until fulfillment of all relevant conditions. Once the applicable pending studies are provided, a conditional marketing authorization can become a "standard" marketing authorization. However, if the conditions are not fulfilled within the timeframe set by the EMA, the marketing authorization will cease to be renewed. Furthermore, marketing authorizations may also be granted "under exceptional circumstances" when the applicant can show that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use even after the product has been authorized and subject to the introduction of specific procedures. This may arise when the intended indications are very rare and, in the present state of scientific knowledge, it is not possible to provide comprehensive information, or when generating data may be contrary to generally accepted ethical principles. This type of marketing authorization is close to a conditional marketing authorization as it is reserved to medicinal products to be approved for severe diseases or unmet medical needs and the applicant does not hold the complete data set legally required for the grant of a marketing authorization. However, unlike a conditional marketing authorization, the applicant does not have to provide the missing data and will never have to. Although a marketing authorization "under exceptional circumstances" is granted definitively, the risk-benefit balance of the medicinal product is reviewed annually and the marketing authorization may be withdrawn where the risk-benefit ratio is no longer favorable.

Prior to seeking accelerated approval or similar expedited approval for any of our product candidates, should we resume development of our product candidates, we may seek feedback from the FDA or other comparable regulatory authorities and will otherwise evaluate our ability to seek and receive accelerated approval or similar expedited approval. Furthermore, if we decide to submit an application for accelerated approval or similar expedited approval, there can be no assurance that such submission or application will be accepted or that any expedited development, review or approval will be granted on a timely basis, or at all. The FDA or other comparable foreign regulatory authorities could also require us to conduct further studies prior to considering our application or granting approval of any type. A failure to obtain accelerated approval or any other form of expedited development, review or approval for our product candidate would result in a longer time period to commercialization of such product candidate or make commercialization unfeasible, and could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

We may seek orphan drug designation for our product candidates should we resume our development activities in the future, but any orphan drug designations we may 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 BLA, to market the same drug for the same disease or condition for seven years, except in limited circumstances. The applicable exclusivity period is ten years in the EU. The European exclusivity period can be reduced to six years if, at the end of the fifth year, 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.

In the future, even if we, or any prospective 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 disease or condition 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 a disease or condition broader than the orphan-designated disease or condition 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 disease or condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same disease or 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 diseases or conditions other than those in which we have been granted orphan drug designation. The same principles are valid for the EU as well.

A Regenerative Medicine Advanced Therapy designation from the FDA, or Advanced Therapy Medicinal Product classification by the EMA, 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.

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

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

In the EU, a specific framework has been implemented for ATMPs to facilitate their access to the EU market. An ATMP can be classified into three main types of medicinal products: (i) gene therapy medicinal products containing genes that lead to

a therapeutic, prophylactic or diagnostic effect, (ii) somatic-cell therapy medicinal products containing cells or tissues that have been manipulated to change their biological characteristics or cells or tissues not intended to be used for the same essential functions in the body which can be used to cure, diagnose or prevent diseases, and (iii) tissue-engineered products containing cells or tissues that have been modified so they can be used to repair, regenerate or replace human tissue. Companies developing product candidates may seek a scientific recommendation from the EMA's CAT on ATMP classification. This optional procedure allows applicants to clarify whether a given product candidate based on genes, cells or tissues meets the scientific criteria which define ATMPs, in order to address, as early as possible, questions of borderline with other areas, which may arise as science develops. ATMP classification recommendation is adopted by the EMA's CAT, after consultation with the EC. The EMA offers a range of advisory services and incentives to support the development of ATMPs such as contribution of the CAT's members in the discussion of the scientific advice and fee waivers. Similarly to RMAT designation, ATMP classification in the EU does not change the standards for product approval, and there is no assurance that such classification will result in expedited review or approval.

Our contract manufacturers, including Oxford Biomedica (US) LLC, are subject to significant regulation with respect to manufacturing our former product candidates. The manufacturing facilities which we have historically and may in the future rely may not meet or continue to meet regulatory requirements, as applicable and as imposed to date, and have limited capacity.

Historically, we have had relationships with a limited number of suppliers for the manufacturing of our viral vectors and product candidates. In March 2022, we closed an agreement with Oxford to establish a new AAV vector manufacturing company, Oxford Biomedica (US) LLC, that incorporates our proven 'plug and play' process development and manufacturing platform, as well as our experienced team and high-quality GMP vector production capabilities that we built and operated since 2019. The related transactions closed on March 10, 2022. 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 GMP or similar requirements outside the United States. 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. Our contract manufacturers must supply all necessary documentation in support of a BLA on a timely basis and must adhere to the FDA's current good laboratory practices, or GLP, and GMP regulations enforced by the FDA through its facilities inspection program. Similar requirements apply in foreign jurisdictions. Some of our contract manufacturers have not produced a commercially-approved product and therefore have not obtained the requisite FDA and foreign regulatory 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 or foreign regulatory authorities 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 our third-party manufacturers fail to maintain regulatory compliance, the FDA or other regulatory authorities 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 and/or marketing authorization application 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 resume development of our product candidates and encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

Should we resume development of our product candidates, the timely completion of clinical trials would depend, 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, should we resume development of our product candidates, our clinical trials would compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition would 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 our product candidates, or could render further development impossible.

Our product candidates have caused and may in the future 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 have caused, and could in the future 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 and/or gene therapy, due to the potential for persistent biological activity of the genetic material or other product components used to carry the genetic material. Accordingly, the FDA typically recommends an extended follow-up period to monitor for such events in patients who have received investigational gene therapies. Although we have communicated to the FDA our intent to withdraw or inactive our previously open INDs and discontinue development of our product candidates, as well as our determination that such long-term follow-up is not necessary for our product candidates, the FDA may disagree, and may continue to recommend that such follow-up be conducted.

If we resume development of our product candidates and unacceptable side effects arise in the development of such product candidates, we, the FDA, the IRBs at the institutions in which our studies are conducted or DMC, 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 we resume development of our product candidates and 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 or implement similar risk management measures;
- 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.

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 have communicated to the FDA our intent to withdraw or inactivate our previously open INDs. It is possible that neither our product candidates previously in development (should we elect to restart our development programs), 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 file for substantive review any 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. Similar risks exist in foreign jurisdictions.

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 authorities, that such product candidates are safe and effective, or in the case of biologics, safe, pure, and potent, for their intended uses. Results from nonclinical studies and clinical trials can be interpreted in different ways. Even if we believe the nonclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. The FDA and other regulatory authorities 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- and other regulatory authorities-required studies, approval of any BLA or application that we submit may be delayed by several years, or may require us to expend significantly more resources than we have available.

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

In addition, even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our products, may grant approval contingent on the performance of costly post-marketing clinical trials, including Phase 4 clinical trials, and/or the implementation of a REMS or similar risk management measures, which may be required to ensure safe use of the drug after approval. The FDA or the applicable foreign regulatory agency also may approve a product candidate for a more limited indication or patient population than we originally requested, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

In addition, changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. For instance, the EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the EC in November 2020. The EC's proposal for revision of several legislative instruments related to medicinal products (including potentially revising the duration of regulatory exclusivity and eligibility for expedited pathways) was published on April 26, 2023. The proposed revisions remain to be agreed and adopted by the European Parliament and European Council (not expected before the end of 2024 or early 2025). The revisions may, however, have a significant impact on the pharmaceutical industry and our business in the long term.

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

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

Even if we restart development of our product candidates and obtain FDA approval for our product candidates in the United States in the future, we may never obtain approval for or commercialize them in any other jurisdiction, which would limit our ability to realize their 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 any 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 restart development of and 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, will be subject to extensive and ongoing requirements of and review by the FDA and other regulatory authorities, including oversight of 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. These requirements include submissions of safety and other post-marketing information and reports, establishment registration and drug listing requirements, continued compliance with GMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping and GCP requirements for any clinical trials that we conduct post-approval. Manufacturers of drug products and their facilities are subject to continual review and periodic, unannounced inspections by the FDA and other regulatory authorities for compliance with GMP or similar regulations and standards.

In addition, any marketing approvals that we may receive for our product candidates may contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, and may include burdensome post-approval study or risk management requirements. For example, the FDA may require a REMS in order to approve our product candidates, which could entail requirements for a medication guide, physician training and communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools.

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 and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. 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 be subject to enforcement action and we may not achieve or sustain profitability.

The FDA and other regulatory authorities actively enforce the laws and regulations prohibiting the promotion of off-label uses.

If we restart development of our product candidates and any of our product candidates are approved, and we are found to have improperly promoted off-label uses of those products, we may become subject to significant liability. The FDA and other regulatory authorities strictly regulate the promotional claims that may be made about prescription products, such as our product candidates, if approved. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling. If we receive marketing approval for a product candidate, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability. The U.S. federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion of our product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

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 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, healthcare 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 our product candidates;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- decreased demand for our product candidates, 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 any of our product candidates, we intend to acquire insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. A successful product liability claim or series of claims brought against us could cause our share price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business, including preventing or limiting the commercialization of any product candidates we develop. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended.

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

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

Misconduct by our employees and independent contractors, including principal investigators, CROs, consultants, vendors, and any third parties we may engage in connection with development and commercialization, could include intentional, reckless or negligent conduct or unauthorized activities that violate: (i) the laws and regulations of the FDA, foreign regulatory authorities 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. Specifically, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws could also involve the improper use or misrepresentation of information obtained in the course of clinical trials, creation of fraudulent data in preclinical studies or clinical trials or illegal misappropriation of drug product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with such laws or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgements, possible exclusion from participation in Medicare, Medicaid, other U.S. federal healthcare programs or healthcare programs in other jurisdictions, individual imprisonment, other sanctions, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations.

Our business and operations may suffer in the event of information technology system failures, cyberattacks or deficiencies in our cybersecurity.

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. Our information technology systems, as well as those of our CROs and other contractors and consultants, are vulnerable to failure or damage from computer viruses and malware (e.g. ransomware), unauthorized access or other cybersecurity attacks, natural disasters (including hurricanes), international terrorism, conflicts and telecommunication and electrical failures. We and certain of our service providers are from time to time subject to cyberattacks and security incidents. While we do not believe that we have experienced any significant system failure, accident or security breach to date, 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, should we resume the development of our product candidates, 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 our product candidates could be delayed.

Despite our security measures, our information technology and infrastructure may be vulnerable to attacks by hackers or internal bad actors, or breached due to human error (e.g., social engineering, phishing), a technical vulnerability, malfeasance or other disruptions. Attacks upon information technology systems are increasing in their frequency, levels of persistence, sophistication and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives and expertise. We may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Even if identified, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques (including artificial intelligence) that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence. Any significant security 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 require significant resources to remediate or recover from the incident, result in legal claims or proceedings (including class actions), 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. Further, our insurance coverage may not be sufficient to cover the financial, legal, business or reputational losses that may result from an interruption or breach of our systems.

Should we resume development of our product candidates, initial, 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.

If we resume development of our product candidates, we may publicly disclose initial, interim, top-line or preliminary data from our clinical trials, which would be based on a preliminary analysis of then-available data, and the results and related findings and conclusions would be subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the initial, top-line or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Initial, top-line or preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the initial, top-line or preliminary data we previously published. Should we resume development of our product candidates, further clinical data from any trials of our candidates may not be consistent with data previously observed and disclosed in preclinical studies or clinical trials. As a result, initial, top-line and preliminary data should be viewed with caution until the final data are available.

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

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

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

To the extent we resume development of our product candidates, 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 have focused 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

If we resume development of our product candidates, enacted and future healthcare legislation could 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 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 Medicare Part D coverage gap discount program, in which manufacturers must agree to offer point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and generic drugs, respectively;
- 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, thereby potentially increasing a manufacturer's Medicaid rebate liability; and
- a Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, the Budget Control Act of 2011 resulted in aggregate reductions of Medicare payments to providers, which went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2031, 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 healthcare 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. On March 11, 2021, the American Rescue Plan Act of 2021 was signed into law, which eliminates the statutory cap on the Medicaid drug rebate, currently set at 100% of a drug's AMP, beginning January 1, 2024.

In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. On August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of Health and Human Services (HHS) to implement many of these provisions through guidance, as opposed to regulation, for the initial years. Further, under the IRA, orphan drugs are exempted from the Medicare drug price negotiation program, but only if they have one orphan designation and for which the only approved indication is for that disease or condition. If a product receives multiple orphan designations or has multiple approved indications, it may not qualify for the orphan drug exemption. The implementation of the IRA is currently the subject of ongoing litigation challenging the constitutionality of the IRA's Medicare drug price negotiation program. The impact of the IRA on our business and the pharmaceutical industry cannot yet be fully determined, but it could have a significant impact. In particular, if a product becomes subject to the IRA negotiation provision

and related price cap, that may significantly alter the economic rationale for developing and commercializing a biosimilar. We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Legally-mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates or put pressure on our product pricing.

In the EU, similar political, economic and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of healthcare 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.

On December 13, 2021, Regulation No 2021/2282 on Health Technology Assessment, or HTA amending Directive 2011/24/EU, was adopted. While the regulation entered into force in January 2022, it will only begin to apply from January 2025 onwards, with preparatory and implementation-related steps to take place in the interim. Once the regulation becomes applicable, it will have a phased implementation depending on the concerned products. The regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products, and providing the basis for cooperation at the EU level for joint clinical assessments in these areas. The regulation will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement.

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. The federal False Claims Act also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the federal False Claims Act and to share in any monetary recovery. 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 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;
- the FDCA, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices;
- the U.S. Public Health Service Act, which prohibits, among other things, the introduction into interstate commerce of a biological product unless a biologics license is in effect for that product;
- the U.S. federal legislation commonly referred to as the Physician Payments Sunshine Act, enacted as part of the ACA, and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program to report annually to the government information related to certain payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician practitioners (physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiologist assistants and certified nurse midwives), 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; and 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
- similar healthcare laws and regulations in the EU and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers. For instance, in the EU, interactions between pharmaceutical companies and healthcare professionals and healthcare organizations, are also governed by strict laws, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct both at EU level and member states level. The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of pharmaceutical products is prohibited in the EU. Relationships with healthcare professionals and associations are subject to stringent anti-gift statutes and anti-bribery laws, the scope of which differs across the EU. In addition, national "Sunshine Acts" may

require pharmaceutical companies to report/publish transfers of value provided to healthcare professionals and associations on a regular (e.g. annual) basis.

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.

Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards and other requirements could adversely affect our business, results of operations, and financial condition.

The global data protection landscape is rapidly evolving, and we are or may become subject to numerous state, federal and foreign laws, requirements and regulations governing the collection, use, disclosure, retention, and security of personal information, such as information that we may collect in connection with clinical trials. In the United States, HIPAA as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, and regulations promulgated thereunder, or collectively, HIPAA, imposes, among other things, certain standards relating to the privacy, security, transmission and breach reporting of individually identifiable health information. Certain states have also adopted comparable privacy and security laws and regulations, some of which may be more stringent than HIPAA. Such laws and regulations will be subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our future customers and strategic partners. For example, California enacted the California Consumer Privacy Act, or CCPA, which went into effect January 1, 2020. The CCPA, increases data privacy obligations for covered companies and provides individual privacy rights to California consumers, including the right to opt out of certain disclosures of their information. The CCPA also creates a private right of action with statutory damages for certain data breaches, thereby potentially increasing the likelihood of and risks associated with a data breach. Although the law includes limited exceptions, including for "protected health information" maintained by a covered entity or business associate, it may regulate or impact our processing of personal information depending on the context. Further, the California Privacy Rights Act, or CPRA, generally went into effect on January 1, 2023 and significantly amends the CCPA. It imposes additional data protection obligations on covered companies doing business in California, including additional consumer rights processes and opt outs for certain uses of sensitive data. It also creates a new California data protection agency specifically tasked to enforce the law, which will likely result in increased regulatory scrutiny of California businesses in the areas of data protection and security. The substantive requirements for businesses subject to the CPRA become enforceable on July 1, 2023. Similar laws have passed in other states and are continuing to be proposed at the state and federal level, reflecting a trend toward more stringent privacy legislation in the United States. The enactment of such laws could have potentially conflicting requirements that would make compliance challenging.

Furthermore, the Federal Trade Commission, or FTC, and many state Attorneys General continue to enforce federal and state consumer protection laws against companies for online collection, use, dissemination and security practices that appear to be unfair or deceptive. For example, according to the FTC, failing to take appropriate steps to keep consumers' personal information secure can constitute unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act. The FTC expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities.

Our operations abroad may also be subject to increased scrutiny or attention from data protection authorities. For example, in Europe, the GDPR imposes obligations and restrictions on the collection and use of personal data relating to individuals located in the European Economic Area, or EEA. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater. Among other requirements, the GDPR regulates transfers of personal data subject to the GDPR to third countries that

have not been found to provide adequate protection to such personal data, including the United States. Case law from the Court of Justice of the European Union, or CJEU, states that reliance on the standard contractual clauses – a standard form of contract approved by the European Commission as an adequate personal data transfer mechanism – alone may not necessarily be sufficient in all circumstances and that transfers must be assessed on a case-by-case basis. Following a period of legal complexity and uncertainty regarding international personal data transfers, particularly to the United States, We expect the regulatory guidance and enforcement landscape to continue to develop, in relation to transfers to the United States and elsewhere. As a result, we may have to make certain operational changes and we will have to implement revised standard contractual clauses and other relevant documentation for existing data transfers within required time frames.

Since the beginning of 2021, we have also been subject to the UK data protection regime, which imposes separate but similar obligations to those under the GDPR and comparable penalties, including fines of up to £17.5 million or 4% of a noncompliant company's global annual revenue for the preceding financial year, whichever is greater. If we continue to expand into other foreign countries and jurisdictions, we may be subject to additional laws and regulations that may affect how we conduct business.

Although we work to comply with applicable laws, regulations and standards, our contractual obligations and other legal obligations, these requirements are evolving and may be modified, interpreted and applied in an inconsistent manner from one jurisdiction to another, and may conflict with one another or other legal obligations with which we must comply. Any failure or perceived failure by us or our employees, representatives, contractors, consultants, collaborators, or other third parties to comply with such requirements or adequately address privacy and security concerns, even if unfounded, could result in additional cost and liability to us, damage our reputation, and adversely affect our business and results of operations.

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 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.

We are currently subject to securities class action litigation and may be subject to similar or other litigation in the future, which will require significant management time and attention, result in significant legal expenses and may result in unfavorable outcomes, which may have a material adverse effect on our business, operating results and financial condition, and negatively affect the price of our common stock.

We are, and may in the future become, subject to various legal proceedings and claims that arise in or outside the ordinary course of business. 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. For example, on March 25, 2022, a stockholder of the Company, Michael C. Pizzuto, filed a putative class action complaint alleging violations of Sections 10(b) and 20(a) of the Securities and Exchange Act of 1934, as amended, against us and certain of our executives. Pizzuto v. Homology Medicines, Inc., No. 2:22– CV – 01968 (C.D. Cal 2022). The complaint alleges that we failed to disclose certain information regarding efficacy and safety in connection with a Phase 1/2 HMI-102 clinical trial, and seeks damages in an unspecified amount. The Company filed a motion to transfer the case to the United States District Court for the District of Massachusetts on September 2, 2022, and a motion to dismiss on October 17, 2022. On April 18, 2023, the court granted the motion to transfer, finding that venue was not proper in the Central District of California and transferring the case to the District of Massachusetts. Following the transfer, the case number changed to 1:23-cv-10858-AK (D. Mass.). On May 9, 2023, the Massachusetts court issued an order permitting the parties to submit updated briefs in connection with the motion to dismiss, which were submitted on June 8, 2023, July 13, 2023, and August 3, 2023. The motion to dismiss remains pending. On March 4, 2024, the Massachusetts court held oral argument on the Company's motion to dismiss, which remains pending. On February 22, 2024, a purported stockholder of the Company, Kevin Welsh, filed a putative class action complaint against the Company and its directors related to the Company's proposed Merger with Q32, alleging violations of Sections 14(a) and 20(a) of the Securities Exchange Act of 1934, as

amended. Welsh v. Homology Medicines, Inc., No. 1:24-cv-00242 (D. Del.). The complaint alleges that the Company and its directors filed a proxy statement containing material omissions regarding financial forecasts and their respective analysis, and seeks damages in an unspecified amount. The case is in its early stages. The Company believes the claims alleged lack merit.

The results of the securities class action lawsuit and any future legal proceedings cannot be predicted with certainty. Also, our insurance coverage may be insufficient, and any amounts not covered by insurance will be borne by the combined company. Furthermore, our assets may be insufficient to cover any amounts that exceed our insurance coverage, and we may have to pay damage awards or otherwise may enter into settlement arrangements in connection with such claims. Any such payments or settlement arrangements in current or future litigation could have a material adverse effect on our business, operating results or financial condition. Even if the plaintiffs' claims are not successful, current or future litigation could result in substantial costs and significantly and adversely impact our reputation and divert management's attention and resources, which could have a material adverse effect on our business, operating results and financial condition, and negatively affect the price of our common stock. In addition, such lawsuits may make it more difficult to finance our operations.

Risks Related to Commercialization

Should we resume development of our product candidates, 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. Should we resume development of our product candidates, we will face competition with respect to any product candidates that we may seek to develop or commercialize 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, MLD, Hunter syndrome, 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.

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

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. We have requested withdrawal or inactivation of our previously open INDs, so we are currently not progressing any product candidates through the development process. 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 opportunities 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.

Should we resume development of our product candidates, 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 or foreign authorities approval. Our ability to achieve acceptable levels of coverage and reimbursement for products by governmental authorities, private health insurers and other organizations will have an effect on our ability to successfully commercialize our product candidates. Assuming we obtain coverage for our product candidates by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Moreover, for drugs and biologics administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such products. We cannot be sure that coverage and reimbursement in the United States, the EU or elsewhere will be available for our product candidates or any product that we may develop, and any reimbursement that may become available may be decreased or eliminated in the future.

Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a product is:

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

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 third-party payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in our product candidates. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates, and may not be able to obtain a satisfactory financial return on our product candidates.

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

No uniform policy for coverage and reimbursement for products exists among third-party payors in the United States. Therefore, coverage and reimbursement for products can differ significantly among third-party payors. 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 third-party 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.

Even if a pharmaceutical product obtains a marketing authorization in the EU, there can be no assurance that reimbursement for such product will be secured on a timely basis or at all. Governments influence the price of medicinal products through their pricing and reimbursement rules and control of national healthcare systems that fund a large part of the cost of those products to consumers. Member states are free to restrict the range of pharmaceutical products for which their national health insurance systems provide reimbursement, and to control the prices and reimbursement levels of pharmaceutical products for human use. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed to by the government. Member states may approve a specific price or level of reimbursement for the pharmaceutical product, or alternatively adopt a system of direct or indirect controls on the profitability of the company responsible for placing the pharmaceutical product on the market, including volume-based arrangements, caps and reference pricing mechanisms. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular product candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines but monitor and control company profits. The downward pressure on healthcare costs in general, particularly prescription medicines, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross border imports from low-priced markets exert a commercial pressure on pricing within a country.

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 healthcare, the increasing influence of health maintenance organizations and additional legislative changes.

Even if any of our product candidates receives marketing approval in the future, it may fail to achieve market acceptance by physicians, patients, third-party payors or others in the medical community necessary for commercial success.

If any of our product candidates receives marketing approval in the future, 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 our product candidates, if approved for commercial sale, will depend on a number of factors, including but not limited to:

- the safety, efficacy and potential advantages compared to alternative treatments;
- effectiveness of sales and marketing efforts;
- the cost of treatment in relation to alternative treatments, including any similar generic treatments;
- our ability to offer our products for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- the timing of market introduction of competitive products;
- the availability of third-party coverage and adequate reimbursement;

- product labeling or product insert requirements of the FDA, EMA or other regulatory authorities, including any limitations or warnings contained in a product's approved labeling;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our product together with other medications.

Because we expect sales of our product candidates, 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.

Should we resume development of our product candidates, 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 our product candidates, if approved. Moreover, provisions in our agreements with Pfizer may inhibit our ability to enter into future collaborations with third parties.

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.

Should we resume development of our product candidates, 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 our product candidates. Additionally, if the commercial launch of any of our product candidates 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 our 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 our product candidates, 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 our product candidates, we may be forced to delay the potential commercialization of our product candidates or reduce the scope of our sales or marketing activities for our product candidates. 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 our product candidates 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 our product candidates, 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 any of our product candidates are approved for commercialization, we intend to enter into agreements with third parties to market it in certain jurisdictions outside the United States. We expect that we will be subject to additional risks related to international pharmaceutical operations, including:

- different regulatory requirements for drug and biologic approvals and rules governing drug and biologic commercialization and country-specific regulations of gene therapies in foreign countries;
- complex and restrictive import/export regulations;
- reduced protection for intellectual property rights;

- foreign reimbursement, pricing and insurance regimes;
- potential noncompliance with the U.S. Foreign Corrupt Practices Act, the U.K. Bribery Act 2010 and similar anti-bribery and anticorruption laws in other jurisdictions;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- political and economic instability, including in light of international terrorism and conflicts;
- fluctuations in currency exchange rates; and
- higher costs of doing business internationally, including increased accounting, travel infrastructure and legal compliance costs.

We have no prior experience in these areas. In addition, there are complex regulatory, tax, labor and other legal requirements imposed by both the EU and many of the EU member states 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.

In the future, any product candidates for which we intend to seek approval as biologic products may face competition sooner than anticipated.

The Patient Protection and Affordable Care Act, signed into law on March 23, 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty.

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. Jurisdictions in addition to the United States have established abbreviated pathways for regulatory approval of biological products that are biosimilar to earlier approved reference products. For example, the EU has had an established regulatory pathway for biosimilars since 2006. 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 have historically contracted with third parties, including Oxford Biomedica (US) LLC, for the manufacture of certain materials for our research programs, preclinical and clinical studies. This reliance on third parties increases the risk that we will not have sufficient quantities of such materials, product candidates, or any medicines that we may develop and commercialize, or that such supply will not be available to us at an acceptable cost or in compliance with regulatory requirements, which could delay, prevent, or impair our development or commercialization efforts if we were to resume such activities.

We have historically relied on third-party manufacturers for the manufacture of materials for research programs, preclinical and clinical studies. We do not have long-term supply agreements with all of the third-party manufacturers, and we purchase our required supply on a purchase order basis. Furthermore, the raw materials for our product candidates are sourced, in some cases, from a single-source supplier. Should we resume development of our product candidates, if we were to experience an unexpected loss of supply of any of our product candidates or any of our future product candidates for any reason, whether as a result of manufacturing, supply or storage issues or otherwise, we could experience delays, disruptions, suspensions or terminations of, or be required to restart or repeat, any pending or ongoing clinical trials.

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;
- reliance on the third party for regulatory compliance, quality assurance, safety, and pharmacovigilance and related reporting;
- inability to meet our drug specifications and quality requirements consistently;
- delay or inability to procure sufficient manufacturing capacity;
- issues related to scale-up of manufacturing;
- costs and validation of new equipment and facilities required for scale-up;
- reliance on single sources for drug components;
- lack of qualified backup suppliers for those components that are currently purchased from a sole or single-source supplier;
- misappropriation of proprietary information, including our trade secrets and know-how;
- the mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or study drug or placebo not being properly identified;
- clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales;
- operations of our third-party manufacturers or suppliers could be disrupted by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier; and
- carrier disruptions or increased costs that are beyond our control.

We do not have complete control over all aspects of the manufacturing process of, and are dependent on, our contract manufacturing partners for compliance with GMP regulations for manufacturing both active drug substances and finished drug products. Third-party manufacturers may not be able to comply with GMP regulations or similar regulatory requirements outside the United States. 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.

Assuming we were to resume the development of our product candidates, any medicines that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under GMP regulations and that might be capable of manufacturing for us. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval.

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

Should we resume development of our product candidates, we would rely on third parties to conduct, supervise and monitor our clinical trials. If those third parties did not successfully carry out their contractual duties, or if they performed in an unsatisfactory manner, it may harm our business.

Should we resume development of our product candidates, we would 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 would 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 would remain responsible for ensuring that each of our studies was conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on the CROs would not relieve us of our regulatory responsibilities.

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

Our CROs will not be our employees, and we will not control whether or not they devote sufficient time and resources to our future clinical and nonclinical programs. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials, or other product development activities which could harm our competitive position. We face the risk of potential unauthorized disclosure or misappropriation of our intellectual property by CROs, which may reduce our trade secret protection and allow our potential competitors to access and exploit our proprietary technology. If our CROs do not successfully carry out their contractual duties or obligations or fail to meet expected deadlines, 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.

Should we resume development of our product candidates, we may collaborate with third parties for the development and commercialization of our product candidates in the future, but there are no assurances that we will succeed in establishing and maintaining such collaborative relationships, which may significantly limit our ability to develop and commercialize our product candidates successfully, if at all.

Should we resume development of our product candidates, we may seek collaborative relationships for the development and commercialization of our product candidates in the future. Failure to obtain a collaborative relationship for any of our product candidates may significantly impair the potential for the product candidate. We would also 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.

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, we could lose such rights that are important to our business.

We are a party to agreements with COH 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.

If we fail to comply with our obligations under the COH 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 all current and 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 our product candidates 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 our former product candidates 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 our former product candidates 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 medicines industries involve both technological complexity and legal complexity. Therefore, obtaining and enforcing biotechnology and genetic medicines 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 as 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 intend to abandon certain national and regional patent applications while they are still pending. The grant proceeding of each national or regional patent is an independent proceeding which may lead to situations in which applications may be rejected by the relevant patent office, while substantively similar applications are granted by others. For example, relative to other countries, China has a heightened requirement for patentability and specifically requires a detailed description of medical uses of a claimed drug. Furthermore, generic drug manufacturers or other competitors may challenge the scope, validity or enforceability of our or our licensors' patents, requiring us or our licensors to engage in complex, lengthy and costly litigation or other proceedings. Generic drug manufacturers may develop, seek approval for and launch generic versions of our products. It is also quite common that depending on the country, the scope of patent protection may vary for the same product candidate or technology.

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

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

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

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

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

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

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

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

- others may be able to make products that are the same as or similar to our product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed;
- others, including inventors or developers of our owned or in-licensed patented technologies who may become involved with competitors, may independently develop similar technologies that function as alternatives or replacements for any of our technologies without infringing our intellectual property rights;
- we or our licensors or our other collaboration partners might not have been the first to conceive and reduce to practice the inventions covered by the patents or patent applications that we own, license or will own or license;

- we or our licensors or our other collaboration partners might not have been the first to file patent applications covering certain of the patents or patent applications that we or they own or have obtained a license, or will own or will have obtained a license;
- we or our licensors may fail to meet obligations to the U.S. government with respect to in-licensed patents and patent applications funded by U.S. government grants, leading to the loss of patent rights;
- it is possible that our pending patent applications will not result in issued patents;
- it is possible that there are prior public disclosures that could invalidate our or our licensors' patents;
- issued patents that we own or exclusively license may not provide us with any competitive advantage, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights, or in countries where research and development safe harbor laws exist, and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- ownership, validity or enforceability of our or our licensors' patents or patent applications may be challenged by third parties; and
- the patents of third parties or pending or future applications of third parties, if issued, may have an adverse effect on our business.

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

We currently in-license certain intellectual property from COH. 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, 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 our current and future product candidates, and we expect to

collaborate with third parties on the development of our current and 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 collaborations 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. As of December 31, 2023 we own four registered trademarks and one pending trademark application in the United States, as well as 39 registered trademarks and five 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 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 Other Risks Related to Our Business

Our recent reduction in force undertaken to significantly reduce our ongoing operating expenses may not result in our intended outcomes and may yield unintended consequences and additional costs.

In July 2023, we implemented a reduction in force affecting approximately 80 employees, or 86% of our workforce, in order to reduce our ongoing operating costs, extend our cash runway and maximize shareholder value as we consider strategic options. In connection with this corporate restructuring, we recorded a restructuring charge for severance and related costs of $10.3 million in the Company's consolidated statements of operations included elsewhere in this Annual Report on Form 10-K during the twelve months ended December 31, 2023. In addition, we had previously granted certain of the terminated employees restricted stock units that vest in annual installments based on continued service to the Company, as well as options to purchase shares of the Company's common stock that typically vest over a period of four years. In connection with the reduction in workforce, the Company agreed to accelerate the vesting of a portion of the RSUs that were unvested as of the employees' termination dates, and also modify the stock options for terminated employees such that subject to the satisfaction of severance conditions, the terminated employees' vested options will remain outstanding and exercisable until the first anniversary of each employee's termination date. These equity modifications resulted in a net reduction to stock based compensation expense of $1.0 million reflected within restructuring and other charges in the Company's consolidated statements of operations included elsewhere in this Annual Report on Form 10-K during the twelve months ended December 31, 2023.

The reduction in force may result in unintended consequences and additional costs, such as the loss of institutional knowledge and expertise, attrition beyond the intended number of employees, decreased morale among our remaining employees, and the risk that we may not achieve the anticipated benefits of the reduction in force. In addition, while positions have been eliminated certain functions necessary to our operations remain, and we may be unsuccessful in distributing the duties and obligations of departed employees among our remaining employees. The reduction in workforce could also make it difficult for us to pursue, or prevent us from pursuing, new opportunities and initiatives due to insufficient personnel, or require us to incur additional and unanticipated costs to hire new personnel to pursue such opportunities or initiatives. If we are unable to realize the anticipated benefits from the reduction in force, or if we experience significant adverse consequences from the reduction in force, our business, financial condition, and results of operations may be materially adversely affected.

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 certain principal members of our management 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.

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

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

Risks Related to Our Common Stock

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

Our executive officers and directors and their respective affiliates, in the aggregate, hold shares representing approximately 10.2% of our outstanding voting stock as of December 31, 2023. As a result, if these stockholders choose to act together, they would be able to control or significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control or significantly influence the election of directors, the composition of our management and approval of any merger, consolidation or sale of all or substantially all of our assets.

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

Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. We have registered all shares of common stock that we may issue under our equity compensation plans, which can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates.

Provisions in our restated certificate of incorporation and amended and restated bylaws and under Delaware law could make an acquisition of our Company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our restated certificate of incorporation and our amended and restated bylaws may discourage, delay or prevent a merger, acquisition or other change in control of our Company that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions include those establishing:

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

potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of us.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Our certificate of incorporation designates the Court of Chancery of the State of Delaware, subject to certain exceptions, as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders and our bylaws designate the federal district courts of the United States as the exclusive forum for actions arising under the Securities Act of 1933, as amended, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our restated certificate of incorporation specifies that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for most legal actions involving claims brought against us by stockholders. In addition, our bylaws provide that the federal district courts of the United States are the exclusive forum for any complaint raising a cause of action arising under the Securities Act of 1933, as amended. 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 and bylaws described above.

We believe these choice of forum provisions benefit 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 or bylaws to be inapplicable or unenforceable in such action. If a court were to find the choice of forum provisions contained in our restated certificate of incorporation or bylaws 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.

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

As of December 31, 2023, we had federal and state net operating loss carryforwards, or NOLs, of approximately $326.2 million and $317.3 million, respectively. Our state NOLs, and federal NOLs generated in taxable years beginning before January 1, 2018, are subject to expiration and will expire at various dates through 2043. Federal NOLs generated in taxable years beginning after December 31, 2017 may be carried forward indefinitely but may only be used to offset 80% of our taxable income in taxable years beginning after December 31, 2020, which may require us to pay federal income taxes in future years despite generating federal NOLs in prior years. As of December 31, 2023, we also had federal and state research and development and other tax credit carryforwards, or credits, including the orphan drug credit, of approximately $65.5 million and $17.2 million, respectively, available to reduce or offset future taxable income. The federal and state credits expire at various dates through 2043. These NOLs and credits could expire unused and be unavailable to offset future taxable income, to the extent subject to expiration. In addition, in general, under Sections 382 and 383 of the Code, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change NOLs or credits to offset future taxable income. For these purposes, an ownership change generally occurs where the aggregate change in stock ownership of one or more stockholders or groups of stockholders owning at least 5% of a corporation's stock exceeds 50 percentage points over a rolling three-year period. Our existing NOLs or credits may be subject to limitations arising from previous ownership changes, if any. In addition, future changes in our stock ownership, many of which are outside of our control, could result in an ownership change. Our state NOLs or credits may also be impaired or subject to limitations under state law. Accordingly, even if we attain profitability, we may not be able to utilize a material portion of our NOLs or credits.

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 and operation 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.

General Risk Factors

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

Our stock price is likely to be volatile. The stock market in general and the market for smaller biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your shares of common stock at or above the price at which you purchased them. The market price for our common stock may be influenced by many factors, including:

- the success of competitive products or technologies;
- actual or expected changes in our growth rate relative to our competitors;
- results of clinical trials of our product candidates or those of our competitors;
- developments related to our existing or any future collaborations;
- regulatory actions with respect to our product candidates or our competitors' products and product candidates;
- regulatory or legal developments in the United States and other countries;
- development of new product candidates that may address our markets and make our product candidates less attractive;
- changes in physician, hospital or healthcare provider practices that may make our product candidates less useful;
- announcements by us, our collaborators or our competitors of significant acquisitions, strategic collaborations, joint ventures or capital commitments;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- failure to meet or exceed financial estimates and projections of the investment community or that we provide to the public;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- actual or expected changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this "Risk Factors" section.

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

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

We continue to evaluate these rules and regulations, and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to furnish a report by our management on our internal control over financial reporting. To achieve compliance with Section 404 within the prescribed period, we have engaged in a process to document and evaluate our internal control over financial reporting, which has been both costly and challenging. We will need to continue to dedicate internal resources, engage outside consultants, adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing whether such controls are functioning as documented, and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could cause us to need to restate our previously issued financial statements and result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

There can be no assurance that we will be able to comply with the continued listing standards of Nasdaq.

If we fail to satisfy Nasdaq's continued listing requirements, Nasdaq may take steps to delist our securities. Such a delisting would likely have a negative effect on the price of the securities and would impair stockholders' ability to sell or purchase the securities when they wish to do so. In the event of a delisting, we can provide no assurance that any action taken by us to restore compliance with listing requirements would allow our securities to become listed again, stabilize the market price or improve the liquidity of our securities, or prevent future non-compliance with Nasdaq's listing requirements.

In the future, 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.

Unstable global political or economic conditions may have serious adverse consequences on our business, financial condition and share price.

The global economy, including credit and financial markets, has recently experienced extreme volatility and disruptions, including severely diminished liquidity and credit availability, rising interest and inflation rates, declines in

consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. If the equity and credit markets continue to deteriorate, or the United States enters a recession, it may make any necessary debt or equity financing more difficult to obtain in a timely manner or on favorable terms, more costly or more dilutive. In addition, international terrorism and conflicts could disrupt or otherwise adversely impact our operations and those of third parties upon which we rely. Related sanctions, export controls or other actions have and may in the future be initiated by nations including the U.S., the EU or Russia (e.g., potential cyberattacks, disruption of energy flows, etc.), which could adversely affect our business and/or our supply chain, our CROs, CMOs and other third parties with which we conduct business. Any of the foregoing could harm our business, results of operations and the price of our common stock may be adversely affected.

We are exposed to fluctuations in inflation, which could negatively affect our business, financial condition and results of operations.

The United States has recently experienced historically high levels of inflation. According to the U.S. Department of Labor, the annual inflation rate for the United States was approximately 8.0% for 2022. If the inflation rate continues to increase, it will likely affect our expenses, including, but not limited to, increased cost of drug product from OXB (US) LLC and other future potential contract manufacturing organizations, supplies and employee compensation expenses. To the extent inflation results in rising interest rates and has other adverse effects on the market, it may adversely affect our business, financial condition and results of operations.

The increasing focus on environmental sustainability and social initiatives could increase our costs, harm our reputation and adversely impact our financial results.

There has been increasing public focus by investors, environmental activists, the media and governmental and nongovernmental organizations on a variety of environmental, social and other sustainability matters. We may experience pressure to make commitments relating to sustainability matters that affect us, including the design and implementation of specific risk mitigation strategic initiatives relating to sustainability. If we are not effective in addressing environmental, social and other sustainability matters affecting our business, or setting and meeting relevant sustainability goals, our reputation and financial results may suffer. In addition, we may experience increased costs in order to execute upon our sustainability goals and measure achievement of those goals, which could have an adverse impact on our business and financial condition.

Moreover, this emphasis on environmental, social and other sustainability matters has resulted and may result in the adoption of new laws and regulations, including new reporting requirements. If we fail to comply with new laws, regulations or reporting requirements, our reputation and business could be adversely impacted.

Item 1B. Unresolved Staff Comments.

None.

Item 1C. Cybersecurity.

Cybersecurity Risk Management and Strategy

We have developed and implemented a cybersecurity risk management program intended to protect the confidentiality, integrity, and availability of our critical systems and information.

We design and assess our program based on the National Institute of Standards and Technology Cybersecurity Framework (NIST CSF). This does not imply that we meet any particular technical standards, specifications, or requirements, only that we use the NIST CSF as a guide to help us identify, assess, and manage cybersecurity risks relevant to our business.

Our cybersecurity risk management program is integrated into our overall risk management program, and shares common methodologies, reporting channels and governance processes that apply across the risk management program to other legal, compliance, strategic, operational, and financial risk areas.

We leverage the support of third-party information technology and security providers, including for periodic security testing and vulnerability scanning, as part of our risk management process, designed to identify, assess, and manage cybersecurity risks. We maintain an incident response and notification plan designed to assist us in identifying, responding to, and recovering from cybersecurity incidents, and we have a process to assess the security practices of certain third-party vendors.

We, like other companies in our industry, face a number of cybersecurity risks in connection with our business. Although such risks have not materially affected us, including our business strategy, results of operations or financial condition, to date, we and/or our vendors have, from time to time, experienced threats to, or security incidents, related to our data and systems or that had the potential to otherwise impact our business. For more information about the cybersecurity risks we face, refer to "Risk Factors – *Our business and operations may suffer in the event of information technology system failures, cyberattacks or deficiencies in our cybersecurity*."

Cybersecurity Governance

Our Board considers cybersecurity risk as part of its risk oversight function and has delegated to the Audit Committee (the "Committee") oversight of cybersecurity risks, including oversight of management's implementation of our cybersecurity risk management program.

The Committee receives periodic reports from management on our cybersecurity risks. In addition, management updates the Committee, as necessary, regarding any significant cybersecurity incidents.

The Committee reports to the full Board regarding its activities, including those related to cybersecurity. The full Board also periodically receives briefings from management on our cyber risk management program. Board members receive presentations on cybersecurity topics from our management team as part of the Board's continuing education on topics that impact public companies.

Our management team, with the assistance of our former Senior Director of Information Technology, now Consultant, and the Company's third-party information technology providers, is responsible for assessing and managing our material risks from cybersecurity threats. The team has primary responsibility for our overall cybersecurity risk management program and supervises both our internal cybersecurity personnel and our retained external cybersecurity consultants. Our former Senior Director of Information Technology's experience includes over 20 years of experience in information technology management and cybersecurity.

Our management team stays informed about and monitors efforts to prevent, detect, mitigate, and remediate cybersecurity risks and incidents through various means, which may include: briefings from internal security personnel; threat intelligence and other information obtained from governmental, public or private sources, including external consultants engaged by us; and alerts and reports produced by security tools deployed in our IT environment.

Item 2. Properties.

We currently occupy approximately 26,850 square feet of office and research and development laboratory space in Bedford, Massachusetts, under a sublease agreement with OXB (US) LLC that is schedule to expire in 2024. We believe that our facilities are sufficient to meet our current needs and that suitable additional space will be available as and when needed.

Item 3. Legal Proceedings.

From time to time, we may become involved in litigation relating to claims arising from the ordinary course of business. Our management believes that there are currently no claims or actions pending against us, the ultimate disposition of which could have a material adverse effect on our results of operations or financial condition.

On March 25, 2022, a stockholder of the Company, Michael C. Pizzuto, filed a putative class action complaint alleging violations of Sections 10(b) and 20(a) of the Securities and Exchange Act of 1934, as amended, against the Company and certain of its executives. Pizzuto v. Homology Medicines, Inc., No. 2:22– CV – 01968 (C.D. Cal 2022). The complaint alleges that the Company failed to disclose certain information regarding efficacy and safety in connection with a Phase I/II HMI-102 clinical trial, and seeks damages in an unspecified amount. The case is in its early stages. The Company believes the claims alleged lack merit and has filed a motion to transfer venue (filed September 2, 2022) and a motion to dismiss (filed October 17, 2022). On April 18, 2023, the court granted the motion to transfer, finding that venue was not proper in the Central District of California and transferring the case to the District of Massachusetts. Following the transfer, the case number changed to 1:23-cv-10858-AK (D. Mass.). On May 9, 2023, the Massachusetts court issued an order permitting the parties to submit updated briefs in connection with the motion to dismiss, which were submitted on June 8, 2023, July 13, 2023, and August 3, 2023. On March 4, 2024, the Massachusetts court held oral argument on the Company's motion to dismiss, which remains pending. As the outcome is not presently determinable, any loss is neither probable nor reasonably estimable.

On February 22, 2024, a purported stockholder of the Company, Kevin Welsh, filed a putative class action complaint against the Company and its directors related to the Company's proposed Merger with Q32, alleging violations of Sections 14(a) and 20(a) of the Securities Exchange Act of 1934, as amended. Welsh v. Homology Medicines, Inc., No. 1:24-cv-00242 (D. Del.). The complaint alleges that the Company and its directors filed a proxy statement containing material omissions

regarding financial forecasts and their respective analysis, and seeks damages in an unspecified amount. The case is in its early stages. The Company believes the claims alleged lack merit. As the outcome is not presently determinable, any loss is neither probable nor reasonably estimable.

Item 4. Mine Safety Disclosures.

Not Applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information

Our common stock has been publicly traded on The Nasdaq Global Select Market under the symbol "FIXX" since March 28, 2018. Prior to that time, there was no public market for our common stock.

Holders

As of March 1, 2024, there were approximately 58,133,540 shares of common stock outstanding with 14 holders of record. This number does not include beneficial owners whose shares are held by nominees in street name.

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 expect to pay 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.

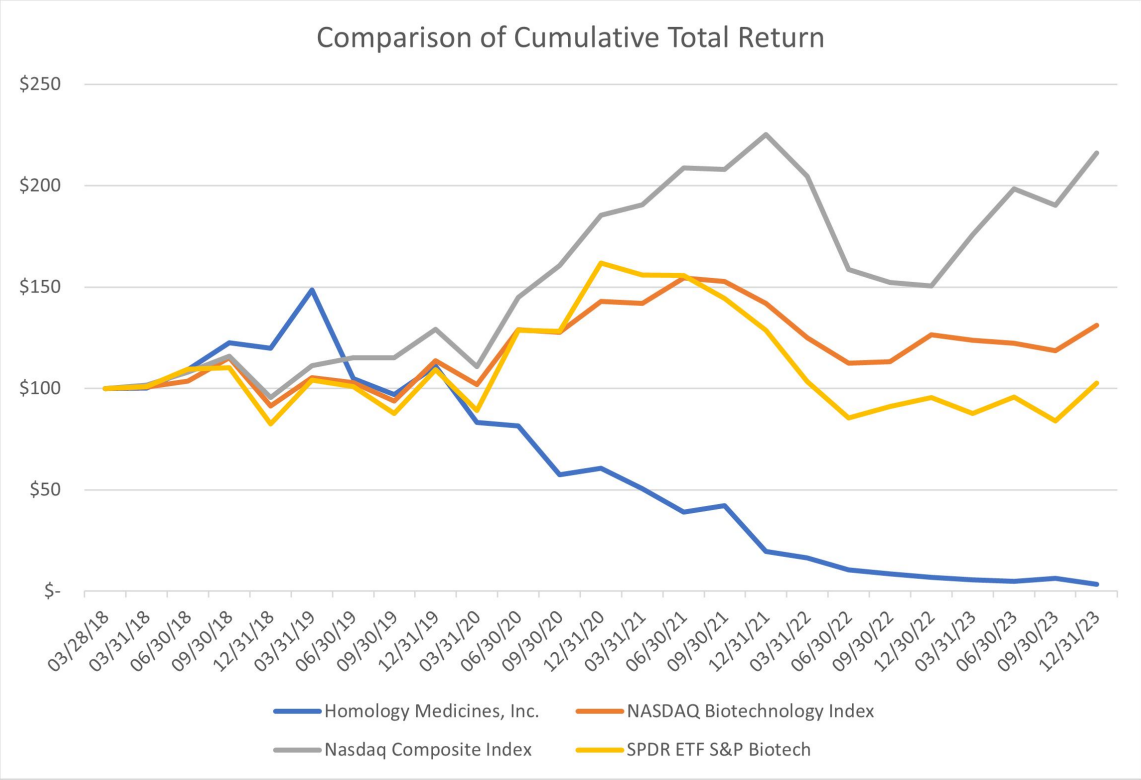
Securities Authorized for Issuance under Equity Compensation Plans

Information about our equity compensation plans is incorporated herein by reference to Item 12, *Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters*, of this Annual Report on Form 10-K.

Stock Performance Graph

This performance graph shall not be deemed "soliciting material" or to be "filed" with the SEC for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities under that Section, and shall not be deemed to be incorporated by reference into any of our filings under the Securities Act of 1933, as amended (the "Securities Act"), or the Exchange Act.

The graph set forth below compares the cumulative total stockholder return on our common stock between March 28, 2018 (the date our common stock commenced trading on The Nasdaq Global Select Market) and December 31, 2023, with the cumulative total return of (a) The Nasdaq Biotechnology Index, (b) The Nasdaq Composite Index and (c) The SPDR S&P Biotech ETF, which is an exchange-traded fund that seeks to replicate the performance of the S&P Biotechnology Select Index, over the same period. This graph assumes an initial investment of $100 on March 28, 2018 in our common stock, The Nasdaq Biotechnology Index, The Nasdaq Composite Index and The SPDR S&P Biotech ETF assumes the reinvestment of dividends, if any. The comparisons in the graph are not intended to forecast or be indicative of possible future performance of our common stock.



Recent Sales of Unregistered Securities; Purchases of Equity Securities by the Issuer or Affiliated Purchaser

We did not repurchase any of our equity securities or issue any securities that were not registered under the Securities Act during the quarter ended December 31, 2023.

Use of Proceeds

Not applicable.

Item 6. [Reserved].

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our "Selected Consolidated Financial Data" and our consolidated financial statements, related notes and other financial information included elsewhere in this Annual Report on Form 10-K. This discussion contains forward-looking statements that involve risks and uncertainties such as our plans, objectives, expectations and intentions. As a result of many important factors, including those set forth in the section captioned "Risk Factors" and elsewhere in this Annual Report on Form 10-K, our actual results could differ materially from the results described in, or implied by, these forward-looking statements.

Overview

We are a clinical-stage genetic medicines company historically focused on transforming the lives of patients suffering from rare genetic diseases with significant unmet medical needs by addressing the underlying cause of the disease. Our proprietary platform is designed to utilize our human hematopoietic stem cell-derived adeno-associated virus vectors, or AAVHSCs, to precisely and efficiently deliver single administration genetic medicines *in vivo* through a nuclease-free gene editing modality, gene therapy, or gene therapy to express antibodies platform, or GTx-mAb, which is designed to produce antibodies throughout the body.

In July 2023, we completed a review of our business and our Board of Directors approved a plan to explore, review and evaluate a range of potential strategic options available to us, including, without limitation, an acquisition, merger, reverse merger, sale of assets, strategic partnerships or other transactions. Based on the financing environment and the anticipated clinical development timeline for our lead program, HMI-103, we stopped further development of our programs and reduced our workforce by 86% to significantly reduce our ongoing operating costs as we evaluated strategic alternatives.

Agreement and Plan of Merger

After a comprehensive review of strategic alternatives, on November 16, 2023, we entered into an Agreement and Plan of Merger, or the Merger Agreement, with Q32 Bio Inc., a Delaware corporation, or Q32, and Kenobi Merger Sub, Inc., a Delaware corporation and our direct, wholly owned subsidiary, or Merger Sub, pursuant to which, among other matters, and subject to the satisfaction or waiver of the conditions set forth in the Merger Agreement, Merger Sub will merge with and into Q32, with Q32 continuing as our wholly owned subsidiary and the surviving corporation of the merger, or the Merger. Our future operations are highly dependent on the success of the Merger and there can be no assurance that the Merger will be successfully consummated. If the Merger is completed, the business of Q32 will continue as the business of the combined company.

Merger Consideration

Subject to the terms and conditions of the Merger Agreement, (i) immediately prior to the effective time of the Merger, or the Effective Time, all Q32 preferred stock will be converted into Q32 common stock pursuant to the organizational documents of Q32, or the Q32 Preferred Stock Conversion, and (ii) at the Effective Time, (a) each outstanding share of Q32 common stock (excluding Q32 common stock issued in the Concurrent Financing, as described below) will be converted into the right to receive a number of shares of our common stock, or the Company Common Stock, calculated in accordance with the Merger Agreement, (b) each outstanding Q32 stock option and warrant that has not previously been exercised prior to the closing of the Merger will be assumed by us and become an option or warrant, as applicable, to purchase a number of shares of Company Common Stock and (c) the Q32 common stock issued in the Concurrent Financing will be converted into the right to receive a number of shares of Company Common Stock calculated in accordance with the Merger Agreement. The shares of Company Common Stock that will be issued to stockholders of Q32 will be calculated using a formula in the Merger Agreement based on the equity value of each of Q32 and us. Q32 has been ascribed an aggregate equity value of $195 million and our equity value is expected to be approximately $80 million subject to adjustment based on the amount of our net cash at closing of the Merger.

Concurrent Financing

Pursuant to the Merger Agreement, immediately prior to the Effective Time, Q32 will consummate a financing through the sale of its common stock for aggregate gross proceeds of $42 million based on the same aggregate equity value of Q32 used in the Merger, or the Concurrent Financing. On November 16, 2023, Q32 entered into subscription agreements with certain accredited investors, or the Investors, for the Concurrent Financing with expected gross proceeds to Q32 of $42 million. In connection with the Concurrent Financing, at the closing of the Merger, Q32 will enter into a registration rights agreement with the Investors providing for the registration under the Securities Act of 1933, as amended, or the Securities Act, of the shares of common stock sold in the Concurrent Financing. The consummation of the transactions contemplated by the subscription

agreements is conditioned on the satisfaction or waiver of the conditions set forth in the Merger Agreement and in the subscription agreements. Shares of Q32 common stock issued pursuant to the Concurrent Financing will be converted into shares of Company Common Stock in the Merger in accordance with the Merger Agreement.

Contingent Value Rights Agreement

At the Effective Time, if any Legacy Assets (as defined below) have not been disposed of in a Legacy Asset Disposition (as defined below) or if additional consideration may be payable for the Legacy Assets (as defined below) after closing of the Merger, the Company and Equiniti Trust Company, LLC, a New York limited liability company, as the initial rights agent, or the Rights Agent, will enter into a Contingent Value Rights Agreement, or the CVR Agreement, pursuant to which our common stockholders of record as of the close of business on the last business day prior to the day on which the Effective Time occurs will receive one contingent value right (each, a "CVR") for each outstanding share of Company Common Stock held by such stockholder on such date.

Each CVR will represent the contractual right to receive payments from us upon the actual receipt by us or our subsidiaries of certain contingent proceeds derived from any cash consideration that is paid to us or our subsidiaries as a result of the sale, transfer, license, assignment or other divestiture, disposition or commercialization of any of our assets, rights and interests relating to our HMI-103, HMI-204, Capsids and AAVHSC Platform, including any equity interests held directly or indirectly by us in Oxford Biomedica (US) LLC (f/k/a Oxford Biomedica Solutions LLC and Roadrunner Solutions LLC), or OXB (US), pursuant to that certain Equity Securities Purchase Agreement, dated as of January 28, 2022, by and between the Company and OXB Solutions, or the Legacy Assets, and such disposition, or a Legacy Asset Disposition, net of certain tax, transaction costs and certain other expenses.

The contingent payments under the CVR Agreement, if they become payable, will become payable to the Rights Agent for subsequent distribution to the holders of the CVRs. There can be no assurance that any holders of CVRs will receive payments with respect thereto. The right to the contingent payments contemplated by the CVR Agreement is a contractual right only and will not be transferable, except in the limited circumstances specified in the CVR Agreement. The CVRs will not be evidenced by a certificate or any other instrument and will not be registered with the Securities and Exchange Commission, or SEC. The CVRs will not have any voting or dividend rights and will not represent any equity or ownership interest in the Company or any of its affiliates. No interest will accrue on any amounts payable in respect of the CVRs.

Former Clinical Programs

Our former clinical programs include: HMI-103, an investigational gene editing candidate for the treatment of patients with phenylketonuria, or PKU; HMI-203, an investigational gene therapy candidate for the treatment of patients with mucopolysaccharidosis type II (MPS II), or Hunter syndrome; and HMI-102, an investigational gene therapy candidate for the treatment of adult patients with PKU. Our former preclinical programs include: HMI-104, a GTx-mAb gene therapy candidate for the treatment of patients with paroxysmal nocturnal hemoglobinuria, or PNH, and HMI-204, a gene therapy candidate for metachromatic leukodystrophy, or MLD. We are currently exploring strategic alternatives for HMI-103 (Adult/Pediatric PKU), HMI-204 (MLD) and our capsids and AAVHSC platform, including the sale of these programs.

In August 2023, we withdrew our Clinical Trial Application, or CTA, for HMI-203 in Canada. In September 2023, we withdrew our IND for HMI-102, which the FDA formally acknowledged in November 2023. In December 2023, we withdrew our IND for HMI-203 and in March 2024, we withdrew our IND for HMI-103. All clinical trial sites have been notified that all studies we had been conducting for our programs have been terminated; sites have been duly notified of their responsibilities. We have also withdrawn all orphan drug designations for our programs in both the United States and the EU.

In September 2023, we inactivated the pheEDIT Phase 1 gene editing clinical trial evaluating HMI-103 in adults with classical PKU (NCT05222178). In October 2023, we reported clinical data from the first dose cohort in the pheEDIT trial. As of the data cut-off date of September 14, 2023, HMI-103 was generally well-tolerated in all three participants with no serious adverse events, and the majority of treatment-related adverse events were mild and transient. All liver function tests remained in the normal range during the prophylactic immunosuppression regimen incorporating the T-cell inhibitor tacrolimus in combination with corticosteroid. Participant 1 experienced a reduction in plasma phenylalanine, or Phe, levels to below the U.S. American College of Medical Genetics and Genomics PKU treatment guideline threshold of <360 μmol/L, and the majority of Phe levels were below 360 mmol/L through 39 weeks post-dose, including after the initiation of dietary protein supplementation. Participant 2 experienced a meaningful plasma Phe reduction of 50% at 23 weeks post-dose. Participant 3 experienced a meaningful plasma Phe reduction of 60% at 14 weeks post-dose.

In August 2023, we terminated both the pheNIX Phase 1/2 gene therapy clinical trial evaluating HMI-102 in adults with classical PKU and the juMPStart Phase 1 gene therapy clinical trial evaluating HMI-203 in adults with Hunter Syndrome. INDs for both the pheNIX Phase 1/2 and juMPStart Phase 1 clinical trials have been withdrawn.

Earlier-Stage Product Candidates

We completed IND-enabling studies with HMI-202, an investigational gene therapy for the treatment of patients with MLD. Applying the learnings from these IND-enabling studies, in August 2022, we announced the details of HMI-204, an optimized, *in vivo*, one-time gene therapy product candidate for the treatment of MLD. Following a single I.V. administration in the MLD murine model, this optimized candidate, which uses one of our proprietary AAVHSC capsids, crossed the blood-brain-barrier to the CNS and reached key peripheral organs involved in MLD. This resulted in expression of human ARSA, or hARSA, levels in multiple brain regions and cell types above the minimum level of enzyme needed to correct the MLD disease phenotype, hARSA activity levels in the brain predictive of functional assay improvements and hARSA activity in the serum. Additionally, these optimizations led to significant improvements in vector yield and superior packaging for the product candidate.

HMI-104 was a candidate from our GTx-mAb platform. This platform represents an additional way that we could potentially leverage our AAVHSCs in an effort to deliver one-time *in vivo* gene therapy to express and secrete antibodies from the liver, which we believe may allow us to target diseases with larger patient populations. In support of this program, we generated and presented preclinical data targeting complement protein 5, demonstrating preclinical proof-of-concept in PNH. A single I.V. dose of an AAVHSC GTx-mAb showed expression of full-length antibodies from the liver consistent with levels associated with anti-C5 therapeutics, sustained and robust Immunoglobulin G, or IgG, expression *in vivo* in a humanized murine liver model and a murine NOD-SCID model, and *in vivo* vector-expressed C5 mAb had potent functional activity as shown by an ex vivo hemolysis assay. Additionally, we observed sustained expression of C5 mAb in the presence of murine and human neonatal fragment crystallizable (Fc) receptor, or FcRn. We completed IND-enabling studies with HMI-104.

Oxford Biomedica (US) LLC Transaction

On March 10, 2022, we closed a transaction with Oxford Biomedica (US) LLC (f/k/a Roadrunner Solutions LLC and Oxford (US) LLC), or OXB (US) LLC, Oxford Biomedica (US), Inc., or OXB, and Oxford Biomedica plc, or OXB Parent, and collectively with OXB, Oxford, pursuant to the Equity Securities Purchase Agreement, or the Purchase Agreement, dated as of January 28, 2022, by and among Homology, OXB (US) LLC and Oxford, whereby, among other things, we and Oxford agreed to collaborate to operate OXB (US) LLC, which provides AAV vector process development and manufacturing services to biotechnology companies, which we refer to as the Oxford Biomedica (US) LLC Transaction, or the OXB (US) LLC Transaction. OXB (US) LLC incorporates our proven 'plug and play' process development and manufacturing platform, as well as our experienced team and high-quality GMP vector production capabilities that we built and operated since 2019.

Pursuant to the terms of the Purchase Agreement and a contribution agreement, or the Contribution Agreement, entered into between us and OXB (US) LLC prior to the closing of the OXB (US) LLC Transaction, or the Closing, we agreed to assign and transfer to OXB (US) LLC all of our assets that are primarily used in the manufacturing of AAV vectors for use in gene therapy or gene editing products, but excluding certain assets related to manufacturing or testing of our proprietary AAV vectors, or collectively, the Transferred Assets, in exchange for 175,000 common equity units in OXB (US) LLC, or Units, and OXB (US) LLC assumed from us, and agreed to pay, perform and discharge when due, all of our duties, obligations, liabilities, interests and commitments of any kind under, arising out of or relating to the Transferred Assets.

Effective as of the Closing, we sold to OXB, and OXB purchased from us, 130,000 Units, or the Transferred Units, in exchange for $130.0 million. In connection with the Closing, OXB contributed $50.0 million in cash to OXB (US) LLC in exchange for an additional 50,000 Units. Immediately following the Closing, (i) OXB owned 180,000 Units, representing 80 percent (80%) of the fully diluted equity interests in OXB (US) LLC, and (ii) we owned 45,000 Units, representing 20 percent (20%) of the fully diluted equity interests in OXB (US) LLC.

Pursuant to the Amended and Restated Limited Liability Company Agreement of OXB (US) LLC, or the OXB (US) LLC Operating Agreement, which was executed in connection with the Closing, at any time following the three-year anniversary of the Closing, (i) OXB will have an option to cause us to sell and transfer to OXB, and (ii) we will have an option to cause OXB to purchase from us, in each case all of our equity ownership interest in OXB (US) LLC at a price equal to 5.5 times the revenue for the immediately preceding 12-month period, subject to a maximum amount of $74.1 million. Pursuant to the terms of the OXB (US) LLC Operating Agreement, we are entitled to designate one director on the board of directors of OXB (US) LLC, currently Paul Alloway, Ph.D., our President and Chief Operating Officer.

Concurrently with the Closing, we entered into certain ancillary agreements with OXB (US) LLC including a license and patent management agreement whereby OXB (US) LLC granted certain licenses to us, a supply agreement, or the Supply Agreement, for a term of three years which includes certain annual minimum purchase commitments, a lease assignment pursuant to which we assigned all of our right, title and interest in, to and under our facility lease to OXB (US) LLC, a sublease agreement whereby OXB (US) LLC subleased certain premises in its facility to us, as well as several additional ancillary agreements.

License Agreements

In April 2016, we entered into an exclusive license agreement with City of Hope, or COH, pursuant to which COH granted us an exclusive, sublicensable, worldwide license, or the COH 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. On August 6, 2021, we received notice from COH that we did not accomplish at least one of the partnering milestones by the applicable deadline, as set forth in the COH License. This notice does not affect our exclusive license in the field of mammalian therapeutics, including all human therapeutics, associated diagnostics, and target validation, or the Mammalian Therapeutic Field, where we retain exclusive rights. Instead, the notice served as written notice that the exclusive license granted pursuant to the COH License in all fields except the Mammalian Therapeutic Field converted from exclusive to non-exclusive effective as of September 20, 2021, which was forty-five days from the receipt of notice. In connection with the conversion, any royalty obligations and sublicensee fees relating to fields outside of the Mammalian Therapeutic Field shall be reduced by a certain percentage. This change to our exclusive worldwide license with COH does not impact any of our therapeutic product development candidates, including HMI-102, HMI-103, HMI-104, HMI-203 and HMI-204.

Corporate Headquarters Lease

In November 2021, we entered into an amendment of our December 2017 lease agreement, or the Lease Amendment, for our corporate headquarters in Bedford, Massachusetts. The Lease Amendment increased the space under the lease by approximately 23,011 square feet, or the Expansion Premises, and extended the expiration date of the existing premises under the lease from February 2027 to June 2030. The term with respect to the Expansion Premises commenced May 1, 2022 and will continue for a period of ten years and five months. The term of the Expansion Premises and the existing premises are not coterminous. Annual base rent for the existing premises under the Lease Amendment is approximately $4.7 million beginning on March 1, 2027, and increases by three percent annually; annual base rent for the Expansion Premises is approximately $1.4 million per year and increases by three percent annually. The Lease Amendment allows for tenant improvement allowances not to exceed $6.3 million in the aggregate. Under the terms of the agreement with Oxford, our lease for our corporate headquarters, including the Expansion Premises, has been assigned to OXB (US) LLC with Homology subleasing a portion of lab and office space back from OXB (US) LLC. Effective October 1, 2023, we were released from being primary obligor under such lease. See Note 10 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for additional information regarding our lease agreement.

Financial Overview

Since our inception in 2015 through December 31, 2023, we have raised approximately $721 million in aggregate net proceeds through our initial public offering, or IPO, in April 2018, follow-on public offerings of common stock in April 2019 and April 2021, proceeds from the sale of common stock under an “at-the-market” sales agreement, equity investments from pharmaceutical companies, preferred stock financings and our agreement with Oxford. Included in our net proceeds is a $130.0 million up-front cash payment from our agreement with Oxford, $50.0 million from a former collaboration partner, comprised of an up-front payment of $35.0 million and a $15.0 million equity investment, and a $60.0 million equity investment from Pfizer Inc., or Pfizer, through a private placement transaction. Should we resume development of one or more of our product candidates, we will require additional capital in order to advance our product candidates through clinical development and commercialization.

We were incorporated and commenced operations in 2015. Since our incorporation and until recently, we have devoted substantially all of our resources to organizing and staffing our Company, business planning, raising capital, developing our technology platform, advancing HMI-102, HMI-103 and HMI-203 through IND-enabling studies and into clinical trials, advancing HMI-202 and HMI-104 into IND-enabling studies, researching and identifying additional product candidates, developing and implementing manufacturing processes and manufacturing capabilities, building out our manufacturing and research and development space, enhancing our intellectual property portfolio and providing general and administrative support for these operations. To date, we have financed our operations primarily through the sale of common stock, through the sale of preferred stock, through funding from our collaboration partner and through proceeds received as a result of our transaction with OXB (US) LLC.

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products in the foreseeable future, if at all. We recognized $1.2 million and $3.2 million in collaboration revenue for the years ended December 31, 2023 and 2022, respectively.

Since inception, we have incurred significant operating losses. Our net losses for the years ended December 31, 2023 and 2022 were $113.0 million and $5.0 million, respectively. On March 10, 2022, we closed our transaction with OXB (US) LLC and recorded a gain of $131.2 million on the sale of our manufacturing business (see Note 6 to our consolidated financial

statements included elsewhere in this Annual Report on Form 10-K for additional information regarding the OXB (US) LLC Transaction). As of December 31, 2023 and 2022, we had an accumulated deficit of $542.1 million and $429.1 million, respectively.

Our total operating expenses were $102.6 million and $136.5 million for the years ended December 31, 2023 and 2022, respectively. We expect our total operating expenses to decrease over the prior year as we reduced our workforce by 86% and stopped all further program development efforts. We expect to continue to incur costs and expenditures in connection with activities related to the Merger and we will continue to incur costs associated with operating as a public company. There can be no assurance, however, that we will be able to successfully consummate the Merger. The process of evaluating strategic transactions has been and, if the Merger is not consummated, may continue to be costly, time-consuming and complex, and we may incur significant costs related to these processes, such as legal, accounting and advisory fees and expenses and other related charges. A considerable portion of these costs were and will continue to be incurred regardless of whether the Merger is completed. Such expenses decrease the remaining cash available for use in our business. Failure to consummate the Merger could significantly impair our ability to enter into any strategic transactions and may significantly diminish or delay any future distributions to our stockholders.

Should we resume development of our product candidates, our ability to generate product revenue sufficient to achieve profitability would depend heavily on the successful development and eventual commercialization of one or more product candidates. Our future operating requirements will depend on many factors, including:

- the costs, timing, and results of research and development efforts for any product candidates, including clinical trials;
- the costs and timing of process development scale-up activities, and the adequacy of supply of any product candidates for preclinical studies and clinical trials through CMOs, including OXB (US) LLC;
- 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.

As of December 31, 2023, we had cash, cash equivalents, and short-term investments of $82.7 million. Based on our current projections, including our recent reduction in force and stopping further program development efforts, we believe that our existing cash, cash equivalents, and short-term investments will enable us to continue operations for at least one year from the date of the filing of our Annual Report on Form 10-K for the year ended December 31, 2023. However, due to the discontinuation of all of our clinical trials and research activities, as well as our recent reduction in force of all but a few custodial employees, our management has concluded that there is a substantial doubt regarding our ability to continue as a going concern for more than twelve months after the date the consolidated financial statements included in its Annual Report on Form 10-K for the year ended December 31, 2023 have been issued. See “Liquidity and Capital Resources.”

Components of Our Results of Operations

Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products in the foreseeable future. We recorded $1.2 million in collaboration revenue for the year ended December 31, 2023, related to the Stock Purchase Agreement with Pfizer (see Note 17 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for additional information regarding revenue recognition discussions).

Operating Expenses

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

Research and Development Expenses

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

- salaries, benefits and other related costs, including stock-based compensation expense, for personnel engaged in research and development functions;
- expenses incurred under agreements with third parties, including contract research organizations, or CROs, and other third parties that conduct research, preclinical activities and clinical trials on our behalf as well as CMOs, including OXB (US) LLC, that manufacture our product candidates for use in our preclinical testing and clinical trials;
- costs of outside consultants, including their fees and related travel expenses;
- the costs of laboratory supplies and acquiring, developing and manufacturing preclinical study and clinical trial materials; and
- allocated expenses for rent and other operating costs.

We expense research and development costs as incurred.

Research and development activities have historically been central to our business model. We expect our research and development expenses to continue to decrease significantly given the discontinuation of all of our clinical trials and research activities. Should we resume development of product candidates, we would expect research and development costs to increase significantly for the foreseeable future as the product candidate development programs progress.

Should we resume development of product candidates, the duration, costs and timing of development activities including clinical trials would depend on a variety of factors, including:

- the scope, rate of progress, expense and results of clinical trials, 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 results, early clinical data, competition, manufacturing capability and commercial viability;
- significant and changing government regulation and regulatory guidance;
- the timing and receipt of any marketing approvals; and
- the expense of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights.

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

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in our executive, finance, human resources, legal, business development and administrative functions. General and administrative expenses also include legal fees relating to intellectual property and corporate matters; professional fees for accounting, auditing, tax and consulting services; insurance costs; travel expenses; and facility-related expenses, which include direct depreciation costs, rent expense, maintenance of facilities and other operating costs including expenses associated with being a public company.

We expect our general and administrative expenses to decrease in the near future due to our recent workforce reduction. We have incurred and expect to continue to incur significant costs, however, related to our exploration of strategic alternatives, including legal, accounting and advisory expenses and other related charges.

Other Income

Other income consists of a gain on the termination of our lease and interest income earned on our cash, cash equivalents, and short-term investments. Our interest income has increased due to significantly higher yields on invested funds during the year ended December 31, 2023 as compared to the prior year period.

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, 2023, we had federal and state net operating loss carryforwards of $326.2 million and $317.3 million, respectively, that expire at various dates through 2043, to the extent subject to expiration. As of December 31, 2023, we also had federal and state research and development tax credit carryforwards of $65.5 million and $17.2 million, respectively, that expire at various dates through 2043. Included in the $65.5 million of federal research and development credit carryforwards is $50.7 million of orphan drug credit carryforwards.

Critical Accounting Policies and Use of Estimates

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

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K, we believe that the following accounting policy is the most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

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 contracts and purchase orders, communicating with our personnel and vendors 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 contract research organizations and other third parties in connection with performing research activities on our behalf and conducting preclinical studies and clinical trials on our behalf and contract manufacturing organizations, including OXB (US) LLC, in connection with producing product for our clinical studies, vendors in connection with preclinical development activities and vendors related to product manufacturing and development and distribution of preclinical supplies.

We base our accrued expenses related to preclinical and clinical 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, including OXB (US) LLC, that manufacture product for our research and development activities on our behalf. The financial terms of these agreements are sometimes 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. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical milestones. 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 expenses actually incurred, if our estimates of the status and timing of services performed differs from the actual status and timing of services performed, we may report 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.

Results of Operations

Comparison of Years Ended December 31, 2023 and 2022

The following table summarizes our results of operations for the years ended December 31, 2023 and 2022:

(in thousands)	For the Year ended December 31, 2023	2022	Change
Collaboration revenue	$ 1,156	$ 3,208	$ (2,052)
Operating expenses:			
Research and development	62,002	98,351	(36,349)
General and administrative	31,256	38,138	(6,882)
Restructuring and other charges	9,327	—	9,327
Total operating expenses	102,585	136,489	(33,904)
Loss from operations	(101,429)	(133,281)	31,852
Other income:			
Gain on sale of business	—	131,249	(131,249)
Gain on lease termination	8,767	—	8,767
Interest income	5,582	3,230	2,352
Total other income	14,349	134,479	(120,130)
Income (loss) before income taxes	(87,080)	1,198	(88,278)
Provision for income taxes	—	(715)	715
Loss from equity method investment	(25,881)	(5,488)	(20,393)
Net loss	$ (112,961)	$ (5,005)	$ (107,956)

Collaboration Revenue

Collaboration revenue for the year ended December 31, 2023 was $1.2 million, compared to $3.2 million for the year ended December 31, 2022. Collaboration revenue in both periods was due to the recognition of deferred revenue related to the Stock Purchase Agreement with Pfizer. We previously recognized deferred revenue from Pfizer over Pfizer's right of first refusal, or ROFR, period of 30 months during which Pfizer could have negotiated a potential collaboration on the development and commercialization of HMI-102 and HMI-103. The ROFR period expired in May 2023.

Research and Development Expenses

(in thousands)	For the Year ended December 31, 2023	2022	Change
External development costs for clinical programs:			
HMI-102	$ 4,514	$ 16,245	$ (11,731)
HMI-103	18,525	19,358	(833)
HMI-203	9,643	15,839	(6,196)
Other development-stage programs' external development costs	13,526	9,794	3,732
Employee-related costs	11,820	29,654	(17,834)
Other research and development costs	3,974	7,461	(3,487)
Total research and development expenses	$ 62,002	$ 98,351	$ (36,349)

Research and development expenses for the year ended December 31, 2023 were $62.0 million, compared to $98.4 million for the year ended December 31, 2022. The decrease of $36.3 million was primarily associated with our decision to stop further development of our programs and reduce our workforce by 86% in July 2023 in an effort to decrease our ongoing operating costs. As of December 31, 2023, we have no remaining obligations with our CRO or any other vendors associated with our former clinical trials and have recognized expense for any remaining contractual obligations owed under our Supply Agreement with OXB (US) LLC; there are no minimum purchase commitments under the Supply Agreement in 2024. All contracts with vendors previously performing research and development activities for us have been terminated and all expenses have been recorded.

General and Administrative Expenses

General and administrative expenses for the year ended December 31, 2023 were $31.3 million, compared to $38.1 million for the year ended December 31, 2022. The decrease of $6.9 million was primarily due to a $4.6 million decrease in employee-related costs as a result of the reduction in workforce we instituted in the third and fourth quarters of 2023. In addition, consulting expenses decreased by $2.8 million as the prior year included a fee of $2.5 million paid to a strategic advisory firm that assisted us with the OXB (US) LLC transaction. There were also decreased market research costs, travel and insurance costs, all associated with our decision to reduce in the second half of 2023 our workforce in an effort to decrease ongoing operating costs.

Restructuring and Other Charges

In connection with the corporate restructuring that reduced our workforce by approximately 80 employees, or 86%, in the third quarter of 2023 and an additional 6 employees in the fourth quarter of 2023, we recorded a restructuring charge for severance and related costs of $10.3 million during the year ended December 31, 2023. We also modified certain stock options and restricted stock units granted to the terminated employees in a prior period. These equity modifications resulted in a net reduction to stock-based compensation expense of $1.0 million reflected within restructuring and other charges during the year ended December 31, 2023. See Notes 9 and 14 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for additional information regarding restructuring and other charges. We did not record restructuring and other charges for the year ended December 31, 2022.

Gain on Sale of Business

Gain on sale of business for the year ended December 31, 2022 was $131.2 million. On March 10, 2022, we closed our transaction with OXB (US) LLC and recorded a gain of $131.2 million on the sale of our manufacturing business. See Note 6 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for details surrounding the sale.

Gain on Termination of Lease

Gain on lease termination for the year ended December 31, 2023 was $8.8 million. Effective October 1, 2023, we were released from being primary obligor under our corporate headquarters lease and therefore derecognized the right-of-use asset and operating lease liability, recording the difference as a gain within other income on the consolidated statements of operations. See Note 10 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for details surrounding the transaction.

Interest Income

Interest income for the year ended December 31, 2023 was $5.6 million, compared to $3.2 million for the year ended December 31, 2022. The increase of $2.4 million was primarily the result of interest income generated at higher yields on invested funds for the year ended December 31, 2023, compared to the year ended December 31, 2022.

Provision for Income Taxes

We recorded an income tax provision of $0.7 million for the year ended December 31, 2022. The tax provision predominately resulted from the gain associated with the sale of our manufacturing business due to the transaction with Oxford. Though we had taxable income for the year ended December 31, 2022, we had federal and state net operating loss carryforwards and research and development tax credits available to offset most of that taxable income for the period. We did not record an income tax provision (benefit) for the year ended December 31, 2023, as the Company was in a taxable loss position for the year.

Loss from Equity Method Investment

We record our share of gains or losses from OXB (US) LLC on a quarterly basis. For the year ended December 31, 2023 and 2022, we recorded a loss from equity method investment of $25.9 million and $5.5 million, respectively, representing our share of OXB (US) LLC's net loss during the year ended December 31, 2023 and the period from March 11, 2022 through December 31, 2022, respectively. For the year ended December 31, 2023, OXB (US) LLC recorded an impairment charge of $119.1 million which significantly increased OXB (US) LLC's net loss for the period. In addition, the loss from equity method investment for the year ended December 31, 2023 includes an other-than-temporary impairment charge of approximately $3.8 million we recorded because it was determined that the fair value of our equity method investment in OXB (US) LLC was less than its carrying value. After recording our share of OXB (US) LLC's net loss, the carrying value of our equity method

investment was reduced to $0.0 million. See Notes 2 and 6 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for more information regarding the equity method of accounting.

Net Loss

Net loss for the year ended December 31, 2023 was $113.0 million, compared to $5.0 million for the year ended December 31, 2022. The increase in our net loss was primarily due to a gain of $131.2 million in the prior year on the sale of our manufacturing business, offset by our operating expenses as described above.

Liquidity and Capital Resources

Since our inception, we have incurred significant operating losses. We do not have any approved products and we have never generated any revenue from product sales. To date, we have financed our operations primarily through the sale of common stock, the sale of preferred stock, through an up-front payment and funding of research candidates from a collaboration partner and through the gross proceeds from our transaction with OXB (US) LLC. Since our inception in 2015, we have raised approximately $721 million in aggregate net proceeds through our IPO in April 2018, follow-on public offerings of common stock in April 2019 and April 2021, proceeds from the sale of common stock under an "at-the-market" sales agreement, equity investments from pharmaceutical companies, preferred stock financings and our agreement with Oxford. Included in our net proceeds is a $130.0 million up-front cash payment from our agreement with Oxford, $50.0 million from a former collaboration partner, comprised of an up-front payment of $35.0 million and a $15.0 million equity investment and a $60.0 million equity investment from Pfizer through a private placement transaction.

ATM Program

On March 9, 2023, we filed a Registration Statement on Form S-3 (File No. 333-270414) (the "Shelf") with the SEC in relation to the registration of up to an aggregate of $250.0 million of our common stock, preferred stock, debt securities, warrants and/or units of any combination thereof for a period up to three years from the date of the filing. The Shelf became effective on March 17, 2023. We also simultaneously entered into a sales agreement with Cowen and Company, LLC ("Cowen"), as sales agent, providing for the offering, issuance and sale by the Company of up to an aggregate of $75.0 million of our common stock from time to time in "at-the-market" offerings under the Shelf (the "ATM"). We did not sell any shares of common stock under the ATM during the year ended December 31, 2023. As of December 31, 2023, there remained $75.0 million of common stock available for sale under the ATM.

Oxford Biomedica (US) LLC Transaction

On March 10, 2022, we closed a transaction with OXB (US) LLC pursuant to the Purchase Agreement, dated as of January 28, 2022, by and among Homology, OXB (US) LLC and Oxford, whereby, among other things, we and Oxford agreed to collaborate to operate OXB (US) LLC, which will provide AAV vector process development services and manufacturing services to pharmaceutical and biotechnology companies. Pursuant to the terms of the agreements entered into as part of the OXB (US) LLC Transaction, we have assigned and transferred to OXB (US) LLC all of our assets that are primarily used in the manufacturing of AAV vectors for use in gene therapy and gene editing products. Oxford paid us $130.0 million upfront and invested $50.0 million to fund the new company in exchange for an 80 percent ownership stake, while we own 20 percent of the new company. Also, at any time following the three-year anniversary of the closing of the transaction, Oxford has an option to cause us to sell and transfer to Oxford and we have an option to cause Oxford to purchase from us, in each case all of our equity ownership interest in OXB (US) LLC at a price equal to 5.5 times the revenue for the immediately preceding 12-month period, subject to a maximum amount of $74.1 million. See Note 6 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for additional information regarding the Oxford transaction.

Strategic Collaborations and Investments

On November 9, 2020, we entered into the Stock Purchase Agreement with Pfizer, pursuant to which Pfizer purchased 5,000,000 shares of our common stock through a private placement transaction at a purchase price of $12.00 per share, for an aggregate purchase price of $60.0 million. Under the Stock Purchase Agreement, Pfizer was granted an exclusive right of first refusal, or ROFR, for a 30-month period to negotiate a potential collaboration on the development and commercialization of HMI-102 and HMI-103. The 30-month ROFR period expired on May 9, 2023. In addition to the ROFR, the Stock Purchase Agreement provided for an information sharing committee comprised of representatives of each company which served as a forum for sharing information regarding the development of HMI-102 and HMI-103 during the ROFR period. Additionally, Pfizer designated a member to join our Scientific Advisory Board to participate in matters related to the development of these programs.

Strategic Review and Reduction in Force

On July 25, 2023, our board of directors approved a process to explore, review and evaluate a range of potential strategic options available to us, including, without limitation, an acquisition, merger, reverse merger, sale of assets, strategic partnerships or other transactions. Therefore, based on cost-reduction initiatives intended to reduce our ongoing operating expenses and maximize shareholder value as we evaluated strategic options, our board of directors also approved a reduction in our workforce by approximately 80 employees during the third quarter of 2023 and an additional 6 employees during the fourth quarter of 2023. In connection with this corporate restructuring, we recorded a restructuring charge for severance and related costs of $10.3 million in its consolidated statements of operations during the year ended December 31, 2023.

Cash Flows

Our cash, cash equivalents and short-term investments totaled $82.7 million and $175.0 million as of December 31, 2023 and 2022, respectively. We had no indebtedness as of December 31, 2023 and 2022.

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

	For the Year ended December 31,	
(in thousands)	**2023**	**2022**
Net cash used in operating activities	$ (96,230)	$ (113,661)
Net cash provided by investing activities	101,326	36,716
Net cash provided by financing activities	184	596
Net change in cash, cash equivalents and restricted cash	$ 5,280	$ (76,349)

Operating Activities

Net cash used in operating activities for the year ended December 31, 2023 was $96.2 million, which was primarily utilized for the funding of our operating expenses of $102.6 million as we incurred expenses associated with research and development activities prior to our decision to stop further development of our programs. Such activities included clinical trial activities associated with our HMI-103 and HMI-203 programs, preclinical development activities for HMI-104 and research activities on other applications for our technology, adjusted for non-cash expenses of $23.9 million. Non-cash expenses includes an $25.9 million loss from our equity method investment in OXB (US) LLC, $7.3 million of stock-based compensation expense and noncash lease expense of $2.1 million, partially offset by an $8.9 million net gain recognized on the termination of our corporate lease and accretion on short-term investments of $2.9 million. The change in operating assets and liabilities of $7.2 million was driven by decreased accrued expenses and other liabilities of $11.7 million, decreased operating lease liabilities of $1.4 million and decreased deferred revenue of $1.2 million, partially offset by decreased prepaid expenses and other current assets of $5.0 million increased accounts payable of $2.1 million.

Net cash used in operating activities for the year ended December 31, 2022 was $113.7 million, which was primarily utilized for the funding of our operating expenses of $136.5 million, as we incurred expenses associated with research and development activities including clinical trial activities associated with our HMI-103, HMI-203 and HMI-102 programs, preclinical development activities including IND-enabling studies for HMI-104 and research activities on other applications for our technology, adjusted for non-cash expenses of $112.0 million, which includes the one-time gain of $131.2 million recognized on the sale of our manufacturing business to Oxford, and a change in operating assets and liabilities of $3.4 million. The change in operating assets and liabilities was driven by increased accrued expenses and other liabilities of $7.4 million largely due to materials produced for us by OXB (US) LLC and accrued for at year-end, offset by decreased deferred revenue of $3.2 million and decreased accounts payable of $1.0 million.

Investing Activities

Net cash provided by investing activities for the year ended December 31, 2023 was $101.3 million, primarily due to proceeds from maturities of short-term investments of $174.2 million, offset by purchases of short-term investments of $73.2 million.

Net cash provided by investing activities for the year ended December 31, 2022 was $36.7 million, primarily due to $130.0 million of cash received from Oxford pursuant to the OXB (US) LLC Transaction (see Note 6 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K). We also had proceeds from maturities of short-term investments of $65.5 million. These two items were offset by purchases of short-term investments of $157.5 million and purchases of property and equipment of $1.3 million.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2023 was $0.2 million, primarily due to proceeds from the issuance of common stock pursuant to our employee stock purchase plan.

Net cash provided by financing activities for the year ended December 31, 2022 was $0.6 million, due to proceeds from the issuance of common stock pursuant to our employee stock purchase plan.

Funding Requirements

Operating expenses decreased during the year ended December 31, 2023 as compared to the year ended December 31, 2022. We expect total operating expenses to continue to decrease due to our decision to stop all further development of our product candidates and the recent implementation of a workforce reduction. We will continue to incur costs associated with operating as a public company. If we decide to resume the development of our product candidates, however, we would expect our expenses to increase in order to advance preclinical activities and clinical trials for product candidates in development. After a comprehensive review of strategic alternatives, on November 16, 2023, we entered into the Merger Agreement. Following the Merger, if successfully consummated, we do not anticipate any further development of our product candidates or programs.

As of December 31, 2023, we had cash, cash equivalents, and short term investments of $82.7 million. Based on our current projections, we believe that our existing cash, cash equivalents, and short-term investments as of December 31, 2023 will enable us to continue operations for at least one year from the date of this Annual Report on Form 10-K for the year ended December 31, 2023. However, in light of the discontinuation of all of our clinical trials and research activities, as well as our recent reduction in force of all but a few custodial employees, we have concluded that there is a substantial doubt regarding our ability to continue as a going concern for more than twelve months after the date the consolidated financial statements included elsewhere in this Annual Report on Form 10-K have been issued.

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. In addition, its resource requirements could materially change if we are unable to consummate the Merger. As a result, we are unable to estimate the exact amount of our working capital requirements. Should we resume development of product candidates in the future, our future funding requirements would depend on and could increase significantly as a result of many factors, including:

- the costs, timing, and results of research and development efforts, including clinical trials;
- the costs and timing of process development scale-up activities, and the adequacy of supply of product candidates for preclinical studies and clinical trials through CMOs, including OXB (US) LLC;
- the costs and timing of preparing, filing, and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims, including any claims by third parties that we are infringing upon their intellectual property rights;
- the effect of competitors and market developments; and
- our ability to establish and maintain strategic collaborations, licensing or other agreements and the financial terms of such agreements for our product candidates.

We maintain the majority of our cash and cash equivalents in accounts with major highly rated multi- national and local financial institutions, and our deposits at these institutions exceed insured limits. Market conditions can impact the viability of these institutions, and any inability to access or delay in accessing these funds could adversely affect our business and financial position. In the event of failure of any of the financial institutions where we maintains our cash and cash equivalents, there can be no assurance that we will be able to access uninsured funds in a timely manner or at all.

Further, the global economy, including credit and financial markets, has recently experienced extreme volatility and disruptions, including severely diminished liquidity and credit availability, rising interest and inflation rates, declines in consumer confidence, declines in economic growth, increases in unemployment rates, uncertainty about economic stability and COVID-19. All of these factors could impact our liquidity and future funding requirements, including but not limited to our ability to raise additional capital when needed on acceptable terms, if at all. The duration of this economic slowdown is uncertain and the impact on our business is difficult to predict. See “Risk Factors— Unstable global political or economic conditions may have serious adverse consequences on our business, financial condition and share price.”

Until such time, if ever, that we can generate product revenue and subject to our pursuit of a potential strategic transaction and the consummation of such potential transaction, we expect to finance our cash needs through a combination of

equity offerings, debt financings, collaboration agreements, other third-party funding, strategic alliances, licensing arrangements and marketing and distribution arrangements.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our stockholders as common stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through other third-party funding, collaboration agreements, strategic alliances, licensing arrangements or marketing and distribution arrangements, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we resume the development of product candidates and 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

As of December 31, 2023, we had non-cancelable operating leases with total future minimum lease payments of $1.4 million, of which all will be payable in 2024. These minimum lease payments exclude our share of the facility operating expenses, real-estate taxes and other costs that are reimbursable to the landlord under the leases. These payments are for operating leases for our corporate headquarters in Bedford, Massachusetts, comprised of office, manufacturing and lab space that expire in June 2030 and May 2032. Under the terms of the OXB (US) LLC Transaction, our leases for this space has been assigned to OXB (US) LLC effective March 10, 2022, with Homology subleasing a portion of lab and office space back from OXB (US) LLC. Our sublease expires on December 31, 2024. On September 25, 2023, we signed and executed a release letter with our lessor related to our headquarters in Bedford, MA. The lessor agreed to release us of all obligations under the lease effective October 1, 2023 in exchange for a $0.1 million cash payment. On October 1, 2023, we derecognized the right-of-use asset and operating lease liability and recorded the difference as a gain within other income on the consolidated statements of operations. See Note 10 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for additional information regarding our lease agreement.

Our agreements with certain institutions to license intellectual property include potential milestone and success fees, sublicense fees, royalty fees, licensing maintenance fees, and reimbursement of patent maintenance costs that we may be required to pay. Our agreements to license intellectual property include potential milestone payments that are dependent upon the development of products using the intellectual property licensed under the agreements and contingent upon the achievement of development or regulatory approval milestones, as well as commercial milestones. These potential obligations are contingent upon the occurrence of future events and the timing and likelihood of such potential obligations are not known with certainty. For further information regarding these agreements, please see Part I, Item 1. “Strategic Collaborations.”

Prior to our decision to stop further development of our products, we entered into contracts in the normal course of business with CROs and CMOs for clinical trials, preclinical research studies and testing, manufacturing and other services and products for operating purposes. These contracts generally did not contain any minimum purchase commitments and were cancelable by us upon prior notice of 30 days. Pursuant to the terms of the Supply Agreement with OXB (US) LLC entered into in March 2022, we agreed to purchase from OXB (US) LLC at least 50% of our clinical supply requirements of AAV-based products during the initial term of the Supply Agreement. We were committed to purchase a minimum number of batches of drug substance and drug product, as well as process development services, totaling approximately $29.7 million in 2023 under the Supply Agreement. We do not have any commitments to purchase products or services from OXB (US) LLC in 2024. The Supply Agreement provides for an initial term of three years, which period may be extended for an additional one-year term. After the initial term, we will have the right to terminate the Supply Agreement for convenience or other reasons specified in the Supply Agreement upon prior written notice. Either Party may terminate the Supply Agreement upon an uncured material breach by the other Party or upon the bankruptcy or insolvency of the other Party.

Item 7A. 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.

Interest Rate Risk

Our interest-earning assets consist of cash, cash equivalents, and short-term investments of $82.7 million, or 97.7% of our total assets at December 31, 2023, and $175.0 million, or 76.6% of our total assets at December 31, 2022. Interest income earned on these assets was approximately $5.6 million in 2023 and $3.2 million in 2022. Our interest income is sensitive to changes in the general level of interest rates, primarily U.S. interest rates. If a 10% change in interest rates were to have immediately occurred on December 31, 2023, this change would not have had a material effect on the fair value of our investment portfolio as of that date. At December 31, 2023, our cash equivalents consisted of bank deposits and money market funds. 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, 2023 and 2022.

Inflation Rate Risk

As of December 31, 2023, we do not believe that inflation has had a material effect on our business, financial condition or results of operations. To the extent inflation results in rising interest rates and has other adverse effects on the market, it may adversely affect our business, financial condition and results of operations.

Item 8. Financial Statements and Supplementary Data.

The financial statements required to be filed pursuant to this item are appended to this report. An index of those financial statements is found in Item 15 of Part IV of this Annual Report on Form 10-K.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Limitations on effectiveness of controls and procedures

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

Evaluation of disclosure controls and procedures

Our management, with the participation of our principal executive officer and our principal financial officer, has evaluated, as of the end of the period covered by this Annual Report on Form 10-K, the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act). Based on such evaluation, our principal executive officer and our principal financial officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2023.

Management's annual report on internal control over financial reporting

Our management is responsible for establishing and maintaining adequate internal control over our financial reporting, as such term is defined in Rule 13a-15(f) under the Exchange Act. Our management conducted an assessment of the effectiveness of our internal control over financial reporting based on the criteria set forth in "Internal Control - Integrated Framework (2013)" issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on this assessment, our management concluded that, as of December 31, 2023, our internal control over financial reporting was effective.

Attestation report of the registered public accounting firm

As a non-accelerated filer, we are not required to provide an attestation report of our independent registered public accounting firm on the effectiveness of our internal control over financial reporting.

Changes in internal control over financial reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the quarter ended December 31, 2023 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

During the three months ended December 31, 2023, no director or officer of the Company adopted a "Rule 10b5-1 trading arrangement" or "non-Rule 10b5-1 trading arrangement," as each term is defined in Item 408(a) of Regulation S-K.

On November 27, 2023, W. Bradford Smith, former Chief Financial and Business Officer, terminated a Rule 10b5-1 trading arrangement intended to satisfy the affirmative defense of Rule 10b5-1(c) and originally adopted on September 23, 2022 for the sale of up to 89,000 shares of the Company's common stock until May 23, 2024.

On December 5, 2023, Arthur Tzianabos, Chairman of our Board of Directors and former Chief Executive Officer, terminated a Rule 10b5-1 trading arrangement intended to satisfy the affirmative defense of Rule 10b5-1(c) and originally adopted on September 23, 2022 for the sale of up to 539,640 shares of the Company's common stock until December 31, 2024.

On December 5, 2023, Paul Alloway, President and Chief Operating Officer, terminated a Rule 10b5-1 trading arrangement intended to satisfy the affirmative defense of Rule 10b5-1(c) and originally adopted on September 23, 2022 for the sale of up to 24,097 shares of the Company's common stock until November 23, 2024.

As of December 31, 2023, all of the Company's "Rule 10b5-1 trading arrangements" and "non-Rule 10b5-1 trading arrangements" have been terminated.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Directors and Executive Officers

Information with respect to this item will be set forth in the Proxy Statement for the 2024 Annual Meeting of Stockholders ("Proxy Statement") or an amendment to this Annual Report on Form 10-K ("Form 10-K/A") under the headings "Election of Directors," "Executive Officers," "Section 16(a) Beneficial Ownership Reporting Compliance" and "Corporate Governance" and is incorporated herein by reference. The Proxy Statement or Form 10-K/A will be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report.

Code of Business Conduct and Ethics

Our board of directors has adopted a Code of Business Conduct and Ethics ("Code of Conduct") applicable to all officers, directors and employees, including our principal executive officer, principal financial officer, principal accounting officer and controller, and persons performing similar functions. A copy of our Code of Conduct is available at the Investors section of our website, located at www.homologymedicines.com, under "Investors—Governance Documents." We intend to disclose on our website any amendments to, or waivers from, our Code of Business Conduct and Ethics that are required to be disclosed pursuant to the rules of the SEC, as well as Nasdaq's requirement to disclose waivers with respect to directors and executive officers. The information contained on our website is not considered part of, or incorporated by reference into, this Annual Report on Form 10-K or any other filing that we make with the SEC.

Audit Committee and Audit Committee Financial Expert

We have a separately-designated standing audit committee ("Audit Committee"). The members of the Audit Committee are Matthew R. Patterson, Jeffrey V. Poulton and Mary Thistle. Ms. Thistle serves as the Chairperson of the Audit Committee. The members of our Audit Committee meet the requirements for financial literacy under the applicable rules of the SEC and Nasdaq. Our board of directors has determined that Ms. Thistle is an "audit committee financial expert" as defined by Item 407(d)(5)(ii) of Regulation S-K.

Family Relationships

There are no family relationships among any of our executive officers or directors.

Item 11. Executive Compensation.

Information with respect to this item will be set forth in the Proxy Statement or Form 10-K/A under the headings "Executive Compensation" and "Non-Employee Director Compensation" and is incorporated herein by reference. The Proxy Statement or Form 10-K/A will be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

Information with respect to this item will be set forth in the Proxy Statement or Form 10-K/A and is incorporated herein by reference. The Proxy Statement or Form 10-K/A will be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

Information with respect to this item will be set forth in the Proxy Statement or Form 10-K/A under the heading "Certain Relationships and Related Transactions, and Director Independence" and is incorporated herein by reference. The Proxy Statement or Form 10-K/A will be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report.

Item 14. Principal Accountant Fees and Services.

Information with respect to this item will be set forth in the Proxy Statement or Form 10-K/A under the heading "Principal Accountant Fees and Services" and is incorporated herein by reference. The Proxy Statement or Form 10-K/A will be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report.

PART IV

Item 15. Exhibits and Financial Statement Schedules.

(a)(1) Financial Statements.

The following documents are included on pages F-1 through F-27 attached hereto and are filed as part of this Annual Report on Form 10-K.

Index to Consolidated Financial Statements

(a)(2) Financial Statement Schedules.

All financial statement schedules have been omitted because they are not applicable, not required or the information required is shown in the financial statements or the notes thereto.

(a)(3) Exhibits.

The following is a list of exhibits filed, furnished or incorporated by reference as part of this Annual Report on Form 10-K.

		Incorporated by Reference				
Exhibit Number	**Description of Exhibit**	**Form**	**File No.**	**Exhibit**	**Filing date**	**Filed Herewith**
2.1^^	Agreement and Plan of Merger, dated November 16, 2023, by and among Homology Medicines, Inc., Kenobi Merger Sub, Inc., and Q32 Bio Inc.	8-K	001-38433	2.1	11/16/23	
3.1	Restated Certificate of Incorporation of Homology Medicines, Inc.	8-K	001-38433	3.1	4/3/18	
3.2	Amended and Restated Bylaws of Homology Medicines, Inc.	8-K	001-38433	3.1	12/18/20	
4.1	Specimen Stock Certificate evidencing the shares of common stock	S-1/A	333-223409	4.2	3/19/18	
4.2	Form of Indenture	S-3	333-230664	4.3	4/1/19	
4.3	Description of Securities					*
10.1#	2015 Stock Incentive Plan, as amended, and forms of agreements thereunder	S-1/A	333-223409	10.1	3/19/18	
10.2#	2018 Incentive Award Plan, and forms of awards thereunder	10-K	001-38433	10.2	3/11/21	
10.3#	2018 Employee Stock Purchase Plan	S-1/A	333-223409	10.3	3/19/18	
10.4#	2018 Employee Stock Purchase Plan – Offering Document	10-Q	001-38433	10.1	11/13/18	
10.5#	Non-Employee Director Compensation Program	10-Q	001-38433	10.1	11/10/22	
10.6#	Form of Indemnification Agreement for Directors and Officers	S-1/A	333-223409	10.5	3/19/18	
10.7	Lease Agreement, dated December 21, 2017, by and between Homology Medicines, Inc. and Patriots Park Owner, LLC, as amended by the First Amendment to Lease, dated February 8, 2019, the Second Amendment to Lease, dated March 15, 2019, and the Third Amendment to Lease, dated November 9, 2021	10-Q	001-38433	10.1	11/15/21	
10.8	Assignment and Assumption Agreement, dated March 10, 2022, between Homology Medicines, Inc. and Roadrunner (US) LLC	10-K	001-38433	10.8	3/23/22	
10.9	Sublease Agreement, dated March 10, 2022, between Homology Medicines, Inc. and Roadrunner (US) LLC	10-K	001-38433	10.9	3/23/22	

10.10#	Amended and Restated Employment Agreement, dated April 21, 2022, by and between Homology Medicines, Inc. and Albert Seymour	8-K	001-38433	10.1	4/21/22	
10.11#	Employment Agreement, dated March 18, 2018, by and between Homology Medicines, Inc. and Bradford Smith	S-1/A	333-223409	10.13	3/19/18	
10.12#	Amendment to Employment Agreement, dated as of September 6, 2022, by and between Homology Medicines, Inc. and W. Bradford Smith	8-K	001-38433	10.2	9/8/22	
10.13#	Consulting Agreement, dated as of September 6, 2022, by and between Homology Medicines, Inc. and Arthur Tzianabos, Ph.D.	8-K	001-38433	10.1	9/8/22	
10.14#	Employment Agreement, dated March 18 2020, by and between Homology Medicines, Inc. and Paul Alloway, Ph.D.	10-K	001-38433	10.13	3/23/22	
10.15#	Amendment to Employment Agreement, dated September 6, 2022, by and between Homology Medicines, Inc. and Paul G. Alloway, Ph.D.	10-Q	001-38433	10.4	11/10/22	
10.16#	Employment Agreement, dated September 1, 2021, by and between Homology Medicines, Inc. and Michael Blum	10-K	001-38433	10.14	3/23/22	
10.17#	Amendment to Employment Agreement, dated September 6, 2022, by and between Homology Medicines, Inc. and Michael Blum	10-Q	001-38433	10.5	11/10/22	
10.18†	Exclusive License Agreement, dated April 28, 2016, between Homology Medicines, Inc. and City of Hope	S-1/A	333-223409	10.16	3/19/18	
10.19^	Stock Purchase Agreement, dated November 9, 2020, by and between Homology Medicines, Inc. and Pfizer Inc.	8-K	001- 38433	10.1	11/9/20	
10.20	Equity Securities Purchase Agreement, dated January 28, 2022, by and among Homology Medicines, Inc., Roadrunner (US) LLC, Oxford Biomedica (US), Inc. and, solely for purposes of Article IX thereof, Oxford Biomedica plc	10-K	001- 38433	10.23	3/23/22	
10.21	Amendment No. 1 to Equity Securities Purchase Agreement dated as of January 28, 2022 by and among Homology Medicines, Inc., Roadrunner (US) LLC, Oxford Biomedica (US), Inc. and, solely for purposes of Article IX thereof, Oxford Biomedica plc	10-K	001- 38433	10.24	3/23/22	
10.22	Contribution Agreement, dated March 10, 2022, between Homology Medicines, Inc. and Roadrunner (US) LLC	10-K	001- 38433	10.25	3/23/22	
10.23^	Amended and Restated Limited Liability Company Agreement, dated March 10, 2022, by and among Oxford Biomedica (US) LLC (f/k/a Roadrunner (US) LLC), Homology Medicines, Inc. and Oxford Biomedica (US) Inc.	10-K	001- 38433	10.26	3/23/22	
10.24^	Manufacturing and Supply Agreement, dated March 10, 2022, by and among Homology Medicines, Inc., Roadrunner (US) LLC and, solely for purposes of Section 2.3(b)(iii) thereof, Oxford Biomedica UK Limited	10-K	001- 38433	10.27	3/23/22	
21.1	Subsidiaries of Homology Medicines, Inc.	S-1	333-223409	21.1	3/2/18	
23.1	Consent of Deloitte & Touche LLP, independent registered public accountant					*
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002					*
31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002					*
32.1	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					**
32.2	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					**

97.1	Policy Relating to Recovery of Erroneously Awarded Compensation	*
101.INS	Inline XBRL Instance Document – the Instance Document does not appear in the interactive data file because its XBRL tags are embedded within the Inline XBRL document	*
101.SCH	Inline XBRL Taxonomy Extension Schema With Embedded Linkbase Documents	*
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)	*

* Filed herewith.

** Furnished herewith.

# Indicates management contract or compensatory plan or arrangement.

† Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment.

^ Portions of this exhibit (indicated by asterisks) have been omitted pursuant to Regulation S-K, Item 601(b)(10)(iv).

^^ Registrant has omitted schedules and exhibits pursuant to Item 601(b)(2) of Regulation S-K. The Registrant agrees to furnish supplementally a copy of the omitted schedules and exhibits to the SEC upon request.

Item 16. Form 10-K Summary.

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized.

Homology Medicines, Inc.

Date: March 12, 2024

By: /s/ Paul Alloway, Ph.D.
Paul Alloway, Ph.D.
President and Chief Operating Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ Paul Alloway, Ph.D. **Paul Alloway, Ph.D.**	President and Chief Operating Officer *(principal executive officer)*	March 12, 2024
/s/ Charles Michaud, Jr. **Charles Michaud, Jr.**	Vice President, Corporate Controller and Treasurer *(principal financial and accounting officer)*	March 12, 2024
/s/ Arthur Tzianabos, Ph.D. **Arthur Tzianabos, Ph.D.**	Chairman of the Board of Directors	March 12, 2024
/s/ Jeffrey V. Poulton **Jeffrey V. Poulton**	Lead Independent Director	March 12, 2024
/s/ Steven Gillis, Ph.D. **Steven Gillis, Ph.D.**	Director	March 12, 2024
/s/ Matthew R. Patterson **Matthew R. Patterson**	Director	March 12, 2024
/s/ Alise S. Reicin, M.D. **Alise S. Reicin, M.D.**	Director	March 12, 2024
/s/ Mary Thistle **Mary Thistle**	Director	March 12, 2024

HOMOLOGY MEDICINES, INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the stockholders and the Board of Directors 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, 2023 and 2022, the related consolidated statements of operations, comprehensive loss, stockholders' equity, 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, 2023 and 2022, 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.

Going Concern

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company’s recurring losses from operations incurred since inception, the expectation of continuing losses for the foreseeable future, and discontinuation of all clinical trials and research activities, as well as the Company’s workforce reduction plan, raise substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

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.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current-period audit of the financial statements that was communicated or required to be communicated to the audit committee and that (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Equity method investment — Refer to Notes 1 and 6 to the financial statements

Critical Audit Matter Description

The Company uses the equity method of accounting to account for its investment in Oxford Biomedica (US) LLC, or OXB (US) LLC. The Company's proportionate share of the net income or loss of OXB (US) LLC is included in consolidated net loss within the caption, loss from equity method investment. During the year-ended December 31, 2023, OXB (US) LLC recorded an impairment of certain long-lived assets, resulting in the Company recording an incremental $14.0 million loss from equity method investment and reducing the balance of the equity method investment to $0 as of December 31, 2023, which required

significant estimates and assumptions related to future revenue projections and the selection of a revenue multiplier used in the market approach model.

We identified the estimation of future revenue projections and the use of a revenue multiplier associated with the valuation of the related asset group of OXB (US) LLC as a critical audit matter due to the significant judgments required in both the estimation of future revenue and the selection of the revenue multiplier used in the market approach model. This required a high degree of auditor judgment and an increased extent of effort when performing audit procedures to evaluate the reasonableness of the estimates and assumptions related to the forecasts of future revenues and selection of revenue multipliers.

How the Critical Audit Matter Was Addressed in the Audit

Our audit procedures related to the estimates and assumptions utilized in the market approach model used for the impairment analysis included the following, among others:

- We (1) evaluated the reasonableness of the forecasts of future revenues by comparing those estimates to historical results and internal communications to management and the Board of Directors and (2) evaluated the reasonableness of the valuation methodology utilized in the fair value estimate.
- We read the audited financial statements of OXB (US) LLC as of and for the year ended December 31, 2023, audited in accordance with auditing standards generally accepted in the United States of America.
- We considered whether other information obtained during the course of our audit represented contradictory evidence in relation to selection of the revenue multiplier in the valuation model or the estimated revenue projections utilized in the model.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
March 12, 2024

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

HOMOLOGY MEDICINES, INC.

CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share amounts)

	December 31,	
	2023	2022
Assets		
Current assets:		
Cash and cash equivalents	$ 39,266	$ 33,986
Short-term investments	43,387	141,040
Assets held for sale	260	—
Prepaid expenses and other current assets	1,001	5,989
Total current assets	83,914	181,015
Equity method investment	—	25,814
Property and equipment, net	—	1,078
Right-of-use assets	650	20,563
Total assets	$ 84,564	$ 228,470
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 3,234	$ 1,144
Accrued expenses and other liabilities	7,021	18,715
Operating lease liabilities	1,318	1,561
Deferred revenue	—	1,156
Total current liabilities	11,573	22,576
Non-current liabilities:		
Operating lease liabilities, net of current portion	—	27,916
Total liabilities	11,573	50,492
Commitments and contingencies (Note 10)		—
Stockholders’ equity:		
Preferred stock, $0.0001 par value, 10,000,000 shares authorized; no shares issued and outstanding at December 31, 2023 and 2022	—	—
Common stock, $0.0001 par value; 200,000,000 shares authorized; 58,017,412 and 57,483,910 shares issued and outstanding as of December 31, 2023 and 2022, respectively	6	6
Additional paid-in capital	615,088	607,513
Accumulated other comprehensive loss	(5)	(404)
Accumulated deficit	(542,098)	(429,137)
Total stockholders’ equity	72,991	177,978
Total liabilities and stockholders' equity	$ 84,564	$ 228,470

See notes to consolidated financial statements.

HOMOLOGY MEDICINES, INC.

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

	For the Year ended December 31,	
	2023	**2022**
Collaboration revenue	$ 1,156	$ 3,208
Operating expenses:		
Research and development	62,002	98,351
General and administrative	31,256	38,138
Restructuring and other charges	9,327	—
Total operating expenses	102,585	136,489
Loss from operations	(101,429)	(133,281)
Other income:		
Gain on sale of business	—	131,249
Gain on lease termination	8,767	—
Interest income	5,582	3,230
Total other income	14,349	134,479
Income (loss) before income taxes	(87,080)	1,198
Provision for income taxes	—	(715)
Loss from equity method investment	(25,881)	(5,488)
Net loss	$ (112,961)	$ (5,005)
Net loss per share-basic and diluted	$ (1.95)	$ (0.09)
Weighted-average common shares outstanding-basic and diluted	57,834,819	57,399,762

See notes to consolidated financial statements.

HOMOLOGY MEDICINES, INC.

CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(in thousands)

	For the Year ended December 31,	
	2023	**2022**
Net loss	$ (112,961)	$ (5,005)
Other comprehensive gain (loss):		
Change in unrealized gain (loss) on available for sale securities, net	399	(397)
Total other comprehensive gain (loss)	399	(397)
Comprehensive loss	$ (112,562)	$ (5,402)

See notes to consolidated financial statements.

HOMOLOGY MEDICINES, INC.

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

	Common Stock $0.0001 Par Value		Additional Paid-in Capital	Accumulated Other Comprehensive Gain (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at January 1, 2022	57,150,274	$ 6	$ 593,784	$ (7)	$ (424,132)	$ 169,651
Issuance of common stock from RSU vesting	106,890	—	—	—	—	—
Issuance of common stock from option exercises	293	—	1	—	—	1
Issuance of common stock pursuant to employee stock purchase plan	226,453	—	595	—	—	595
Stock-based compensation	—	—	13,054	—	—	13,054
Stock-based compensation for equity method investee	—	—	79	—	—	79
Other comprehensive loss	—	—	—	(397)	—	(397)
Net loss	—	—	—	—	(5,005)	(5,005)
Balance at December 31, 2022	57,483,910	$ 6	$ 607,513	$ (404)	$ (429,137)	$ 177,978
Issuance of common stock from RSU vesting	373,519	—	—	—	—	—
Issuance of common stock from option exercises	26,166	—	16	—	—	16
Issuance of common stock pursuant to employee stock purchase plan	133,817	—	168	—	—	168
Stock-based compensation	—	—	7,324	—	—	7,324
Stock-based compensation for equity method investee	—	—	67	—	—	67
Other comprehensive gain	—	—	—	399	—	399
Net loss	—	—	—	—	(112,961)	(112,961)
Balance at December 31, 2023	58,017,412	$ 6	$ 615,088	$ (5)	$ (542,098)	$ 72,991

See notes to consolidated financial statements.

HOMOLOGY MEDICINES, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	For the Year ended December 31,	
	2023	**2022**
Cash flows from operating activities:		
Net loss	$ (112,961)	$ (5,005)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	578	1,293
Noncash lease expense	2,065	1,306
Loss from equity method investment	25,881	5,488
Stock-based compensation expense	7,324	13,054
Accretion of discount on short-term investments	(2,948)	(1,947)
Non-cash gain on lease termination	(8,866)	—
(Gain) loss on disposal of property and equipment	(94)	49
Gain on sale of business	—	(131,249)
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	4,988	840
Accounts payable	2,090	(981)
Accrued expenses and other liabilities	(11,686)	7,418
Deferred revenue	(1,156)	(3,208)
Operating lease liabilities	(1,445)	(719)
Net cash used in operating activities	(96,230)	(113,661)
Cash flows from investing activities:		
Purchases of short-term investments	(73,240)	(157,460)
Maturities of short-term investments	174,240	65,461
Proceeds from sale of business	—	130,000
Proceeds from sale of property and equipment	554	—
Purchases of property and equipment	(228)	(1,285)
Net cash provided by investing activities	101,326	36,716
Cash flows from financing activities:		
Proceeds from issuance of common stock pursuant to employee stock purchase plan	168	595
Proceeds from issuance of common stock from option exercises	16	1
Net cash provided by financing activities	184	596
Net change in cash, cash equivalents and restricted cash	5,280	(76,349)
Cash, cash equivalents and restricted cash, beginning of period	33,986	110,335
Cash, cash equivalents and restricted cash, end of period	$ 39,266	$ 33,986
Supplemental disclosures of noncash investing and financing activities:		
Lease liability settled through termination of lease	$ 28,338	$ —
Lease liability obtained in exchange for right-of-use asset	$ 1,625	$ —
Cash paid for income taxes	$ —	$ 720
Unrealized gain (loss) on available for sale securities, net	$ 399	$ (397)
Property and equipment additions included in accrued expenses and other liabilities	$ —	$ 8

See notes to consolidated financial statements.

1. NATURE OF BUSINESS AND BASIS OF PRESENTATION

Nature of Business—Homology Medicines, Inc. (the “Company” or "Homology") is a clinical-stage genetic medicines company historically focused on transforming the lives of patients suffering from rare diseases by addressing the underlying cause of the disease with one-time gene therapy and gene editing treatments. The Company was founded in March 2015 as a Delaware corporation. Its principal offices are in Bedford, Massachusetts.

On July 27, 2023, the Company announced that it had completed a review of its business and the Company's Board of Directors had approved a plan to explore, review and evaluate a range of potential strategic options available to the Company, including, without limitation, an acquisition, merger, reverse merger, sale of assets, strategic partnerships or other transactions. Based on the financing environment and the Company's anticipated clinical development timeline for its lead program, HMI-103, the Company also announced that it was stopping further development of its programs and reduced its workforce by 86% in an effort to significantly reduce its ongoing operating costs as it evaluated strategic alternatives. The workforce reduction was substantially completed in the third quarter of 2023 (see Note 9).

Agreement and Plan of Merger

After a comprehensive review of strategic alternatives, on November 16, 2023, the Company entered into an Agreement and Plan of Merger (the "Merger Agreement"), with Q32 Bio Inc., a Delaware corporation ("Q32"), and Kenobi Merger Sub, Inc., a Delaware corporation and the Company's direct, wholly owned subsidiary ("Merger Sub"), pursuant to which, among other matters, and subject to the satisfaction or waiver of the conditions set forth in the Merger Agreement, Merger Sub will merge with and into Q32, with Q32 continuing as the Company's wholly owned subsidiary and the surviving corporation of the merger (the "Merger"). The Company's future operations are highly dependent on the success of the Merger and there can be no assurance that the Merger will be successfully consummated. If the Merger is completed, the business of Q32 will continue as the business of the combined company.

Merger Consideration

Subject to the terms and conditions of the Merger Agreement, (i) immediately prior to the effective time of the Merger (the “Effective Time”), all Q32 preferred stock will be converted into Q32 common stock pursuant to the organizational documents of Q32 (the “Q32 Preferred Stock Conversion”), and (ii) at the Effective Time, (a) each outstanding share of Q32 common stock (excluding Q32 common stock issued in the Concurrent Financing, as described below) will be converted into the right to receive a number of shares of the Company’s common stock (“Company Common Stock”), calculated in accordance with the Merger Agreement, (b) each outstanding Q32 stock option and warrant that has not previously been exercised prior to the closing of the Merger will be assumed by the Company and become an option or warrant, as applicable, to purchase a number of shares of Company Common Stock and (c) the Q32 common stock issued in the Concurrent Financing will be converted into the right to receive a number of shares of the Company’s Common Stock calculated in accordance with the Merger Agreement. The shares of Company Common Stock that will be issued to stockholders of Q32 will be calculated using a formula in the Merger Agreement based on the equity value of each of Q32 and the Company. Q32 has been ascribed an aggregate equity value of $195 million and the Company’s equity value is expected to be approximately $80 million subject to adjustment based on the amount of net cash of the Company at closing of the Merger.

Concurrent Financing

Pursuant to the Merger Agreement, immediately prior to the Effective Time, Q32 will consummate a financing through the sale of its common stock for aggregate gross proceeds of $42 million based on the same aggregate equity value of Q32 used in the Merger (the “Concurrent Financing”). On November 16, 2023, Q32 entered into subscription agreements with certain accredited investors (the “Investors”) for the Concurrent Financing with expected gross proceeds to Q32 of $42 million. In connection with the Concurrent Financing, at the closing of the Merger, Q32 will enter into a registration rights agreement with the Investors providing for the registration under the Securities Act of 1933, as amended (the “Securities Act”) of the shares of common stock sold in the Concurrent Financing. The consummation of the transactions contemplated by the subscription agreements is conditioned on the satisfaction or waiver of the conditions set forth in the Merger Agreement and in the subscription agreements. Shares of Q32 common stock issued pursuant to the Concurrent Financing will be converted into shares of Company Common Stock in the Merger in accordance with the Merger Agreement.

Contingent Value Rights Agreement

At the Effective Time, if any Legacy Assets (as defined below) have not been disposed of in a Legacy Asset Disposition (as defined below) or if additional consideration may be payable for the Legacy Assets (as defined below) after closing of the Merger, the Company and Equiniti Trust Company, LLC, a New York limited liability company, as the initial rights agent ("Rights Agent"), will enter into a Contingent Value Rights Agreement (the "CVR Agreement"), pursuant to which the Company's common stockholders of record as of the close of business on the last business day prior to the day on which the Effective Time occurs will receive one contingent value right (each, a "CVR") for each outstanding share of Company Common Stock held by such stockholder on such date.

Each CVR will represent the contractual right to receive payments from the Company upon the actual receipt by the Company or its subsidiaries of certain contingent proceeds derived from any cash consideration that is paid to the Company or its subsidiaries as a result of the sale, transfer, license, assignment or other divestiture, disposition or commercialization of any of the Company's assets, rights and interests relating to the Company's HMI-103, HMI-204, Capsids and AAVHSC Platform, including any equity interests held directly or indirectly by the Company in Oxford Biomedica Solutions, LLC or its affiliates ("OXB Solutions") pursuant to that certain Equity Securities Purchase Agreement, dated as of January 28, 2022, by and between the Company and OXB Solutions (the "Legacy Assets" and such disposition, a "Legacy Asset Disposition"), net of certain tax, transaction costs and certain other expenses.

The contingent payments under the CVR Agreement, if they become payable, will become payable to the Rights Agent for subsequent distribution to the holders of the CVRs. There can be no assurance that any holders of CVRs will receive payments with respect thereto. The right to the contingent payments contemplated by the CVR Agreement is a contractual right only and will not be transferable, except in the limited circumstances specified in the CVR Agreement. The CVRs will not be evidenced by a certificate or any other instrument and will not be registered with the Securities and Exchange Commission (the "SEC"). The CVRs will not have any voting or dividend rights and will not represent any equity or ownership interest in the Company or any of its affiliates. No interest will accrue on any amounts payable in respect of the CVRs.

Other Recent Developments

On March 9, 2023, the Company filed a Registration Statement on Form S-3 (File No. 333-270414) (the "Shelf") with the SEC in relation to the registration of up to an aggregate of $250.0 million of its common stock, preferred stock, debt securities, warrants and/or units of any combination thereof for a period up to three years from the date of the filing. The Shelf became effective on March 17, 2023. The Company also simultaneously entered into a sales agreement with Cowen and Company, LLC ("Cowen"), as sales agent, providing for the offering, issuance and sale by the Company of up to an aggregate of $75.0 million of its common stock from time to time in "at-the-market" offerings under the Shelf (the "ATM"). The Company did not sell any shares of common stock under the ATM during the year ended December 31, 2023. As of December 31, 2023, there remained $75.0 million of common stock available for sale under the ATM.

On March 10, 2022, the Company closed a transaction with Oxford Biomedica (US) LLC ("OXB (US)"), to establish a new adeno-associated virus ("AAV") vector manufacturing company, Oxford Biomedica (US) LLC ("OXB (US) LLC") that provides AAV vector process development and manufacturing services to biotechnology companies. Under the terms of the agreement, the Company contributed its manufacturing team of 125 employees, manufacturing facility and equipment, manufacturing-related intellectual property and know-how and certain other assets. Oxford paid the Company $130.0 million of upfront cash and invested $50.0 million of cash to fund OXB (US) LLC in exchange for an 80 percent ownership interest, while Homology retained a 20 percent ownership interest in the new company and received a put option on this ownership position (see Note 6).

Since its inception and until recently, the Company has devoted substantially all of its resources to recruiting personnel, developing its technology platform and advancing its pipeline of product candidates through discovery, preclinical and clinical trials, developing and implementing manufacturing processes, building out manufacturing and research and development space, and maintaining and building its intellectual property portfolio. The Company is subject to a number of risks similar to those of other companies conducting high-risk, early-stage research and development of product candidates. Principal among these risks are dependency on key individuals and intellectual property, competition from other products and companies, and the technical and regulatory risks associated with the successful research, development and manufacturing of its product candidates.

To date, the Company has not generated any revenue from product sales and does not expect to generate any revenue from the sale of product in the foreseeable future. Through December 31, 2023, the Company has financed its operations primarily through public offerings of its common stock, the issuance of convertible preferred stock, and with proceeds from its transaction with Oxford (see Note 6), its collaboration and license agreement with a former collaboration partner and its private

placement with Pfizer (see Note 17). During the year ended December 31, 2023, the Company incurred a loss from operations of $101.4 million and as of December 31, 2023, had $542.1 million in accumulated deficit.

The Company has incurred and expects to continue to incur costs and expenditures in connection with the process of evaluating strategic alternatives. Though the Company has executed the Merger Agreement with Q32 effective November 16, 2023, there can be no assurance that the Company will be able to successfully consummate the Merger or any other strategic transaction. The process of evaluating strategic options has been and may continue to be costly, time-consuming and complex and the Company may incur significant costs related to this continued evaluation, such as legal, accounting and advisory fees and expenses and other related charges.

Based on current projections, management believes that the Company's cash and cash equivalents and short-term investments as of December 31, 2023 will enable the Company to continue its operations for at least one year from the date of this filing. However, due to the consideration of certain qualitative factors, including the discontinuation of all clinical trials and research activities, as well as the Company's workforce reduction of all but a few custodial employees, management has concluded there is substantial doubt regarding the Company's ability to continue as a going concern for more than twelve months from the date that the consolidated financial statements included in this Annual Report on Form 10-K have been issued. These financial statements do not include any adjustments that might result from the outcome of this uncertainty. Should the Company resume the development of product candidates, it would need to obtain substantial additional funding in connection with continuing operations, particularly if the Company were to resume its preclinical activities and clinical trials for its product candidates. There can be no assurance that the Company will be able to obtain sufficient capital to cover its costs on acceptable terms, if at all.

Basis of Presentation—The accompanying consolidated financial statements have been 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.

2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Principles of Consolidation—The Company's consolidated financial statements include the accounts of the Company and its subsidiary, Homology Medicines Securities Corporation, a wholly owned Massachusetts corporation, for the sole purpose of buying, selling, and holding securities on the Company's behalf. All intercompany balances and transactions have been eliminated in the 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, revenue recognition, accrued research and development expenses and the valuation of the Company's equity method investment. The Company assesses estimates on an ongoing basis; however, actual results could materially differ from those estimates.

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

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

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 have maturities of greater than 90 days at the time of purchase and mature within one-year from the balance sheet date. Investments in marketable securities are recorded at fair value, with any unrealized gains and losses, reported within accumulated other comprehensive income as a separate component of stockholders' equity until realized or until a determination is made that an other-than-temporary decline in market value has occurred. Any premium or discount arising at purchase is amortized and/or accreted to interest income and/or expense over the life of the underlying security. Such amortization and accretion, together with interest on securities, are included in interest income in the Company's 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.

Concentrations of Credit Risk—Financial instruments that potentially subject the Company to significant concentration of credit risk consist primarily of cash, cash equivalents and short-term investments. Periodically, the Company may maintain deposits in financial institutions in excess of government insured limits. The Company believes that it is not exposed to significant credit risk as its 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. The Company 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, 2023, the Company's cash and cash equivalents were held with two financial institutions. The Company believes that the market risk arising from its 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.

Equity Method Investment—The Company uses the equity method of accounting to account for an investment in an entity that it does not control, but in which it has the ability to exercise significant influence over operating and financial policies. The Company's proportionate share of the net income or loss of the entity is included in consolidated net loss. Judgments regarding the level of influence over the equity method investment include consideration of key factors such as the Company's ownership interest, representation on the board of directors or other management body and participation in policy-making decisions.

Under the equity method of accounting, the Company's investment is initially recorded at fair value on the consolidated balance sheets. Upon initial investment, the Company evaluates whether there are basis differences between the carrying value and fair value of the Company's proportionate share of the investee's underlying net assets. Typically, the Company amortizes basis differences identified on a straight-line basis over the underlying assets' estimated useful lives when calculating the attributable earnings or losses, excluding the basis differences attributable to in-process research and development that has no alternative future use. If the Company is unable to attribute all of the basis differences to specific assets or liabilities of the investee, the residual excess of the cost of the investment over the proportional fair value of the investee's assets and liabilities is considered to be equity method goodwill and is recognized within the equity investment balance, which is tracked separately within the Company's memo accounts. The Company subsequently records in the statements of operations its share of income or loss of the other entity within other income/expense, which results in an increase or decrease to the carrying value of the investment. If the share of losses exceeds the carrying value of the Company's investment, the Company will suspend recognizing additional losses and will continue to do so unless it commits to providing additional funding; however, if there are intra-entity profits this can cause the investment balance to go negative.

The Company evaluates its equity method investments for impairment whenever events or changes in circumstances indicate that a decline in value has occurred that is other than temporary. Evidence considered in this evaluation includes, but would not necessarily be limited to, the financial condition and near-term prospects of the investee, recent operating trends and forecasted performance of the investee, market conditions in the geographic area or industry in which the investee operates and the Company's strategic plans for holding the investment in relation to the period of time expected for an anticipated recovery of its carrying value. If the investment is determined to have a decline in value deemed to be other than temporary it is written down to estimated fair value.

At December 31, 2023, the Company accounted for its investment in OXB (US) LLC using the equity method of accounting (see Note 6).

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

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

At the commencement date, operating lease liabilities and their corresponding right-of-use assets are recorded based on the present value of future lease payments over the expected lease term. The Company's lease agreements do not provide an implicit rate. As a result, the Company utilizes an estimated incremental borrowing rate to discount lease payments, which is

based on the rate of interest the Company would have to pay to borrow a similar amount on a collateralized basis over a similar term. Certain adjustments to the right-of-use asset may be required for items such as initial direct costs paid or lease incentives received. Operating lease cost is recognized over the expected term on a straight-line basis. The expected lease term includes noncancelable lease periods and, when applicable, periods covered by an option to extend the lease if the Company is reasonably certain to exercise that option, as well as periods covered by an option to terminate the lease if the Company is reasonably certain not to exercise that option. Variable lease cost is recognized as incurred. Right-of-use assets are periodically evaluated for impairment.

The Company subleases a portion of its headquarters that is now occupied by OXB (US) LLC (see Note 18). Homology assigned all of its right, title and interest in, to and under this lease to OXB (US) LLC and effective October 1, 2023, the Company was released from being the primary obligor under such lease. Therefore, the related right-of-use asset and operating lease liability were derecognized as of October 1, 2023 and a new right-of-use asset and operating lease liability representing the present value of the future sublease payments to be made to OXB (US) LLC was recorded (see Note 10).

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, 2023, 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
Manufacturing equipment	5 - 7 years
Leasehold improvements	Shorter of the lease term or estimated useful life

Assets Held for Sale—The Company classifies assets as held for sale when the following conditions are met: (1) management has committed to a plan to sell, (2) the assets are available for immediate sale in their present condition, (3) the Company has initiated an active program to identify a buyer, (4) it is probable that a sale will occur within one year, (5) the assets are actively marketed for sale at a reasonable price in relation to their current fair value, and (6) there is a low likelihood of significant changes to the plan or that the plan will be withdrawn. If all of the criteria are met as of the balance sheet date, the assets are presented separately in the consolidated balance sheet as held for sale at the lower of the carrying amount or fair value less costs to sell. The assets are then no longer depreciated or amortized while classified as held for sale.

Impairment of Long-Lived Assets—The Company evaluates its long-lived assets, which consist primarily of property and equipment and right-of-use assets, 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.

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

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

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. 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 of benefit that is greater than 50% likely of being realized upon ultimate settlement. 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 Company accounts for interest and penalties related to uncertain tax positions as part of its provision for income taxes. Since inception, 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 has not been determined to be more likely than not.

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

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

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

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

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

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

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

Stock-based Compensation—The Company recognizes compensation expense for awards to employees and non-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 fair value of options on the date of grant is calculated using the Black-Scholes option pricing model based on key assumptions such as stock price, expected volatility and expected term. The Company's estimates of these assumptions are primarily based on the trading price of the Company's stock, historical data, peer company data and judgment regarding future trends and factors. The Company recognizes forfeitures as they occur.

The purchase price of common stock under the Company's employee stock purchase plan ("ESPP") is equal to 85% of the lesser of (i) the fair market value per share of the common stock on the first business day of an offering period and (ii) the fair market value per share of the common stock on the purchase date. The fair value of the look-back provision under the ESPP is calculated using the Black-Scholes option pricing model. The fair value of the look-back provision plus the 15% discount is recognized as compensation expense over the 180-day purchase period.

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

Common stock equivalent shares are excluded from the computation of diluted net loss per share if their effect is antidilutive. In periods in which the Company reports a net loss attributable to common stockholders, diluted net loss per share

attributable to common stockholders is generally the same as basic net loss per share attributable to common stockholders, since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive.

Recent Accounting Pronouncements—The Jumpstart Our Business Startups Act of 2012 permits an emerging growth company to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. The Company ceased to qualify as an emerging growth company effective December 31, 2023.

In June 2016, the FASB issued ASU No. 2016-13, Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments ("ASU 2016-13") to improve financial reporting by requiring more timely recording of credit losses on loans and other financial instruments held by financial institutions and other organizations. ASU 2016-13 requires the measurement of all expected credit losses for financial assets held at the reporting date based on historical experience, current conditions and reasonable and supportable forecasts. ASU 2016-13 also requires enhanced disclosures to help investors and other financial statement users better understand significant estimates and judgments used in estimating credit losses, as well as the credit quality and underwriting standards of an organization's portfolio. The Company adopted ASU 2016-13 on January 1, 2023. The adoption of ASU 2016-13 did not have a material impact on the Company's consolidated financial statements and related disclosures.

3. CASH AND CASH EQUIVALENTS

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:

	December 31,	
	2023	2022
	(in thousands)	
Cash	$ 749	$ 19
Money market funds	38,517	33,967
Total cash and cash equivalents	$ 39,266	$ 33,986

4. SHORT-TERM INVESTMENTS

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

The following table summarizes the Company's short-term investments as of December 31, 2023 and December 31, 2022:

As of December 31, 2023	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
		(in thousands)		
US Treasury securities	$ 31,817	$ 6	$ (5)	$ 31,818
Corporate debt securities	11,575	—	(6)	11,569
Total	$ 43,392	$ 6	$ (11)	$ 43,387

As of December 31, 2022	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
		(in thousands)		
Commercial paper	$ 57,138	$ —	$ —	$ 57,138
US Treasury securities	65,160	—	(335)	64,825
Corporate debt securities	19,146	—	(69)	19,077
Total	$ 141,444	$ —	$ (404)	$ 141,040

The Company utilizes the specific identification method in computing realized gains and losses. The Company had no realized gains and losses on its available-for-sale securities for the years ended December 31, 2023 and 2022. The contractual maturity dates of all of the Company's investments are less than one year.

5. FAIR VALUE MEASUREMENTS

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

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

Description	December 31, 2023	Quoted Prices (Unadjusted) in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
		(in thousands)		
Cash equivalents:				
Money market mutual funds	$ 38,517	$ 38,517	$ —	$ —
Total cash equivalents	$ 38,517	$ 38,517	$ —	$ —
Short-term investments:				
US Treasury securities	31,818	—	31,818	—
Corporate debt securities	11,569	—	11,569	—
Total short-term investments	$ 43,387	$ —	$ 43,387	$ —
Total financial assets	$ 81,904	$ 38,517	$ 43,387	$ —

Description	December 31, 2022	Quoted Prices (Unadjusted) in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
		(in thousands)		
Cash equivalents:				
Money market mutual funds	$ 33,967	$ 33,967	$ —	$ —
Total cash equivalents	$ 33,967	$ 33,967	$ —	$ —
Short-term investments:				
Commercial paper	$ 57,138	$ —	$ 57,138	$ —
US Treasury securities	64,825	—	64,825	—
Corporate debt securities	19,077	—	19,077	—
Total short-term investments	$ 141,040	$ —	$ 141,040	$ —
Total financial assets	$ 175,007	$ 33,967	$ 141,040	$ —

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

There were no transfers between fair value measurement levels during the years ended December 31, 2023 and 2022.

6. EQUITY METHOD INVESTMENT

Summary of Transaction

On March 10, 2022, the Company closed a transaction with OXB (US) LLC, Oxford Biomedica (US), Inc., ("OXB"), and Oxford, pursuant to the Equity Securities Purchase Agreement (the "Purchase Agreement"), dated as of January 28, 2022, by and among Homology, OXB (US) LLC and Oxford, whereby, among other things, Homology and Oxford agreed to collaborate to operate OXB (US) LLC, which provides AAV vector process development and manufacturing services to pharmaceutical and biotechnology companies (the "OXB (US) LLC Transaction").

Pursuant to the terms of the Purchase Agreement and a contribution agreement (the "Contribution Agreement") entered into between Homology and OXB (US) LLC prior to the closing of the OXB (US) LLC Transaction (the "Closing"), Homology contributed its manufacturing team of 125 employees and assigned and transferred to OXB (US) LLC all of its assets that are primarily used in the manufacturing of AAV vectors for use in gene therapy and gene editing products, including its manufacturing facility and equipment and manufacturing-related intellectual property and know-how, but excluding certain assets related to manufacturing or testing of Homology's proprietary AAV vectors (collectively, the "Transferred Assets"), in exchange for 175,000 common equity units in OXB (US) LLC ("Units"), representing 100 percent (100%) of the ownership interest of OXB (US) LLC, and OXB (US) LLC assumed from the Company, and agreed to pay, perform and discharge when due, all of the Company's duties, obligations, liabilities, interests and commitments of any kind under, arising out of or relating to the Transferred Assets.

Effective as of the Closing, Homology sold to OXB, and OXB purchased from Homology, 130,000 Units, (the "Transferred Units") in exchange for $130.0 million of cash consideration. In connection with the Closing, OXB contributed $50.0 million in cash to OXB (US) LLC in exchange for an additional, newly issued 50,000 Units. Immediately following the Closing, (i) OXB owned 180,000 Units, representing 80 percent (80%) of the fully diluted equity interests in OXB (US) LLC, and (ii) Homology owned 45,000 Units, representing 20 percent (20%) of the fully diluted equity interests in OXB (US) LLC.

Pursuant to the Amended and Restated Limited Liability Company Agreement of OXB (US) LLC (the "OXB (US) LLC Operating Agreement") which was executed in connection with the Closing, at any time following the three-year anniversary of the Closing, (i) OXB will have an option to cause Homology to sell and transfer to OXB, and (ii) Homology will have an option to cause OXB to purchase from Homology, in each case all of Homology's equity ownership interest in OXB (US) LLC at a price equal to 5.5 times the revenue for the immediately preceding 12-month period (together, the "Options"), subject to a maximum amount of $74.1 million. Pursuant to the terms of the OXB (US) LLC Operating Agreement, Homology is entitled to designate one director to the board of directors of OXB (US) LLC, currently Paul Alloway, Homology's President and Chief Operating Officer.

Pursuant to the OXB (US) LLC Transaction, the Company also assigned all of its right, title and interest in, to and under its facility lease to OXB (US) LLC, with Homology subleasing a portion of lab and office space back from OXB (US) LLC. Effective October 1, 2023, the Company was released from being primary obligor under such lease. Therefore, the related right-of-use asset and operating lease liability were derecognized as of October 1, 2023 and a new right-of-use asset and operating lease liability representing the present value of the future sublease payments to be made to OXB (US) LLC was recorded (see Note 10).

Equity Method of Accounting

The Company has significant influence over, but does not control, OXB (US) LLC through its noncontrolling representation on OXB’s board of directors and the Company’s equity interest in OXB (US) LLC. In addition, the Company and OXB (US) LLC have intra-entity transactions through a series of agreements entered into in conjunction with the OXB (US) LLC Transaction, OXB (US) LLC granted certain licenses to the Company, and the Company has representation on the joint steering committee which oversees the activities governed by the Supply Agreement. Accordingly, the Company does not consolidate the financial statements of OXB (US) LLC and accounts for its investment using the equity method of accounting.

The Company recorded its equity method investment in OXB (US) LLC at fair value upon deconsolidation of OXB (US) LLC as of the Closing. The fair value of the equity method investment was determined based on the market approach. This approach estimated the fair value of OXB (US) LLC based on the implied value for the entity using the consideration paid, including the Options, for a controlling interest in OXB (US) LLC at the entity’s formation. As part of its fair value analysis, the Company determined that the Options are embedded in the common equity units because the Options are not legally detachable or separately exercisable. Accordingly, the equity method investment and the Options represent one unit of account and the fair value recorded reflects the value of the equity interest and the Options. The valuation included certain subjective

assumptions including discounts for lack of control and marketability given the consideration paid for OXB (US) LLC was for a controlling interest in the entity and the Company owns a noncontrolling interest.

As of March 10, 2022, the Closing, the fair value of the Company's investment in OXB (US) LLC was $31.2 million and the Company recorded a gain of $131.2 million on the sale of its manufacturing business in other income in the Company's consolidated statements of operations. The gain was computed as follows:

(in thousands)	March 10, 2022
Cash received	$ 130,000
Plus: Fair value of equity method investment	31,223
Less: Carrying value of transferred assets	(29,974)
Gain on sale of business	$ 131,249

During the year ended December 31, 2023, the Company determined that the fair value of its investment in OXB (US) LLC was negatively impacted due to a change in OXB (US) LLC' forecasted performance relative to expected performance when the Company initially invested in OXB (US) LLC. The Company determined that the decline in value was deemed to be other than temporary and recorded an impairment charge of $3.8 million to reduce its equity method investment to fair value. The impairment charge is included in the loss on equity method investment in the Company's consolidated statements of operations.

In addition, the Company records its share of income or losses from OXB (US) LLC on a quarterly basis. For the year ended December 31, 2023, OXB (US) LLC recorded an impairment charge of $119.1 million which significantly increased OXB (US) LLC's net loss for the period. After recording its share of OXB (US) LLC's net loss, the carrying value of the Company's equity method investment was reduced to $0.0 million.

Summarized Financial Information

Summarized financial information for OXB (US) LLC is as follows:

	December 31,	
	2023	2022
Balance Sheet Data	(in thousands)	
Current assets	$ 10,763	$ 39,237
Noncurrent assets	$ 74,461	$ 228,745
Current liabilities	$ 6,151	$ 12,352
Noncurrent liabilities	$ 42,835	$ 37,718

	December 31,	
	2023	2022
Statement of Operations Data	(in thousands)	
Revenues	$ 30,699	$ 29,380
Net loss	$ 167,062	$ 29,036

See Note 18 for information regarding the Company's related party transactions with OXB (US) LLC.

7. PROPERTY AND EQUIPMENT

Property and equipment, net consists of the following:

	December 31,	
	2023	2022
	(in thousands)	
Laboratory equipment	$ —	$ 6,025
Computers and purchased software	—	644
Furniture and fixtures	—	645
Property and equipment, at cost	—	7,314
Less: accumulated depreciation and amortization	—	(6,236)
Property and equipment, net	$ —	$ 1,078

In August 2023, consistent with its decision to stop further development of its programs and explore, review and evaluate a range of potential strategic options available to the Company, the Company committed to a plan to sell its remaining property and equipment and therefore has classified the amount as assets held for sale on the consolidated balance sheet as of December 31, 2023. The assets held for sale were reported at the lower of the carrying amount or fair value with no depreciation expense taken after August 2023. The Company expects to dispose of all assets held for sale during the first quarter of 2024.

Depreciation expense for the years ended December 31, 2023 and 2022 was approximately $0.6 million and $1.3 million, respectively. The Company disposed of approximately $0.5 million and $0.1 million of property and equipment, net during each of the years ended December 31, 2023 and 2022, respectively.

8. ACCRUED EXPENSES AND OTHER LIABILITIES

Accrued expenses and other liabilities consist of the following:

	December 31,	
	2023	2022
	(in thousands)	
Accrued compensation and benefits	$ 5,755	$ 5,953
Accrued research and development expenses	—	9,447
Accrued professional fees	941	1,052
Accrued other	325	2,263
Total accrued expenses and other liabilities	$ 7,021	$ 18,715

Accrued compensation and benefits includes a restructuring accrual for severance and related costs of approximately $4.6 million (see Note 9).

9. RESTRUCTURING AND OTHER CHARGES

On July 25, 2023, the Company's Board of Directors approved a process to explore, review and evaluate a range of potential strategic options available to the Company, including, without limitation, an acquisition, merger, reverse merger, sale of assets, strategic partnerships or other transactions. Therefore, based on cost-reduction initiatives intended to reduce the Company’s ongoing operating expenses and maximize shareholder value as the Company plans to pursue strategic options, the Company's Board of Directors approved a reduction in the Company’s workforce by approximately 80 employees, or 86% of the Company's workforce as of July 2023. Simultaneous with the signing of the Merger Agreement, the Company terminated another 6 employees in November 2023.

In connection with the reduction in force, the Company recorded a restructuring charge for severance and related costs of $10.3 million in the Company's consolidated statements of operations during the year ended December 31, 2023. The Company’s restructuring liability, which was included in accrued compensation and benefits, consisted of the following:

(in thousands)	Employee-Related Costs
Accrued restructuring balance at January 1, 2023	$ —
Expenses incurred	10,279
Payments	(5,666)
Accrued restructuring balance at December 31, 2023	$ 4,613

The Company had previously granted certain of the terminated employees restricted stock units (“RSUs”) that vest in annual installments based on continued service to the Company, as well as options to purchase shares of the Company’s common stock that typically vest over a period of four years. In connection with the reduction in workforce, the Company agreed to accelerate the vesting of a portion of the RSUs that were unvested as of the employees’ termination dates, and also modify the stock options for terminated employees such that subject to the satisfaction of severance conditions, the terminated employees’ vested options will remain outstanding and exercisable until the first anniversary of each employee’s termination date. These equity modifications, described in detail in Note 14, resulted in a net reduction to stock based compensation

expense of approximately $1.0 million reflected within restructuring and other charges in the Company's consolidated statements of operations during the year ended December 31, 2023.

10. COMMITMENTS AND CONTINGENCIES

Operating Leases—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. Prior to a subsequent amendment described below, the lease was set to expire in February 2027 with an option for an additional five-year term. Rent became due under the lease in two phases; rent on the first 46,000 square feet started in September 2018 and rent on the remaining 21,000 square feet started in March 2019. The initial annual base rent was $39.50 per square foot and increases by three percent annually. The Company is obligated to pay, on a pro-rata basis, real estate taxes and operating costs related to the premises. The lease agreement allowed for a tenant improvement allowance not to exceed $10.9 million, which the Company received in full, to be applied to the total cost of tenant improvements to the leased premises. The unamortized balance of the tenant improvement allowance was included in deferred rent incentives and recorded as a reduction to operating right-of-use asset upon adoption of the new leasing standards.

In November 2021, the Company entered into an amendment of its December 2017 lease agreement (the “Lease Amendment”) for its corporate headquarters in Bedford, Massachusetts. The Lease Amendment increased the space under lease by approximately 23,011 square feet (the "Expansion Premises") and extended the expiration date of the existing premises under the lease from February 2027 to June 2030. The payment term with respect to the Expansion Premises commenced on May 1, 2022, and continues for a period of ten years and five months. The term of the Expansion Premises and the existing premises are not coterminous. Annual base rent for the existing premise under the Lease Amendment is approximately $4.7 million beginning on March 1, 2027, and increases by three percent annually; annual base rent for the Expansion Premises is approximately $1.4 million per year and increases by three percent annually. The Lease Amendment allows for tenant improvement allowances not to exceed $6.3 million in the aggregate. The Lease Amendment was accounted for as a lease modification and the right-of-use asset and operating lease liability for the existing premises were remeasured at the modification date, which resulted in an increase of $10.9 million to both the right-of-use asset and operating lease liabilities. In February 2022, the Company revised its assumption for when it expected to utilize the tenant improvement allowances. This change in assumption was accounted for as a lease modification and the right-of-use asset and operating lease liability for the existing premises were remeasured at the modification date, which resulted in an increase of $0.2 million to both the right-of-use asset and operating lease liabilities.

In March 2022, in accordance with its transaction with OXB (US) LLC, the Company assigned all of its right, title and interest in, to and under its corporate headquarters lease to OXB (US) LLC and entered into a sublease agreement whereby OXB (US) LLC subleased certain premises in its facility to Homology. However, as the Company remained jointly and severally liable for the payment of rent under this lease, the Company was not released from being the primary obligor and therefore the related right-of-use asset and lease liability were not derecognized and remained on the Company’s balance sheet.

In September 2022, the Company concluded that 100% of the tenant improvement allowances would be utilized by OXB (US) LLC. This change in assumption was accounted for as a lease modification and the right-of-use asset and operating lease liability for the existing premises were remeasured at the modification date, which resulted in an increase of $6.1 million to both the right-of-use asset and operating lease liabilities.

On September 25, 2023, the Company signed and executed a release letter with its lessor related to its corporate headquarters lease. The lessor agreed to release the Company of all obligations under the lease effective October 1, 2023 (the "Release Date") in exchange for a $0.1 million cash payment. On October 1, 2023, the Company derecognized the right-of-use asset and operating lease liability and recorded the difference as a gain of $8.8 million within other income on the consolidated statements of operations. Because the Company’s sublease agreement with OXB (US) LLC remains in effect after termination of the head lease, the Company recorded a new right-of-use asset and an operating lease liability of $1.6 million, which equals the present value of the future sublease payments owed to OXB (US) LLC for the remaining term of the sublease. The Company's sublease expires on December 31, 2024.

During the fourth quarter of fiscal year 2023, the Company significantly reduced active use of its corporate headquarters, with the plan to fully abandon the space in the first quarter of fiscal year 2024. Accordingly, the Company shortened the remaining useful of its right-of-use asset to equal the time remaining until the planned abandonment date. This had no impact on the operating lease liability.

Prior to being released from obligation under the lease, the Company was acting as sublessor to OXB (US) LLC for accounting purposes. For the years ended December 31, 2023 and 2022, the Company received $2.3 million and $2.0 million, respectively, in sublease payments from OXB (US) LLC, which was recorded as a reduction to lease cost.

The following table summarizes operating lease costs and variable lease costs, as well as sublease income:

	For the Year ended December 31,	
	2023	2022
	(in thousands)	
Operating lease costs	$ 4,273	$ 3,913
Variable lease costs	1,771	2,142
Sublease income	(2,312)	(1,979)
Net lease cost	$ 3,732	$ 4,076

The maturities of the Company's operating lease liabilities and minimum lease payments as of December 31, 2023 were as follows:

For the Years Ending December 31,	Amount (in thousands)
2024	$ 1,380
Total undiscounted lease payments	$ 1,380
Less: imputed interest	(62)
Present value of operating lease liabilities	$ 1,318

The following table summarizes the lease term and discount rate as of December 31, 2023:

	December 31, 2023
Weighted-average remaining lease term (years)	
Operating leases	1.0
Weighted-average discount rate	
Operating leases	10.5%

The following table summarizes the supplemental cash flow information related to the Company's operating leases:

	For the Year ended December 31,	
	2023	2022
	(in thousands)	
Cash paid for amounts included in the measurement of lease liabilities	$ 3,653	$ 3,326
Increase in lease liabilities and right-of-use assets due to lease remeasurements	$ —	$ 6,262

Legal Proceedings—On March 25, 2022, the Company and certain of its executives were named as defendants in a putative securities class action lawsuit filed in the United States District Court for the Central District of California; Pizzuto v. Homology Medicines, Inc., No. 2:22–CV–01968 (C.D. Cal 2022). The complaint alleges that the Company failed to disclose certain information regarding efficacy and safety in connection with a Phase I/II HMI-102 clinical trial, and seeks damages in an unspecified amount. The case is in its early stages. The Company believes the claims alleged lack merit and has filed a motion to transfer venue (filed September 2, 2022) and a motion to dismiss (filed October 17, 2022). On April 18, 2023, the court granted the motion to transfer, finding that venue was not proper in the Central District of California and transferring the case to the District of Massachusetts. Following the transfer, the case number changed to 1:23-cv-10858-AK (D. Mass.). On May 9, 2023, the Massachusetts court issued an order permitting the parties to submit updated briefs in connection with the motion to dismiss, which were submitted on June 8, 2023, July 13, 2023, and August 3, 2023. On March 4, 2024, the Massachusetts court held oral argument on the Company's motion to dismiss, which remains pending. As the outcome is not presently determinable, any loss is neither probable nor reasonably estimable.

On February 22, 2024, a purported stockholder of the Company, Kevin Welsh, filed a putative class action complaint against the Company and its directors related to the Company's proposed Merger with Q32, alleging violations of Sections 14(a) and 20(a) of the Securities Exchange Act of 1934, as amended. Welsh v. Homology Medicines, Inc., No. 1:24-cv-00242 (D. Del.). The complaint alleges that the Company and its directors filed a proxy statement containing material omissions regarding financial forecasts and their respective analysis, and seeks damages in an unspecified amount. The case is in its early stages. The Company believes the claims alleged lack merit. As the outcome is not presently determinable, any loss is neither probable nor reasonably estimable.

11. LICENSE AGREEMENTS

City of Hope

In April 2016, the Company entered into an exclusive license agreement with City of Hope, or COH, an academic research and medical center. COH granted the Company an exclusive, sublicensable, worldwide license, or the COH 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.

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. Other than the annual license fee, there were no payments to COH in 2022. In January 2023, the Company paid $50,000 to COH upon dosing the first patient in the pheEDIT Phase 1 clinical trial.

On August 6, 2021, the Company received notice from COH that it did not accomplish at least one of the partnering milestones by the applicable deadline, as set forth in the COH License. This notice does not affect the Company's exclusive license in the field of mammalian therapeutics, including all human therapeutics, associated diagnostics, and target validation, or the Mammalian Therapeutic Field, where the Company retains exclusive rights. Instead, the notice served as written notice that the exclusive license granted pursuant to the COH License in all fields except the Mammalian Therapeutic Field converted from exclusive to non-exclusive effective as of September 20, 2021, which was forty-five days from the receipt of notice. In connection with the conversion, any royalty obligations and sublicensee fees relating to fields outside of the Mammalian Therapeutic Field shall be reduced by a certain percentage. This change to the Company's exclusive worldwide license with COH does not impact any of its product candidates, including HMI-102, HMI-103, HMI-104, HMI-203 and HMI-204.

12. INCOME TAXES

Provision for income taxes consists of the following:

	For the Year ended December 31,	
	2023	2022
	(in thousands)	
Federal tax provision:		
Current	$ —	$ 698
Deferred	—	—
Total federal tax provision	—	698
State tax provision:		
Current	—	17
Deferred	—	—
Total state tax provision	—	17
Total tax provision	$ —	$ 715

A reconciliation between the U.S. federal statutory tax and the Company’s tax provision is summarized below.

	For the Year ended December 31,	
	2023	2022
	(in thousands)	
Federal statutory rate	$ (23,722)	$ (901)
Tax credits	(7,699)	(13,955)
State taxes, net of federal tax benefit	(8,496)	(2,994)
Non-deductible expenses	595	875
Other	(2,351)	1,410
Change in valuation allowance	41,673	16,280
Tax provision	$ —	$ 715

The principal components of the Company's deferred tax assets and liabilities consist of the following:

	For the Year ended December 31,	
	2023	2022
	(in thousands)	
Deferred tax assets:		
Net operating losses	$ 88,552	$ 76,735
R&D credits	79,094	66,761
Equity compensation	8,215	7,888
Operating lease liabilities	356	8,003
Accrued expense and other	9,351	1,479
Deferred revenue	—	314
Capitalized R&D costs	35,987	24,477
Total deferred tax assets	221,555	185,657
Deferred tax liabilities:		
Right-of-use assets	(176)	(5,583)
Depreciation	(54)	(171)
Other	—	(251)
Total deferred tax liabilities	(230)	(6,005)
Valuation allowance	(221,325)	(179,652)
Net deferred taxes	$ —	$ —

The Company recorded an income tax provision of $0.7 million for the year ended December 31, 2022. This prior year-to-date tax provision predominately resulted from the gain associated with the sale of the Company's manufacturing business due to the transaction with Oxford (see Note 6), offset by available federal and state net operating loss carryforwards and research and development tax credits which are subject to certain limitations as to their utilization. The Company did not record an income tax provision (benefit) for the year ended December 31, 2023.

At December 31, 2023, the Company had $326.2 million and $317.3 million of federal and state net operating loss carryforwards, respectively. Federal net operating loss carryforwards of $0.4 million, generated before 2018, will begin expiring in varying amounts through 2035 unless utilized. The remaining federal net operating loss carryforwards of $325.8 million, generated after 2017, will be carried forward indefinitely. The state net operating losses will begin expiring in varying amounts through 2043 unless utilized. At December 31, 2023, the Company had $65.5 million and $17.2 million of federal and state research and development credit carryforwards, respectively, that expire at various dates through 2043. Included in the $65.5 million of federal research and development credit carryforwards is $50.7 million of orphan drug credit carryforwards.

A valuation allowance is recorded against deferred tax assets if it is more likely than not that some or all of the deferred tax assets will not be realized. Due to the uncertainty surrounding the realization of the favorable tax attributes in future tax returns, the Company has recorded a full valuation allowance against the Company's otherwise recognizable net deferred tax assets. A roll forward of the valuation allowance is as follows:

(in thousands)	Valuation Allowance
Balance at December 31, 2022	$ (179,652)
Utilization of net operating losses against taxable income	—
Increase in net deferred taxes	(41,673)
Balance at December 31, 2023	$ (221,325)

For all years through December 31, 2023, the Company generated research credits but has not conducted a study to document the qualified activities. This study may result in an adjustment to the Company's research and development credit carryforwards. Since a full valuation allowance has been provided against the Company's research and development credits, any reduction in the gross deferred tax asset established for the research and development credit carryforwards would not result in any net impact to the Company's consolidated financial statements.

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 completed a study to assess ownership changes through December 31,

2021. Based on this analysis, the net operating losses are limited but the Company does not believe that any of its net operating losses or research and development credit carryforwards will expire unutilized due to Section 382 limitations.

The Company files tax returns in the United States, Massachusetts and several other states. 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, 2023, 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, 2023 and 2022.

13. 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 are 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 any preferential dividends to which the holders of 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.

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 any 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.

There were 58,017,412 and 57,483,910 shares of common stock outstanding at December 31, 2023 and 2022, respectively.

Preferred Stock—As of December 31, 2023 and 2022, there were no shares of preferred stock issued and outstanding.

14. STOCK INCENTIVE PLANS

2015 Stock Incentive Plan

In December 2015, the Company's Board of Directors adopted the 2015 Stock Incentive Plan (the "2015 Plan"), which provided for the grant of incentive stock options, nonqualified stock options and restricted stock awards to the Company's employees, officers, directors, advisors, and outside consultants. Stock options granted under the 2015 Plan 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, 2023, there were no additional shares available for future grant under the 2015 Plan.

2018 Incentive Award Plan

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

The 2018 Plan provides for the grant of incentive stock options, nonqualified stock options, restricted stock awards, restricted stock units, stock appreciation rights and other stock or cash-based awards to employees and consultants of the Company and certain affiliates and directors of the Company. The number of shares of common stock initially available for issuance under the 2018 Plan was 3,186,205 shares of common stock plus the number of shares subject to awards outstanding under the 2015 Plan that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by the Company on

or after the effective date of the 2018 Plan. In addition, the number of shares of common stock available for issuance under the 2018 Plan is subject to an annual increase on the first day of each calendar year beginning on January 1, 2019 and ending on and including January 1, 2028 equal to the lesser of (i) 4% of the Company's outstanding shares of common stock on the final day of the immediately preceding calendar year and (ii) such smaller number of shares of common stock as determined by the Company's Board of Directors, provided that not more than 20,887,347 shares of common stock may be issued under the 2018 Plan upon the exercise of incentive stock options. As of December 31, 2023, there were 4,978,083 shares available for future grant under the 2018 Plan. On January 1, 2024, an additional 2,320,696 shares were added to the 2018 Plan, representing 4% of total common shares outstanding at December 31, 2023.

2018 Employee Stock Purchase Plan

In March 2018, the Company's Board of Directors adopted, and the Company's stockholders approved, the Homology Medicines, Inc. 2018 Employee Stock Purchase Plan (the "2018 ESPP"). The 2018 ESPP allows employees to buy Company stock through after-tax payroll deductions at a discount from market value. The 2018 ESPP is intended to qualify as an "employee stock purchase plan" under Section 423 of the Internal Revenue Code. The number of shares of common stock initially available for issuance under the 2018 ESPP was 353,980 shares of common stock plus an annual increase on the first day of each calendar year beginning on January 1, 2019 and ending on and including January 1, 2028 equal to the lesser of (i) 1% of the Company's outstanding shares of common stock on the final day of the immediately preceding calendar year and (ii) such smaller number of shares of common stock as determined by the Company's Board of Directors, provided that not more than 4,778,738 shares of common stock may be issued under the 2018 ESPP. As of December 31, 2023, there were 2,693,911 shares available for future grant under the 2018 ESPP. On January 1, 2024, an additional 580,174 shares were added to the 2018 ESPP, representing 1% of total common shares outstanding at December 31, 2023.

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

During the year ended December 31, 2023, 133,817 shares were issued under the 2018 ESPP for aggregate proceeds to the Company of $0.2 million. During the year ended December 31, 2022, 226,453 shares were issued under the 2018 ESPP for aggregate proceeds to the Company of $0.6 million. Pursuant to the 2018 ESPP, the Company recorded stock-based compensation of less than $0.1 million for each of the years ended December 31, 2023 and 2022, respectively.

Stock Options

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 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 assumed dividend yield is based upon the Company's expectation of not paying dividends in the foreseeable future. The risk-free rate is based on the U.S. Treasury yield curve in effect at the time of grant for periods commensurate with the expected term of the award. The Company recognizes forfeitures as they occur.

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

	For the Year ended December 31,	
	2023	2022
Expected volatility	69.2% - 69.7%	68.7% - 70.1%
Weighted-average risk-free interest rate	3.45% - 4.22%	1.46% - 4.16%
Expected dividend yield	— %	— %
Expected term (in years)	5.5 - 6.25	5.5 - 6.25
Underlying common stock fair value	$0.92-$1.60	$1.40-$4.17

The following table summarizes the Company's stock option activity during the year ended December 31, 2023:

	Number of Options	Weighted-Average Exercise Price per Share	Weighted-Average Remaining Contractual Term (in Years)	Aggregate Intrinsic Value (in thousands)
Outstanding at January 1, 2023	9,865,734	$ 10.96	7.2	$ 493
Granted	3,188,150	$ 1.53		
Exercised	(26,166)	$ 0.61		
Cancelled/Forfeited	(3,476,677)	$ 7.05		
Outstanding at December 31, 2023	9,551,041	$ 9.26	5.2	$ 66
Vested and expected to vest at December 31, 2023	9,551,041	$ 9.26	5.2	$ 66
Exercisable at December 31, 2023	7,061,128	$ 11.35	4.3	$ 66

The total intrinsic value of options exercised during the year ended December 31, 2023 and 2022 was insignificant for each period. The weighted-average grant date fair value of options granted during the years ended December 31, 2023 and 2022 was $1.01 and $1.68, respectively.

Stock Awards Modifications - Corporate Restructuring

In connection with the Company's reduction in force implemented in July and November of 2023 (see Note 9), the Company terminated approximately 86 employees and modified approximately 6.3 million existing stock options and approximately 1.0 million existing restricted stock units ("RSUs") granted to these terminated employees in prior periods. The modification of the vested stock options to permit terminated employees up to one year following their termination date to exercise their options, rather than the 90-day window for terminated employees, is accounted for as a modification under FASB ASC Topic 718, Compensation—Stock Compensation ("ASC 718"). Accordingly, the Company recognized incremental compensation cost on the modification date in an amount equal to the difference between the fair value of the awards before and after the modification. The fair value of the awards immediately before assumes an expected term equal to 90 days from the termination date, whereas the fair value immediately after assumes an expected term equal to one year from the termination date. Total incremental compensation cost recognized for the year ended December 31, 2023 related to awards that were vested prior to modification was less than $0.1 million. Certain terminated employees' unvested stock options were also modified such that the stock options will vest in full upon a change of control occurring within 45 days of termination. The remaining unvested stock options were forfeited upon termination and the Company reversed all compensation cost previously recorded on the forfeited awards. Total compensation cost reversed in the year ended December 31, 2023 was approximately $0.4 million.

The terminated employees' RSUs were modified to accelerate the vesting of a portion of the RSUs that were unvested as of the employees' termination dates. The accelerated vesting of certain RSUs is accounted for as a Type III (improbable to probable) modification under ASC 718. Accordingly, the Company reversed all compensation cost previously recorded on the awards that are not expected to vest under the original terms. Certain terminated employees' unvested RSUs were also modified such that the RSUs will vest in full upon a change of control occurring within 45 days of termination. Total compensation cost reversed in the year ended December 31, 2023 was approximately $0.5 million. Total compensation cost of approximately $0.2 million, equal to the modification date fair value, was recognized over the remaining service period, beginning on the modification date and ending on each employee's termination date.

Stock Awards Modifications - OXB (US) LLC Transaction

As part of the transaction with OXB (US) LLC (see Note 6), the Company transferred employees to OXB (US) LLC and modified approximately 1.6 million existing stock options and approximately 0.1 million existing restricted stock units granted to these transferred employees in prior periods in order to permit such individuals to continue vesting in their awards and exercise their vested options as long as they are employed by and provide services to OXB (US) LLC. The modification of the unvested stock awards to continue vesting was accounted for as a Type III (improbable to probable) modification under ASC 718. Accordingly, the Company reversed all compensation cost previously recorded on the awards that were not expected to vest under the original terms. Total compensation cost reversed in the year ended December 31, 2022 was less than $0.1 million. Total compensation cost of $0.8 million, equal to the modification date fair value, will be recognized over the

remaining service period. A portion of this total compensation cost will be included as a component of the loss from equity method investment.

The modification of the vested stock awards to permit transferred employees to exercise their options over the remaining life of the award, rather than the 90-day window for terminated employees, was accounted for as a modification under ASC 718. Accordingly, the Company recognized incremental compensation cost on the modification date in an amount equal to the difference between the fair value of the awards before and after modification. The fair value of the awards immediately before modification assumed a 90-day expected term, whereas the fair value immediately after assumed an expected term equal to the remaining life of the modified options. Total incremental compensation cost recognized in the year ended December 31, 2022 related to awards that were vested as of the modification date was $0.4 million.

Restricted Stock Units

The fair value of RSUs is based on the fair market value of the Company's common stock on the date of grant. Each RSU represents a contingent right to receive one share of the Company's common stock upon vesting. In general, RSUs vest annually in two or three equal installments on January 1st of each year after the grant date. The following table summarizes the Company's RSU activity for the year ended December 31, 2023:

	Number of Restricted Stock Units	Weighted-Average Grant Date Fair Value
Outstanding at January 1, 2023	543,179	$ 6.12
Granted	483,850	$ 1.60
Vested	(373,519)	$ 4.86
Forfeited	(312,171)	$ 2.59
Outstanding at December 31, 2023	341,339	$ 2.95

Stock-based Compensation Expense

The Company recognizes compensation expense for awards to employees based on the grant date fair value of stock-based awards on a straight-line basis over the period during which an award holder provides service in exchange for the award, which is generally the vesting period. The Company recorded stock-based compensation expense related to stock options, shares purchased under the 2018 ESPP, restricted stock units and stock award modifications as follows:

	For the Year ended December 31,	
	2023	2022
	(in thousands)	
General and administrative	$ 5,952	$ 7,867
Research and development	1,372	5,187
	$ 7,324	$ 13,054

As of December 31, 2023, there was $13.1 million of unrecognized compensation expense related to unvested employee and non-employee share-based compensation arrangements granted under the Plans. The unrecognized compensation expense is estimated to be recognized over a period of 2.0 years at December 31, 2023.

15. NET LOSS PER SHARE

The Company’s potential dilutive securities have been excluded from the computation of diluted net loss per share as the effect would be to reduce the net loss per share. Therefore, the weighted average number of common shares outstanding used to calculate both basic and diluted net loss per share attributable to common stockholders is the same. The Company excluded the following potential common shares, presented based on amounts outstanding at December 31, 2023 and 2022, from the

computation of diluted net loss per share attributable to common stockholders because including them would have had an anti-dilutive effect:

	December 31,	
	2023	2022
Stock options to purchase common stock	9,551,041	9,865,734
Restricted stock units	341,339	543,179
Total	9,892,380	10,408,913

16. 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, while the Company contributes to the plan at the discretion of the Board of Directors. The Company's discretionary match made under the 401(k) Plan for the years ended December 31, 2023 and 2022 was $0.4 million and $0.6 million, respectively.

17. PFIZER STOCK PURCHASE AGREEMENT

On November 9, 2020, the Company entered into a common stock purchase agreement (the "Stock Purchase Agreement") with Pfizer Inc. ("Pfizer"), pursuant to which the Company agreed to issue and sell to Pfizer 5,000,000 shares of the Company's common stock through a private placement transaction (the "Private Placement") at a purchase price of $12.00 per share, for an aggregate purchase price of $60.0 million. The shares of common stock sold to Pfizer were subject to a one-year lock-up from closing, during which time Pfizer was prohibited from selling or otherwise disposing of such shares.

Under the Stock Purchase Agreement, Pfizer was granted an exclusive right of first refusal (the "ROFR") for a 30-month period (the "ROFR Period") beginning on the date of the closing of the Private Placement (collectively, the "ROFR Provision"), to negotiate a potential collaboration on the development and commercialization of HMI-102 and HMI-103. The ROFR Period expired on May 9, 2023. In addition to the ROFR, the Stock Purchase Agreement provided for an information sharing committee (the "Information Committee"), comprised of representatives of each company which will serve as a forum for sharing information regarding the development of HMI-102 and HMI-103 during the ROFR Period.

The Company recorded the issuance of common stock at its estimated fair value of $52.0 million, which reflected a discount for the lack of marketability of the shares. The remaining $8.0 million of aggregate purchase price was allocated to the other elements of the Stock Purchase Agreement, which represented a contract with a customer. The Company concluded that the Information Committee represented the only performance obligation under the contract. The ROFR did not provide Pfizer with a material right and was therefore not a performance obligation. As such, the Company allocated the $8.0 million to the Information Committee obligation.

The Company recognized revenue over time as the measure of progress which it believed best depicted the transfer of control to Pfizer. The Information Committee met regularly over the ROFR Period to share information which resulted in recognition of the transaction price over the 30-month ROFR Period.

The Company recognized collaboration revenue of $1.2 million and $3.2 million during the years ended December 31, 2023 and 2022, respectively. There was no deferred revenue related to the Company's obligation to Pfizer as of December 31, 2023. As of December 31, 2022, there was approximately $1.2 million of deferred revenue related to the Company's obligation to Pfizer.

18. RELATED PARTY TRANSACTIONS

Oxford Biomedica (US) LLC

As described in Note 6, the Company has significant influence over, but does not control, OXB (US) LLC through its noncontrolling representation on OXB Solution's board of directors and the Company's equity interest in OXB (US) LLC. In March 2022, concurrently with the closing of the transaction with OXB (US) LLC, the Company entered into certain ancillary agreements with OXB (US) LLC including a supply agreement, a lease assignment and assumption agreement, a sublease agreement and a transitional services agreement.

Supply Agreement

Pursuant to the terms of the Manufacturing and Supply Agreement with OXB (US) LLC entered into in March 2022 (the "Supply Agreement"), the Company agreed to purchase from OXB (US) LLC at least 50% of its clinical supply requirements of AAV-based products during the initial term of the supply agreement. The Supply Agreement provides for an initial term of three years, which may be extended for an additional one-year term. Under the Supply Agreement, the Company was committed to purchase a minimum number of batches of drug substance and drug product, as well as process development services, for a total commitment of approximately $29.7 million in 2023. As of December 31, 2023, the Company had no remaining purchase obligations to OXB (US) LLC pursuant to the Supply Agreement; there are no minimum purchase commitments in 2024 (year three) of the Supply Agreement. After the initial term, the Company will have the right to terminate the Supply Agreement for convenience or other reasons specified in the Supply Agreement upon prior written notice. Either party may terminate the Supply Agreement upon an uncured material breach by the other party or upon the bankruptcy or insolvency of the other party.

During the years ended December 31, 2023 and 2022, the Company recorded purchases of drug substance from OXB (US) LLC related to the Supply Agreement of approximately $21.7 million and $13.9 million, respectively, purchases of process development services of approximately $7.4 million and $12.5 million, respectively, and stability and other support of approximately $1.0 million and $1.8 million, respectively. These amounts are included within research and development expenses on the Company's consolidated statements of operations. The amounts due to OXB (US) LLC under the Supply Agreement were $3.1 million and $5.2 million as of December 31, 2023 and 2022, respectively, and were included in accounts payable and accrued expenses and other liabilities on the Company's consolidated balance sheets.

Lease Assignment and Sublease Agreement

As described in Note 10, the Company leases space for research and development, manufacturing and general office space in Bedford, Massachusetts. In March 2022, the Company and OXB (US) LLC entered into a lease assignment and assumption agreement pursuant to which Homology assigned all of its right, title and interest in, to and under this lease to OXB (US) LLC and a sublease agreement whereby OXB (US) LLC subleased certain premises in its facility to Homology. However, as the Company remained jointly and severally liable for the payment of rent under this lease, the Company was not released from being the primary obligor under such lease and therefore the related right-of-use asset and operating lease liability were not derecognized and the Company recorded sublease income from OXB (US) LLC as if it were subleasing the space to OXB (US) LLC. See Note 10 for details.

During the years ended December 31, 2023 and 2022, the Company recorded sublease income of $2.3 million and $2.0 million, respectively, related to the sublease agreement with OXB (US) LLC. This amount was recognized as a reduction to lease expense in the Company's consolidated statements of operations.

During 2023, OXB (US) LLC assumed responsibility for paying the landlord for invoices related to the leased property and, as such, the Company began making direct payments to OXB (US) LLC for amounts due to OXB (US) LLC under the sublease. Therefore, as of December 31, 2023, the amount of sublease income payable to OXB (US) LLC was $0.3 million and was included in accrued expenses on the Company's consolidated balance sheets. As of December 31, 2022, the amount of sublease income receivable from OXB (US) LLC was $0.5 million and was included in prepaid expenses and other current assets on the Company's consolidated balance sheets.

Transitional Services Agreement

Under the transitional services agreement with OXB (US) LLC (the “Services Agreement”), the Company is performing certain services for the benefit of OXB (US) LLC and OXB (US) LLC is performing certain services for the benefit of the Company. The term of the Services Agreement will not exceed eighteen months and lasts until the earlier of termination for convenience, termination for cause in the event of an uncured material breach, termination as a result of bankruptcy of either party, and expiration or termination of the only remaining outstanding service as set forth in the Services Agreement. Each company is fully reimbursing the other for these services. As of December 31, 2023, the Services Agreement was substantially complete.

Expenses incurred by the Company for services provided by OXB (US) LLC recognized under the Services Agreement totaled approximately $0.3 million and $0.7 million for the years ended December 31, 2023 and 2022, respectively, and are presented within research and development expenses in the consolidated statements of operations as the services related to facilities support within the Company's research and development labs. The Company did not have a payable balance to OXB (US) LLC under the Services Agreement as of December 31, 2023. As of December 31, 2022, the amount due to OXB (US) LLC under the Services Agreement was $0.1 million and was included in accrued expenses and other liabilities on the Company's consolidated balance sheets.

The Company provided finance, human resources, IT and legal services to OXB (US) LLC under the Services Agreement and recognized $0.5 million and $1.7 million for the years ended December 31, 2023 and 2022, respectively, for amounts reimbursed by OXB (US) LLC as a reduction to general and administrative expense in the Company's consolidated statements of operations. The Company did not provide reimbursable services to OXB (US) LLC under the Services Agreement during the second half of 2023 and did not have a receivable balance from OXB (US) LLC as of December 31, 2023. As of December 31, 2022, the Company had a receivable balance of $0.3 million from OXB (US) LLC which was recorded as a component of prepaid expenses and other current assets in the Company's condensed consolidated balance sheets. Pursuant to the Services Agreement, the Company had been paying vendors on OXB (US) LLC's behalf; this process was fully transitioned to OXB (US) LLC in 2023. As of December 31, 2022, the amount receivable from OXB (US) LLC for amounts paid to vendors on their behalf was $1.1 million and was included in prepaid expenses and other current assets on the Company's consolidated balance sheets. In addition, as of December 31, 2022, the Company had an amount due to OXB (US) LLC of $2.0 million as a result of a year-end reconciliation between the two companies related to vendor invoicing.

* * * * *

Exhibit 4.3

DESCRIPTION OF CAPITAL STOCK

The following description of the capital stock of Homology Medicines, Inc. (the "Company," "we," "us" and "our") is not complete and may not contain all the information you should consider before investing in our capital stock. This description is summarized from, and qualified in its entirety by reference to, our restated certificate of incorporation and our amended and restated bylaws, each of which has been publicly filed with the Securities and Exchange Commission ("SEC").

Our authorized capital stock consists 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.

Common Stock

Our common stock is listed on the Nasdaq Global Select Market under the symbol "FIXX."

Voting Rights. 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 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 restated certificate of incorporation. See below under "-Anti-Takeover Effects of Delaware Law and Our Certificate of Incorporation and Bylaws-Amendment of Charter Provisions."

Rights Upon Liquidation. 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.

Other Rights. 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 under this prospectus 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.

Transfer Agent

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

Dividend

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 outstanding preferred stock. We have never declared or paid any cash dividends on our common stock. We do not intend to declare or pay cash dividends for the foreseeable future. We currently expect to retain all future earnings, if any, for use in the development, operation and expansion of our business. Any determination to pay cash dividends in the future will depend upon, among other things, our results of operations, plans for expansion, tax considerations, available net profits and reserves, limitations under law, financial condition, capital requirements and other factors that our board of directors considers to be relevant.

Preferred Stock

Under the terms of our restated certificate of incorporation, our board of directors is authorized 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.

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 amended and 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 amended and 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 amended and 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. 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 and amended and restated bylaws provide that, subject to the rights of holders of any series of preferred stock, 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 capital stock entitled to vote in the election of directors. Subject to the rights of holders of any series of preferred stock, any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office, unless our board of directors determines by resolution that any such vacancy or newly created directorship shall be filled by our stockholders.

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 an alternative forum, 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 restated certificate of incorporation or amended and restated bylaws; or (4) any action asserting a claim governed by the internal affairs doctrine. In addition, our bylaws provide that the federal district courts of the United States are the exclusive forum for any complaint raising a cause of action arising under the Securities Act. 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 these choice of forum provisions. It is possible that a court of law could find the choice of forum provisions contained in our restated certificate of incorporation or bylaws to be inapplicable or unenforceable if 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 capital stock entitled to vote thereon.

The provisions of Delaware law, our restated certificate of incorporation and our amended and 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.

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Registration Statement Nos. 333-270414 and 333-237131 on Form S-3 and Registration Statement Nos. 333-270398 and 333-224030 on Form S-8 of our report dated March 12, 2024, relating to the financial statements of Homology Medicines, Inc. appearing in this Annual Report on Form 10-K for the year ended December 31, 2023.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
March 12, 2024

Exhibit 31.1

CERTIFICATION

I, Paul Alloway, Ph.D., certify that:

1. I have reviewed this Annual Report on Form 10-K for the fiscal year ended December 31, 2023 of Homology Medicines, Inc.;

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

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

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

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

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

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

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

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

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

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

Date: March 12, 2024

By: /s/ Paul Alloway, Ph.D.

Paul Alloway, Ph.D..
President and Chief Operating Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION

I, Charles Michaud, Jr., certify that:

1. I have reviewed this Annual Report on Form 10-K for the fiscal year ended December 31, 2023 of Homology Medicines, Inc.;

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

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

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

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

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

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

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

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

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

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

Date: March 12, 2024

By: /s/ Charles Michaud, Jr.

Charles Michaud, Jr.
Vice President, Corporate Controller and Treasurer
(Principal Financial and Accounting Officer)

Exhibit 32.1

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

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

(1) The Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2023 (the "Report") fully complies with the requirements of Sections 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

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

Date: March 12, 2024

By: /s/ Paul Alloway, Ph.D.

Paul Alloway, Ph.D.
President and Chief Operating Officer
(Principal Executive Officer)

Exhibit 32.2

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

I, Charles Michaud, Jr., Vice President, Corporate Controller and Treasurer of Homology Medicines, Inc. (the "Company") hereby certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that to the best of my knowledge:

(1) The Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2023 (the "Report") fully complies with the requirements of Sections 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

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

Date: March 12, 2024

By: /s/ Charles Michaud, Jr.

Charles Michaud, Jr.
Vice President, Corporate Controller and Treasurer
(Principal Financial and Accounting Officer)

Exhibit 97.1

HOMOLOGY MEDICINES, INC.

POLICY FOR RECOVERY OF ERRONEOUSLY AWARDED COMPENSATION

Homology Medicines, Inc. (the "***Company***") has adopted this Policy for Recovery of Erroneously Awarded Compensation (the "***Policy***"), effective as of October 6, 2023 (the "***Effective Date***"). Capitalized terms used in this Policy but not otherwise defined herein are defined in Section 11.

1. Persons Subject to Policy

This Policy shall apply to current and former Officers of the Company. Each Officer shall be required to sign an acknowledgment pursuant to which such Officer will agree to be bound by the terms of, and comply with, this Policy; however, any Officer's failure to sign any such acknowledgment shall not negate the application of this Policy to the Officer.

2. Compensation Subject to Policy

This Policy shall apply to Incentive-Based Compensation received on or after the Effective Date. For purposes of this Policy, the date on which Incentive-Based Compensation is "received" shall be determined under the Applicable Rules, which generally provide that Incentive-Based Compensation is "received" in the Company's fiscal period during which the relevant Financial Reporting Measure is attained or satisfied, without regard to whether the grant, vesting or payment of the Incentive-Based Compensation occurs after the end of that period.

3. Recovery of Compensation

In the event that the Company is required to prepare a Restatement, the Company shall recover, reasonably promptly, the portion of any Incentive-Based Compensation that is Erroneously Awarded Compensation, unless the Committee has determined that recovery would be Impracticable. Recovery shall be required in accordance with the preceding sentence regardless of whether the applicable Officer engaged in misconduct or otherwise caused or contributed to the requirement for the Restatement and regardless of whether or when restated financial statements are filed by the Company. For clarity, the recovery of Erroneously Awarded Compensation under this Policy will not give rise to any person's right to voluntarily terminate employment for "good reason," or due to a "constructive termination" (or any similar term of like effect) under any plan, program or policy of or agreement with the Company or any of its affiliates.

4. Manner of Recovery; Limitation on Duplicative Recovery

The Committee shall, in its sole discretion, determine the manner of recovery of any Erroneously Awarded Compensation, which may include, without limitation, reduction or cancellation by the Company or an affiliate of the Company of Incentive-Based Compensation or Erroneously Awarded Compensation, reimbursement or repayment by any person subject to this Policy of the Erroneously Awarded Compensation, and, to the extent permitted by law, an offset of the Erroneously Awarded Compensation against other compensation payable by the Company or an affiliate of the Company to such person. Notwithstanding the foregoing, unless otherwise prohibited by the Applicable Rules, to the extent this Policy provides for recovery of Erroneously Awarded Compensation already recovered by the Company pursuant to Section 304 of the Sarbanes-Oxley Act of 2002 or Other Recovery Arrangements, the amount of Erroneously Awarded Compensation already recovered by the Company from the recipient of such

Erroneously Awarded Compensation may be credited to the amount of Erroneously Awarded Compensation required to be recovered pursuant to this Policy from such person.

5. Administration

This Policy shall be administered, interpreted and construed by the Committee, which is authorized to make all determinations necessary, appropriate or advisable for such purpose. The Board of Directors of the Company (the "***Board***") may re-vest in itself the authority to administer, interpret and construe this Policy in accordance with applicable law, and in such event references herein to the "Committee" shall be deemed to be references to the Board. Subject to any permitted review by the applicable national securities exchange or association pursuant to the Applicable Rules, all determinations and decisions made by the Committee pursuant to the provisions of this Policy shall be final, conclusive and binding on all persons, including the Company and its affiliates, equityholders and employees. The Committee may delegate administrative duties with respect to this Policy to one or more directors or employees of the Company, as permitted under applicable law, including any Applicable Rules.

6. Interpretation

This Policy will be interpreted and applied in a manner that is consistent with the requirements of the Applicable Rules, and to the extent this Policy is inconsistent with such Applicable Rules, it shall be deemed amended to the minimum extent necessary to ensure compliance therewith.

7. No Indemnification; No Liability

The Company shall not indemnify or insure any person against the loss of any Erroneously Awarded Compensation pursuant to this Policy, nor shall the Company directly or indirectly pay or reimburse any person for any premiums for third-party insurance policies that such person may elect to purchase to fund such person's potential obligations under this Policy. None of the Company, an affiliate of the Company or any member of the Committee or the Board shall have any liability to any person as a result of actions taken under this Policy.

8. Application; Enforceability

Except as otherwise determined by the Committee or the Board, the adoption of this Policy does not limit, and is intended to apply in addition to, any other clawback, recoupment, forfeiture or similar policies or provisions of the Company or its affiliates, including any such policies or provisions of such effect contained in any employment agreement, bonus plan, incentive plan, equity-based plan or award agreement thereunder or similar plan, program or agreement of the Company or an affiliate or required under applicable law (the "***Other Recovery Arrangements***"). The remedy specified in this Policy shall not be exclusive and shall be in addition to every other right or remedy at law or in equity that may be available to the Company or an affiliate of the Company.

9. Severability

The provisions in this Policy are intended to be applied to the fullest extent of the law; provided, however, to the extent that any provision of this Policy is found to be unenforceable or invalid under any applicable law, such provision will be applied to the maximum extent permitted, and shall automatically be deemed amended in a manner consistent with its objectives to the extent necessary to conform to any limitations required under applicable law.

10. Amendment and Termination

The Board or the Committee may amend, modify or terminate this Policy in whole or in part at any time and from time to time in its sole discretion. This Policy will terminate automatically when the Company does not have a class of securities listed on a national securities exchange or association.

11. Definitions

"***Applicable Rules***" means Section 10D of the Exchange Act, Rule 10D-1 promulgated thereunder, the listing rules of the national securities exchange or association on which the Company's securities are listed, and any applicable rules, standards or other guidance adopted by the Securities and Exchange Commission or any national securities exchange or association on which the Company's securities are listed.

"***Committee***" means the committee of the Board responsible for executive compensation decisions comprised solely of independent directors (as determined under the Applicable Rules), or in the absence of such a committee, a majority of the independent directors serving on the Board.

"***Erroneously Awarded Compensation***" means the amount of Incentive-Based Compensation received by a current or former Officer that exceeds the amount of Incentive-Based Compensation that would have been received by such current or former Officer based on a restated Financial Reporting Measure, as determined on a pre-tax basis in accordance with the Applicable Rules.

"***Exchange Act***" means the Securities Exchange Act of 1934, as amended.

"***Financial Reporting Measure***" means any measure determined and presented in accordance with the accounting principles used in preparing the Company's financial statements, and any measures derived wholly or in part from such measures, including GAAP, IFRS and non-GAAP/IFRS financial measures, as well as stock or share price and total equityholder return.

"***GAAP***" means United States generally accepted accounting principles.

"***IFRS***" means international financial reporting standards as adopted by the International Accounting Standards Board.

"***Impracticable***" means (a) the direct costs paid to third parties to assist in enforcing recovery would exceed the Erroneously Awarded Compensation; provided that the Company has (i) made reasonable attempts to recover the Erroneously Awarded Compensation, (ii) documented such attempt(s), and (iii) provided such documentation to the relevant listing exchange or association, (b) to the extent permitted by the Applicable Rules, the recovery would violate the Company's home country laws pursuant to an opinion of home country counsel; provided that the Company has (i) obtained an opinion of home country counsel, acceptable to the relevant listing exchange or association, that recovery would result in such violation, and (ii) provided such opinion to the relevant listing exchange or association, or (c) recovery would likely cause an otherwise tax-qualified retirement plan, under which benefits are broadly available to employees of the Company, to fail to meet the requirements of 26 U.S.C. 401(a)(13) or 26 U.S.C. 411(a) and the regulations thereunder.

"***Incentive-Based Compensation***" means, with respect to a Restatement, any compensation that is granted, earned, or vested based wholly or in part upon the attainment of one or more Financial Reporting Measures and received by a person: (a) after beginning service as an Officer; (b) who served as an Officer at any time during the performance period for that compensation; (c) while the Company has a class of its securities listed on a national securities exchange or association; and (d) during the applicable Three-Year Period.

"***Officer***" means each person who serves as an executive officer of the Company, as defined in Rule 10D-1(d) under the Exchange Act.

"***Restatement***" means an accounting restatement to correct the Company's material noncompliance with any financial reporting requirement under securities laws, including restatements that correct an error in previously issued financial statements (a) that is material to the previously issued financial statements or (b) that would result in a material misstatement if the error were corrected in the current period or left uncorrected in the current period.

"***Three-Year Period***" means, with respect to a Restatement, the three completed fiscal years immediately preceding the date that the Board, a committee of the Board, or the officer or officers of the Company authorized to take such action if Board action is not required, concludes, or reasonably should have concluded, that the Company is required to prepare such Restatement, or, if earlier, the date on which a court, regulator or other legally authorized body directs the Company to prepare such Restatement. The "Three-Year Period" also includes any transition period (that results from a change in the Company's fiscal year) within or immediately following the three completed fiscal years identified in the preceding sentence. However, a transition period between the last day of the Company's previous fiscal year end and the first day of its new fiscal year that comprises a period of nine to 12 months shall be deemed a completed fiscal year.

Approved by the Board of Directors on October 6, 2023

ACKNOWLEDGMENT AND CONSENT TO
POLICY FOR RECOVERY OF ERRONEOUSLY AWARDED COMPENSATION

The undersigned has received a copy of the Policy for Recovery of Erroneously Awarded Compensation (the "***Policy***") adopted by Homology Medicines, Inc. (the "***Company***").

For good and valuable consideration, the receipt of which is acknowledged, the undersigned agrees to the terms of the Policy and agrees that compensation received by the undersigned may be subject to reduction, cancellation, forfeiture and/or recoupment to the extent necessary to comply with the Policy, notwithstanding any other agreement to the contrary. The undersigned further acknowledges and agrees that the undersigned is not entitled to indemnification in connection with any enforcement of the Policy and expressly waives any rights to such indemnification under the Company's organizational documents or otherwise.

_____ _____

Date Signature

_____

Name

_____

Title