

The information in this preliminary prospectus supplement is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities and they are not soliciting an offer to buy these securities in any state where the offer or sale thereof is not permitted.

Subject to Completion
Preliminary Prospectus Supplement dated April 6, 2021

PROSPECTUS SUPPLEMENT

\$50,000,000



Common Stock

We are offering shares of our common stock with an aggregate offering price of \$50,000,000.

Our shares trade on The Nasdaq Global Select Market under the symbol "FIXX." On April 5, 2021, the last sale price of our shares as reported on the Nasdaq Global Select Market was \$9.64 per share.

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

Investing in our common stock involves risks that are described in the "[Risk Factors](#)" beginning on page S-4 of this prospectus supplement, page 4 of the accompanying prospectus and under similar headings in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus.

The underwriter has agreed to purchase our common stock from us at a price of \$ _____ per share. The underwriter proposes to offer the shares of common stock from time to time for sale in one or more transactions on The Nasdaq Global Select Market, in the over-the-counter market, through negotiated transactions or otherwise, at market prices prevailing at the time of sale, at prices related to prevailing market prices or at negotiated prices, subject to receipt and acceptance by it and subject to its right to reject any order in whole or in part. The underwriter may also exercise its option to purchase additional shares of our common stock from us with an aggregate offering price of up to \$7.5 million for 30 days after the date of this prospectus supplement. We estimate that the proceeds to us in this offering will be approximately \$ _____ million, or approximately \$ _____ million if the underwriter exercises in full its option to purchase additional shares, in each case before deducting estimated offering expenses payable by us. See "Underwriting."

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

The shares will be ready for delivery on or about _____, 2021.

Book-Running Manager

BTIG

The date of this prospectus supplement is _____, 2021

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

ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part, the prospectus supplement, describes the specific terms of this offering of shares of our common stock and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference herein and into the accompanying prospectus. The second part, the accompanying prospectus, provides more general information. If the information in this prospectus supplement is inconsistent with the accompanying prospectus or any document incorporated by reference therein filed prior to the date of this prospectus supplement, you should rely on the information in this prospectus supplement.

We and the underwriter have not authorized anyone to provide you with any information or to make any representations other than those included or incorporated by reference in this prospectus supplement and the accompanying prospectus and any relevant free writing prospectus. If you receive any information not authorized by us, we and the underwriter take no responsibility for, and can provide no assurance as to the reliability of, such information. We are not making an offer to sell the shares of common stock in any jurisdiction where the offer or sale is not permitted. You should not assume that the information contained or incorporated by reference in this prospectus supplement or the accompanying prospectus or any relevant free writing prospectus is accurate as of any date other than its respective date, regardless of its time of delivery or any sale of shares of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date.

It is important for you to read and consider all of the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus in making your investment decision. We include cross-references in this prospectus supplement and the accompanying prospectus to captions in these materials where you can find additional related discussions. The table of contents in this prospectus supplement provides the pages on which these captions are located. You should read both this prospectus supplement and the accompanying prospectus, together with the additional information described in the sections entitled “Where You Can Find More Information” on page S-23 and “Incorporation by Reference” on page S-24 of this prospectus supplement, before investing in our common stock.

We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the accompanying prospectus and the offering of the common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus supplement and the accompanying prospectus outside the United States. This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

Unless the context otherwise requires, “Homology,” the “company,” “we,” “us,” “our” and similar names refer to Homology Medicines, Inc. and its consolidated subsidiaries.

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the accompanying prospectus, including the documents that we incorporate by reference, contain forward-looking statements within the meaning of 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. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. These statements are often, but are not always, made through the use of words or phrases such as “may,” “will,” “could,” “should,” “expects,” “intends,” “target,” “plans,” “anticipates,” “believes,” “estimates,” “predicts,” “projects,” “contemplate,” “potential,” “continue,” and similar expressions, or the negative of these terms. Accordingly, these statements involve estimates, assumptions and uncertainties which could cause actual results to differ materially from those expressed in them. Any forward-looking statements are qualified in their entirety by reference to the factors discussed throughout this prospectus supplement and the accompanying prospectus, and in particular those factors referenced in the section “Risk Factors.”

This prospectus supplement and the accompanying prospectus contain forward-looking statements that are based on our management’s belief and assumptions and on information currently available to our management. These statements relate to future events or our future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

- the initiation, timing, progress and results of our research and development programs and future preclinical and clinical trials;
- our ability to advance any product candidates into, and successfully complete, clinical trials and obtain regulatory approval for them;
- our ability to identify additional product candidates using our proprietary genetic medicines platform;
- the timing or likelihood of regulatory filings and approvals;
- the commercialization, marketing and manufacturing of our product candidates, if approved;
- the pricing and reimbursement of our product candidates, if approved;
- the rate and degree of market acceptance and clinical utility of any products for which we receive marketing approval;
- the implementation of our strategic plans for our business, product candidates and technology;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology;
- our expectations related to the use of proceeds from our public offering, and estimates of our expenses, future revenues, capital requirements and our needs for additional financing;
- our ability to maintain and establish collaborations;
- our financial performance;
- developments relating to our competitors and our industry, including the impact of government regulation;
- the period of time for which our existing cash and cash equivalents will enable us to fund our operations; and
- our intended use of proceeds from this offering.

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Given these uncertainties, readers should not place undue reliance on our forward-looking statements. These forward-looking statements speak only as of the date on which the statements were made and are not guarantees of future performance. Except as may be required by applicable law, we do not undertake to update any forward-looking statements after the date of this prospectus supplement or the respective dates of documents incorporated by reference herein or therein that include forward-looking statements.

PROSPECTUS SUPPLEMENT SUMMARY

The following summary is qualified in its entirety by, and should be read together with, the more detailed information and financial statements and related notes thereto appearing elsewhere or incorporated by reference in this prospectus supplement and the accompanying prospectus. Before you decide to invest in our securities, you should read the entire prospectus supplement and the accompanying prospectus carefully, including the risk factors and the financial statements and related notes included or incorporated by reference in this prospectus supplement and the accompanying prospectus.

Our Company

Overview

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

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

Patent Portfolio Update

Our patent portfolio includes a combination of issued patents and pending patent applications that we own or are licensed from third parties. As of December 31, 2020, we have an exclusive license or co-exclusive license under 16 United States issued patents, two European patents and 35 patent applications pending in the United States and internationally. In addition, we own a granted U.S. patent relating to our HMI-102 composition that is expected to expire in 2039 and may be eligible for patent term extension depending on the regulatory pathway of the product covered by the patent.

Company Information

We were incorporated under the laws of the State of Delaware in 2015 under the name Homology Medicines, Inc. Our executive offices are located at One Patriots Park, Bedford, Massachusetts 01730, and our

telephone number is (781) 301-7277. Our website address is www.homologymedicines.com. We do not incorporate the information on or accessible through our website into this prospectus supplement, and you should not consider any information on, or that can be accessed through, our website as part of this prospectus supplement.

Implications of Being an Emerging Growth Company

We qualify as an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, as amended, or the JOBS Act. As an emerging growth company, we may take advantage of reduced reporting requirements that are otherwise applicable generally to public companies. These provisions include, but are not limited to:

- the option to present only two years of audited financial statements in addition to any required unaudited interim financial statements and only two years of related “Management’s Discussion and Analysis of Financial Condition and Results of Operations” disclosure;
- reduced disclosure obligations regarding executive compensation in our periodic reports, proxy statements and registration statements;
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved;
- exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting; and
- an exemption from new or revised financial accounting standards until they would apply to private companies and from compliance with any new requirements adopted by the Public Company Accounting Oversight Board requiring mandatory audit firm rotation.

We may take advantage of these exemptions for up to five years or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company on the date that is the earliest of (i) the last day of the fiscal year in which we have total annual gross revenues of \$1.07 billion or more; (ii) December 31, 2023; (iii) the date on which we have issued more than \$1 billion in non-convertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. We have elected to take advantage of this extended transition period.

THE OFFERING

Common stock offered by us	shares of common stock.
Option to purchase additional shares	We have granted the underwriter an option for a period of 30 days after the date of this prospectus supplement to purchase up to an additional shares of common stock at the public offering price, less the underwriting discount.
Common stock to be outstanding immediately after this offering	shares of common stock (or shares of common stock if the underwriter exercises its option to purchase additional shares in full).
Use of proceeds	We intend to use the net proceeds from this offering, in addition to our existing cash resources, (i) to continue to advance our lead gene therapy candidate, HMI-102, for the treatment of phenylketonuria, or PKU, in adults through our ongoing Phase 2 pheNIX clinical trial, (ii) to advance HMI-203, our gene therapy candidate for the treatment of Hunter syndrome, and HMI-103, our first gene editing candidate, which is for the treatment of PKU in the pediatric population, through IND-enabling studies and into clinical trials, (iii) to advance our other pipeline programs through preclinical development, (iv) to further expand our intellectual property portfolio, (v) to potentially further expand our manufacturing capacity and (iv) for working capital and general corporate and administrative expenses. See “Use of Proceeds” on page S-6.
Risk factors	This investment involves a high degree of risk. You should read the description of risks set forth under “Risk Factors” beginning on page S-4 of this prospectus supplement or otherwise incorporated by reference in this prospectus supplement for a discussion of factors to consider before deciding to purchase our securities.
Nasdaq Global Select Market symbol	“FIXX”

The number of shares of our common stock to be outstanding immediately after this offering is based on 50,268,666 shares outstanding as of December 31, 2020, which included 3,091 shares of unvested restricted stock subject to repurchase, and excludes:

- 1,661,468 shares of common stock issuable upon exercise of stock options outstanding under our 2015 Stock Incentive Plan, or 2015 Plan, at a weighted-average exercise price of \$3.95 per share, as of December 31, 2020;
- 4,179,356 shares of common stock issuable upon the exercise of stock options granted under our 2018 Incentive Award Plan, or the 2018 Plan, at a weighted-average exercise price of \$19.65 per share, as of December 31, 2020;
- 2,397,547 shares of our common stock available for future issuance under our 2018 Plan, as of December 31, 2020, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under our 2018 Plan; and
- 1,039,650 shares of common stock available for future issuance under our 2018 Employee Stock Purchase Plan, or 2018 ESPP, as of December 31, 2020, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under our 2018 ESPP.

RISK FACTORS

Investing in our common stock involves risk. Before deciding whether to invest in our common stock, you should consider carefully the risks and uncertainties described below. You should also consider the risks, uncertainties and assumptions discussed under the heading “Risk Factors” included in our most recent annual report on Form 10-K for the year ended December 31, 2020, which is on file with the SEC and is incorporated herein by reference, and which may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future. There may be other unknown or unpredictable economic, business, competitive, regulatory or other factors that could have material adverse effects on our future results. If any of these risks actually occurs, our business, business prospects, financial condition or results of operations could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment. Please also read carefully the section above entitled “Cautionary Statement Regarding Forward-Looking Statements.”

Risks Related to this Offering

A significant portion of our total outstanding shares is restricted from immediate resale but may be sold into the market in the near future, which could cause the market price of our common stock to decline significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. As of March 1, 2021, we had 50,482,124 shares of outstanding common stock, of which approximately 12.4 million shares held by our executive officers, directors and certain of our affiliates are subject to restrictions on transfer under the lock-up arrangements with the underwriter of this offering as described in the section entitled “Underwriting—No Sales of Similar Securities.” Specifically, we and our executive officers and directors have agreed not to sell or transfer any common stock or securities convertible into, exchangeable for, exercisable for, or repayable with common stock, for 45 days after the date of this prospectus supplement without first obtaining the written consent of BTIG, LLC. In addition, certain of our affiliates holding collectively approximately 10.3 million shares of our common stock have also agreed not to sell or transfer any common stock or securities convertible into, exchangeable for, exercisable for, or repayable with common stock, for 45 days after the date of this prospectus supplement without first obtaining the written consent of BTIG, LLC; *provided, however*, that such affiliates may sell collectively up to approximately 1.0 million shares of such common stock after 30 days from the date of this prospectus supplement. The expiration of these restrictions will result in a substantial number of these shares becoming eligible for public sale at that time if they are registered under the Securities Act or if they qualify for an exemption from registration under the Securities Act including under Rules 144 or 701.

Moreover, based on filings with the SEC as of the date of this prospectus supplement, holders of up to an aggregate of approximately 10.3 million shares of our common stock have rights, subject to conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We have also registered shares of our common stock issued and available for issuance under our equity compensation plans, which can be freely sold in the public market, subject to vesting requirements, volume limitations applicable to affiliates and lock-up agreements. If these additional shares are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

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

Our management will have broad discretion in the application of the net proceeds from this offering, including for any of the purposes described in the section entitled “Use of Proceeds,” as well as our existing cash,

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cash equivalents and short-term investments, and you will be relying on the judgment of our management regarding such application. You will not have the opportunity, as part of your investment decision, to assess whether the net proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. Our management might not apply the net proceeds or our existing cash in ways that ultimately increase the value of your investment. If we do not invest or apply the net proceeds from this offering or our existing cash and cash equivalents in ways that enhance stockholder value, we may fail to achieve expected business and financial results, which could cause our stock price to decline. Pending their use, we may invest the net proceeds from this offering in short-term, investment-grade, interest-bearing securities. These investments may not yield a favorable return to our stockholders.

You will experience immediate dilution in the book value per share of the securities you purchase in this offering.

Because the price per share of our common stock being offered is substantially higher than the net tangible book value per share of our common stock, you will suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. Based on an assumed public offering price of \$ per share, and a net tangible book value per share of our common stock of \$3.90 as of December 31, 2020, if you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of \$ per share in the net tangible book value of the common stock you purchase. Any exercise of outstanding stock options, warrants or other equity awards will result in further dilution. See “Dilution” for a more detailed discussion of the dilution you will incur if you purchase our securities in this offering.

USE OF PROCEEDS

We estimate that the net proceeds from the sale of the shares of common stock we are offering will be \$ million after deducting the estimated underwriting discounts and commissions and estimated offering costs payable by us. If the underwriter exercises in full its option to purchase additional shares, we estimate that our net proceeds from this offering will be approximately \$ million after deducting the estimated underwriting discounts and commissions and estimated offering costs payable by us.

The principal purpose of this offering is to obtain additional capital to support our operations. We expect to use the net proceeds of this offering, in addition to our existing cash resources, for the following purposes:

- continue to advance our lead gene therapy candidate, HMI-102, for the treatment of PKU in adults through our ongoing Phase 2 pheNIX clinical trial;
- advance HMI-203, our gene therapy candidate for the treatment of Hunter syndrome, and HMI-103, our first gene editing candidate, which is for the treatment of PKU in the pediatric population, through IND-enabling studies and into clinical trials;
- advance our other pipeline programs through preclinical development;
- further expand our intellectual property portfolio;
- potentially further expand our manufacturing capacity; and
- the remainder for working capital and general corporate and administrative expenses.

This expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our use of the net proceeds from this offering will depend on a number of factors, such as the timing and progress of our research and development efforts, the timing and progress of any collaborative or strategic partnering efforts, and the competitive environment for our planned products. As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses for the net proceeds to us from this offering. The amounts and timing of our actual expenditures and the extent of clinical development may vary significantly depending on numerous factors, including the progress of our development efforts, the status of and results from pre-clinical studies and any ongoing clinical trials or clinical trials we may commence in the future, as well as any collaborations that we may enter into with third parties for our product candidates and any unforeseen cash needs. Accordingly, our management will have broad discretion in the timing and application of these proceeds. Pending application of the net proceeds as described above, we intend to temporarily invest the proceeds in short-term interest-bearing instruments.

Based on the planned use of proceeds described above, we believe that the net proceeds from this offering and our existing cash and cash equivalents will be sufficient to enable us to fund our operating expenses and capital expenditure requirements into the first quarter of 2023. We have based this estimate on assumptions that may prove to be incorrect, and we could use our available capital resources sooner than we currently expect. We may satisfy our future cash needs through the sale of equity securities, debt financings, working capital lines of credit, corporate collaborations or license agreements, grant funding, interest income earned on invested cash balances or a combination of one or more of these sources.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our common stock. We intend to retain future earnings, if any, to finance the operation and expansion of our business and do not anticipate paying any cash dividends on our common stock 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.

DILUTION

If you purchase shares of our common stock in this offering, your interest will be immediately diluted to the extent of the difference between the public offering price per share of our common stock and the net tangible book value per share of our common stock immediately after this offering. Our net tangible book value as of December 31, 2020 was \$196.0 million, or \$3.90 per share of common stock. “Net tangible book value” is total assets minus the sum of liabilities and intangible assets. “Net tangible book value per share” is net tangible book value divided by the total number of shares of common stock outstanding.

After giving effect to the sale by us of _____ shares of common stock in this offering, based on an assumed public offering price of \$ _____ per share, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses that we will pay, our as adjusted net tangible book value as of December 31, 2020, would have been approximately \$ _____ million, or \$ _____ per share of common stock. This amount represents an immediate increase in net tangible book value of \$ _____ per share to existing stockholders and an immediate dilution in tangible book value of \$ _____ per share to purchasers of our common stock in this offering.

The following table illustrates the dilution:

Assumed public offering price per share of common stock	\$
Historical net tangible book value per share as of December 31, 2020	\$3.90
Increase in net tangible book value per share attributable to this offering	<u> </u>
As adjusted net tangible book value per share after this offering	<u> </u>
Dilution per share to investors in this offering	<u> </u> <u> </u>

If the underwriter exercises its option to purchase _____ additional shares in full at the assumed public offering price of \$ _____ per share, the as adjusted net tangible book value will increase to \$ _____ per share, representing an immediate increase in net tangible book value of \$ _____ per share of our common stock to existing stockholders and an immediate dilution of \$ _____ per share to purchasers of our common stock in this offering.

The above table and discussion are based on 50,268,666 shares of our common stock outstanding as of December 31, 2020, which included 3,091 shares of unvested restricted stock subject to repurchase. The number of shares outstanding as of December 31, 2020 does not include:

- 1,661,468 shares of common stock issuable upon exercise of stock options outstanding under our 2015 Plan at a weighted-average exercise price of \$3.95 per share, as of December 31, 2020;
- 4,179,356 shares of common stock issuable upon the exercise of stock options granted under our 2018 Plan at a weighted-average exercise price of \$19.65 per share, as of December 31, 2020;
- 2,397,547 shares of our common stock available for future issuance under our 2018 Plan, as of December 31, 2020, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under our 2018 Plan; and
- 1,039,650 shares of common stock available for future issuance under our 2018 ESPP, as of December 31, 2020, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under our 2018 ESPP.

To the extent that any options are exercised, new options are issued or we otherwise issue additional shares of common stock in the future at a price less than the public offering price, there may be further dilution to purchasers of our common stock in this offering.

UNDERWRITING

BTIG, LLC is acting as the underwriter. Subject to the terms and conditions set forth in an underwriting agreement among us and the underwriter, we have agreed to sell to the underwriter, and the underwriter has agreed to purchase from us, the number of shares of common stock set forth opposite its name below.

<u>Underwriter</u>	<u>Number of Shares</u>
BTIG, LLC	

Subject to the terms and conditions set forth in the underwriting agreement, the underwriter has agreed to purchase all of the shares sold under the underwriting agreement if any of these shares are purchased.

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

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

Commissions and Discounts

The underwriter may offer the shares of common stock from time to time for sale in one or more transactions on the Nasdaq Global Select Market, in the over-the-counter market, through negotiated transactions or otherwise at market prices prevailing at the time of sale, at prices related to prevailing market prices or negotiated prices, subject to receipt and acceptance by it and subject to its right to reject any order in whole or in part. In connection with the sale of the shares of common stock offered hereby, the underwriter may be deemed to have received compensation in the form of underwriting discounts. The underwriter may effect such transactions by selling shares of common stock to or through dealers, and such dealers may receive compensation in the form of discounts, concessions or commissions from the underwriter and/or purchasers of shares of common stock for whom it may act as agent or to whom it may sell as principal. The difference between the price at which the underwriter purchases shares and the price at which the underwriter resells such shares, may be deemed underwriting compensation.

The following table shows the proceeds before expenses to us. The information assumes either no exercise or full exercise by the underwriter of its option to purchase additional shares.

	<u>Per Share</u>	<u>Without Option</u>	<u>With Option</u>
Proceeds, before expenses, to us	\$	\$	\$

The expenses of the offering, not including the underwriting discount, are estimated at \$572,685 and are payable by us. We have also agreed to reimburse the underwriter for its expenses relating to clearance of this offering with the Financial Industry Regulatory Authority in an amount up to \$30,000. The underwriter has agreed to reimburse us for certain fees, costs and expenses and other amount related to or in connection with this offering.

Option to Purchase Additional Shares

We have granted an option to the underwriter, exercisable for 30 days after the date of this prospectus supplement, to purchase up to additional shares at the public offering price, less the underwriting discount.

No Sales of Similar Securities

We and our executive officers and directors have agreed not to sell or transfer any common stock or securities convertible into, exchangeable for, exercisable for, or repayable with common stock, for 45 days after the date of this prospectus supplement without first obtaining the written consent of BTIG, LLC. In addition, certain of our affiliates holding collectively approximately 10.3 million shares of our common stock have also agreed not to sell or transfer any common stock or securities convertible into, exchangeable for, exercisable for, or repayable with common stock, for 45 days after the date of this prospectus supplement without first obtaining the written consent of BTIG, LLC; *provided, however*, that such affiliates may sell collectively up to approximately 1.0 million shares of such common stock after 30 days from the date of this prospectus supplement. Specifically, we and these other persons have agreed, with certain limited exceptions, not to directly or indirectly during the lock-up periods described above:

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

This lock-up provision applies to common stock and to securities convertible into or exchangeable or exercisable for or repayable with common stock. It also applies to common stock owned now or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition. BTIG, LLC, in its sole discretion, may release the common stock and other securities subject to the lock-up agreements described above in whole or in part at any time with or without notice. This lock-up provision will not prohibit sales of our common stock by certain of our directors and officers pursuant to 10b5-1 trading plans that comply with Rule 10b5-1 under the Exchange Act that have been entered into by such individuals prior to this offering. In addition, in the event that any stockholder holding our outstanding shares is granted an early release from the lock-up restrictions with respect to our securities in an aggregate amount in excess of one percent of our issued and outstanding shares (whether in one or multiple releases), then each other Major Holder automatically will be granted an equivalent early release from its obligations under the lock-up agreement on a pro-rata basis. Such release shall not be applicable in the event of an underwritten primary or secondary public offering or sale of our common stock during the period ending 30 days or 45 days, as applicable, after the date of this prospectus supplement. For purposes of this paragraph each of the following persons is a “Major Holder”: 5AM Ventures IV, L.P., 5AM Co-Investors IV, L.P., ARCH Venture Fund VIII Overage, L.P. and ARCH Venture Fund VIII, L.P.

Nasdaq Global Select Market Listing

The shares are listed on the Nasdaq Global Select Market under the symbol “FIXX.”

Price Stabilization, Short Positions

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

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

Similar to other purchase transactions, the underwriter’s purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. The underwriters may conduct these transactions on the Nasdaq Global Select Market, in the over-the-counter market or otherwise.

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

Passive Market Making

In connection with this offering, underwriters and selling group members may engage in passive market making transactions in the common stock on the Nasdaq Global Select Market in accordance with Rule 103 of Regulation M under the Exchange Act during a period before the commencement of offers or sales of common stock and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker’s bid, that bid must then be lowered when specified purchase limits are exceeded. Passive market making may cause the price of our common stock to be higher than the price that otherwise would exist in the open market in the absence of those transactions. The underwriter and dealers are not required to engage in passive market making and may end passive market making activities at any time.

Electronic Distribution

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

Other Relationships

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

In addition, in the ordinary course of their business activities, the underwriter and its affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers.

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Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriter and its affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

European Economic Area

In relation to each Member State of the European Economic Area (each a “Relevant State”), no Shares have been offered or will be offered pursuant to this offering to the public in that Relevant State prior to the publication of a prospectus in relation to the shares offered hereby (“Shares”) which has been approved by the competent authority in that Relevant State or, where appropriate, approved in another Relevant State and notified to the competent authority in that Relevant State, all in accordance with the Prospectus Regulation), except that offers of Shares may be made to the public in that Relevant State at any time under the following exemptions under the Prospectus Regulation:

- a. to any legal entity which is a qualified investor as defined under the Prospectus Regulation;
- b. to fewer than 150 natural or legal persons (other than qualified investors as defined under the Prospectus Regulation), subject to obtaining the prior consent of the underwriter for any such offer; or
- c. in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of Shares shall require us or the underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation.

Each person in a Relevant State who initially acquires any Shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with us and the underwriter that it is a qualified investor within the meaning of the Prospectus Regulation.

In the case of any Shares being offered to a financial intermediary as that term is used in Article 5(1) of the Prospectus Regulation, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the Shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer to the public other than their offer or resale in a Relevant State to qualified investors, in circumstances in which the prior consent of the underwriter has been obtained to each such proposed offer or resale.

We, the underwriter and their respective affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

For the purposes of this provision, the expression an “offer to the public” in relation to any Shares in any Relevant State means the communication in any form and by any means of sufficient information on the terms of the offer and any Shares to be offered so as to enable an investor to decide to purchase or subscribe for any Shares, and the expression “Prospectus Regulation” means Regulation (EU) 2017/1129.

Notice to Prospective Investors in the United Kingdom

In relation to the United Kingdom (“UK”), no shares have been offered or will be offered pursuant to this offering to the public in the UK prior to the publication of a prospectus in relation to the shares which has been approved by the Financial Conduct Authority in the UK in accordance with the UK Prospectus Regulation and the FSMA, except that offers of shares may be made to the public in the UK at any time under the following exemptions under the UK Prospectus Regulation and the FSMA:

- a. to any legal entity which is a qualified investor as defined under the UK Prospectus Regulation;

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- b. to fewer than 150 natural or legal persons (other than qualified investors as defined under the UK Prospectus Regulation), subject to obtaining the prior consent of the underwriter for any such offer; or
- c. at any time in other circumstances falling within section 86 of the FSMA,

provided that no such offer of shares shall require us or the underwriter to publish a prospectus pursuant to Section 85 of the FSMA or Article 3 of the UK Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the UK Prospectus Regulation.

Each person in the UK who initially acquires any shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with us and the underwriter that it is a qualified investor within the meaning of the UK Prospectus Regulation.

In the case of any shares being offered to a financial intermediary as that term is used in Article 5(1) of the UK Prospectus Regulation, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer to the public other than their offer or resale in the UK to qualified investors, in circumstances in which the prior consent of the underwriter has been obtained to each such proposed offer or resale.

We, the underwriter and their affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

For the purposes of this provision, the expression an “offer to the public” in relation to any shares in the UK means the communication in any form and by any means of sufficient information on the terms of the offer and any shares to be offered so as to enable an investor to decide to purchase or subscribe for any shares, the expression “UK Prospectus Regulation” means Regulation (EU) 2017/1129 as it forms part of domestic law by virtue of the European Union (Withdrawal) Act 2018, and the expression “FSMA” means the Financial Services and Markets Act 2000.

This document is for distribution only to persons who (i) have professional experience in matters relating to investments and who qualify as investment professionals within the meaning of Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (as amended, the “Financial Promotion Order”), (ii) are persons falling within Article 49(2)(a) to (d) (“high net worth companies, unincorporated associations etc.”) of the Financial Promotion Order, (iii) are outside the UK, or (iv) are persons to whom an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the FSMA) in connection with the issue or sale of any securities may otherwise lawfully be communicated or caused to be communicated (all such persons together being referred to as “relevant persons”). This document is directed only at relevant persons and must not be acted on or relied on by persons who are not relevant persons. Any investment or investment activity to which this document relates is available only to relevant persons and will be engaged in only with relevant persons.

Notice to Prospective Investors in Switzerland

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

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

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

Notice to Prospective Investors in the Dubai International Financial Centre

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

Notice to Prospective Investors in Australia

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

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

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

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

Notice to Prospective Investors in Hong Kong

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

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

Notice to Prospective Investors in Japan

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

Notice to Prospective Investors in Singapore

This prospectus supplement has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, the shares were not offered or sold or caused to be made the subject of an invitation for subscription or purchase and will not be offered or sold or caused to be made the subject of an invitation for subscription or purchase, and this prospectus supplement or any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares, has not been circulated or distributed, nor will it be circulated or distributed, whether directly or indirectly, to any person in Singapore other than (i) to an institutional investor (as defined under section 274 of the Securities and Futures Act (Chapter 289) of Singapore, as modified or amended from time to time (the “SFA”)) pursuant to Section 274 of the SFA, (ii) to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA, in each case subject to compliance with conditions set forth in the SFA. Pursuant to Section 309B(1)(c) of the SFA, the Notes are “prescribed capital markets products” (as defined in the Securities and Futures (Capital Markets Products) Regulations 2018) and “Excluded Investment Products” (as defined in MAS Notice SFA04-N12: Notice on the sale of Investment Products and MAS Notice FAA-N16: Notice on Recommendations on Investment Products).

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

- (a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

securities or securities-based derivatives contracts (each term as defined in Section 2(1) of the SFA) of that corporation or the beneficiaries’ rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares pursuant to an offer made under Section 275 of the SFA except:

- (a) to an institutional investor (for corporations, under Section 274 of the SFA) or to a relevant person defined in Section 275(2) of the SFA, or to any person pursuant to an offer that is made on terms that

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such shares, debentures and units of shares and debentures of that corporation or such rights and interest in that trust are acquired at a consideration of not less than S\$200,000 (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets, and further for corporations, in accordance with the conditions specified in Section 275 of the SFA;

- (b) where no consideration is or will be given for the transfer;
- (c) where the transfer is by operation of law; or
- (d) as specified in Section 276(7) of the SFA.

Notice to Prospective Investors in Canada

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

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

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

MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES TO NON-U.S. HOLDERS OF OUR COMMON STOCK

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

This discussion is limited to Non-U.S. Holders that hold our common stock as a “capital asset” within the meaning of Section 1221 of the Code (generally, property held for investment). This discussion does not address all U.S. federal income tax consequences relevant to a Non-U.S. Holder’s particular circumstances, including the impact of the Medicare contribution tax on net investment income and the alternative minimum tax. In addition, it does not address consequences relevant to Non-U.S. Holders subject to particular rules, including, without limitation:

- U.S. expatriates and former citizens or long-term residents of the United States;
- persons holding our common stock as part of a hedge, straddle, or other risk reduction strategy or as part of a conversion transaction or other integrated investment;
- banks, insurance companies, and other financial institutions;
- brokers, dealers, or traders in securities or currencies;
- “controlled foreign corporations,” “passive foreign investment companies,” and corporations that accumulate earnings to avoid U.S. federal income tax;
- partnerships or other entities or arrangements treated as partnerships for U.S. federal income tax purposes (and investors therein);
- tax-exempt organizations or governmental organizations;
- persons deemed to sell our common stock under the constructive sale provisions of the Code;
- persons who hold or receive our common stock pursuant to the exercise of any employee stock option or otherwise as compensation;
- tax-qualified retirement plans; and
- “qualified foreign pension funds” as defined in Section 897(l)(2) of the Code and entities all of the interests of which are held by qualified foreign pension funds.

If a partnership (or other entity treated as a partnership for U.S. federal income tax purposes) holds our common stock, the tax treatment of a partner in the partnership will depend on the status of the partner, the activities of the partnership, and certain determinations made at the partner level. Accordingly, partnerships holding our common stock and the partners in such partnerships should consult their tax advisors regarding the U.S. federal income tax consequences to them.

THIS DISCUSSION IS FOR INFORMATIONAL PURPOSES ONLY AND IS NOT LEGAL OR TAX ADVICE. INVESTORS SHOULD CONSULT THEIR TAX ADVISORS WITH RESPECT TO THE

APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS TO THEIR PARTICULAR SITUATIONS AS WELL AS ANY TAX CONSEQUENCES OF THE PURCHASE, OWNERSHIP AND DISPOSITION OF OUR COMMON STOCK ARISING UNDER THE U.S. FEDERAL ESTATE OR GIFT TAX LAWS OR UNDER THE LAWS OF ANY STATE, LOCAL, OR NON-U.S. TAXING JURISDICTION OR UNDER ANY APPLICABLE INCOME TAX TREATY.

Definition of a Non-U.S. Holder

For purposes of this discussion, a “Non-U.S. Holder” is any beneficial owner of our common stock that is neither a “U.S. person” nor an entity treated as a partnership for U.S. federal income tax purposes. A U.S. person is any person that, for U.S. federal income tax purposes, is or is treated as any of the following:

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

Distributions

As described in the section entitled “Dividend Policy,” we do not anticipate paying any cash dividends on our common stock in the foreseeable future. However, if we do make distributions of cash or property on our common stock, such distributions will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Amounts not treated as dividends for U.S. federal income tax purposes will constitute a return of capital and first be applied against and reduce a Non-U.S. Holder’s adjusted tax basis in our common stock, but not below zero. Any excess will be treated as capital gain and will be treated as described below under “—Sale or Other Taxable Disposition.”

Subject to the discussion below on effectively connected income, dividends paid to a Non-U.S. Holder will be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the dividends (or such lower rate specified by an applicable income tax treaty, provided the Non-U.S. Holder furnishes a valid IRS Form W-8BEN or W-8BEN-E (or other applicable documentation) certifying qualification for the lower treaty rate). A Non-U.S. Holder that does not timely furnish the required documentation, but that qualifies for a reduced treaty rate, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS. Non-U.S. Holders should consult their tax advisors regarding their entitlement to benefits under any applicable income tax treaty.

If dividends paid to a Non-U.S. Holder are effectively connected with the Non-U.S. Holder’s conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the Non-U.S. Holder maintains a permanent establishment in the United States to which such dividends are attributable), the Non-U.S. Holder will be exempt from the U.S. federal withholding tax described above. To claim the exemption, the Non-U.S. Holder must furnish to the applicable withholding agent a valid IRS Form W-8ECI, certifying that the dividends are effectively connected with the Non-U.S. Holder’s conduct of a trade or business within the United States.

Any such effectively connected dividends will be subject to U.S. federal income tax on a net income basis at the regular rates. A Non-U.S. Holder that is a corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected dividends, as adjusted for certain items. Non-U.S. Holders should consult their tax advisors regarding any applicable tax treaties that may provide for different rules.

Sale or Other Taxable Disposition

A Non-U.S. Holder will not be subject to U.S. federal income tax on any gain realized upon the sale or other taxable disposition of our common stock unless:

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

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

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

With respect to the third bullet point above, we believe we currently are not, and do not anticipate becoming, a USRPHC. Because the determination of whether we are a USRPHC depends, however, on the fair market value of our USRPIs relative to the fair market value of our non-U.S. real property interests and our other business assets, there can be no assurance we currently are not a USRPHC or will not become one in the future. Even if we are or were to become a USRPHC, gain arising from the sale or other taxable disposition of our common stock by a Non-U.S. Holder will not be subject to U.S. federal income tax if our common stock is "regularly traded," as defined by applicable Treasury Regulations, on an established securities market, and such Non-U.S. Holder owned, actually and constructively, 5% or less of our common stock throughout the shorter of the five-year period ending on the date of the sale or other taxable disposition or the Non-U.S. Holder's holding period.

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

Information Reporting and Backup Withholding

Payments of dividends on our common stock will not be subject to backup withholding, provided the applicable withholding agent does not have actual knowledge or reason to know the holder is a United States person and the holder either certifies its non-U.S. status, such as by furnishing a valid IRS Form W-8BEN, W-8BEN-E, or W-8ECI, or otherwise establishes an exemption. However, information returns are required to be filed with the IRS in connection with any distributions on our common stock paid to the Non-U.S. Holder, regardless of whether such distributions constitute dividends or whether any tax was actually withheld. In addition, proceeds of the sale or other taxable disposition of our common stock within the United States or conducted through certain U.S.-related brokers generally will not be subject to backup withholding or information reporting if the applicable withholding agent receives the certification described above and does not have actual knowledge or reason to know that such holder is a United States person or the holder otherwise establishes an exemption. Proceeds of a disposition of our common stock conducted through a non-U.S. office of a non-U.S. broker generally will not be subject to backup withholding or information reporting.

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Copies of information returns that are filed with the IRS may also be made available under the provisions of an applicable treaty or agreement to the tax authorities of the country in which the Non-U.S. Holder resides or is established.

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

Additional Withholding Tax on Payments Made to Foreign Accounts

Withholding taxes may be imposed under Sections 1471 to 1474 of the Code (such Sections commonly referred to as the Foreign Account Tax Compliance Act, or FATCA) on certain types of payments made to non-U.S. financial institutions and certain other non-U.S. entities. Specifically, a 30% withholding tax may be imposed on dividends on, or (subject to the proposed Treasury Regulations discussed below) gross proceeds from the sale or other disposition of, our common stock paid to a "foreign financial institution" or a "non-financial foreign entity" (each as defined in the Code), unless (1) the foreign financial institution undertakes certain diligence and reporting obligations, (2) the non-financial foreign entity either certifies it does not have any "substantial United States owners" (as defined in the Code) or furnishes identifying information regarding each substantial United States owner, or (3) the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from these rules. If the payee is a foreign financial institution and is subject to the diligence and reporting requirements in clause (1) above, it must enter into an agreement with the U.S. Department of the Treasury requiring, among other things, that it undertake to identify accounts held by certain "specified United States persons" or "United States owned foreign entities" (each as defined in the Code), annually report certain information about such accounts, and withhold 30% on certain payments to non-compliant foreign financial institutions and certain other account holders. Foreign financial institutions located in jurisdictions that have an intergovernmental agreement with the United States governing FATCA may be subject to different rules.

Under the applicable Treasury Regulations and administrative guidance, withholding under FATCA generally applies to payments of dividends on our common stock. While withholding under FATCA would have applied also to payments of gross proceeds from the sale or other disposition of stock on or after January 1, 2019, proposed Treasury Regulations eliminate FATCA withholding on payments of gross proceeds entirely. Taxpayers generally may rely on these proposed Treasury Regulations until final Treasury Regulations are issued.

Prospective investors should consult their tax advisors regarding the potential application of withholding under FATCA to their investment in our common stock.

LEGAL MATTERS

The validity of the common stock being offered hereby will be passed upon for us by Latham & Watkins LLP. Shearman & Sterling LLP, New York, New York, is acting as counsel for the underwriter in connection with certain legal matters related to this offering.

EXPERTS

The financial statements incorporated in this prospectus supplement by reference from our Annual Report on Form 10-K have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report, which is incorporated herein by reference. Such financial statements have been so incorporated in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the information requirements of the Exchange Act and, in accordance therewith, file annual, quarterly and special reports, proxy statements and other information with the SEC. These documents may be accessed through the SEC's electronic data gathering, analysis and retrieval system, or EDGAR, via electronic means, including the SEC's home page on the Internet (www.sec.gov).

We have the authority to designate and issue more than one class or series of stock having various preferences, conversion and other rights, voting powers, restrictions, limitations as to dividends, qualifications, and terms and conditions of redemption. See "Description of Capital Stock" in the accompanying prospectus. We will furnish a full statement of the relative rights and preferences of each class or series of our stock which has been so designated and any restrictions on the ownership or transfer of our stock to any shareholder upon request and without charge. Written requests for such copies should be directed to Homology Medicines, Inc., One Patriots Park, Bedford, MA 01730, or by telephone request to (781) 301-7277. Our website is located at www.homologymedicines.com. Information contained on or accessible through our website is not incorporated by reference into this prospectus supplement and, therefore, is not part of this prospectus supplement or the accompanying prospectus.

INCORPORATION BY REFERENCE

The SEC allows us to “incorporate by reference” information that we file with them. Incorporation by reference allows us to disclose important information to you by referring you to those other documents. The information incorporated by reference is an important part of this prospectus supplement and the accompanying prospectus, and information that we file later with the SEC will automatically update and supersede this information. We filed a registration statement on Form S-3 under the Securities Act, with the SEC with respect to the securities being offered pursuant to this prospectus supplement and the accompanying prospectus. This prospectus supplement and the accompanying prospectus omit certain information contained in the registration statement, as permitted by the SEC. You should refer to the registration statement, including the exhibits, for further information about us and the securities being offered pursuant to this prospectus supplement and the accompanying prospectus. Statements in this prospectus supplement and the accompanying prospectus regarding the provisions of certain documents filed with, or incorporated by reference in, the registration statement are not necessarily complete and each statement is qualified in all respects by that reference. Copies of all or any part of the registration statement, including the documents incorporated by reference or the exhibits, may be obtained upon payment of the prescribed rates at the offices of the SEC listed above in “Where You Can Find More Information.” The documents we are incorporating by reference are (other than those documents or the portions of those documents not deemed to be filed):

- the description of our common stock contained in our Registration Statement on [Form 8-A](#), filed on March 19, 2018;
- our Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2020, filed on March 11, 2021; and
- our Current Reports on Form 8-K filed on [February 8](#), 2021 and [March 1](#), 2021.

In addition, all documents (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed in such forms that are related to such items unless such Form 8-K expressly provides to the contrary) subsequently filed by us pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act, before the date our offering is terminated or completed are deemed to be incorporated by reference into, and to be a part of, this prospectus supplement and the accompanying prospectus.

Any statement contained in this prospectus supplement and the accompanying prospectus or in a document incorporated or deemed to be incorporated by reference into this prospectus supplement and the accompanying prospectus will be deemed to be modified or superseded for purposes of this prospectus supplement and the accompanying prospectus to the extent that a statement contained in this prospectus supplement and the accompanying prospectus or any other subsequently filed document that is deemed to be incorporated by reference into this prospectus supplement and the accompanying prospectus modifies or supersedes the statement. Any statement so modified or superseded will not be deemed, except as so modified or superseded, to constitute a part of this prospectus supplement and the accompanying prospectus.

We will furnish without charge to you, on written or oral request, a copy of any or all of the documents incorporated by reference, including exhibits to these documents. You should direct any requests for documents to Homology Medicines, Inc., One Patriots Park, Bedford, MA 01730, or by telephone request to (781) 301-7277.

PROSPECTUS



\$350,000,000

**Common Stock
Preferred Stock
Debt Securities
Warrants
Units**

We may offer and sell up to \$350,000,000 in the aggregate of the securities identified above from time to time in one or more offerings. This prospectus provides you with a general description of the securities.

Each time we offer and sell securities, we will provide a supplement to this prospectus that contains specific information about the offering and the amounts, prices and terms of the securities. The prospectus supplement may also add, update or change information contained in this prospectus with respect to that offering. You should carefully read this prospectus and the applicable prospectus supplement before you invest in any of our securities.

We may offer and sell the securities described in this prospectus and any prospectus supplement to or through one or more underwriters, dealers and agents, or directly to purchasers, or through a combination of these methods. If any underwriters, dealers or agents are involved in the sale of any of the securities, their names and any applicable purchase price, fee, commission or discount arrangement between or among them will be set forth, or will be calculable from the information set forth, in the applicable prospectus supplement. See the sections of this prospectus entitled "About this Prospectus" and "Plan of Distribution" for more information. No securities may be sold without delivery of this prospectus and the applicable prospectus supplement describing the method and terms of the offering of such securities.

INVESTING IN OUR SECURITIES INVOLVES RISKS. SEE THE "[RISK FACTORS](#)" ON PAGE 4 OF THIS PROSPECTUS AND ANY SIMILAR SECTION CONTAINED IN THE APPLICABLE PROSPECTUS SUPPLEMENT AND IN THE DOCUMENTS INCLUDED BY REFERENCE IN THIS PROSPECTUS OR ANY PROSPECTUS SUPPLEMENT CONCERNING FACTORS YOU SHOULD CONSIDER BEFORE INVESTING IN OUR SECURITIES.

Our common stock is listed on the Nasdaq Global Select Market under the symbol "FIXX." On March 9, 2021, the last reported sale price of our common stock on the Nasdaq Global Select Market was \$10.07 per share.

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

The date of this prospectus is March 12, 2021.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the U.S. Securities and Exchange Commission, or the SEC using a “shelf” registration process. By using a shelf registration statement, we may sell securities from time to time and in one or more offerings up to a total dollar amount of \$350,000,000 as described in this prospectus. Each time that we offer and sell securities, we will provide a prospectus supplement to this prospectus that contains specific information about the securities being offered and sold and the specific terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement or free writing prospectus may also add, update or change information contained in this prospectus with respect to that offering. If there is any inconsistency between the information in this prospectus and the applicable prospectus supplement or free writing prospectus, you should rely on the prospectus supplement or free writing prospectus, as applicable. Before purchasing any securities, you should carefully read both this prospectus and the applicable prospectus supplement (and any applicable free writing prospectuses), together with the additional information described under the heading “Where You Can Find More Information; Incorporation by Reference.”

We have not authorized anyone to provide you with any information or to make any representations other than those contained in this prospectus, any applicable prospectus supplement or any free writing prospectuses prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We will not make an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus and the applicable prospectus supplement to this prospectus is accurate only as of the date on its respective cover, that the information appearing in any applicable free writing prospectus is accurate only as of the date of that free writing prospectus, and that any information incorporated by reference is accurate only as of the date of the document incorporated by reference, unless we indicate otherwise. Our business, financial condition, results of operations and prospects may have changed since those dates. This prospectus incorporates by reference, and any prospectus supplement or free writing prospectus may contain and incorporate by reference, market data and industry statistics and forecasts that are based on independent industry publications and other publicly available information. Although we believe these sources are reliable, we do not guarantee the accuracy or completeness of this information and we have not independently verified this information. In addition, the market and industry data and forecasts that may be included or incorporated by reference in this prospectus, any prospectus supplement or any applicable free writing prospectus may involve estimates, assumptions and other risks and uncertainties and are subject to change based on various factors, including those discussed under the heading “Risk Factors” contained in this prospectus, the applicable prospectus supplement and any applicable free writing prospectus, and under similar headings in other documents that are incorporated by reference into this prospectus. Accordingly, investors should not place undue reliance on this information.

When we refer to “Homology,” “we,” “our company,” “our,” “us” and the “Company” in this prospectus, we mean Homology Medicines, Inc. and its consolidated subsidiaries, unless otherwise specified. When we refer to “you,” we mean the potential holders of the applicable series of securities.

WHERE YOU CAN FIND MORE INFORMATION; INCORPORATION BY REFERENCE

Available Information

We file reports, proxy statements and other information with the SEC. The SEC maintains a website that contains reports, proxy and information statements and other information about issuers, such as us, who file electronically with the SEC. The address of that website is <http://www.sec.gov>.

Our website address is <http://www.homologymedicines.com>. The information on our website, however, is not, and should not be deemed to be, a part of this prospectus.

This prospectus and any prospectus supplement are part of a registration statement that we filed with the SEC and do not contain all of the information in the registration statement. The full registration statement may be obtained from the SEC or us, as provided below. Forms of the indenture and other documents establishing the terms of the offered securities are or may be filed as exhibits to the registration statement or documents incorporated by reference in the registration statement. Statements in this prospectus or any prospectus supplement about these documents are summaries and each statement is qualified in all respects by reference to the document to which it refers. You should refer to the actual documents for a more complete description of the relevant matters. You may inspect a copy of the registration statement through the SEC's website, as provided above.

Incorporation by Reference

The SEC's rules allow us to "incorporate by reference" information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus, and subsequent information that we file with the SEC will automatically update and supersede that information. Any statement contained in this prospectus or a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or a subsequently filed document incorporated by reference modifies or replaces that statement.

This prospectus and any accompanying prospectus supplement incorporate by reference the documents set forth below that have previously been filed with the SEC (other than those documents or the portions of those documents not deemed to be filed):

- Our Annual Report on [Form 10-K](#) for the year ended December 31, 2020, filed with the SEC on March 11, 2021.
- Our Current Reports on Form 8-K filed with the SEC on [February 8, 2021](#) and [March 1, 2021](#).
- The description of our Common Stock contained in our Registration Statement on [Form 8-A](#), filed with the SEC on March 19, 2018, and any amendment or report filed with the SEC for the purpose of updating the description.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, which we refer to as the "Exchange Act" in this prospectus, prior to the termination of this offering, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus and deemed to be part of this prospectus from the date of the filing of such reports and documents.

You may request a free copy of any of the documents incorporated by reference in this prospectus by writing or telephoning us at the following address:

Homology Medicines, Inc.
One Patriots Park
Bedford, Massachusetts 01730
(781) 301-7277

Exhibits to the filings will not be sent, however, unless those exhibits have specifically been incorporated by reference in this prospectus or any accompanying prospectus supplement.

THE COMPANY

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

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

We were incorporated under the laws of the State of Delaware in 2015. Our principal executive offices are located at One Patriots Park, Bedford, Massachusetts 01730, and our telephone number is (781) 301-7277. Our website address is www.homologymedicines.com. The information contained on our website is not incorporated by reference into this prospectus, and you should not consider any information contained on, or that can be accessed through, our website as part of this prospectus or in deciding whether to purchase our securities. Our common stock is listed on the Nasdaq Global Select Market under the symbol "FIXX."

RISK FACTORS

Investment in any securities offered pursuant to this prospectus and the applicable prospectus supplement involves significant risks. You should carefully consider the risk factors incorporated by reference to our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q or Current Reports on Form 8-K, and all other information contained or incorporated by reference into this prospectus, as updated by our subsequent filings under the Exchange Act, and the risk factors and other information contained in the applicable prospectus supplement and any applicable free writing prospectus before making a decision about investing in our securities. The risks and uncertainties we have described are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our operations. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered securities.

USE OF PROCEEDS

We intend to use the net proceeds from the sale of the securities as set forth in the applicable prospectus supplement.

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock 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 certificate of incorporation, which has been publicly filed with the SEC. See “Where You Can Find More Information; Incorporation by Reference.”

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.

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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.

Registration Rights

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

Form S-1 Registration Rights

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

Piggyback Registration Rights

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

Form S-3 Registration Rights

If, at any time after we become entitled under the Securities Act to register our shares on a registration statement on Form S-3, the holders of the registrable securities request in writing that we effect a registration with respect to registrable securities at an aggregate price to the public in the offering of at least \$5,000,000, we will be required to effect such registration; provided, however, that we will not be required to effect such a registration if, within any 12-month period, we have already effected two registrations on Form S-3 for the holders of registrable securities.

Expenses and Indemnification

Ordinarily, other than underwriting discounts and commissions, we will be required to pay all expenses incurred by us related to any registration effected pursuant to the exercise of these registration rights. These expenses may

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include all registration and filing fees, printing expenses, fees and disbursements of our counsel, reasonable fees and disbursements of a counsel for the selling security holders and blue sky fees and expenses. Additionally, we have agreed to indemnify selling stockholders for damages, and any legal or other expenses reasonably incurred, arising from or based upon any untrue statement of a material fact contained in any registration statement, an omission or alleged omission to state a material fact in any registration statement or necessary to make the statements therein not misleading, or any violation or alleged violation by the indemnifying party of securities laws, subject to certain exceptions.

Termination of Registration Rights

The registration rights terminate as to any holder of registrable securities upon the earlier of (i) April 2, 2021, (ii) the closing of a deemed liquidation event, as defined in the investors' rights agreement, (iii) such time at which all shares held by such holder can be sold in any three month period without registration or volume limitations in compliance with Rule 144 or another similar exemption and (iv) such time at which such holder is not an affiliate (as defined under the Securities Act of 1933, as amended) of us.

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.

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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. Our restated certificate of incorporation also provides that any

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person or entity purchasing or otherwise acquiring any interest in shares of our capital stock will be deemed to have notice of and to have consented to this choice of forum provision. It is possible that a court of law could rule that the choice of forum provision contained in our restated certificate of incorporation is inapplicable or unenforceable if it is challenged in a proceeding or otherwise.

In addition, our amended and restated bylaws provide that unless we consent in writing to the selection of an alternative forum, to the fullest extent permitted by law, the federal district courts of the United States of America shall be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act of 1933, as amended, and any person or entity purchasing or otherwise acquiring or holding any interest in our shares of capital stock shall be deemed to have notice of and consented to this choice of forum provision.

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.

DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplement or free writing prospectus, summarizes certain general terms and provisions of the debt securities that we may offer under this prospectus. When we offer to sell a particular series of debt securities, we will describe the specific terms of the series in a supplement to this prospectus. We will also indicate in the supplement to what extent the general terms and provisions described in this prospectus apply to a particular series of debt securities.

We may issue debt securities either separately, or together with, or upon the conversion or exercise of or in exchange for, other securities described in this prospectus. Debt securities may be our senior, senior subordinated or subordinated obligations and, unless otherwise specified in a supplement to this prospectus, the debt securities will be our direct, unsecured obligations and may be issued in one or more series.

The debt securities will be issued under an indenture between us and a trustee to be named in the applicable indenture. We have summarized select portions of the indenture below. The summary is not complete. The form of the indenture has been filed as an exhibit to the registration statement and you should read the indenture for provisions that may be important to you. In the summary below, we have included references to the section numbers of the indenture so that you can easily locate these provisions. Capitalized terms used in the summary and not defined herein have the meanings specified in the indenture.

As used in this section only, “Homology,” “we,” “our” or “us” refer to Homology Medicines, Inc., excluding our subsidiaries, unless expressly stated or the context otherwise requires.

General

The terms of each series of debt securities will be established by or pursuant to a resolution of our board of directors and set forth or determined in the manner provided in a resolution of our board of directors, in an officer’s certificate or by a supplemental indenture. (Section 2.2) The particular terms of each series of debt securities will be described in a prospectus supplement relating to such series (including any pricing supplement or term sheet).

We can issue an unlimited amount of debt securities under the indenture that may be in one or more series with the same or various maturities, at par, at a premium, or at a discount. (Section 2.1) We will set forth in a prospectus supplement (including any pricing supplement or term sheet) relating to any series of debt securities being offered, the aggregate principal amount and the following terms of the debt securities, if applicable:

- the title and ranking of the debt securities (including the terms of any subordination provisions);
- the price or prices (expressed as a percentage of the principal amount) at which we will sell the debt securities;
- any limit on the aggregate principal amount of the debt securities;
- the date or dates on which the principal of the securities of the series is payable;
- the rate or rates (which may be fixed or variable) per annum or the method used to determine the rate or rates (including any commodity, commodity index, stock exchange index or financial index) at which the debt securities will bear interest, the date or dates from which interest will accrue, the date or dates on which interest will commence and be payable and any regular record date for the interest payable on any interest payment date;
- the place or places where principal of, and interest, if any, on, the debt securities will be payable (and the method of such payment), where the securities of such series may be surrendered for registration of transfer or exchange, and where notices and demands to us in respect of the debt securities may be delivered;

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- the period or periods within which, the price or prices at which and the terms and conditions upon which we may redeem the debt securities;
- any obligation we have to redeem or purchase the debt securities pursuant to any sinking fund or analogous provisions or at the option of a holder of debt securities and the period or periods within which, the price or prices at which and in the terms and conditions upon which securities of the series shall be redeemed or purchased, in whole or in part, pursuant to such obligation;
- the dates on which and the price or prices at which we will repurchase debt securities at the option of the holders of debt securities and other detailed terms and provisions of these repurchase obligations;
- the denominations in which the debt securities will be issued, if other than denominations of \$1,000 and any integral multiple thereof;
- whether the debt securities will be issued in the form of certificated debt securities or global debt securities;
- the portion of principal amount of the debt securities payable upon declaration of acceleration of the maturity date, if other than the principal amount;
- the currency of denomination of the debt securities, which may be U.S. Dollars or any foreign currency, and if such currency of denomination is a composite currency, the agency or organization, if any, responsible for overseeing such composite currency;
- the designation of the currency, currencies or currency units in which payment of principal of, premium and interest on the debt securities will be made;
- if payments of principal of, premium on or interest on the debt securities will be made in one or more currencies or currency units other than that or those in which the debt securities are denominated, the manner in which the exchange rate with respect to these payments will be determined;
- the manner in which the amounts of payment of principal of, premium, if any, or interest on the debt securities will be determined, if these amounts may be determined by reference to an index based on a currency or currencies or by reference to a commodity, commodity index, stock exchange index or financial index;
- any provisions relating to any security provided for the debt securities;
- any addition to, deletion of or change in the Events of Default described in this prospectus or in the indenture with respect to the debt securities and any change in the acceleration provisions described in this prospectus or in the indenture with respect to the debt securities;
- any addition to, deletion of or change in the covenants described in this prospectus or in the indenture with respect to the debt securities;
- any depositaries, interest rate calculation agents, exchange rate calculation agents or other agents with respect to the debt securities;
- the provisions, if any, relating to conversion or exchange of any debt securities of such series, including, if applicable, the conversion or exchange price and period, provisions as to whether conversion or exchange will be mandatory, the events requiring an adjustment of the conversion or exchange price and provisions affecting conversion or exchange;
- any other terms of the debt securities, which may supplement, modify or delete any provision of the indenture as it applies to that series, including any terms that may be required under applicable law or regulations or advisable in connection with the marketing of the securities; and
- whether any of our direct or indirect subsidiaries will guarantee the debt securities of that series, including the terms of subordination, if any, of such guarantees. (Section 2.2)

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We may issue debt securities that provide for an amount less than their stated principal amount to be due and payable upon declaration of acceleration of their maturity pursuant to the terms of the indenture. We will provide you with information on the federal income tax considerations and other special considerations applicable to any of these debt securities in the applicable prospectus supplement.

If we denominate the purchase price of any of the debt securities in a foreign currency or currencies or a foreign currency unit or units, or if the principal of and any premium and interest on any series of debt securities is payable in a foreign currency or currencies or a foreign currency unit or units, we will provide you with information on the restrictions, elections, general tax considerations, specific terms and other information with respect to that issue of debt securities and such foreign currency or currencies or foreign currency unit or units in the applicable prospectus supplement.

Transfer and Exchange

Each debt security will be represented by either one or more global securities registered in the name of The Depository Trust Company, or the Depository, or a nominee of the Depository (we will refer to any debt security represented by a global debt security as a “book-entry debt security”), or a certificate issued in definitive registered form (we will refer to any debt security represented by a certificated security as a “certificated debt security”) as set forth in the applicable prospectus supplement. Except as set forth under the heading “Global Debt Securities and Book-Entry System” below, book-entry debt securities will not be issuable in certificated form.

Certificated Debt Securities. You may transfer or exchange certificated debt securities at any office we maintain for this purpose in accordance with the terms of the indenture. (Section 2.4) No service charge will be made for any transfer or exchange of certificated debt securities, but we may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection with a transfer or exchange. (Section 2.7)

You may effect the transfer of certificated debt securities and the right to receive the principal of, premium and interest on certificated debt securities only by surrendering the certificate representing those certificated debt securities and either reissuance by us or the trustee of the certificate to the new holder or the issuance by us or the trustee of a new certificate to the new holder.

Global Debt Securities and Book-Entry System. Each global debt security representing book-entry debt securities will be deposited with, or on behalf of, the Depository, and registered in the name of the Depository or a nominee of the Depository. Please see “Global Securities.”

Covenants

We will set forth in the applicable prospectus supplement any restrictive covenants applicable to any issue of debt securities. (Article IV)

No Protection in the Event of a Change of Control

Unless we state otherwise in the applicable prospectus supplement, the debt securities will not contain any provisions which may afford holders of the debt securities protection in the event we have a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control) which could adversely affect holders of debt securities.

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Consolidation, Merger and Sale of Assets

We may not consolidate with or merge with or into, or convey, transfer or lease all or substantially all of our properties and assets to any person (a “successor person”) unless:

- we are the surviving corporation or the successor person (if other than Homology) is a corporation organized and validly existing under the laws of any U.S. domestic jurisdiction and expressly assumes our obligations on the debt securities and under the indenture; and
- immediately after giving effect to the transaction, no Default or Event of Default, shall have occurred and be continuing.

Notwithstanding the above, any of our subsidiaries may consolidate with, merge into or transfer all or part of its properties to us. (Section 5.1)

Events of Default

“Event of Default” means with respect to any series of debt securities, any of the following:

- default in the payment of any interest upon any debt security of that series when it becomes due and payable, and continuance of such default for a period of 30 days (unless the entire amount of the payment is deposited by us with the trustee or with a paying agent prior to the expiration of the 30-day period);
- default in the payment of principal of any security of that series at its maturity;
- default in the performance or breach of any other covenant or warranty by us in the indenture (other than a covenant or warranty that has been included in the indenture solely for the benefit of a series of debt securities other than that series), which default continues uncured for a period of 60 days after we receive written notice from the trustee or we and the trustee receive written notice from the holders of not less than 25% in principal amount of the outstanding debt securities of that series as provided in the indenture;
- certain voluntary or involuntary events of bankruptcy, insolvency or reorganization of Homology; or
- any other Event of Default provided with respect to debt securities of that series that is described in the applicable prospectus supplement. (Section 6.1)

No Event of Default with respect to a particular series of debt securities (except as to certain events of bankruptcy, insolvency or reorganization) necessarily constitutes an Event of Default with respect to any other series of debt securities. (Section 6.1) The occurrence of certain Events of Default or an acceleration under the indenture may constitute an event of default under certain indebtedness of ours or our subsidiaries outstanding from time to time.

We will provide the trustee written notice of any Default or Event of Default within 30 days of becoming aware of the occurrence of such Default or Event of Default, which notice will describe in reasonable detail the status of such Default or Event of Default and what action we are taking or propose to take in respect thereof. (Section 6.1)

If an Event of Default with respect to debt securities of any series at the time outstanding occurs and is continuing, then the trustee or the holders of not less than 25% in principal amount of the outstanding debt securities of that series may, by a notice in writing to us (and to the trustee if given by the holders), declare to be due and payable immediately the principal of (or, if the debt securities of that series are discount securities, that portion of the principal amount as may be specified in the terms of that series) and accrued and unpaid interest, if any, on all debt securities of that series. In the case of an Event of Default resulting from certain events of bankruptcy, insolvency or reorganization, the principal (or such specified amount) of and accrued and unpaid

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interest, if any, on all outstanding debt securities will become and be immediately due and payable without any declaration or other act on the part of the trustee or any holder of outstanding debt securities. At any time after a declaration of acceleration with respect to debt securities of any series has been made, but before a judgment or decree for payment of the money due has been obtained by the trustee, the holders of a majority in principal amount of the outstanding debt securities of that series may rescind and annul the acceleration if all Events of Default, other than the non-payment of accelerated principal and interest, if any, with respect to debt securities of that series, have been cured or waived as provided in the indenture. (Section 6.2) We refer you to the prospectus supplement relating to any series of debt securities that are discount securities for the particular provisions relating to acceleration of a portion of the principal amount of such discount securities upon the occurrence of an Event of Default.

The indenture provides that the trustee may refuse to perform any duty or exercise any of its rights or powers under the indenture unless the trustee receives indemnity satisfactory to it against any cost, liability or expense which might be incurred by it in performing such duty or exercising such right or power. (Section 7.1(e)) Subject to certain rights of the trustee, the holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee with respect to the debt securities of that series. (Section 6.12)

No holder of any debt security of any series will have any right to institute any proceeding, judicial or otherwise, with respect to the indenture or for the appointment of a receiver or trustee, or for any remedy under the indenture, unless:

- that holder has previously given to the trustee written notice of a continuing Event of Default with respect to debt securities of that series; and
- the holders of not less than 25% in principal amount of the outstanding debt securities of that series have made written request, and offered indemnity or security satisfactory to the trustee, to the trustee to institute the proceeding as trustee, and the trustee has not received from the holders of not less than a majority in principal amount of the outstanding debt securities of that series a direction inconsistent with that request and has failed to institute the proceeding within 60 days. (Section 6.7)

Notwithstanding any other provision in the indenture, the holder of any debt security will have an absolute and unconditional right to receive payment of the principal of, premium and any interest on that debt security on or after the due dates expressed in that debt security and to institute suit for the enforcement of payment. (Section 6.8)

The indenture requires us, within 120 days after the end of our fiscal year, to furnish to the trustee a statement as to compliance with the indenture. (Section 4.3) If a Default or Event of Default occurs and is continuing with respect to the securities of any series and if it is known to a responsible officer of the trustee, the trustee shall mail to each Securityholder of the securities of that series notice of a Default or Event of Default within 90 days after it occurs or, if later, after a responsible officer of the trustee has knowledge of such Default or Event of Default. The indenture provides that the trustee may withhold notice to the holders of debt securities of any series of any Default or Event of Default (except in payment on any debt securities of that series) with respect to debt securities of that series if the trustee determines in good faith that withholding notice is in the interest of the holders of those debt securities. (Section 7.5)

Modification and Waiver

We and the trustee may modify, amend or supplement the indenture or the debt securities of any series without the consent of any holder of any debt security:

- to cure any ambiguity, defect or inconsistency;

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- to comply with covenants in the indenture described above under the heading “Consolidation, Merger and Sale of Assets”;
- to provide for uncertificated securities in addition to or in place of certificated securities;
- to add guarantees with respect to debt securities of any series or secure debt securities of any series;
- to surrender any of our rights or powers under the indenture;
- to add covenants or events of default for the benefit of the holders of debt securities of any series;
- to comply with the applicable procedures of the applicable depository;
- to make any change that does not adversely affect the rights of any holder of debt securities;
- to provide for the issuance of and establish the form and terms and conditions of debt securities of any series as permitted by the indenture;
- to effect the appointment of a successor trustee with respect to the debt securities of any series and to add to or change any of the provisions of the indenture to provide for or facilitate administration by more than one trustee; or
- to comply with requirements of the SEC in order to effect or maintain the qualification of the indenture under the Trust Indenture Act. (Section 9.1)

We may also modify and amend the indenture with the consent of the holders of at least a majority in principal amount of the outstanding debt securities of each series affected by the modifications or amendments. We may not make any modification or amendment without the consent of the holders of each affected debt security then outstanding if that amendment will:

- reduce the amount of debt securities whose holders must consent to an amendment, supplement or waiver;
- reduce the rate of or extend the time for payment of interest (including default interest) on any debt security;
- reduce the principal of or premium on or change the fixed maturity of any debt security or reduce the amount of, or postpone the date fixed for, the payment of any sinking fund or analogous obligation with respect to any series of debt securities;
- reduce the principal amount of discount securities payable upon acceleration of maturity;
- waive a default in the payment of the principal of, premium on or interest on any debt security (except a rescission of acceleration of the debt securities of any series by the holders of at least a majority in aggregate principal amount of the then outstanding debt securities of that series and a waiver of the payment default that resulted from such acceleration);
- make the principal of, premium or interest on any debt security payable in currency other than that stated in the debt security;
- make any change to certain provisions of the indenture relating to, among other things, the right of holders of debt securities to receive payment of the principal of, premium and interest on those debt securities and to institute suit for the enforcement of any such payment and to waivers or amendments; or
- waive a redemption payment with respect to any debt security. (Section 9.3)

Except for certain specified provisions, the holders of at least a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all debt securities of that series waive our compliance with provisions of the indenture. (Section 9.2) The holders of a majority in principal amount of the

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outstanding debt securities of any series may on behalf of the holders of all the debt securities of such series waive any past default under the indenture with respect to that series and its consequences, except a default in the payment of the principal of, premium or any interest on any debt security of that series; provided, however, that the holders of a majority in principal amount of the outstanding debt securities of any series may rescind an acceleration and its consequences, including any related payment default that resulted from the acceleration. (Section 6.13)

Defeasance of Debt Securities and Certain Covenants in Certain Circumstances

Legal Defeasance. The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, we may be discharged from any and all obligations in respect of the debt securities of any series (subject to certain exceptions). We will be so discharged upon the irrevocable deposit with the trustee, in trust, of money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. Dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money or U.S. government obligations in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities.

This discharge may occur only if, among other things, we have delivered to the trustee an opinion of counsel stating that we have received from, or there has been published by, the U.S. Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable U.S. federal income tax law, in either case to the effect that, and based thereon such opinion shall confirm that, the holders of the debt securities of that series will not recognize income, gain or loss for U.S. federal income tax purposes as a result of the deposit, defeasance and discharge and will be subject to U.S. federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit, defeasance and discharge had not occurred. (Section 8.3)

Defeasance of Certain Covenants. The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, upon compliance with certain conditions:

- we may omit to comply with the covenant described under the heading “Consolidation, Merger and Sale of Assets” and certain other covenants set forth in the indenture, as well as any additional covenants that may be set forth in the applicable prospectus supplement; and
- any omission to comply with those covenants will not constitute a Default or an Event of Default with respect to the debt securities of that series (“covenant defeasance”).

The conditions include:

- depositing with the trustee money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. Dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal of, premium on and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities; and
- delivering to the trustee an opinion of counsel to the effect that the holders of the debt securities of that series will not recognize income, gain or loss for U.S. federal income tax purposes as a result of the deposit and related covenant defeasance and will be subject to U.S. federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit and related covenant defeasance had not occurred. (Section 8.4)

No Personal Liability of Directors, Officers, Employees or Securityholders

None of our past, present or future directors, officers, employees or securityholders, as such, will have any liability for any of our obligations under the debt securities or the indenture or for any claim based on, or in respect or by reason of, such obligations or their creation. By accepting a debt security, each holder waives and releases all such liability. This waiver and release is part of the consideration for the issue of the debt securities.

However, this waiver and release may not be effective to waive liabilities under U.S. federal securities laws, and it is the view of the SEC that such a waiver is against public policy.

Governing Law

The indenture and the debt securities, including any claim or controversy arising out of or relating to the indenture or the securities, will be governed by the laws of the State of New York.

The indenture will provide that we, the trustee and the holders of the debt securities (by their acceptance of the debt securities) irrevocably waive, to the fullest extent permitted by applicable law, any and all right to trial by jury in any legal proceeding arising out of or relating to the indenture, the debt securities or the transactions contemplated thereby.

The indenture will provide that any legal suit, action or proceeding arising out of or based upon the indenture or the transactions contemplated thereby may be instituted in the federal courts of the United States of America located in the City of New York or the courts of the State of New York in each case located in the City of New York, and we, the trustee and the holder of the debt securities (by their acceptance of the debt securities) irrevocably submit to the non-exclusive jurisdiction of such courts in any such suit, action or proceeding. The indenture will further provide that service of any process, summons, notice or document by mail (to the extent allowed under any applicable statute or rule of court) to such party's address set forth in the indenture will be effective service of process for any suit, action or other proceeding brought in any such court. The indenture will further provide that we, the trustee and the holders of the debt securities (by their acceptance of the debt securities) irrevocably and unconditionally waive any objection to the laying of venue of any suit, action or other proceeding in the courts specified above and irrevocably and unconditionally waive and agree not to plead or claim any such suit, action or other proceeding has been brought in an inconvenient forum. (Section 10.10)

DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of shares of our common stock or preferred stock or of debt securities. We may issue warrants independently or together with other securities, and the warrants may be attached to or separate from any offered securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and the investors or a warrant agent. The following summary of material provisions of the warrants and warrant agreements are subject to, and qualified in their entirety by reference to, all the provisions of the warrant agreement and warrant certificate applicable to a particular series of warrants. The terms of any warrants offered under a prospectus supplement may differ from the terms described below. We urge you to read the applicable prospectus supplement and any related free writing prospectus, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants.

The particular terms of any issue of warrants will be described in the prospectus supplement relating to the issue. Those terms may include:

- the number of shares of common stock or preferred stock purchasable upon the exercise of warrants to purchase such shares and the price at which such number of shares may be purchased upon such exercise;
- the designation, stated value and terms (including, without limitation, liquidation, dividend, conversion and voting rights) of the series of preferred stock purchasable upon exercise of warrants to purchase preferred stock;
- the principal amount of debt securities that may be purchased upon exercise of a debt warrant and the exercise price for the warrants, which may be payable in cash, securities or other property;
- the date, if any, on and after which the warrants and the related debt securities, preferred stock or common stock will be separately transferable;
- the terms of any rights to redeem or call the warrants;
- the date on which the right to exercise the warrants will commence and the date on which the right will expire;
- U.S. federal income tax consequences applicable to the warrants; and
- any additional terms of the warrants, including terms, procedures and limitations relating to the exchange, exercise and settlement of the warrants.

Holders of equity warrants will not be entitled:

- to vote, consent or receive dividends;
- receive notice as stockholders with respect to any meeting of stockholders for the election of our directors or any other matter; or
- exercise any rights as stockholders of Homology.

Each warrant will entitle its holder to purchase the principal amount of debt securities or the number of shares of preferred stock or common stock at the exercise price set forth in, or calculable as set forth in, the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to the specified time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

A holder of warrant certificates may exchange them for new warrant certificates of different denominations, present them for registration of transfer and exercise them at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement. Until any warrants to purchase debt securities are

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exercised, the holder of the warrants will not have any rights of holders of the debt securities that can be purchased upon exercise, including any rights to receive payments of principal, premium or interest on the underlying debt securities or to enforce covenants in the applicable indenture. Until any warrants to purchase common stock or preferred stock are exercised, the holders of the warrants will not have any rights of holders of the underlying common stock or preferred stock, including any rights to receive dividends or payments upon any liquidation, dissolution or winding up on the common stock or preferred stock, if any.

DESCRIPTION OF UNITS

We may issue units consisting of any combination of the other types of securities offered under this prospectus in one or more series. We may evidence each series of units by unit certificates that we will issue under a separate agreement. We may enter into unit agreements with a unit agent. Each unit agent will be a bank or trust company that we select. We will indicate the name and address of the unit agent in the applicable prospectus supplement relating to a particular series of units.

The following description, together with the additional information included in any applicable prospectus supplement, summarizes the general features of the units that we may offer under this prospectus. You should read any prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of units being offered, as well as the complete unit agreements that contain the terms of the units. Specific unit agreements will contain additional important terms and provisions, and we will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from another report that we file with the SEC, the form of each unit agreement relating to units offered under this prospectus.

If we offer any units, certain terms of that series of units will be described in the applicable prospectus supplement, including, without limitation, the following, as applicable:

- the title of the series of units;
- identification and description of the separate constituent securities comprising the units;
- the price or prices at which the units will be issued;
- the date, if any, on and after which the constituent securities comprising the units will be separately transferable;
- a discussion of certain U.S. federal income tax considerations applicable to the units; and
- any other terms of the units and their constituent securities.

GLOBAL SECURITIES

Book-Entry, Delivery and Form

Unless we indicate differently in any applicable prospectus supplement or free writing prospectus, the securities initially will be issued in book-entry form and represented by one or more global notes or global securities, or, collectively, global securities. The global securities will be deposited with, or on behalf of, The Depository Trust Company, New York, New York, as depository, or DTC, and registered in the name of Cede & Co., the nominee of DTC. Unless and until it is exchanged for individual certificates evidencing securities under the limited circumstances described below, a global security may not be transferred except as a whole by the depository to its nominee or by the nominee to the depository, or by the depository or its nominee to a successor depository or to a nominee of the successor depository.

DTC has advised us that it is:

- a limited-purpose trust company organized under the New York Banking Law;
- a “banking organization” within the meaning of the New York Banking Law;
- a member of the Federal Reserve System;
- a “clearing corporation” within the meaning of the New York Uniform Commercial Code; and
- a “clearing agency” registered pursuant to the provisions of Section 17A of the Exchange Act.

DTC holds securities that its participants deposit with DTC. DTC also facilitates the settlement among its participants of securities transactions, such as transfers and pledges, in deposited securities through electronic computerized book-entry changes in participants’ accounts, thereby eliminating the need for physical movement of securities certificates. “Direct participants” in DTC include securities brokers and dealers, including underwriters, banks, trust companies, clearing corporations and other organizations. DTC is a wholly-owned subsidiary of The Depository Trust & Clearing Corporation, or DTCC. DTCC is the holding company for DTC, National Securities Clearing Corporation and Fixed Income Clearing Corporation, all of which are registered clearing agencies. DTCC is owned by the users of its regulated subsidiaries. Access to the DTC system is also available to others, which we sometimes refer to as indirect participants, that clear through or maintain a custodial relationship with a direct participant, either directly or indirectly. The rules applicable to DTC and its participants are on file with the SEC.

Purchases of securities under the DTC system must be made by or through direct participants, which will receive a credit for the securities on DTC’s records. The ownership interest of the actual purchaser of a security, which we sometimes refer to as a beneficial owner, is in turn recorded on the direct and indirect participants’ records. Beneficial owners of securities will not receive written confirmation from DTC of their purchases. However, beneficial owners are expected to receive written confirmations providing details of their transactions, as well as periodic statements of their holdings, from the direct or indirect participants through which they purchased securities. Transfers of ownership interests in global securities are to be accomplished by entries made on the books of participants acting on behalf of beneficial owners. Beneficial owners will not receive certificates representing their ownership interests in the global securities, except under the limited circumstances described below.

To facilitate subsequent transfers, all global securities deposited by direct participants with DTC will be registered in the name of DTC’s partnership nominee, Cede & Co., or such other name as may be requested by an authorized representative of DTC. The deposit of securities with DTC and their registration in the name of Cede & Co. or such other nominee will not change the beneficial ownership of the securities. DTC has no knowledge of the actual beneficial owners of the securities. DTC’s records reflect only the identity of the direct participants to whose accounts the securities are credited, which may or may not be the beneficial owners. The participants are responsible for keeping account of their holdings on behalf of their customers.

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So long as the securities are in book-entry form, you will receive payments and may transfer securities only through the facilities of the depository and its direct and indirect participants. We will maintain an office or agency in the location specified in the prospectus supplement for the applicable securities, where notices and demands in respect of the securities and the indenture may be delivered to us and where certificated securities may be surrendered for payment, registration of transfer or exchange.

Conveyance of notices and other communications by DTC to direct participants, by direct participants to indirect participants and by direct participants and indirect participants to beneficial owners will be governed by arrangements among them, subject to any legal requirements in effect from time to time.

Redemption notices will be sent to DTC. If less than all of the securities of a particular series are being redeemed, DTC's practice is to determine by lot the amount of the interest of each direct participant in the securities of such series to be redeemed.

Neither DTC nor Cede & Co. (or such other DTC nominee) will consent or vote with respect to the securities. Under its usual procedures, DTC will mail an omnibus proxy to us as soon as possible after the record date. The omnibus proxy assigns the consenting or voting rights of Cede & Co. to those direct participants to whose accounts the securities of such series are credited on the record date, identified in a listing attached to the omnibus proxy.

So long as securities are in book-entry form, we will make payments on those securities to the depository or its nominee, as the registered owner of such securities, by wire transfer of immediately available funds. If securities are issued in definitive certificated form under the limited circumstances described below and unless if otherwise provided in the description of the applicable securities herein or in the applicable prospectus supplement, we will have the option of making payments by check mailed to the addresses of the persons entitled to payment or by wire transfer to bank accounts in the United States designated in writing to the applicable trustee or other designated party at least 15 days before the applicable payment date by the persons entitled to payment, unless a shorter period is satisfactory to the applicable trustee or other designated party.

Redemption proceeds, distributions and dividend payments on the securities will be made to Cede & Co., or such other nominee as may be requested by an authorized representative of DTC. DTC's practice is to credit direct participants' accounts upon DTC's receipt of funds and corresponding detail information from us on the payment date in accordance with their respective holdings shown on DTC records. Payments by participants to beneficial owners will be governed by standing instructions and customary practices, as is the case with securities held for the account of customers in bearer form or registered in "street name." Those payments will be the responsibility of participants and not of DTC or us, subject to any statutory or regulatory requirements in effect from time to time. Payment of redemption proceeds, distributions and dividend payments to Cede & Co., or such other nominee as may be requested by an authorized representative of DTC, is our responsibility; disbursement of payments to direct participants is the responsibility of DTC, and disbursement of payments to the beneficial owners is the responsibility of direct and indirect participants.

Except under the limited circumstances described below, purchasers of securities will not be entitled to have securities registered in their names and will not receive physical delivery of securities. Accordingly, each beneficial owner must rely on the procedures of DTC and its participants to exercise any rights under the securities and the indenture.

The laws of some jurisdictions may require that some purchasers of securities take physical delivery of securities in definitive form. Those laws may impair the ability to transfer or pledge beneficial interests in securities.

DTC may discontinue providing its services as securities depository with respect to the securities at any time by giving reasonable notice to us. Under such circumstances, in the event that a successor depository is not obtained, securities certificates are required to be printed and delivered.

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As noted above, beneficial owners of a particular series of securities generally will not receive certificates representing their ownership interests in those securities. However, if:

- DTC notifies us that it is unwilling or unable to continue as a depository for the global security or securities representing such series of securities or if DTC ceases to be a clearing agency registered under the Exchange Act at a time when it is required to be registered and a successor depository is not appointed within 90 days of the notification to us or of our becoming aware of DTC's ceasing to be so registered, as the case may be;
- we determine, in our sole discretion, not to have such securities represented by one or more global securities; or
- an Event of Default has occurred and is continuing with respect to such series of securities,

we will prepare and deliver certificates for such securities in exchange for beneficial interests in the global securities. Any beneficial interest in a global security that is exchangeable under the circumstances described in the preceding sentence will be exchangeable for securities in definitive certificated form registered in the names that the depository directs. It is expected that these directions will be based upon directions received by the depository from its participants with respect to ownership of beneficial interests in the global securities.

Euroclear and Clearstream

If so provided in the applicable prospectus supplement, you may hold interests in a global security through Clearstream Banking S.A., which we refer to as "Clearstream," or Euroclear Bank S.A./N.V., as operator of the Euroclear System, which we refer to as "Euroclear," either directly if you are a participant in Clearstream or Euroclear or indirectly through organizations that are participants in Clearstream or Euroclear. Clearstream and Euroclear will hold interests on behalf of their respective participants through customers' securities accounts in the names of Clearstream and Euroclear, respectively, on the books of their respective U.S. depositories, which in turn will hold such interests in customers' securities accounts in such depositories' names on DTC's books.

Clearstream and Euroclear are securities clearance systems in Europe. Clearstream and Euroclear hold securities for their respective participating organizations and facilitate the clearance and settlement of securities transactions between those participants through electronic book-entry changes in their accounts, thereby eliminating the need for physical movement of certificates.

Payments, deliveries, transfers, exchanges, notices and other matters relating to beneficial interests in global securities owned through Euroclear or Clearstream must comply with the rules and procedures of those systems. Transactions between participants in Euroclear or Clearstream, on one hand, and other participants in DTC, on the other hand, are also subject to DTC's rules and procedures.

Investors will be able to make and receive through Euroclear and Clearstream payments, deliveries, transfers and other transactions involving any beneficial interests in global securities held through those systems only on days when those systems are open for business. Those systems may not be open for business on days when banks, brokers and other institutions are open for business in the United States.

Cross-market transfers between participants in DTC, on the one hand, and participants in Euroclear or Clearstream, on the other hand, will be effected through DTC in accordance with the DTC's rules on behalf of Euroclear or Clearstream, as the case may be, by their respective U.S. depositories; however, such cross-market transactions will require delivery of instructions to Euroclear or Clearstream, as the case may be, by the counterparty in such system in accordance with the rules and procedures and within the established deadlines (European time) of such system. Euroclear or Clearstream, as the case may be, will, if the transaction meets its settlement requirements, deliver instructions to its U.S. depository to take action to effect final settlement on its behalf by delivering or receiving interests in the global securities through DTC, and making or receiving

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payment in accordance with normal procedures for same-day fund settlement. Participants in Euroclear or Clearstream may not deliver instructions directly to their respective U.S. depositories.

Due to time zone differences, the securities accounts of a participant in Euroclear or Clearstream purchasing an interest in a global security from a direct participant in DTC will be credited, and any such crediting will be reported to the relevant participant in Euroclear or Clearstream, during the securities settlement processing day (which must be a business day for Euroclear or Clearstream) immediately following the settlement date of DTC. Cash received in Euroclear or Clearstream as a result of sales of interests in a global security by or through a participant in Euroclear or Clearstream to a direct participant in DTC will be received with value on the settlement date of DTC but will be available in the relevant Euroclear or Clearstream cash account only as of the business day for Euroclear or Clearstream following DTC's settlement date.

Other

The information in this section of this prospectus concerning DTC, Clearstream, Euroclear and their respective book-entry systems has been obtained from sources that we believe to be reliable, but we do not take responsibility for this information. This information has been provided solely as a matter of convenience. The rules and procedures of DTC, Clearstream and Euroclear are solely within the control of those organizations and could change at any time. Neither we nor the trustee nor any agent of ours or of the trustee has any control over those entities and none of us takes any responsibility for their activities. You are urged to contact DTC, Clearstream and Euroclear or their respective participants directly to discuss those matters. In addition, although we expect that DTC, Clearstream and Euroclear will perform the foregoing procedures, none of them is under any obligation to perform or continue to perform such procedures and such procedures may be discontinued at any time. Neither we nor any agent of ours will have any responsibility for the performance or nonperformance by DTC, Clearstream and Euroclear or their respective participants of these or any other rules or procedures governing their respective operations.

PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods or through underwriters or dealers, through agents and/or directly to one or more purchasers. The securities may be distributed from time to time in one or more transactions:

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

Each time that we sell securities covered by this prospectus, we will provide a prospectus supplement or supplements that will describe the method of distribution and set forth the terms and conditions of the offering of such securities, including the offering price of the securities and the proceeds to us, if applicable.

Offers to purchase the securities being offered by this prospectus may be solicited directly. Agents may also be designated to solicit offers to purchase the securities from time to time. Any agent involved in the offer or sale of our securities will be identified in a prospectus supplement.

If a dealer is utilized in the sale of the securities being offered by this prospectus, the securities will be sold to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale.

If an underwriter is utilized in the sale of the securities being offered by this prospectus, an underwriting agreement will be executed with the underwriter at the time of sale and the name of any underwriter will be provided in the prospectus supplement that the underwriter will use to make resales of the securities to the public. In connection with the sale of the securities, we or the purchasers of securities for whom the underwriter may act as agent, may compensate the underwriter in the form of underwriting discounts or commissions. The underwriter may sell the securities to or through dealers, and those dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters and/or commissions from the purchasers for which they may act as agent. Unless otherwise indicated in a prospectus supplement, an agent will be acting on a best efforts basis and a dealer will purchase securities as a principal, and may then resell the securities at varying prices to be determined by the dealer.

Any compensation paid to underwriters, dealers or agents in connection with the offering of the securities, and any discounts, concessions or commissions allowed by underwriters to participating dealers will be provided in the applicable prospectus supplement. Underwriters, dealers and agents participating in the distribution of the securities may be deemed to be underwriters within the meaning of the Securities Act of 1933, as amended, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions. We may enter into agreements to indemnify underwriters, dealers and agents against civil liabilities, including liabilities under the Securities Act, or to contribute to payments they may be required to make in respect thereof and to reimburse those persons for certain expenses.

Any common stock will be listed on the Nasdaq Global Select Market, but any other securities may or may not be listed on a national securities exchange. To facilitate the offering of securities, certain persons participating in the offering may engage in transactions that stabilize, maintain or otherwise affect the price of the securities. This may include over-allotments or short sales of the securities, which involve the sale by persons participating in the offering of more securities than were sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising their over-allotment option, if any. In addition, these persons may stabilize or maintain the price of the securities by bidding for or

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purchasing securities in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if securities sold by them are repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. These transactions may be discontinued at any time.

We may engage in at the market offerings into an existing trading market in accordance with Rule 415(a)(4) under the Securities Act. In addition, we may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement so indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter and, if not identified in this prospectus, will be named in the applicable prospectus supplement (or a post-effective amendment). In addition, we may otherwise loan or pledge securities to a financial institution or other third party that in turn may sell the securities short using this prospectus and an applicable prospectus supplement. Such financial institution or other third party may transfer its economic short position to investors in our securities or in connection with a concurrent offering of other securities.

The specific terms of any lock-up provisions in respect of any given offering will be described in the applicable prospectus supplement.

The underwriters, dealers and agents may engage in transactions with us, or perform services for us, in the ordinary course of business for which they receive compensation.

LEGAL MATTERS

Latham & Watkins LLP will pass upon certain legal matters relating to the issuance and sale of the securities offered hereby on behalf of Homology Medicines, Inc. Additional legal matters may be passed upon for us or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The financial statements incorporated in this prospectus by reference from our Annual Report on Form 10-K have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report, which is incorporated herein by reference. Such financial statements have been so incorporated in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

\$50,000,000



Common Stock

PROSPECTUS SUPPLEMENT

BTIG

, 2021
