

PROSPECTUS SUPPLEMENT
(To prospectus dated February 14, 2023)



Up to \$150,000,000

Common Stock

We previously entered into a sales agreement (as amended, the “sales agreement”) with SVB Securities LLC (“SVB Securities”) and Cantor Fitzgerald & Co. (“Cantor” and together with SVB Securities, the “Sales Agents”) relating to shares of our common stock, \$0.001 par value per share. Under this prospectus supplement and the accompanying prospectus, and in accordance with the terms of the sales agreement, we may offer and sell shares of our common stock having an aggregate offering price of up to \$150,000,000 from time to time through the Sales Agents.

Our common stock is listed on the Nasdaq Global Market under the trading symbol “ETNB.” On February 13, 2023, the last reported sale price of our common stock was \$13.73 per share.

Sales of our common stock, if any, under this prospectus supplement and the accompanying prospectus may be made in sales deemed to be an “at the market offering” as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended (the “Securities Act”). The Sales Agents are not required to sell any specific number or dollar amounts of securities, but will act as sales agents using commercially reasonable efforts consistent with their normal trading and sales practices, on mutually agreed terms between the Sales Agents and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

The Sales Agents will be entitled to compensation at a commission up to 3.0% of the aggregate gross sales price per share sold under the sales agreement. In connection with the sale of our common stock on our behalf, the Sales Agents will be deemed to be “underwriters” within the meaning of the Securities Act and the compensation of the Sales Agents will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contributions to the Sales Agents against certain civil liabilities, including liabilities under the Securities Act. See “Plan of Distribution” beginning on page S-11 of this prospectus supplement for additional information regarding the Sales Agents’ compensation.

Investing in our common stock involves a high degree of risk. Before making an investment decision, you should review carefully and consider all of the information set forth in this prospectus supplement, the accompany prospectus and the documents incorporated by reference in this prospectus supplement. See “[Risk Factors](#)” beginning on page S-4 of this prospectus supplement and in the documents incorporated by reference herein.

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.

We are an “emerging growth company” under the federal securities laws and are subject to reduced public company reporting requirements.

SVB Securities

Cantor

The date of this prospectus supplement is February 15, 2023.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement is part of a registration statement that we have filed with the Securities and Exchange Commission (“SEC”) utilizing a “shelf” registration process. Under the shelf registration statement we may offer shares of our common stock, preferred stock, debt securities, warrants and units, including common stock or preferred stock upon conversion of debt securities, common stock upon conversion of preferred stock, or common stock, preferred stock or debt securities upon the exercise of warrants, having an aggregate offering price of up to \$500,000,000. Under this prospectus supplement, we may offer shares of our common stock having an aggregate offering price of up to \$150,000,000 from time to time at prices and on terms to be determined by market conditions at the time of offering.

We provide information to you about this offering of shares of our common stock in two separate documents that are bound together: (1) this prospectus supplement, which describes the specific details regarding this offering; and (2) the accompanying prospectus, which provides general information, some of which may not apply to this offering. Generally, when we refer to this “prospectus,” we are referring to both documents combined. If information in this prospectus supplement is inconsistent with the accompanying prospectus, you should rely on this prospectus supplement. However, if any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in this prospectus supplement—the statement in the document having the later date modifies or supersedes the earlier statement as our business, financial condition, results of operations and prospects may have changed since the earlier dates.

We have not, and the Sales Agents have not, authorized any other person to provide you with any information or to make any representations other than those contained in or incorporated by reference in this prospectus supplement, the accompanying prospectus and any free writing prospectus prepared by or on behalf of us or to which we have referred you. We and the Sales Agents take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We and the Sales Agents are not making an offer to sell or soliciting an offer to buy our securities in any jurisdiction in which an offer or solicitation is not authorized or in which the person making that offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make an offer or solicitation. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference into this prospectus supplement and in any free writing prospectus that we may authorize for use in connection with this offering, is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference into this prospectus supplement and any free writing prospectus that we may authorize for use in connection with this offering, in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you in the sections of this prospectus supplement captioned “Where You Can Find More Information” and “Incorporation of Certain Information by Reference.”

We are offering to sell, and seeking offers to buy, shares of 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 our 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 our common stock and the distribution of this prospectus supplement and the accompanying prospectus supplement 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.

This prospectus supplement, the accompanying prospectus and the information incorporated herein and therein by reference include trademarks, servicemarks and tradenames owned by us or other companies. All trademarks, servicemarks and tradenames included or incorporated by reference in this prospectus supplement or the accompanying prospectus are the property of their respective owners.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information and does not contain all of the information that you should consider before deciding to invest in our common stock. You should read the entire prospectus supplement, including the information incorporated by reference herein, the accompanying prospectus and any related free writing prospectus, carefully, including the section titled “Risk Factors” contained in this prospectus supplement, the accompanying prospectus and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus supplement, and our financial statements and notes thereto included in our most recent Annual Report on Form 10-K, which are incorporated by reference herein, before making an investment decision. Some of the statements in this summary constitute forward-looking statements, see “Special Note Regarding Forward-Looking Statements.” In this prospectus supplement, unless the context requires otherwise, references to “we,” “us,” “our,” “89bio” or the “company” refer to 89bio, Inc., in each case together with its consolidated subsidiaries.

Our Company

Overview

We are a clinical-stage biopharmaceutical company focused on the development and commercialization of innovative therapies for the treatment of liver and cardio-metabolic diseases. Our lead product candidate, pegozafermin (previously BIO89-100), a specifically engineered glycoPEGylated analog of fibroblast growth factor 21, is currently being developed for the treatment of severe hypertriglyceridemia and nonalcoholic steatohepatitis.

Corporate Information

We were incorporated in January 2018 in Israel under the name 89Bio Ltd. 89bio, Inc., the registrant whose name appears on the cover page of this prospectus supplement, was incorporated in June 2019 for the purpose of an internal reorganization transaction.

Our principal executive offices are located at 142 Sansome Street, San Francisco, California 94104 and our telephone number is (415) 432-9270. Our website is www.89bio.com. The information contained on our website is not incorporated by reference into this prospectus supplement or the accompanying prospectus, and you should not consider any information contained on, or that can be accessed through, our website as part of this prospectus supplement and the accompanying prospectus in deciding whether to purchase our shares of common stock.

THE OFFERING

Common stock offered by us	Shares of our common stock having an aggregate offering price of up to \$150,000,000.
Common stock to be outstanding after this offering	Up to 54,549,606 shares, assuming sales of 10,924,981 shares of our common stock in this offering at an assumed offering price of \$13.73 per share, which was the last reported sale price of our common stock on the Nasdaq Global Market on February 13, 2023. The actual number of shares issued will vary depending on the sales prices at which our common stock is sold under this offering.
Plan of Distribution	“At the market offering” that may be made from time to time through the Sales Agents. See “Plan of Distribution” on page S-11 of this prospectus supplement.
Use of Proceeds	We currently intend to use the net proceeds from this offering, if any, for development, manufacturing and scale-up, as well as for working capital and general corporate purposes. See “Use of Proceeds” on page S-8 of this prospectus supplement.
Risk Factors	You should read the “Risk Factors” section of this prospectus supplement and the accompanying prospectus and in the documents incorporated by reference into this prospectus supplement for a discussion of factors you should carefully consider before deciding to purchase shares of our common stock.
Nasdaq Global Market symbol	“ETNB”

The number of our shares of common stock outstanding is based on 43,624,625 shares of common stock outstanding as of September 30, 2022, and excludes the following, all as of September 30, 2022:

- 3,123,221 shares of our common stock issuable upon the exercise of stock options outstanding as of September 30, 2022, under our 2019 Equity Incentive Plan (as amended and restated, the “2019 Plan”) at a weighted-average exercise price of \$13.05 per share;
- 103,000 shares of our common stock issuable upon the exercise of stock options granted subsequent to September 30, 2022, under the 2019 Plan at a weighted-average exercise price of \$8.12 per share;
- 25,000 shares of our common stock issuable upon exercise of an outstanding warrant at an exercise price of \$22.06 per share (which expires on June 30, 2025);
- 33,923 shares of our common stock issuable upon exercise of an outstanding warrant at an exercise price of \$19.12 per share (which expires on May 28, 2031);
- 241,946 shares of our common stock reserved for future issuance under our 2019 Plan, as well as any automatic increase in the number of shares of common stock reserved for future issuance thereunder; and
- 731,603 shares of our common stock reserved for future issuance under our 2019 Employee Stock Purchase Plan, as well as any automatic increase in the number of shares of common stock reserved for future issuance thereunder.

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should consider carefully the risks and uncertainties described below and discussed under the heading “Risk Factors” contained in our most recent Annual Report on Form 10-K, and in our subsequent Quarterly Reports on Form 10-Q, as well as any amendments thereto reflected in subsequent filings with the SEC, which are incorporated by reference into this prospectus supplement in their entirety, together with other information in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference and any free writing prospectus that we may authorize for use in connection with this offering. The risks described in these documents are not the only ones we face, but those that we consider to be material. There may be other unknown or unpredictable economic, business, competitive, regulatory or other factors that could have material adverse effects on our future results. Past financial performance may not be a reliable indicator of future performance, and historical trends should not be used to anticipate results or trends in future periods. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow 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 below entitled “Special Note Regarding Forward-Looking Statements.”

Additional Risks Related to This Offering

Management will have broad discretion as to the use of the proceeds from this offering, and may not use the proceeds effectively.

Because we have not designated the amount of net proceeds from this offering to be used for any particular purpose, our management will have broad discretion as to the application of the net proceeds from this offering and could use them for purposes other than those contemplated at the time of the offering. Our management may use the net proceeds for corporate purposes that may not improve our financial condition or market value.

You may experience immediate and substantial dilution.

The offering price per share in this offering may exceed the net tangible book value per share of our common stock outstanding prior to this offering. Assuming that 10,924,981 shares of our common stock are sold in this offering, based on an assumed sale price of \$13.73 per share, the last sale price of a share of our common stock on the Nasdaq Global Market on February 13, 2023, you will experience immediate dilution, representing the difference between the price you pay and our as adjusted net tangible book value per share as of September 30, 2022, after giving effect to this offering, of \$8.28 per share. The exercise of outstanding stock options may result in further dilution of your investment. See the section titled “Dilution” below for a more detailed illustration of the dilution you would incur if you participate in this offering.

You may experience future dilution as a result of future equity offerings.

To raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price per share in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price per share paid by investors in this offering.

It is not possible to predict the aggregate proceeds resulting from sales made under the sales agreement.

Subject to certain limitations in the sales agreement and compliance with applicable law, we have the discretion to deliver placement notices to the Sales Agents at any time throughout the term of the sales agreement. The number of shares that are sold through the applicable Sales Agent after delivering a placement notice will fluctuate based on a number of factors, including the market price of our common stock during the sales period, any limits we may set with the applicable Sales Agent in any applicable placement notice and the demand for our common stock. Because the price per share of each share sold pursuant to the sales agreement will fluctuate over time, it is not currently possible to predict the aggregate proceeds to be raised in connection with sales under the sales agreement.

Sales of common stock offered hereby will be in an “at the market offering,” and investors who buy shares at different times will likely pay different prices.

Investors who purchase shares in this offering at different times will likely pay different prices, and accordingly may experience different levels of dilution and different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices and number of shares sold in this offering. In addition, subject to the final determination by our board of directors or any restrictions we may place in any applicable placement notice delivered to the applicable Sales Agent, there is no minimum or maximum sales price for shares to be sold in this offering. Investors may experience a decline in the value of the shares they purchase in this offering as a result of sales made at prices lower than the prices they paid.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the accompanying prospectus contain “forward-looking statements” within the meaning of the federal securities laws, which statements involve substantial risks and uncertainties. In some cases, you can identify forward-looking statements by terms such as “may,” “might,” “will,” “objective,” “intend,” “should,” “could,” “can,” “would,” “expect,” “believe,” “design,” “estimate,” “predict,” “potential,” “plan,” “anticipate,” “target,” “forecast” or the negative of these terms, and similar expressions intended to identify forward-looking statements.

Forward-looking statements involve known and unknown risks, uncertainties and other factors that could cause our actual results to differ materially from the forward-looking statements expressed or implied in this prospectus supplement and the accompanying prospectus. Such risks, uncertainties and other factors include, among others, the factors disclosed in the section titled “Risk Factors” in this prospectus supplement and the accompanying prospectus and the sections titled “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” in our most recent Annual Report on Form 10-K, and in our subsequent Quarterly Reports on Form 10-Q, which are incorporated by reference herein, and the following risks, uncertainties and factors:

- our plans to develop and commercialize pegozafermin or any future product candidates;
- our ongoing and planned clinical trials;
- our positive results from a clinical study may not necessarily be predictive of the results of future or ongoing clinical studies;
- the timing of and our ability to obtain regulatory approvals for pegozafermin or any future product candidates;
- the effect of the ongoing COVID-19 pandemic on our business;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our ability to identify additional products or product candidates with significant commercial potential that are consistent with our commercial objectives;
- the rate and degree of market acceptance and clinical utility of pegozafermin or any future product candidates, if approved;
- our commercialization, marketing and manufacturing capabilities and strategy;
- substantial competition in our industry and with respect to the product candidates that we are developing;
- our intellectual property position;
- loss of key members of management;
- failure to successfully execute our growth strategy, including any delays in our planned future growth;
- our failure to maintain effective internal controls;
- our expected use of net proceeds from this offering; and
- other risks and uncertainties, including those listed or incorporated by reference in “Risk Factors.”

We caution you that the risks, uncertainties and other factors referred to above, elsewhere in this prospectus supplement and the accompanying prospectus and in the documents incorporated by reference herein may not contain all of the risks, uncertainties and other factors that may affect our future results and operations. Moreover, new risks will emerge from time to time. It is not possible for our management to predict all risks. In

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addition, we cannot assure you that we will realize the results, benefits or developments that we expect or anticipate or, even if substantially realized, that they will result in the consequences or affect us or our business in the way expected. Forward-looking statements are not historical facts, and reflect our current views with respect to future events. Given the significant uncertainties, you should evaluate all forward-looking statements made in this prospectus supplement and the accompanying prospectus in the context of these risks and uncertainties and not place undue reliance on these forward-looking statements as predictions of future events.

All forward-looking statements in this prospectus supplement apply only as of the date made and are expressly qualified in their entirety by the cautionary statements included in this prospectus supplement. We disclaim any intent to publicly update or revise any forward-looking statements to reflect subsequent events or circumstances, except as required by law.

USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate sales proceeds of up to \$150,000,000 from time to time. Because there is no minimum offering amount required pursuant to the sales agreement, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. Actual net proceeds will depend on the number of shares we sell and the prices at which such sales occur. There can be no assurance that we will sell any shares under or fully utilize the sales agreement with the Sales Agents as a source of financing.

We currently intend to use the net proceeds from this offering, if any, for development, manufacturing and scale-up, as well as for working capital and general corporate purposes. We may also use a portion of the proceeds to license, acquire or invest in new programs or for drug development activities related to such programs, however, we have no current commitments to do so.

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 partnering and commercialization efforts, technological advances and the competitive environment for our 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 the sale of the securities offered by us hereunder. 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.

DILUTION

If you purchase common stock in this offering, your ownership interest will be diluted to the extent of the difference between the purchase price per share and the as adjusted net tangible book value per share after giving effect to this offering. We calculate net tangible book value per share by dividing the net tangible book value, which is total tangible assets less total liabilities, by the number of outstanding shares of our common stock. Dilution represents the difference between the portion of the amount per share paid by purchasers of shares in this offering and the as adjusted net tangible book value per share of our common stock immediately after giving effect to this offering. Our net tangible book value as of September 30, 2022, was approximately \$152.4 million, or \$3.49 per share.

After giving effect to the assumed sale of 10,924,981 shares of our common stock at a sale price of \$13.73 per share, the last sale price of our common stock on the Nasdaq Global Market on February 13, 2023, after deducting commissions and estimated aggregate offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2022, would have been \$297.5 million, or \$5.45 per share of common stock. This represents an immediate increase in the as adjusted net tangible book value of \$1.96 per share to our existing stockholders and an immediate dilution of \$8.28 per share to new investors purchasing shares in this offering. The following table illustrates this per share dilution:

Assumed offering price per share	\$13.73
Net tangible book value per share as of September 30, 2022	\$3.49
Increase in net tangible book value per share attributable to new investors in offering	<u>\$1.96</u>
As adjusted net tangible book value per share as of September 30, 2022, after giving effect to this offering	\$ 5.45
Dilution per share to new investors in this offering	<u>\$ 8.28</u>

The above illustration of dilution per share to investors participating in this offering assumes no exercise of outstanding options to purchase our common stock.

Changes in the assumed public offering price of \$13.73 per share would not affect our as adjusted net tangible book value after this offering because this offering is currently limited to \$150,000,000. However, each \$1.00 increase (decrease) in the assumed public offering price of \$13.73 per share would increase (decrease) the dilution per share to new investors by approximately \$0.92 per share ((\$0.92) per share), assuming that the aggregate dollar amount of shares offered by us, as set forth above, remains at \$150,000,000 and after deducting the commissions and estimated offering expenses payable by us. The information discussed above is illustrative only and will adjust based on the actual public offering price, the actual number of shares that we offer in this offering, and other terms of this offering determined at the time of each offer and sale.

The number of our shares of common stock outstanding is based on 43,624,625 shares of common stock outstanding as of September 30, 2022, and excludes the following, all as of September 30, 2022:

- 3,123,221 shares of our common stock issuable upon the exercise of stock options outstanding as of September 30, 2022, under our 2019 Equity Incentive Plan (as amended and restated, the “2019 Plan”) at a weighted-average exercise price of \$13.05 per share;
- 103,000 shares of our common stock issuable upon the exercise of stock options granted subsequent to September 30, 2022, under the 2019 Plan at a weighted-average exercise price of \$8.12 per share;
- 25,000 shares of our common stock issuable upon exercise of an outstanding warrant at an exercise price of \$22.06 per share (which expires on June 30, 2025);

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- 33,923 shares of our common stock issuable upon exercise of an outstanding warrant at an exercise price of \$19.12 per share (which expires on May 28, 2031);
- 241,946 shares of our common stock reserved for future issuance under our 2019 Plan, as well as any automatic increase in the number of shares of common stock reserved for future issuance thereunder; and
- 731,603 shares of our common stock reserved for future issuance under our 2019 Employee Stock Purchase Plan, as well as any automatic increase in the number of shares of common stock reserved for future issuance thereunder.

To the extent that options outstanding as of September 30, 2022, have been or are exercised, or other shares are issued, investors purchasing shares in this offering could experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

PLAN OF DISTRIBUTION

We previously entered into a sales agreement with SVB Securities and Cantor Fitzgerald & Co., under which we may offer and sale from time to time. Sales of our common stock, if any, will be made at market prices by any method that is deemed to be an “at the market offering” as defined in Rule 415(a)(4) under the Securities Act, including sales made directly on the Nasdaq Global Market or any other trading market for our common stock. Under this prospectus supplement and the accompanying prospectus, and in accordance with the terms of the sales agreement, as amended, we may offer and sell up to \$150,000,000 of shares of our common stock.

The below description of the material provisions of the sales agreement does not purport to be a complete statement of its terms and conditions.

The Sales Agents will offer our common stock subject to the terms and conditions of the sales agreement on a daily basis or as otherwise agreed upon by us and the Sales Agents. We will designate the maximum amount of common stock to be sold through the Sales Agents on a daily basis or otherwise determine such maximum amount together with the Sales Agents. Subject to the terms and conditions of the sales agreement, the Sales Agents will use their commercially reasonable efforts consistent with their normal trading and sales practices to sell such shares up to the amount specified on such terms. We may instruct the Sales Agents not to sell common stock if the sales cannot be effected at or above the price designated by us in any such instruction. The Sales Agents or we may suspend the offering of our common stock being made through the Sales Agents under the sales agreement upon proper notice to the other party. The Sales Agents and we each have the right, by giving written notice as specified in the sales agreement, to terminate the sales agreement in each party’s sole discretion at any time.

The aggregate compensation payable to the Sales Agents is up to 3.0% of the aggregate gross sales price of the shares sold through it pursuant to the sales agreement. We have also agreed to reimburse the Sales Agents up to an aggregate of \$50,000 of the Sales Agents’ actual outside legal expenses incurred by the Sales Agents in connection with this offering and certain ongoing expenses. We estimate that the total expenses of the offering payable by us, excluding commissions payable to the Sales Agents under the sales agreement, will be approximately \$350,000.

The remaining sales proceeds, after deducting any expenses payable by us and any transaction fees imposed by any governmental, regulatory, or self-regulatory organization in connection with the sales, will equal our net proceeds for the sale of such common stock.

A Sales Agent will provide written confirmation to us following the close of trading on The Nasdaq Global Market on each day in which common stock is sold through it as sales agent under the sales agreement. Each confirmation will include the number of shares of common stock sold through it as sales agent on that day, the volume weighted average price of the shares sold, the percentage of the daily trading volume and the net proceeds to us.

We will report at least quarterly the number of shares of common stock sold through the Sales Agents under the sales agreement, the net proceeds to us and the compensation paid by us to the Sales Agents in connection with the sales of common stock.

Settlement for sales of common stock will occur on the second business day that is also a trading day following the date on which any sales were made in return for payment of the net proceeds to us. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

In connection with the sales of our common stock on our behalf, the Sales Agents will each be deemed to be an “underwriter” within the meaning of the Securities Act and the compensation paid to the Sales Agents will be deemed to be underwriting commissions or discounts. We have agreed in the sales agreement to provide

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indemnification and contribution to the Sales Agents against certain liabilities, including liabilities under the Securities Act. As Sales Agents, SVB Securities and Cantor will not engage in any transactions that stabilize our common stock.

Our common stock is listed on the Nasdaq Global Market and trades under the symbol “ETNB.” The transfer agent of our common stock is currently American Stock Transfer and Trust Company, LLC.

The Sales Agents and/or their affiliates have provided, and may in the future provide, various investment banking, commercial banking, financial advisory and other financial services for us and our affiliates for which services they have received and, may in the future receive, customary fees.

LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by Gibson, Dunn & Crutcher LLP. SVB Securities LLC and Cantor Fitzgerald & Co. are being represented in this offering by Cooley LLP, New York, New York.

EXPERTS

The consolidated financial statements of 89bio, Inc. as of December 31, 2021 and 2020, and for each of the years in the two-year period ended December 31, 2021, have been incorporated by reference herein and in the registration statement in reliance upon the report of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus supplement is part of the registration statement on Form S-3 we filed with the SEC under the Securities Act and does not contain all the information set forth in the registration statement. Whenever a reference is made in this prospectus supplement to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference into this prospectus supplement for a copy of such contract, agreement or other document. Because we are subject to the information and reporting requirements of the Exchange Act, we file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at www.sec.gov.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference the information and reports we file with it, which means that we can disclose important information to you by referring you to those publicly available documents. The information incorporated by reference is an important part of this prospectus supplement, and information that we file after the date hereof with the SEC will automatically update and supersede the information already incorporated by reference. We are incorporating by reference the documents listed below:

- Annual Report on [Form 10-K](#) for the year ended December 31, 2021 filed with the SEC on March 24, 2022 (and any portions of our [Definitive Proxy Statement on Schedule 14A](#) filed on April 14, 2022 that are incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2021);
- Quarterly Reports on Form 10-Q for the quarters ended [March 31, 2022](#), [June 30, 2022](#) and [September 30, 2022](#), filed with the SEC on May 12, 2022, August 11, 2022 and November 10, 2022, respectively;
- Current Reports on Form 8-K filed with the SEC on [June 7, 2022](#), [June 28, 2022](#), [July 1, 2022](#), [January 6, 2023](#) (as amended on [February 2, 2023](#)) and [February 15, 2023](#); and
- the description of our common stock contained in our registration statement on [Form 8-A](#) filed with the SEC on November 1, 2019, including any amendments or reports filed for the purposes of updating this description.

Because we are incorporating by reference future filings with the SEC, this prospectus supplement is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus supplement. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus supplement or in any document previously incorporated by reference have been modified or superseded.

This prospectus supplement incorporates by reference the documents listed above and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act between the date of the initial registration statement and the effectiveness of the registration statement and following the effectiveness of the registration statement until the offering of the securities under the registration statement is terminated or completed, except that we are not incorporating by reference any information furnished (and not filed) with the SEC, including any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K (unless expressly provided to the contrary).

You may request a copy of these filings (other than exhibits to such documents unless such exhibits are specifically incorporated by reference herein), at no cost, by contacting us, either orally or in writing, at the following:

89bio, Inc.
142 Sansome Street, 2nd Floor
San Francisco, California 94104
(415) 432-9270

Information about us, including our reports filed with the SEC, is available through our website at www.89bio.com. Such reports are accessible at no charge through our website and are made available as soon as reasonably practicable after such material is filed with or furnished to the SEC. Our website and the information contained on that website, or connected to that website, are not incorporated by reference in this prospectus supplement. We have authorized no one to provide you with any information that differs from that contained in this prospectus supplement. Accordingly, we take no responsibility for any other information that others may give you. You should not assume that the information in this prospectus supplement is accurate as of any date other than the date of the front cover of this prospectus supplement.

PROSPECTUS



**COMMON STOCK
PREFERRED STOCK
DEBT SECURITIES
WARRANTS
UNITS**

From time to time, we may issue, in one or more series or classes, up to \$500,000,000 in aggregate principal amount of our common stock, preferred stock, debt securities, warrants and/or units, at prices and on terms that we will determine at the time of the offering.

This prospectus provides you with a general description of the securities we may offer. Each time we offer securities, we will provide specific terms of the securities offered in a supplement to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may also add, update or change information contained in this prospectus. We may not sell any securities under this prospectus without delivery of the applicable prospectus supplement. If information in any prospectus supplement is inconsistent with the information in this prospectus, then the information in that prospectus supplement will apply and will supersede the information in this prospectus.

You should read this prospectus, the applicable prospectus supplement and any related free writing prospectus carefully, as well as any documents incorporated by reference, before you invest in any of the securities being offered.

Our shares of common stock are listed on the Nasdaq Global Market under the symbol “ETNB.” The last reported sale price of our common stock on the Nasdaq Global Market on January 27, 2023 was \$11.50 per share. We recommend that you obtain current market quotations for our common stock prior to making an investment decision.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading “[Risk Factors](#)” contained in this prospectus beginning on page 5 and any applicable prospectus supplement, and under similar headings in the other documents that are incorporated by reference into this prospectus.

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

Prospectus dated February 14, 2023

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ABOUT THIS PROSPECTUS

This prospectus is a part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission (the “SEC” or the “Commission”) utilizing a “shelf” registration process. Under this shelf registration process, we may sell any combination of the securities described in this prospectus in one or more offerings up to a total dollar amount of \$500,000,000. This prospectus provides you with a general description of the securities we may offer.

Each time we sell securities under this prospectus, we will provide a prospectus supplement that will contain specific information about the 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 and any related free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in any documents that we have incorporated by reference into this prospectus. You should carefully read both this prospectus and any prospectus supplement together with additional information under the headings “Where You Can Find More Information” and “Incorporation of Certain Information by Reference.”

We have not authorized anyone to provide you with any information other than that contained or incorporated by reference in this prospectus and any applicable prospectus supplement, along with the information contained in any free writing prospectuses we have authorized for use in connection with a specific offering. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. This prospectus, any applicable supplement to this prospectus or any related free writing prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this prospectus, any applicable supplement to this prospectus or any related free writing prospectus constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction.

You should not assume that the information contained in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus, any applicable prospectus supplement or any related free writing prospectus is delivered, or securities are sold, on a later date.

Unless the context otherwise requires, we use the terms “89bio,” “company,” “we,” “us,” and “our” in this prospectus to refer to 89bio, Inc. and, where appropriate, our subsidiaries.

CAUTIONARY STATEMENT CONCERNING FORWARD-LOOKING STATEMENTS

This prospectus, including the documents that we incorporate by reference, contains “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933, as amended (the “Securities Act”), and Section 21E of the Securities Exchange Act of 1934, as amended (the “Exchange Act”). All statements, other than statements of historical facts contained in this prospectus, including statements concerning our plans, objectives, goals, strategies, future events, future revenues or performance, financing needs, plans or intentions relating to acquisitions, business trends and other information referred to in the section entitled “Risk Factors” in this prospectus and the sections entitled “Business,” “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” in our Annual Report on Form 10-K for the year ended December 31, 2021, which is incorporated by reference herein, are forward-looking statements. Forward-looking statements generally relate to future events or our future financial or operating performance. In some cases, you can identify forward-looking statements by terms such as “may,” “might,” “will,” “objective,” “intend,” “should,” “could,” “can,” “would,” “expect,” “believe,” “design,” “estimate,” “predict,” “potential,” “plan,” “anticipate,” “target,” “forecast,” or the negative of these terms, and similar expressions intended to identify forward-looking statements. Forward-looking statements are not historical facts and reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements.

There are a number of risks, uncertainties and other important factors that could cause our actual results to differ materially from the forward-looking statements contained in this prospectus. Such risks, uncertainties and other important factors include, among others, the risks, uncertainties and factors set forth in “Risk Factors,” and the following risks, uncertainties and factors:

- our plans to develop and commercialize pegozafermin or any future product candidates;
- our ongoing and planned clinical trials;
- our positive results from a clinical study may not necessarily be predictive of the results of future or ongoing clinical studies;
- the timing of and our ability to obtain regulatory approvals for pegozafermin or any future product candidates;
- the effect of the ongoing COVID-19 pandemic on our business;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our ability to identify additional products or product candidates with significant commercial potential that are consistent with our commercial objectives;
- the rate and degree of market acceptance and clinical utility of pegozafermin or any future product candidates, if approved;
- our commercialization, marketing and manufacturing capabilities and strategy;
- substantial competition in our industry and with respect to the product candidates that we are developing;
- our intellectual property position;
- loss of key members of management;
- failure to successfully execute our growth strategy, including any delays in our planned future growth;
- our failure to maintain effective internal controls; and
- other risks and uncertainties, including those incorporated by reference in “Risk Factors.”

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There may be other factors that may cause our actual results to differ materially from the forward-looking statements, including factors disclosed in “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” in our Annual Report on Form 10-K for the year ended December 31, 2021, which is incorporated by reference herein. You should evaluate all forward-looking statements made in this prospectus in the context of these risks and uncertainties.

These factors should not be construed as exhaustive and should be read in conjunction with the other cautionary statements that are included in this prospectus, any accompanying prospectus supplement, information incorporated by reference herein or therein, and any related free-writing prospectus. In addition, we cannot assure you that we will realize the results, benefits or developments that we expect or anticipate or, even if substantially realized, that they will result in the consequences or affect us or our business in the way expected. All forward-looking statements contained in this prospectus are made as of the date of hereof and we undertake no obligation to publicly update or review any forward-looking statements to reflect subsequent events or circumstances.

THE COMPANY

We are a clinical-stage biopharmaceutical company focused on the development and commercialization of innovative therapies for the treatment of liver and cardio-metabolic diseases. Our lead product candidate, pegozafermin (previously BIO89-100), a specifically engineered glycoPEGylated analog of fibroblast growth factor 2, is currently being developed for the treatment of severe hypertriglyceridemia and nonalcoholic steatohepatitis.

Corporate Information

We were incorporated in January 2018 in Israel under the name 89Bio Ltd. 89bio, Inc., the registrant whose name appears on the cover page of this prospectus, was incorporated in June 2019 for the purpose of an internal reorganization transaction.

Our principal executive offices are located at 142 Sansome Street, San Francisco, California 94104 and our telephone number is (415) 432-9270. Our website is www.89bio.com. The information on, or that can be accessed through, our website is not part of this prospectus and is not incorporated by reference herein.

RISK FACTORS

Investing in our securities involves risks. You should carefully consider the risks, uncertainties and other factors described in our most recent Annual Report on Form 10-K, as supplemented and updated by subsequent Quarterly Reports on Form 10-Q and Current Reports on Form 8-K that we have filed or will file with the SEC, and in other documents which are incorporated by reference into this prospectus, as well as the risk factors and other information contained in or incorporated by reference into any accompanying prospectus supplement before investing in any of our securities. Our business, financial condition, results of operations, cash flows or prospects could be materially and adversely affected by any of these risks. The risks and uncertainties described in the documents incorporated by reference herein are not the only risks and uncertainties that you may face.

For more information about our SEC filings, please see “Where You Can Find More Information” and “Incorporation of Certain Information by Reference.”

USE OF PROCEEDS

We will retain broad discretion over the use of the net proceeds from the sale of the securities offered hereby. Unless otherwise specified in a prospectus supplement accompanying this prospectus, the net proceeds from the sale by us of the securities to which this prospectus relates will be used for development, manufacturing and scale-up, as well as for working capital and general corporate purposes. We may also use a portion of the proceeds to license, acquire or invest in new programs or for drug development activities related to such programs, however, we have no current commitments to do so. Our expected use of proceeds from the sale of the securities offered hereby represents our current intentions based on our present plans and business condition. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the proceeds to be received from the sale of the securities offered hereby or the amounts that we will actually spend on the uses set forth above.

Pending the use of the net proceeds, we may invest the proceeds in interest-bearing, investment-grade securities, certificates of deposit or government securities. When we offer and sell the securities to which this prospectus relates, the prospectus supplement related to such offering will set forth our intended use of the proceeds, if any, received from the sale of such securities.

SECURITIES WE MAY OFFER

This prospectus contains summary descriptions of the securities we may offer from time to time. These summary descriptions are not meant to be complete descriptions of each security. The particular terms of any security will be described in the applicable prospectus supplement.

DESCRIPTION OF SECURITIES

The following is a summary of the material terms of our capital stock, as well as other material terms of certain provisions of Delaware law, our second amended and restated certificate of incorporation (as amended from time to time, our “certificate of incorporation”), and our second amended and restated bylaws (as amended from time to time, our “bylaws”). This summary does not purport to be complete and is qualified in its entirety by the provisions of our certificate of incorporation and our bylaws. For more information on how you can obtain our certificate of incorporation and our bylaws, see the heading “Where You Can Find More Information.”

Our authorized capital stock consists of 100,000,000 shares of common stock, par value \$0.001 per share, and 10,000,000 shares of preferred stock, par value \$0.001 per share.

As of December 31, 2022, 50,560,590 shares of our common stock were issued and outstanding.

Common Stock

Our certificate of incorporation authorizes the issuance of up to 100,000,000 shares of our common stock. All outstanding shares of our common stock are validly issued, fully paid and nonassessable.

The holders of our common stock are entitled to one vote per share on all matters submitted to a vote of stockholders. A majority vote of the shares present in person or represented by proxy and entitled to vote on the subject matter is required for the holders of our common stock to take action on all matters (except for election of directors (as discussed below)), except as otherwise required by law, our certificate of incorporation or our bylaws. Our certificate of incorporation does not provide for cumulative voting in the election of directors. The holders of our common stock will receive ratably any dividends declared by our board of directors out of funds legally available therefor. In the event of our liquidation, dissolution or winding-up, the holders of our common stock will be entitled to share ratably in all assets remaining after payment of or provision for any liabilities.

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

Our certificate of incorporation and our bylaws include a number of provisions that may have the effect of delaying, deferring or preventing another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts.

- **Issuance of undesignated preferred stock:** Under our certificate of incorporation, our board of directors has the authority, without further action by the stockholders, to issue up to 10,000,000 shares of undesignated preferred stock with rights and preferences, including voting rights, designated from time to time by our board of directors. The existence of authorized but unissued shares of preferred stock enables our board of directors to make it more difficult to attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise.
- **Classified board:** Our certificate of incorporation establishes a classified board of directors consisting of three classes of directors, with staggered three-year terms. Only one class of directors will be elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms. This provision may have the effect of delaying a change in control of our board of directors.
- **Election and removal of directors and board vacancies:** Our bylaws provide that directors will be elected by a plurality vote. Our certificate of incorporation and bylaws also provide that our board of directors has the right to increase or decrease the size of the board and to fill vacancies on the board. Directors may be removed only for cause by the affirmative vote of the holders of at least 66 2/3% of the votes that all our stockholders would be entitled to cast in an annual election of directors. Only our

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board of directors is authorized to fill vacant directorships. In addition the number of directors constituting our board of directors may be set only by resolution adopted by a majority vote of the directors then in office. These provisions prevent stockholders from increasing the size of our board of directors and gaining control of our board of directors by filling the resulting vacancies with its own nominees.

- **Requirements for advance notification of stockholder nominations and proposals:** Our bylaws establish advance notice procedures with respect to stockholder proposals and the nomination of candidates for election as directors that specify certain requirements as to the timing, form and content of a stockholder's notice. Business that may be conducted at an annual meeting of stockholders will be limited to those matters properly brought before the meeting. These provisions may make it more difficult for our stockholders to bring matters before our annual meeting of stockholders or to nominate directors at annual meetings of stockholders.
- **No written consent of stockholders:** Our certificate of incorporation provides that all stockholder actions be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting. This limit may lengthen the amount of time required to take stockholder actions and would prevent the amendment of our bylaws or removal of directors by our stockholders without holding a meeting of stockholders.
- **No stockholder ability to call special meetings:** Our certificate of incorporation and bylaws provide that only a majority of the members of our board of directors then in office may be able to call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders.
- **Amendments to certificate of incorporation and bylaws:** Any amendment to our certificate of incorporation will be required to be approved by a majority of our board of directors as well as, if required by law or the certificate of incorporation, a majority of the outstanding shares entitled to vote on the amendment and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of provisions to board classification, stockholder action, certificate amendments, and liability of directors must be approved by not less than 66 2/3% of the outstanding shares entitled to vote on the amendment, voting together as a single class. Any amendment to our bylaws must be approved by either a majority of our board of directors or not less than 66 2/3% of the outstanding shares entitled to vote on the amendment, voting together as a single class.

These provisions are designed to enhance the likelihood of continued stability in the composition of our board of directors and its policies, to discourage certain types of transactions that may involve an actual or threatened acquisition of us and to reduce our vulnerability to an unsolicited acquisition proposal. We also designed these provisions to discourage certain tactics that may be used in proxy fights. However, these provisions could have the effect of discouraging others from making tender offers for our shares and, as a consequence, they may also reduce fluctuations in the market price of our shares that could result from actual or rumored takeover attempts.

Section 203 of the Delaware General Corporation Law

We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner.

Choice of Forum

Our certificate of incorporation requires that the Court of Chancery of the State of Delaware be the exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: (1) any derivative action or proceeding brought on our behalf; (2) any action asserting a breach of fiduciary duty owed

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by any director, officer or other employee to us or our stockholders; (3) any action asserting a claim against us or any director or officer or other employee arising pursuant to the Delaware General Corporation Law, our certificate of incorporation or our bylaws; or (4) any action asserting a claim against us or any director or officer or other employee that is governed by the internal affairs doctrine. This provision would not apply to claims brought to enforce a duty or liability created by the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction. Our certificate of incorporation provides further that the federal district courts of the United States will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, subject to and contingent upon a final adjudication in the State of Delaware of the enforceability of such exclusive forum provision. Although we believe these provisions benefit us by providing increased consistency in the application of Delaware law for the specified types of actions and proceedings, the provisions may have the effect of discouraging lawsuits against us or our directors or officers.

Transfer Agent and Registrar

American Stock Transfer and Trust Company, LLC serves as the transfer agent and registrar for our common stock.

Listing

Our common stock is listed on the Nasdaq Global Market under the symbol “ETNB.”

Preferred Stock

Under the terms of our certificate of incorporation, our board of directors has the authority, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, to fix the dividend, voting and other rights, preferences and privileges of the shares of each wholly unissued series and any qualifications, limitations or restrictions thereon, and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding.

Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of our common stock. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in our control and may adversely affect the market price of our common stock and the voting and other rights of the holders of our common stock. As of December 31, 2022, there were no shares of preferred stock issued and outstanding, and we have no current plans to issue any shares of preferred stock.

Debt Securities

The paragraphs below describe the general terms and provisions of the debt securities we may issue. When we offer to sell a particular series of debt securities, we will describe the specific terms of the securities in a supplement to this prospectus, including any additional covenants or changes to existing covenants relating to such series. The prospectus supplement also will indicate whether the general terms and provisions described in this prospectus apply to a particular series of debt securities. You should read the actual indenture if you do not fully understand a term or the way we use it in this prospectus.

If we issue debt securities at a discount from their principal amount, then, for purposes of calculating the aggregate initial offering price of the offered securities issued under this prospectus, we will include only the initial offering price of the debt securities and not the principal amount of the debt securities.

We have summarized below the material provisions of the indenture, or indicated which material provisions will be described in the related prospectus supplement. The prospectus supplement relating to any particular securities

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offered will describe the specific terms of the securities, which may be in addition to or different from the general terms summarized in this prospectus. We have included the form of the indenture as an exhibit to our registration statement of which this prospectus is a part, and it is incorporated into this prospectus by reference. Because the summary in this prospectus and in any prospectus supplement does not contain all of the information that you may find useful, you should read the documents relating to the securities that are described in this prospectus or in any applicable prospectus supplement. Please read “Where You Can Find More Information” in this prospectus to find out how you can obtain a copy of those documents. References below to an “indenture” are references to the indenture, as supplemented, under which a particular series of debt securities is issued. As used under this caption, the term “debt securities” includes the debt securities being offered by this prospectus and all other debt securities issued by us under the indenture.

General

The indenture:

- does not limit the amount of debt securities that we may issue;
- allows us to issue debt securities in one or more series;
- does not require us to issue all of the debt securities of a series at the same time; and
- allows us to reopen a series to issue additional debt securities without the consent of the holders of the debt securities of such series.

The prospectus supplement for each offering of debt securities will provide the following terms, where applicable:

- the title of the debt securities and whether they are senior, senior subordinated or subordinated debt securities;
- the aggregate principal amount of the debt securities being offered and any limit on their aggregate principal amount, and, if the series is to be issued at a discount from its face amount, the method of computing the accretion of such discount;
- the price at which the debt securities will be issued, expressed as a percentage of the principal and, if other than the full principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof or, if applicable, the portion of the principal amount of such debt securities that is convertible into common stock or preferred stock or the method by which any such portion shall be determined;
- if convertible, the terms on which such debt securities are convertible, including the initial conversion price or rate or the method of calculation, how and when the conversion price or exchange ratio may be adjusted, whether conversion or exchange is mandatory, at the option of the holder or at our option, the conversion or exchange period, and any other provision in relation thereto, and any applicable limitations on the ownership or transferability of common stock or preferred stock received on conversion;
- the date or dates, or the method for determining the date or dates, on which the principal of the debt securities will be payable;
- the fixed or variable interest rate or rates of the debt securities, or the method by which the interest rate or rates is determined;
- the date or dates, or the method for determining the date or dates, from which interest will accrue;
- the dates on which interest will be payable;
- the record dates for interest payment dates, or the method by which we will determine those dates;

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- the persons to whom interest will be payable;
- the basis upon which interest will be calculated if other than that of a 360-day year of twelve 30-day months;
- Any collateral securing the performance of our obligations under the debt securities;
- the place or places where the principal of, premium, if any, and interest on, the debt securities will be payable;
- where the debt securities may be surrendered for registration of transfer or conversion or exchange;
- where notices or demands to or upon us in respect of the debt securities and the applicable indenture may be served;
- any provisions regarding our right to redeem or purchase debt securities or the right of holders to require us to redeem or purchase debt securities;
- any right or obligation we have to redeem, repay or purchase the debt securities pursuant to any sinking fund or analogous provision;
- the currency or currencies (including any composite currency) in which the debt securities are denominated and payable if other than United States dollars, and the currency or currencies (including any composite currency) in which principal, premium, if any, and interest, if any, will be payable, and if such payments may be made in a currency other than that in which the debt securities are denominated, the manner for determining such payments, including the time and manner of determining the exchange rate between the currency in which such securities are denominated and the currency in which such securities or any of them may be paid, and any additions to, modifications of or deletions from the terms of the debt securities to provide for or to facilitate the issuance of debt securities denominated or payable in a currency other than U.S. dollars;
- whether the amount of payments of principal of, premium, if any, or interest on, the debt securities may be determined according to an index, formula or other method and how such amounts will be determined;
- whether the debt securities will be in registered form, bearer form or both, and the terms of these forms;
- whether the debt securities will be issued in whole or in part in the form of a global security and, if applicable, the identity of the depository for such global security;
- any provision for electronic issuance of the debt securities or issuance of the debt securities in uncertificated form;
- whether and upon what terms the debt securities of such series may be defeased or discharged, if different from the provisions set forth in the indenture for the series to which the supplemental indenture or authorizing resolution relates;
- any provisions granting special rights to holders of securities upon the occurrence of such events as specified in the applicable prospectus supplement;
- any deletions from, modifications of, or additions to our events of default or covenants or other provisions set forth in the indenture for the series to which the supplemental indenture or authorizing resolution relates; and
- any other material terms of the debt securities, which may be different from the terms set forth in this prospectus.

We may issue debt securities at a discount below their principal amount and provide for less than the entire principal amount thereof to be payable upon declaration of acceleration of the maturity of the debt securities. We

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refer to any such debt securities throughout this prospectus as “original issue discount securities.” The applicable prospectus supplement will describe the United States federal income tax consequences and other relevant considerations applicable to original issue discount securities.

Neither the Delaware General Corporation Law nor our governing instruments define the term “substantially all” as it relates to the sale of assets. Additionally, Delaware cases interpreting the term “substantially all” rely upon the facts and circumstances of each particular case. Consequently, to determine whether a sale of “substantially all” of our assets has occurred, a holder of debt securities must review the financial and other information that we have disclosed to the public.

The applicable prospectus supplement will also describe any material covenants to which a series of debt securities will be subject and the applicability of those covenants to any of our subsidiaries to be restricted thereby, which are referred to herein as “restricted subsidiaries.” The applicable prospectus supplement will also describe provisions for restricted subsidiaries to cease to be restricted by those covenants.

Events of Default

Unless the applicable prospectus supplement states otherwise, when we refer to “events of default” as defined in the indentures with respect to any series of debt securities, we mean:

- our failure to pay interest on any debt security of such series when the same becomes due and payable and the continuance of any such failure for a period of 30 days;
- our failure to pay the principal or premium of any debt security of such series when the same becomes due and payable at maturity, upon acceleration, redemption or otherwise;
- our failure or the failure of any restricted subsidiary to comply with any of its agreements or covenants in, or provisions of, the debt securities of such series or the indenture (as they relate thereto) and such failure continues for a period of 60 days after our receipt of notice of the default from the trustee or from the holders of at least 25 percent in aggregate principal amount of the then outstanding debt securities of that series (except in the case of a default with respect to the provisions of the indenture regarding the consolidation, merger, sale, lease, conveyance or other disposition of all or substantially all of the assets of us (or any other provision specified in the applicable supplemental indenture or authorizing resolution), which will constitute an event of default with notice but without passage of time); or
- certain events of bankruptcy, insolvency or reorganization occur with respect to 89bio or any restricted subsidiary of 89bio that is a significant subsidiary (as defined in the indenture).

If an event of default occurs and is continuing with respect to debt securities of any series outstanding, then the trustee or the holders of 25% or more in principal amount of the outstanding debt securities of that series will have the right to declare the principal amount of all the debt securities of that series to be due and payable immediately. However, the holders of at least a majority in principal amount of outstanding debt securities of such series may rescind and annul such declaration and its consequences, except an acceleration due to nonpayment of principal or interest on such series, if the rescission would not conflict with any judgment or decree and if all existing events of default with respect to such series have been cured or waived.

The indenture also provides that the holders of at least a majority in principal amount of the outstanding debt securities of any series, by notice to the trustee, may, on behalf of all holders, waive any existing default and its consequences with respect to such series of debt securities, other than any event of default in payment of principal or interest.

The indenture will require the trustee to give notice to the holders of debt securities within 90 days after the trustee obtains knowledge of a default that has occurred and is continuing. However, the trustee may withhold

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notice to the holders of any series of debt securities of any default, except a default in payment of principal or interest, if any, with respect to such series of debt securities, if the trustee considers it in the interest of the holders of such series of debt securities to do so.

The holders of a majority of the outstanding principal amount of the debt securities of any series will have the right to direct the time, method and place of conducting any proceedings for any remedy available to the trustee with respect to such series, subject to limitations specified in the indenture.

Amendment, Supplement and Waiver

Without notice to or the consent of any holder, we and the trustee may amend or supplement the indenture or the debt securities of a series:

- to cure any ambiguity, omission, defect or inconsistency;
- to comply with the provisions of the indenture regarding the consolidation, merger, sale, lease, conveyance or other disposition of all or substantially all of our assets;
- to provide that specific provisions of the indenture shall not apply to a series of debt securities not previously issued or to make a change to specific provisions of the indenture that only applies to any series of debt securities not previously issued or to additional debt securities of a series not previously issued;
- to create a series and establish its terms;
- to provide for uncertificated debt securities in addition to or in place of certificated debt securities;
- to release a guarantor in respect of any series which, in accordance with the terms of the indenture applicable to such series, ceases to be liable in respect of its guarantee;
- to add a guarantor subsidiary in respect of any series of debt securities;
- to secure any series of debt securities;
- to add to the covenants of 89bio for the benefit of the holders or surrender any right or power conferred upon 89bio;
- to appoint a successor trustee with respect to the securities;
- to comply with requirements of the SEC in order to effect or maintain the qualification of the indenture under the Trust Indenture Act;
- to make any change that does not adversely affect the rights of holders; or
- to conform the provisions of the indenture to the final offering document in respect of any series of debt securities.

The indenture will provide that we and the trustee may amend or supplement any provision of the debt securities of a series or of the indenture relating to such series with the written consent of the holders of at least a majority in principal amount of the outstanding debt securities of such series. However, without the consent of each holder of a debt security the terms of which are directly amended, supplemented or waived, an amendment, supplement or waiver may not:

- reduce the amount of debt securities of such series whose holders must consent to an amendment, supplement or waiver;
- reduce the rate of or extend the time for payment of interest, including defaulted interest;
- reduce the principal of or extend the fixed maturity of any debt security or alter the provisions with respect to redemptions or mandatory offers to repurchase debt securities of a series in a manner adverse to holders;

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- make any change that adversely affects any right of a holder to convert or exchange any debt security into or for shares of our common stock or other securities, cash or other property in accordance with the terms of such security;
- modify the ranking or priority of the debt securities of the relevant series;
- release any guarantor of any series from any of its obligations under its guarantee or the indenture otherwise than in accordance with the terms of the indenture;
- make any change to any provision of the indenture relating to the waiver of existing defaults, the rights of holders to receive payment of principal and interest on the debt securities, or to the provisions regarding amending or supplementing the indenture or the debt securities of a particular series with the written consent of the holders of such series, except to increase the percentage required for modification or waiver or to provide for consent of each affected holder of debt securities of such series;
- waive a continuing default or event of default in the payment of principal of or interest on the debt securities; or
- make any debt security payable at a place or in money other than that stated in the debt security, or impair the right of any holder of a debt security to bring suit as permitted by the indenture.

The holders of a majority in aggregate principal amount of the outstanding debt securities of such series may, on behalf of all holders of debt securities of that series, waive any existing default under, or compliance with, any provision of the debt securities of a particular series or of the indenture relating to a particular series of debt securities, other than any event of default in payment of interest or principal.

Defeasance

The indenture will permit us to terminate all our respective obligations under the indenture as they relate to any particular series of debt securities, other than the obligation to pay interest, if any, on and the principal of the debt securities of such series and certain other obligations, at any time by:

- depositing in trust with the trustee, under an irrevocable trust agreement, money or government obligations in an amount sufficient to pay principal of and interest, if any, on the debt securities of such series to their maturity or redemption; and
- complying with other conditions, including delivery to the trustee of an opinion of counsel to the effect that holders will not recognize income, gain or loss for federal income tax purposes as a result of our exercise of such right and will be subject to federal income tax on the same amount and in the same manner and at the same times as would have been the case otherwise.

The indenture will also permit us to terminate all of our respective obligations under the indenture as they relate to any particular series of debt securities, including the obligations to pay interest, if any, on and the principal of the debt securities of such series and certain other obligations, at any time by:

- depositing in trust with the trustee, under an irrevocable trust agreement, money or government obligations in an amount sufficient to pay principal and interest, if any, on the debt securities of such series to their maturity or redemption; and
- complying with other conditions, including delivery to the trustee of an opinion of counsel to the effect that (A) we have received from, or there has been published by, the Internal Revenue Service a ruling, or (B) since the date such series of debt securities were originally issued, there has been a change in the applicable federal income tax law, in either case to the effect that, and based thereon such opinion of counsel shall state that, holders will not recognize income, gain or loss for federal income tax purposes as a result of our exercise of such right and will be subject to federal income tax on the same amount and in the same manner and at the same times as would have been the case otherwise.

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In addition, the indenture will permit us to terminate substantially all our respective obligations under the indenture as they relate to a particular series of debt securities by depositing with the trustee money or government obligations sufficient to pay all principal and interest on such series at its maturity or redemption date if the debt securities of such series will become due and payable at maturity within one year or are to be called for redemption within one year of the deposit.

Transfer and Exchange

A holder will be able to transfer or exchange debt securities only in accordance with the indenture. The registrar may require a holder, among other things, to furnish appropriate endorsements and transfer documents, and to pay any taxes and fees required by law or permitted by the indenture.

Concerning the Trustee

The indenture will contain limitations on the rights of the trustee, should it become our creditor, to obtain payment of claims in specified cases or to realize on property received in respect of any such claim as security or otherwise. The indenture will permit the trustee to engage in other transactions; however, if it acquires any conflicting interest, it must eliminate such conflict or resign.

The indenture will provide that in case an event of default occurs and is not cured, the trustee will be required, in the exercise of its power, to use the degree of care of a prudent person in similar circumstances in the conduct of such person's own affairs. The trustee shall be under no obligation to exercise any of the rights or powers vested in it by the indenture at the request or direction of any of the holders pursuant to the indenture, unless such holders shall have offered to the trustee security or indemnity satisfactory to the trustee against the costs, expenses and liabilities which might be incurred by it in compliance with such request or direction.

No Recourse Against Others

The indenture will provide that there is no recourse under any obligation, covenant or agreement in the applicable indenture or with respect to any debt security against any of our or our successor's past, present or future stockholders, employees, officers or directors.

Governing Law

The laws of the State of New York will govern the indenture and the debt securities.

Warrants

We may issue warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series, from time to time. We may issue warrants independently or together with common stock, preferred stock and/or debt securities, and the warrants may be attached to or separate from those securities.

If we issue warrants, they will be evidenced by warrant agreements or warrant certificates issued under one or more warrant agreements, which are contracts between us and an agent for the holders of the warrants. We urge you to read the prospectus supplement related to any series of warrants we may offer, as well as the complete warrant agreement and warrant certificate that contain the terms of the warrants. If we issue warrants, forms of warrant agreements and warrant certificates relating to warrants for the purchase of common stock, preferred stock and debt securities will be incorporated by reference into the registration statement of which this prospectus is a part from reports we would subsequently file with the SEC.

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

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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 United States federal income tax considerations applicable to the units; and
- any other terms of the units and their constituent securities.

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. We may sell the securities to or through underwriters or dealers, through agents, or directly to one or more purchasers. We may distribute securities 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.

We may also sell equity securities covered by this registration statement in an “at the market offering” as defined in Rule 415(a)(4) under the Securities Act. Such offering may be made into an existing trading market for such securities in transactions at other than a fixed price, either:

- on or through the facilities of the Nasdaq Global Market or any other securities exchange or quotation or trading service on which such securities may be listed, quoted or traded at the time of sale; and/or
- to or through a market maker otherwise than on the Nasdaq Global Market or such other securities exchanges or quotation or trading services.

Such at the market offerings, if any, may be conducted by underwriters acting as principal or agent.

A prospectus supplement or supplements (and any related free writing prospectus that we may authorize to be provided to you) will describe the terms of the offering of the securities, including, to the extent applicable:

- the name or names of any underwriters, dealers or agents, if any;
- the purchase price of the securities and the proceeds we will receive from the sale;
- any options under which underwriters may purchase additional securities from us;
- any agency fees or underwriting discounts and other items constituting agents’ or underwriters’ compensation;
- any public offering price;
- any discounts or concessions allowed or re-allowed or paid to dealers; and
- any securities exchange or market on which the securities may be listed.

Only underwriters named in the prospectus supplement are underwriters of the securities offered by the prospectus supplement.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement. Any public offering price and any discounts or concessions allowed or re-allowed or paid to dealers may change from time to time. We may use underwriters with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, the nature of any such relationship.

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We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities, and we will describe any commissions we will pay the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

We may provide agents and underwriters with indemnification against civil liabilities related to offerings pursuant to this prospectus, including liabilities under the Securities Act, or contribution with respect to payments that the agents or underwriters may make with respect to these liabilities. Agents and underwriters may engage in transactions with, or perform services for, us in the ordinary course of business.

All securities we offer, other than our shares of common stock, will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities.

Any underwriter may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Overallotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a stabilizing or covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time. These transactions may be effected on any exchange or over-the-counter market or otherwise.

Any underwriters who are qualified market makers on the Nasdaq Global Market may engage in passive market making transactions in the securities on the Nasdaq Global Market in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded. Passive market making may stabilize the market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

LEGAL MATTERS

Certain legal matters, including the legality of the securities offered, will be passed upon for us by Gibson, Dunn & Crutcher LLP, San Francisco, California. 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 consolidated financial statements of 89bio, Inc. as of December 31, 2021 and 2020, and for each of the years in the two-year period ended December 31, 2021, have been incorporated by reference herein and in the registration statement in reliance upon the report of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and special reports, proxy statements and other information with the SEC, and we have filed with the SEC a registration statement on Form S-3 under the Securities Act with respect to the securities offered by this prospectus. This prospectus, which forms part of the registration statement, does not contain all of the information included in the registration statement, including its exhibits and schedules. For further information about us and the securities described in this prospectus, you should refer to the registration statement, its exhibits and schedules and our reports, proxies, information statements and other information filed with the SEC.

Our filings are available to the public on the Internet, through a database maintained by the SEC at www.sec.gov. We also maintain a website at www.89bio.com. We have included our website address for the information of prospective investors and do not intend it to be an active link to our website. Information contained on our website does not constitute a part of this prospectus or any applicable prospectus supplement (or any document incorporated by reference herein or therein).

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference the information and reports we file with it, which means that we can disclose important information to you by referring you to those publicly available documents. The information incorporated by reference is an important part of this prospectus, and information that we file after the date hereof with the SEC will automatically update and supersede the information already incorporated by reference. We are incorporating by reference the documents listed below:

- Annual Report on [Form 10-K](#) for the year ended December 31, 2021 filed with the SEC on March 24, 2022 (and any portions of our [Definitive Proxy Statement on Schedule 14A](#) filed on April 14, 2022 that are incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2021);
- Quarterly Reports on Form 10-Q for the quarters ended [March 31, 2022](#), [June 30, 2022](#) and [September 30, 2022](#), filed with the SEC on May 12, 2022, August 11, 2022 and November 10, 2022, respectively;
- Current Reports on Form 8-K filed with the SEC on [June 7, 2022](#), [June 28, 2022](#), [July 1, 2022](#) and [January 6, 2023](#); and
- the description of our common stock contained in our registration statement on [Form 8-A](#) filed with the SEC on November 1, 2019, including any amendments or reports filed for the purposes of updating this description.

Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any document previously incorporated by reference have been modified or superseded.

This prospectus incorporates by reference the documents listed above and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act between the date of the initial registration statement and the effectiveness of the registration statement and following the effectiveness of the registration statement until the offering of the securities under the registration statement is terminated or completed, except that we are not incorporating by reference any information furnished (and not filed) with the SEC, including any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K (unless expressly provided to the contrary).

You may request a copy of these filings (other than exhibits to such documents unless such exhibits are specifically incorporated by reference herein), at no cost, by contacting us, either orally or in writing, at the following:

89bio, Inc.
142 Sansome Street, 2nd Floor
San Francisco, California 94104
(415) 432-9270

Information about us, including our reports filed with the SEC, is available through our website at www.89bio.com. Such reports are accessible at no charge through our website and are made available as soon as reasonably practicable after such material is filed with or furnished to the SEC. Our website and the information contained on that website, or connected to that website, are not incorporated by reference in this prospectus. We have authorized no one to provide you with any information that differs from that contained in this prospectus. Accordingly, we take no responsibility for any other information that others may give you. You should not assume that the information in this prospectus is accurate as of any date other than the date of the front cover of this prospectus.



Up to \$150,000,000

Common Stock

PROSPECTUS SUPPLEMENT

SVB Securities

Cantor

February 15, 2023
