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

# **SCHEDULE 13D**

Under the Securities Exchange Act of 1934 (Amendment No. 1)\*

89bio, Inc.
(Name of Issuer)
COMMON STOCK
(Title of Class of Securities)
282559103
(CUSIP Number)
OrbiMed Advisors LLC OrbiMed Advisors Israel II Limited OrbiMed Israel GP II, L.P. OrbiMed Capital GP VI LLC  601 Lexington Avenue, 54th Floor New York, NY 10022 Telephone: (212) 739-6400  (Name, Address and Telephone Number of Person Authorized to
Receive Notices and Communications)
July 10, 2020
(Date of Event which Requires Filing of this Statement)
If the filing person has previously filed a statement on Schedule 13G to report the acquisition that is the subject of this Schedule 13D, and is filing this schedule because of §§240.13d-1(e), 240.13d-1(f) or 240.13d-1(g), check the following box. □
<b>Note:</b> Schedules filed in paper format shall include a signed original and five copies of the schedule, including all exhibits. See §240.13d-7(b) for other parties to whom copies are to be sent.

\* The remainder of this cover page shall be filled out for a Reporting Person's initial filing on this form with respect to the subject class of securities, and for any subsequent amendment containing information which would alter disclosures provided in a prior cover page.

The information required on the remainder of this cover page shall not be deemed to be "filed" for the purpose of Section 18 of the Securities Exchange Act of 1934 ("Act") or otherwise subject to the liabilities of that section of the Act but shall be subject to all other provisions of the Act (however, see the Notes).

1	Names of Reporting Persons. OrbiMed Advisors LLC			
2	Check the Appropriate Box if a Member of a Group (See Instructions). (a) o (b) o			
3	SEC Use Only			
4	Source of Funds (See Instructions)  AF			
5	Check if Disclosure of Legal Proceedings Is Required Pursuant to Items 2(d) or 2(e)			
6	Citizenship or Place of Organization Delaware			
	IUMBER OF SHARES ENEFICIALLY DWNED BY EACH REPORTING PERSON WITH	7	Sole Voting Power 0	
BEI O R		8	Shared Voting Power 2,002,221	
		9	Sole Dispositive Power 0	
				Shared Dispositive Power 2,002,221
11	Aggregate Amount Beneficially Owned by Each Reporting Person 2,002,221			
12	12 Check if the Aggregate Amount in Row (11) Excludes Certain Shares (See Instructions) o			
13	Percent of Class Represented by Amount in Row (11) 11.9%*			
14	14 Type of Reporting Person (See Instructions) IA			

<sup>\*</sup> This percentage is calculated based upon 16,852,244 shares of common stock outstanding of 89bio, Inc. (the "Issuer"), as set forth in the Issuer's Rule 424(b)(4) Prospectus filed with the Securities and Exchange Commission ("SEC") on July 8, 2020 and giving effect to the additional 397,440 shares of common stock issued and sold by the Issuer to the underwriters pursuant to the underwriters' option.

1	Names of Reporting Persons. OrbiMed Advisors Israel II Limited				
2	Check the App (a) o (b) o				
3	SEC Use Only	r			
4	Source of Fund AF	ds (See Ir	nstructions)		
5	Check if Disclosure of Legal Proceedings Is Required Pursuant to Items 2(d) or 2(e)				
6	Citizenship or Place of Organization Cayman Islands				
	UMBER OF SHARES JEFICIALLY WNED BY EACH PORTING PERSON WITH	7	Sole Voting Power 0		
BEN		8	Shared Voting Power 2,002,221		
RE		9	Sole Dispositive Power 0		
		10	Shared Dispositive Power 2,002,221		
11	Aggregate Amount Beneficially Owned by Each Reporting Person 2,002,221				
12	Check if the Aggregate Amount in Row (11) Excludes Certain Shares (See Instructions)				
13	Percent of Class Represented by Amount in Row (11) 11.9%*				
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<sup>\*</sup> This percentage is calculated based upon 16,852,244 shares of common stock outstanding of 89bio, Inc. (the "Issuer"), as set forth in the Issuer's Rule 424(b)(4) Prospectus filed with the Securities and Exchange Commission ("SEC") on July 8, 2020 and giving effect to the additional 397,440 shares of common stock issued and sold by the Issuer to the underwriters pursuant to the underwriters' option.

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1	Names of Reporting Persons. OrbiMed Israel GP II, L.P.				
2	Check the Appropriate Box if a Member of a Group (See Instructions). (a) o (b) o				
3	SEC Use Only				
4	Source of Fund AF	ds (See Iı	nstructions)		
5	Check if Discl	osure of	Legal Proceedings Is Required Pursuant to Items 2(d) or 2(e)	0	
6	Citizenship or Place of Organization Cayman Islands				
	_	7	Sole Voting Power 0		
BEN		8	Shared Voting Power 2,002,221		
RE		REPORTING PERSON		Sole Dispositive Power 0	
_				Shared Dispositive Power 2,002,221	
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12	Check if the Aggregate Amount in Row (11) Excludes Certain Shares (See Instructions)				
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14	Type of Reporting Person (See Instructions) OO				

<sup>\*</sup> This percentage is calculated based upon 16,852,244 shares of common stock outstanding of 89bio, Inc. (the "Issuer"), as set forth in the Issuer's Rule 424(b)(4) Prospectus filed with the Securities and Exchange Commission ("SEC") on July 8, 2020 and giving effect to the additional 397,440 shares of common stock issued and sold by the Issuer to the underwriters pursuant to the underwriters' option.

1	Names of Reporting Persons. OrbiMed Capital GP VI LLC						
2	Check the Appropriate Box if a Member of a Group (See Instructions). (a) o (b) o						
3	SEC Use Only						
4	Source of Funds ( AF	See Instr	uctions)				
5	Check if Disclosure of Legal Proceedings Is Required Pursuant to Items 2(d) or 2(e)						
6	Citizenship or Place of Organization Delaware						
NUMBER OF SHARES		7	Sole Voting Power 0				
BEI	NEFICIALLY WNED BY	8	Shared Voting Power 2,002,221				
	EACH EPORTING PERSON WITH	REPORTING		REPORTING		Sole Dispositive Power 0	
		10	Shared Dispositive Power 2,002,221				
11	Aggregate Amount Beneficially Owned by Each Reporting Person 2,002,221						
12	Check if the Aggregate Amount in Row (11) Excludes Certain Shares (See Instructions)						
13	Percent of Class Represented by Amount in Row (11) 11.9%*						
14	Type of Reporting Person (See Instructions) OO						

<sup>\*</sup> This percentage is calculated based upon 16,852,244 shares of common stock outstanding of 89bio, Inc. (the "<u>Issuer</u>"), as set forth in the Issuer's Rule 424(b)(4) Prospectus filed with the Securities and Exchange Commission ("<u>SEC</u>") on July 8, 2020 and giving effect to the additional 397,440 shares of common stock issued and sold by the Issuer to the underwriters pursuant to the underwriters' option.

#### Item 1. Security and Issuer

This Amendment No. 1 ("<u>Amendment No. 1</u>") to Schedule 13D supplements and amends the Statement on Schedule 13D of OrbiMed Advisors LLC, OrbiMed Advisors Israel II Limited, OrbiMed Israel GP II, L.P., and OrbiMed Capital GP VI (the "<u>Statement</u>") originally filed with the Securities and Exchange Commission (the "<u>SEC</u>") on November 25, 2020. This Statement relates to the common stock, par value \$0.001 per share (the "<u>Shares</u>") of 89bio, Inc., a corporation organized under the laws of Delaware (the "<u>Issuer</u>"), with its principal executive offices located at 535 Mission Street, 14<sup>th</sup> Floor, San Francisco, California 94105. The Shares are listed on the NASDAQ Global Market under the ticker symbol "ETNB". Information given in response to each item shall be deemed incorporated by reference in all other items, as applicable.

On July 10, 2020, the Issuer completed an underwritten public offering of 2,649,600 Shares at an offering price of \$27.50 per Share (the "Offering"). In addition, the Issuer granted the underwriters an option to purchase, at the public offering price less any underwriting discounts and commissions, up to an additional 397,440 Shares. None of the Reporting Persons participated in the Offering. As a result of the Offering, the percentage of outstanding Shares that the Reporting Persons may be deemed to beneficially own was reduced by more than one percent of the Issuer's Shares outstanding since the filing of the Statement.

#### Item 2. Identity and Background

- (a) This Schedule 13D is being filed by OrbiMed Advisors LLC ("OrbiMed Advisors"), OrbiMed Advisors Israel II Limited ("OrbiMed Limited"), OrbiMed Israel GP II, L.P. ("OrbiMed Israel"), and OrbiMed Capital GP VI LLC ("OrbiMed Capital") (collectively, the "Reporting Persons").
- (b) (c), (f) OrbiMed Advisors, a limited liability company organized under the laws of Delaware and a registered investment adviser under the Investment Advisers Act of 1940, as amended, is the managing member or general partner of certain entities as more particularly described in Item 6 below. OrbiMed Advisors has its principal offices at 601 Lexington Avenue, 54th Floor, New York, New York 10022.

OrbiMed Limited, a corporation organized under the laws of the Cayman Islands, is the general partner of a limited partnership as more particularly described in Item 6 below. OrbiMed Limited has its principal offices at 89 Medinat Hayehudim St., building E, Herzliya 4614001 Israel.

OrbiMed Israel, a limited partnership organized under the laws of the Cayman Islands, is the general partner of a limited partnership as more particularly described in Item 6 below. OrbiMed Israel has its principal offices at 89 Medinat Hayehudim St., building E, Herzliya 4614001 Israel.

OrbiMed Capital, a limited liability company organized under the laws of Delaware, is the general partner of a limited partnership as more particularly described in Item 6 below. OrbiMed Capital has its principal offices at 601 Lexington Avenue, 54th Floor, New York, New York 10022.

The directors and executive officers of OrbiMed Advisors, OrbiMed Limited, OrbiMed Israel and OrbiMed Capital are set forth on Schedules I, II, III and IV, respectively, attached hereto. Schedules I, II, III and IV set forth the following information with respect to each such person:

- (i) name;
- (ii) business address;
- (iii) present principal occupation of employment and the name, principal business and address of any corporation or other organization in which such employment is conducted; and
  - (iv) citizenship.
- (d) (e) During the last five years, neither the Reporting Persons nor any Person named in Schedules I through IV has been (i) convicted in a criminal proceeding (excluding traffic violations or similar misdemeanors) or (ii) a party to a civil proceeding of a judicial or administrative body of competent jurisdiction and as a result of such proceeding was or is subject to a judgment, decree or final order enjoining future violations of, or prohibiting or mandating activities subject to, federal or state securities laws or finding any violation with respect to such laws.

#### Item 3. Source and Amount of Funds or Other Consideration

Not applicable.

#### **Item 4. Purpose of Transaction**

The Shares acquired by the Reporting Persons were acquired for the purpose of making an investment in the Issuer and not with the intention of acquiring control of the Issuer's business on behalf of the Reporting Persons' respective advisory clients.

The Reporting Persons from time to time intend to review their investment in the Issuer on the basis of various factors, including the Issuer's business, financial condition, results of operations and prospects, general economic and industry conditions, the securities markets in general and those for the Issuer's Shares in particular, as well as other developments and other investment opportunities. Based upon such review, the Reporting Persons will take such actions in the future as the Reporting Persons may deem appropriate in light of the circumstances existing from time to time. If the Reporting Persons believe that further investment in the Issuer is attractive, whether because of the market price of Shares or otherwise, they may acquire Shares or other securities of the Issuer either in the open market or in privately negotiated transactions. Similarly, depending on market and other factors, the Reporting Persons may determine to dispose of some or all of the Shares currently owned by the Reporting Persons or otherwise acquired by the Reporting Persons either in the open market or in privately negotiated transactions.

Except as set forth in this Statement, the Reporting Persons have not formulated any plans or proposals which relate to or would result in: (a) the acquisition by any person of additional securities of the Issuer or the disposition of securities of the Issuer, (b) an extraordinary corporate transaction, such as a merger, reorganization or liquidation, involving the Issuer or any of its subsidiaries, (c) a sale or transfer of a material amount of the assets of the Issuer or any of its subsidiaries, (d) any change in the present Board of Directors or management of the Issuer, including any plans or proposals to change the number or term of directors or to fill any existing vacancies on the board, (e) any material change in the Issuer's capitalization or dividend policy of the Issuer, (f) any other material change in the Issuer's business or corporate structure, (g) any change in the Issuer's charter or bylaws or other instrument corresponding thereto or other action which may impede the acquisition of control of the Issuer by any person, (h) causing a class of the Issuer's securities to be deregistered or delisted from a national securities exchange or to cease to be authorized to be quoted in an inter-dealer quotation system of a registered national securities association, (i) a class of equity securities of the Issuer becoming eligible for termination of registration pursuant to Section 12(g)(4) of the Act or (j) any action similar to any of those enumerated above.

#### Item 5. Interest in Securities of the Issuer

(a) — (b) The following disclosure is based upon 16,852,244 outstanding Shares of the Issuer, as set forth in the Issuer's Rule 424(b)(4) Prospectus filed with the Securities and Exchange Commission on July 8, 2020.

As of the date of this filing, OrbiMed Israel Partners II, L.P. ("OIP II"), a limited partnership organized under the laws of the Cayman Islands, holds 2,002,221 Shares constituting approximately 11.9% of the issued and outstanding Shares. OrbiMed Israel is the general partner of OIP II pursuant to the terms of the limited partnership agreement of OIP II, and OrbiMed Limited is the general partner of OrbiMed Israel pursuant to the terms of the limited partnership agreement of OrbiMed Israel. As a result, OrbiMed Israel and OrbiMed Limited share the power to direct the vote and disposition of the Shares held by OIP II, and both OrbiMed Israel and OrbiMed Limited may be deemed directly or indirectly, including by reason of their mutual affiliation, to be the beneficial owners of the Shares held by OIP II. OrbiMed Limited exercises this investment power through an investment committee comprised of Carl L. Gordon, Jonathan Silverstein, Nissim Darvish, Anat Naschitz, and Erez Chimovits each of whom disclaims beneficial ownership of the Shares held by OIP II.

As of the date of this filing, OrbiMed Private Investments VI, LP ("OPI VI"), a limited partnership organized under the laws of Delaware, holds 2,002,221 Shares constituting approximately 11.9% of the issued and outstanding Shares. OrbiMed Capital is the general partner of OPI VI, pursuant to the terms of the limited partnership agreement of OPI VI, and OrbiMed Advisors is the managing member of OrbiMed Capital, pursuant to the terms of the limited liability company agreement of OrbiMed Capital. As a result, OrbiMed Advisors and OrbiMed Capital share power to direct the vote and disposition of the Shares held by OPI VI and may be deemed directly or indirectly, including by reason of their mutual affiliation, to be the beneficial owners of the Shares held by OPI VI. Each of OrbiMed Advisors and OrbiMed Capital disclaims any beneficial ownership over the shares of the other Reporting Persons. OrbiMed Advisors exercises this investment and voting power through a management committee comprised of Carl L. Gordon, Sven H. Borho and Jonathan T. Silverstein, each of whom disclaims beneficial ownership of the Shares held by OPI VI.

- (c) The Reporting Persons have not effected any transactions during the past sixty (60) days in any Shares.
- (d) Not applicable.
- (e) Not applicable.

#### Item 6. Contracts, Arrangements, Understandings or Relationships with Respect to Securities of the Issuer

In addition to the relationships between the Reporting Persons described in Items 2 and 5 above, OrbiMed Capital is the general partner of OPI VI, pursuant to the terms of the limited partnership agreement of OPI VI. Pursuant to this agreement and relationship, OrbiMed Capital has discretionary investment management authority with respect to the assets of OPI VI. Such authority includes the power to vote and otherwise dispose of securities held by OPI VI. The number of outstanding Shares of the Issuer attributable to OPI VI is 2,002,221. OrbiMed Capital, pursuant to its authority under the limited partnership agreement of OPI VI, may be considered to hold indirectly 2,002,221 Shares.

OrbiMed Advisors is the managing member of OrbiMed Capital, pursuant to the terms of the limited liability company agreement of OrbiMed Capital. Pursuant to these agreements and relationships, OrbiMed Advisors and OrbiMed Capital have discretionary investment management authority with respect to the assets of OPI VI. Such authority includes the power of OrbiMed Capital to vote and otherwise dispose of securities held by OPI VI. The number of outstanding Shares attributable to OPI VI is 2,002,221 Shares. OrbiMed Advisors, pursuant to its authority under the terms of the limited liability company agreement of OrbiMed Capital, may also be considered to hold indirectly 2,002,221 Shares.

OrbiMed Israel is the general partner of OIP II pursuant to the terms of the limited partnership agreement of OIP II. OrbiMed Limited is the general partner of OrbiMed Israel pursuant to the terms of the limited partnership agreement of OrbiMed Israel. Pursuant to these agreements and relationships, OrbiMed Israel has discretionary investment management authority with respect to the assets of OIP II and such discretionary investment management authority is exercised through OrbiMed Limited by action of the committee. Such authority includes the power to vote and otherwise dispose of securities held by OIP II. The number of outstanding Shares of the Issuer attributable to OIP II is 2,002,221. OrbiMed Israel, as the general partner of OIP II, may be considered to hold indirectly 2,002,221 Shares, and OrbiMed Limited, as the general partner of OrbiMed Israel, may be considered to hold indirectly 2,002,221 Shares.

Anat Naschitz ("Naschitz"), an employee of OrbiMed Limited, is a member of the Board of Directors of the Issuer and, accordingly, the Reporting Persons may have the ability to affect and influence control of the Issuer. From time to time, Naschitz may receive stock options or other awards of equity-based compensation pursuant to the Issuer's compensation arrangements for non-employee directors. Pursuant to an agreement with the Reporting Persons, Naschitz is obligated to transfer any securities issued under any such stock options or other awards, or the economic benefit thereof, to the Reporting Persons, which will in turn ensure that such securities or economic benefits are provided to OPI VI and OIP II.

#### **Investors Rights Agreement**

In addition, OPI VI and certain other stockholders of the Issuer entered into an amended and restated investors' rights agreement with the Issuer a summary of which is set forth at Item 6 of the Statement.

#### Lock-Up Agreement

In connection with the Offering, OPI VI, OIP II, and certain other stockholders entered into Lock-Up Agreements with the Issuer's underwriters. Pursuant to their Lock-Up Agreements, OPI VI and OIP II agreed that it will not, during the period ending 90 days after the date of the underwriting agreement used in connection with the Offering (the "Lock-Up Period"), directly or indirectly (1) sell, assign, transfer, pledge, contract to sell, or otherwise dispose of, any Shares or securities convertible into or exercisable or exchangeable for Shares with respect to which OPI VI or OIP II has or acquires the power of disposition or (2) enter into any swap or other agreement that transfers, in whole or in part, the economic risk of ownership of any such Shares.

After the Lock-Up Period expires, the Reporting Persons' Shares will be eligible for sale in the public market, subject to any applicable limitations under Rule 144 under the Securities Act, and other applicable U.S. securities laws.

The foregoing description of the Lock-Up Agreement does not purport to be complete and is qualified in its entirety by reference to the full text of the Lock-Up Agreement, which is filed as Exhibit 3 and incorporated herein by reference.

Other than as described in this Amendment No. 1, to the best of the Reporting Persons' knowledge, there are no other contracts, arrangements, understandings or relationships (legal or otherwise) among the persons named in Item 2 and between such persons and any person with respect to any securities of the Issuer.

### Item 7. Material to Be Filed as Exhibits

Exhibit	Description
1.	Joint Filing Agreement among OrbiMed Advisors LLC, OrbiMed Advisors Israel II Limited, OrbiMed Israel GP II, L.P., and OrbiMed Capital GP VI LLC.
2.	Investors' Rights Agreement by and among the Issuer and each of the persons listed on the signature page thereto, dated as of September 17, 2019 (incorporated by reference to Exhibit 4.2 to the Issuer's Registration Statement on Form S-1 (SEC 333-234174)).
3.	Form of Lock-Up Agreement.

### Signature

After reasonable inquiry and to the best of my knowledge and belief, I certify that the information set forth in this statement is true, complete and correct.

Dated: July 10, 2020 ORBIMED ADVISORS LLC

By: /s/ Carl L. Gordon

Name: Carl L. Gordon Title: Member

ORBIMED ADVISORS ISRAEL II LIMITED

By: /s/ Carl L. Gordon

Name: Carl L. Gordon Title: Director

ORBIMED ISRAEL GP II, L.P.

By: ORBIMED ADVISORS ISRAEL II LIMITED, its general partner

By: /s/ Carl L. Gordon

Name: Carl L. Gordon

Title: Director of OrbiMed Advisors Israel II

Limited

ORBIMED CAPITAL GP VI LLC

By: ORBIMED ADVISORS LLC, its managing member

By: /s/ Carl L. Gordon

Carl L. Gordon

Member of OrbiMed Advisors LLC  $\,$ 

# SCHEDULE I

The names and present principal occupations of each of the executive officers and directors of OrbiMed Advisors LLC are set forth below. Unless otherwise noted, each of these persons is a United States citizen and has a business address of 601 Lexington Avenue, 54th Floor, New York, NY 10022.

<u>Name</u>	Position with Reporting Person	Principal Occupation
Carl L. Gordon	Member	Member OrbiMed Advisors LLC
Sven H. Borho German and Swedish Citizen	Member	Member OrbiMed Advisors LLC
Jonathan T. Silverstein	Member	Member OrbiMed Advisors LLC
W. Carter Neild	Member	Member OrbiMed Advisors LLC
Geoffrey C. Hsu	Member	Member OrbiMed Advisors LLC
C. Scotland Stevens	Member	Member ObiMed Advisors LLC
David P. Bonita	Member	Member OrbiMed Advisors LLC
Trey Block	Chief Financial Officer	Chief Financial Officer OrbiMed Advisors LLC

# SCHEDULE II

The names and present principal occupations of each of the executive officers and directors of OrbiMed Advisors Israel II Limited are set forth below. Unless otherwise noted, each of these persons is a United States citizen and has a business address of 89 Medinat Hayehudim St., building E, Herzliya 4614001 Israel.

<u>Name</u>	Position with Reporting Person	Principal Occupation
Carl L. Gordon	Director	Director OrbiMed Advisors Israel II Limited
Jonathan T. Silverstein	Director	Director OrbiMed Advisors Israel II Limited
Nissim Darvish Israeli Citizen	Director	Director OrbiMed Advisors Israel II Limited
Anat Naschitz Israeli Citizen	Director	Director OrbiMed Advisors Israel II Limited
Erez Chimovits Israeli Citizen	Director	Director OrbiMed Advisors Israel II Limited

# SCHEDULE III

The business and operations of OrbiMed Israel GP II, L.P. are managed by the executive officers and directors of its general partner, OrbiMed Advisors Israel II Limited, set forth on Schedule II attached hereto.

# SCHEDULE IV

The business and operations of OrbiMed Capital GP VI LLC are managed by the executive officers and directors of its managing member, OrbiMed Advisors LLC, set forth in Schedule I attached hereto.

# EXHIBIT INDEX

Exhibit	Description
1.	Joint Filing Agreement among OrbiMed Advisors LLC, OrbiMed Advisors Israel II Limited, OrbiMed Israel GP II, L.P., and OrbiMed Capital GP VI LLC.
2.	Investors' Rights Agreement by and among the Issuer and each of the persons listed on the signature page thereto, dated as of September 17, 2019 (incorporated by reference to Exhibit 4.2 to the Issuer's Registration Statement on Form S-1 (SEC 333-234174)).
3.	Form of Lock-Up Agreement.

### JOINT FILING AGREEMENT

The undersigned hereby agree that the Amendment No. 1 to Schedule 13D, dated July 10, 2020, with respect to the ordinary shares of 89bio, Inc. is filed on behalf of each of us pursuant to and in accordance with the provisions of Rule 13d-1(k) under the Securities Exchange Act of 1934, as amended. Each of the undersigned agrees to be responsible for the timely filing of this Statement, and for the completeness and accuracy of the information concerning itself contained therein. This Agreement may be executed in any number of counterparts, all of which taken together shall constitute one and the same instrument.

IN WITNESS WHEREOF, the undersigned have executed this Agreement as of the 10<sup>th</sup> day of July 2020.

# ORBIMED ADVISORS LLC

By: /s/ Carl L. Gordon

Name: Carl L. Gordon Title: Member

# ORBIMED ADVISORS ISRAEL II LIMITED

By: /s/ Carl L. Gordon

Name: Carl L. Gordon Title: Director

# ORBIMED ISRAEL GP II, L.P.

By: ORBIMED ADVISORS ISRAEL II LIMITED, its general partner

By: /s/ Carl L. Gordon

Name: Carl L. Gordon

Title: Director of OrbiMed Advisors Israel II

Limited

# ORBIMED CAPITAL GP VI LLC

By: ORBIMED ADVISORS LLC, its managing member

By: /s/ Carl L. Gordon

Carl L. Gordon

Member of OrbiMed Advisors LLC

#### LOCK-UP AGREEMENT

BofA Securities, Inc. SVB Leerink LLC RBC Capital Markets, LLC

> as Representatives of the several Underwriters to be named in the within-mentioned Underwriting Agreement

c/o BofA Securities, Inc.
One Bryant Park
New York, New York 10036

c/o SVB Leerink LLC 255 California Street, 12th Floor San Francisco, California 94111

c/o RBC Capital Markets, LLC 200 Vesey Street New York, New York 10281

Re: Proposed Public Offering by 89bio, Inc.

#### Ladies and Gentlemen:

The undersigned, a securityholder, an officer and/or a director, as applicable, of 89bio, Inc., a Delaware corporation (the "Company"), understands that BofA Securities, Inc. ("BofAS"), SVB Leerink LLC ("SVB Leerink") and RBC Capital Markets, LLC ("RBC," and, collectively with BofAS and SVB Leerink, the "Representatives") propose to enter into an Underwriting Agreement (the "Underwriting Agreement") with the Company, providing for the public offering (the "Public Offering") of shares of the Company's common stock, par value \$0.001 per share ("Common Stock"). In recognition of the benefit that the Public Offering will confer upon the undersigned as a securityholder, an officer and/or a director, as applicable, of the Company, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the undersigned agrees with each underwriter to be named in the Underwriting Agreement that, during the period beginning on the date hereof and ending on the date that is 90 days from the date of the Underwriting Agreement (the "Lock-Up Period"), the undersigned will not, without the prior written consent of the Representatives, (i) directly or indirectly, offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase or otherwise transfer or dispose of any shares of Common Stock or any securities convertible into or exercisable or exchangeable for shares of Common Stock, whether now owned or hereafter acquired by the undersigned or with respect to which the undersigned has or hereafter acquires the power of disposition (collectively, the "Lock-Up Securities"), or exercise any right with respect to the registration of any of the Lock-Up Securities, or file, cause to be filed or cause to be confidentially submitted any registration statement in connection therewith, under the Securities Act of 1933, as amended, or (ii) enter into any swap or any other agreement or any transaction that transfers, in whole or in part, directly or indirectly, the economic consequence of ownership of the Lock-Up Securities, whether any such swap or transaction is to be settled by delivery of shares of Common Stock or other securities, in cash or otherwise. If the undersigned is an officer or director of the Company, the undersigned further agrees that the foregoing provisions shall be equally applicable to any issuer-directed Common Stock the undersigned may purchase in the Public Offering.

Notwithstanding the foregoing, and subject to the conditions below, the undersigned may transfer the Lock-Up Securities without the prior written consent of the Representatives:

- (1) as a *bona fide* gift or gifts, *provided* that (i) the Representatives receive a signed lock-up agreement for the balance of the Lock-Up Period from each transferee prior to such transfer, (ii) any such transfer shall not involve a disposition for value, (iii) any such transfer is not required to be publicly filed or reported during the Lock-Up Period, and (iv) the undersigned does not otherwise voluntarily effect any public filing or report regarding such transfers during the Lock-Up Period;
- (2) by will or intestate succession upon the death of the undersigned, including to the transferee's nominee or custodian, *provided* that (i) the Representatives receive a signed lock-up agreement for the balance of the Lock-Up Period from each transferee prior to such transfer, (ii) any such transfer shall not involve a disposition for value, (iii) if required, any public filing or report under Section 16 of the Securities Exchange Act of 1934, as amended (the "Exchange Act") during the Lock-Up Period shall clearly indicate in the footnotes thereto that the such transfer is being made pursuant to the circumstances described in this clause, and (iv) no public filings or reports regarding such transfers shall be otherwise voluntarily effected during the Lock-Up Period;
- (3) to the immediate family of the undersigned or any trust, partnership or similar entity for the direct or indirect benefit of the undersigned or the immediate family of the undersigned (for purposes of this Lock-Up Agreement, "immediate family" shall mean any relationship by blood, marriage or adoption, not more remote than first cousin) or if the undersigned is a trust, to any beneficiary of the undersigned (including such beneficiary's estate), *provided* that (i) the Representatives receive a signed lock-up agreement for the balance of the Lock-Up Period from each transferee prior to such transfer, (ii) any such transfer shall not involve a disposition for value, (iii) any such transfer is not required to be publicly filed or reported during the Lock-Up Period, and (iv) the undersigned does not otherwise voluntarily effect any public filing or report regarding such transfers during the Lock-Up Period;
- (4) if the undersigned is a non-natural person, as a distribution to limited partners, general partners, limited liability company members, stockholders or other equity holders of the undersigned, *provided* that (i) the Representatives receive a signed lock-up agreement for the balance of the Lock-Up Period from each transferee prior to such transfer, (ii) any such transfer shall not involve a disposition for value, (iii) any such transfer is not required to be publicly filed or reported during the Lock-Up Period, and (iv) the undersigned does not otherwise voluntarily effect any public filing or report regarding such transfers during the Lock-Up Period;
- (5) to the undersigned's affiliates or to any investment fund or other entity controlled or managed by the undersigned (including, for the avoidance of doubt, where the undersigned is a partnership, to its general partner or a successor partnership or fund, or any other funds managed by such partnership), *provided* that (i) the Representatives receive a signed lock-up agreement for the balance of the Lock-Up Period from each transferee prior to such transfer, (ii) any such transfer shall not involve a disposition for value, (iii) any such transfer is not required to be publicly filed or reported during the Lock-Up Period, and (iv) the undersigned does not otherwise voluntarily effect any public filing or report regarding such transfers during the Lock-Up Period;

- (6) to the Company upon exercise of any right in respect of any option granted under any incentive plan of the Company described in the final prospectus relating to the Public Offering or any document incorporated by reference therein, including the surrender of shares of Common Stock to the Company in "net" or "cashless" exercise of any option, provided, that (i) the shares of Common Stock received by the undersigned upon exercise continue to be subject to the restrictions on transfer set forth in this Lock-Up Agreement, (ii) if required, any public filing or report under Section 16 of the Exchange Act during the Lock-Up Period shall clearly indicate in the footnotes thereto that the filing relates to the exercise of a stock option, that no shares were sold by the reporting person and that the shares received upon exercise of the stock option are subject to this Lock-Up Agreement, and (iii) the undersigned does not otherwise voluntarily effect any public filing or report regarding such transfers during the Lock-Up Period;
- (7) pursuant to an order of a court of competent jurisdiction or in connection with a qualified domestic order or divorce settlement, *provided*, that (i) the Representatives receive a signed lock-up agreement for the balance of the Lock-Up Period from each transferee prior to such transfer, (ii) if required, any public filing or report under Section 16 of the Exchange Act during the Lock-Up Period shall clearly indicate in the footnotes thereto that the such transfer is being made pursuant to the circumstances described in this clause, and (iii) the undersigned does not otherwise voluntarily effect any public filing or report regarding such transfers during the Lock-Up Period; or
- (8) to a *bona fide* third party pursuant to a merger, consolidation, tender offer or other similar transaction made to all holders of Common Stock and involving a Change of Control of the Company and approved by the Company's board of directors, *provided*, that (i) in the event that such Change of Control is not completed, the undersigned's Lock-Up Securities shall remain subject to the restrictions contained herein, and (ii) any shares of Common Stock not transferred in such merger, consolidation, tender offer or similar transaction shall remain subject to the restrictions contained herein. "Change of Control" shall mean the transfer (whether by tender offer, merger, consolation or other similar transaction), in one transaction or a series of related transactions, to a person or group of affiliated persons (other than an underwriter pursuant to the Public Offering), of the Company's voting securities if, after such transfer, such person or group of affiliated persons would hold more than 50% of the outstanding voting securities of the Company (or the surviving entity).

Furthermore, during the Lock-Up Period, the undersigned may sell shares of Common Stock purchased by the undersigned in the Public Offering or in the open market transactions following the Public Offering if and only if (i) such sales are not required to be publicly filed or reported during the Lock-Up Period and (ii) the undersigned does not otherwise voluntarily effect any public filing or report regarding such sales during the Lock-Up Period.

Nothing herein shall prevent the undersigned from establishing a 10b5-1 trading plan that complies with Rule 10b5-1 under the Exchange Act (a "10b5-1 trading plan") so long as any such plan does not permit sales of Lock-Up Securities during the Lock-Up Period; and *provided* that the establishment of a 10b5-1 trading plan shall only be permitted if (i) the establishment of such plan is not required to be reported in any public filing or report with the Securities and Exchange Commission, or otherwise and (ii) the undersigned does not otherwise voluntarily effect any public filing or report regarding the establishment of such plan during the Lock-Up Period.

The undersigned also agrees and consents to the entry of stop transfer instructions with the Company's transfer agent and registrar against the transfer of the Lock-Up Securities, except in compliance with the foregoing restrictions.

If any record or beneficial owner of any securities of the Company is granted an early release from the restrictions described herein during the Lock-Up Period with respect to more than 1% in the aggregate of the Company's total outstanding common stock (whether in one or multiple releases), then each Major Holder (as defined below) shall also be granted an early release from its obligations hereunder on a pro rata basis with all other record or beneficial holders of similarly restricted securities of the Company based on the maximum percentage of shares held by any such record or beneficial holder being released from such holder's Lock-Up Agreement; provided, however, that in the case of an early release from the restrictions described herein during the Lock-Up Period in connection with an underwritten public offering, whether or not such offering or sale is wholly or partially a secondary offering of the Company's Common Stock (an "Underwritten Sale"), such early release shall only apply with respect to such Major Holder's participation in such Underwritten Sale. Notwithstanding any other provisions of this Lock-Up Agreement, if the Representatives in their reasonable judgment determines that a record or beneficial owner of any securities should be granted an early release from a Lock-Up Agreement due to circumstances of an emergency or hardship, then the Major Holders shall not have any right to be granted an early release pursuant to the terms of this paragraph. For purposes of this Lock-Up Agreement, each of the following persons is a "Major Holder": each record or beneficial owner, as of the date hereof, of more than 5% of the outstanding shares of securities of the Company (for purposes of determining record or beneficial ownership of a stockholder, all shares of securities held by investment funds affiliated with such stockholder shall be aggregated).

Notwithstanding anything to the contrary contained herein, this Lock-Up Agreement will automatically terminate and the undersigned will be released from all of his, her or its obligations hereunder upon the earliest to occur, if any, of (i) if the Representatives, on the one hand, or the Company, on the other hand, informs the other, prior to the execution of the Underwriting Agreement, that it has determined not to proceed with the Public Offering, (ii) the date the Company files an application with the Securities and Exchange Commission to withdraw the registration statement related to the Public Offering, (iii) the date the Underwriting Agreement is terminated prior to payment for and delivery of the shares of Common Stock to be sold thereunder or (iv) July 31, 2020, in the event that the Underwriting Agreement has not been executed by such date.

[signature page follows]

Very truly yours,
[Signature Page to Lock-Up Agreement]