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

SCHEDULE 13D

Under the Securities Exchange Act of 1934
(Amendment No. 4)*

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)

January 24, 2023

(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.

Note: 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).

CUSIP No. 282559103

| | | |
|--|--|---------------------------------------|
| 1 | Names of Reporting Persons. OrbiMed Advisors LLC | |
| 2 | Check the Appropriate Box if a Member of a Group (See Instructions). (a) <input type="radio"/> (b) <input type="radio"/> | |
| 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) <input type="radio"/> | |
| 6 | Citizenship or Place of Organization Delaware | |
| NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH | 7 | Sole Voting Power 0 |
| | 8 | Shared Voting Power 1,504,433 |
| | 9 | Sole Dispositive Power 0 |
| | 10 | Shared Dispositive Power 1,504,433 |
| 11 | Aggregate Amount Beneficially Owned by Each Reporting Person 1,504,433 | |
| 12 | Check if the Aggregate Amount in Row (11) Excludes Certain Shares (See Instructions) <input type="radio"/> | |
| 13 | Percent of Class Represented by Amount in Row (11) 3.2%* | |
| 14 | Type of Reporting Person (See Instructions) IA | |

* This percentage is calculated based upon 46,536,970 shares of common stock outstanding of 89bio, Inc. (the "Issuer"), as set forth in the Issuer's Quarterly Report for the quarter ending September 30, 2022 filed with the Securities and Exchange Commission ("SEC") on November 10, 2022.

CUSIP No. 282559103

| | | |
|--|--|---------------------------------------|
| 1 | Names of Reporting Persons. OrbiMed Advisors Israel II Limited | |
| 2 | Check the Appropriate Box if a Member of a Group (See Instructions). (a) <input type="radio"/> (b) <input type="radio"/> | |
| 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) <input type="radio"/> | |
| 6 | Citizenship or Place of Organization Cayman Islands | |
| NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH | 7 | Sole Voting Power 0 |
| | 8 | Shared Voting Power 1,504,436 |
| | 9 | Sole Dispositive Power 0 |
| | 10 | Shared Dispositive Power 1,504,436 |
| 11 | Aggregate Amount Beneficially Owned by Each Reporting Person 1,504,436 | |
| 12 | Check if the Aggregate Amount in Row (11) Excludes Certain Shares (See Instructions) <input type="radio"/> | |
| 13 | Percent of Class Represented by Amount in Row (11) 3.2%* | |
| 14 | Type of Reporting Person (See Instructions) OO | |

* This percentage is calculated based upon 46,536,970 shares of common stock outstanding of 89bio, Inc. (the "Issuer"), as set forth in the Issuer's Quarterly Report for the quarter ending September 30, 2022 filed with the Securities and Exchange Commission ("SEC") on November 10, 2022.

CUSIP No. 282559103

| | | |
|--|--|---------------------------------------|
| 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) <input type="radio"/> (b) <input type="radio"/> | |
| 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) <input type="radio"/> | |
| 6 | Citizenship or Place of Organization Cayman Islands | |
| NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH | 7 | Sole Voting Power 0 |
| | 8 | Shared Voting Power 1,504,436 |
| | 9 | Sole Dispositive Power 0 |
| | 10 | Shared Dispositive Power 1,504,436 |
| 11 | Aggregate Amount Beneficially Owned by Each Reporting Person 1,504,436 | |
| 12 | Check if the Aggregate Amount in Row (11) Excludes Certain Shares (See Instructions) <input type="radio"/> | |
| 13 | Percent of Class Represented by Amount in Row (11) 3.2%* | |
| 14 | Type of Reporting Person (See Instructions) OO | |

* This percentage is calculated based upon 46,536,970 shares of common stock outstanding of 89bio, Inc. (the "Issuer"), as set forth in the Issuer's Quarterly Report for the quarter ending September 30, 2022 filed with the Securities and Exchange Commission ("SEC") on November 10, 2022.

CUSIP No. 282559103

| | | |
|--|--|---------------------------------------|
| 1 | Names of Reporting Persons. OrbiMed Capital GP VI LLC | |
| 2 | Check the Appropriate Box if a Member of a Group (See Instructions). (a) <input type="radio"/> (b) <input type="radio"/> | |
| 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) <input type="radio"/> | |
| 6 | Citizenship or Place of Organization Delaware | |
| NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH | 7 | Sole Voting Power 0 |
| | 8 | Shared Voting Power 1,504,433 |
| | 9 | Sole Dispositive Power 0 |
| | 10 | Shared Dispositive Power 1,504,433 |
| 11 | Aggregate Amount Beneficially Owned by Each Reporting Person 1,504,433 | |
| 12 | Check if the Aggregate Amount in Row (11) Excludes Certain Shares (See Instructions) <input type="radio"/> | |
| 13 | Percent of Class Represented by Amount in Row (11) 3.2%* | |
| 14 | Type of Reporting Person (See Instructions) OO | |

* This percentage is calculated based upon 46,536,970 shares of common stock outstanding of 89bio, Inc. (the "Issuer"), as set forth in the Issuer's Quarterly Report for the quarter ending September 30, 2022 filed with the Securities and Exchange Commission ("SEC") on November 10, 2022.

Item 1. Security and Issuer

This Amendment No. 4 ("Amendment No. 4") 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 LLC (the "Statement") originally filed with the Securities and Exchange Commission (the "SEC") on November 25, 2019, as amended by Amendment No. 1 filed with the SEC on July 13, 2020, Amendment No. 2 filed with the SEC on September 23, 2020, and Amendment No. 3 filed with the SEC on July 5, 2022. This Statement relates to the common stock, par value \$0.001 per share (the "Shares") of 89bio, Inc., a corporation organized under the laws of Delaware (the "Issuer"), with its principal executive offices located at 142 Sansome Street, Second Floor, San Francisco, California 94104. 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.

This Amendment No. 4 is being filed to report that the beneficial ownership of the outstanding Shares held by the Reporting Persons (as defined below) was reduced by more than 1% since the last filing following the transaction described in Item 5(c) below.

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 ("GP VI") (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 1 Shankar St., Herzliya 4672501, 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 1 Shankar St., Herzliya 4672501, Israel.

GP VI, 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. GP VI 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 GP VI 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 46,536,970 outstanding Shares of the Issuer, as set forth in the Issuer's Quarterly Report on Form 10-Q for the quarter ending September 30, 2022 filed with the Securities and Exchange Commission on November 10, 2022.

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 1,504,436 Shares constituting approximately 3.2% 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, David P. Bonita, 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 1,504,433 Shares constituting approximately 3.2% of the issued and outstanding Shares. GP VI 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 GP VI, pursuant to the terms of the limited liability company agreement of GP VI. As a result, OrbiMed Advisors and GP VI 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 GP VI 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 W. Carter Neild, each of whom disclaims beneficial ownership of the Shares held by OPI VI.

(c)

| Seller | Date of Transaction | Transaction | Number of Shares | Price Per Share |
|--------|---------------------|-------------|------------------|-----------------|
| OIP II | January 24, 2023 | Sold | 15,381 | \$12.25 |
| OPI VI | January 24, 2023 | Sold | 15,380 | \$12.25 |
| OIP II | January 24, 2023 | Sold | 285,011 | \$12.33 |
| OPI VI | January 24, 2023 | Sold | 285,011 | \$12.33 |
| OIP II | January 25, 2023 | Sold | 24,608 | \$12.06 |
| OIP VI | January 25, 2023 | Sold | 24,609 | \$12.06 |

(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, GP VI 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, GP VI 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 1,504,433. GP VI, pursuant to its authority under the limited partnership agreement of OPI VI, may be considered to hold indirectly 1,504,433 Shares.

OrbiMed Advisors is the managing member of GP VI, pursuant to the terms of the limited liability company agreement of GP VI. Pursuant to these agreements and relationships, OrbiMed Advisors and GP VI have discretionary investment management authority with respect to the assets of OPI VI. Such authority includes the power of GP VI to vote and otherwise dispose of securities held by OPI VI. The number of outstanding Shares attributable to OPI VI is 1,504,433 Shares. OrbiMed Advisors, pursuant to its authority under the terms of the limited liability company agreement of GP VI, may also be considered to hold indirectly 1,504,433 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 1,504,436. OrbiMed Israel, as the general partner of OIP II, may be considered to hold indirectly 1,504,436 Shares, and OrbiMed Limited, as the general partner of OrbiMed Israel, may be considered to hold indirectly 1,504,436 Shares.

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.

Other than as described in this Amendment No. 3, 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)). |

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: January 26, 2023

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

Name: Carl L. Gordon

Title: 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> | <u>Position with Reporting Person</u> | <u>Principal Occupation</u> |
|---|---------------------------------------|---|
| Carl L. Gordon | Member | Member OrbiMed Advisors LLC |
| Sven H. Borho German and Swedish Citizen | 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 OrbiMed Advisors LLC |
| David P. Bonita | Member | Member OrbiMed Advisors LLC |
| Peter A. Thompson | Member | Member OrbiMed Advisors LLC |
| Matthew S. Rizzo | 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 1 Shankar St., Herzliya 4672501 Israel.

| <u>Name</u> | <u>Position with Reporting Person</u> | <u>Principal Occupation</u> |
|-----------------------------------|---------------------------------------|--|
| Carl L. Gordon | Director | Director OrbiMed Advisors Israel II Limited |
| David P. Bonita | 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)). |

JOINT FILING AGREEMENT

The undersigned hereby agree that the Amendment No. 4 to Schedule 13D, dated January 24, 2023, 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 26th day of January 2023.

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
Name: Carl L. Gordon
Title: Member of OrbiMed Advisors LLC
