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

SCHEDULE 13D
Under the Securities Exchange Act of 1934
(Amendment No. 5)*

Synlogic, Inc.
(Name of Issuer)

Common Stock, par value \$0.001 per share
(Title of Class of Securities)

87166L100
(CUSIP Number)

OrbiMed Advisors LLC
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)

April 20, 2021
(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. 87166L100

1	NAME OF REPORTING PERSON OrbiMed Advisors LLC	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions) (a) <input type="checkbox"/> (b) <input type="checkbox"/>	
3	SEC USE ONLY	
4	SOURCE OF FUNDS (See Instructions) AF	
5	CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) or 2(e) <input type="checkbox"/>	
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 3,696,662
	9	SOLE DISPOSITIVE POWER 0
	10	SHARED DISPOSITIVE POWER 3,696,662
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 3,696,662	
12	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (See Instructions) <input type="checkbox"/>	
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11) 7.4%*	
14	TYPE OF REPORTING PERSON (See Instructions) IA	

* This percentage is calculated based upon 49,683,273 shares of common stock outstanding of Synlogic, Inc. (the "Issuer"), as set forth in the Issuer's Rule 424(b)(5) Prospectus filed with the Securities and Exchange Commission on April 19, 2021.

CUSIP No. 87166L100

1	NAME OF REPORTING PERSON OrbiMed Capital GP VI LLC	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions) (a) <input type="checkbox"/> (b) <input type="checkbox"/>	
3	SEC USE ONLY	
4	SOURCE OF FUNDS (See Instructions) AF	
5	CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) or 2(e) <input type="checkbox"/>	
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14	TYPE OF REPORTING PERSON (See Instructions) OO	

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Item 1. Security and Issuer

This Amendment No. 5 ("Amendment No. 5") to Schedule 13D supplements and amends the statement on Schedule 13D (the "Statement") originally filed by OrbiMed Advisors LLC, OrbiMed Capital GP VI LLC, and Samuel D. Isaly with the Securities and Exchange Commission (the "SEC") on September 7, 2017, as amended by Amendment No. 1 ("Amendment No. 1") filed with the SEC on January 26, 2018, Amendment No. 2 filed with the SEC on April 12, 2018, Amendment No. 3 filed with the SEC on August 12, 2019, and Amendment No. 4 filed with the SEC on March 29, 2021 ("Amendment No. 4"). This Statement relates to the common stock, par value \$0.001 per share (the "Shares"), of Synlogic, Inc., a Delaware corporation formerly known as Mirna Therapeutics, Inc. (the "Issuer"), with its principal offices located at 301 Binney St., Suite 402, Cambridge, Massachusetts 02142. The Shares are listed on The NASDAQ Capital Market under the ticker symbol "SYBX". Information given in response to each item shall be deemed incorporated by reference in all other items, as applicable. As reported in Amendment No. 1, Samuel D. Isaly has ceased to be a reporting person for purposes of the Statement.

This Amendment No. 5 is being filed to report that the beneficial ownership of the outstanding Shares held by the Reporting Persons increased by more than 1% since the filing of Amendment No. 4 following the purchase of Shares as more particularly described in Item 3, below.

Item 2. Identity and Background

(a) This Statement is being filed by OrbiMed Advisors LLC ("OrbiMed Advisors"), a limited liability company organized under the laws of Delaware, and OrbiMed Capital GP VI LLC ("GP VI"), a limited liability company organized under the laws of Delaware (collectively, the "Reporting Persons").

(b) – (c), (f) OrbiMed Advisors, a registered investment adviser under the Investment Advisers Act of 1940, as amended, is the managing member of GP VI, which is the general partner of OrbiMed Private Investments VI, LP ("OPI VI"), which holds Shares, as more particularly described in Item 3 below. Advisors has its principal offices at 601 Lexington Avenue, 54th Floor, New York, New York 10022.

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 and GP VI are set forth on Schedules I and II, attached hereto. Schedules I and II set forth the following information with respect to each such person:

(i) name;

(ii) business address;

(iii) present principal occupation or 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 Schedule I or II have 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

On April 20, 2021, the Issuer closed an underwritten public offering of 10,000,000 Shares at a purchase price of \$3.00 per Share (the “Offering”). OrbiMed Advisors and GP VI, pursuant to their authority under the limited partnership agreement of OPI VI, as more particularly referred to in Item 6 below, caused OPI VI to purchase an aggregate of 1,666,666 Shares in the Offering. The source of funds for such purchases was the working capital of OPI VI.

As a result of the transaction described in this Item 3, GP VI, as the general partner of OPI VI, may be deemed to be the beneficial owners of approximately 7.4% of the outstanding Shares. OrbiMed Advisors, as the managing member of GP VI, may be deemed to be the beneficial owner of approximately 7.4% of the outstanding Shares.

Item 4. Purpose of Transaction

The Shares were initially acquired by the Reporting Persons for the purpose of making an investment in the Issuer and not with the intention of acquiring control of the Issuer’s business.

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 the 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) As of the date of this filing, the Reporting Persons may be deemed, for purposes of Rule 13d-3 of the Securities Exchange Act of 1934, as amended, directly or indirectly, including by reason of their mutual affiliation, to be the beneficial owners of the Shares described in Item 6 below. Based upon information contained in the Issuer’s Rule 424(b)(5) Prospectus, filed with the Securities and Exchange Commission on April 19, 2021, such Shares deemed to be indirectly beneficially owned by the Reporting Persons constitutes approximately 7.4% of the issued and outstanding Shares. OrbiMed Advisors, pursuant to its authority as the managing member of GP VI, the general partner of OPI VI, may be deemed to indirectly beneficially own the Shares held by OPI VI. GP VI, pursuant to its authority as the general partner of OPI VI, may be deemed to indirectly beneficially own the Shares held by OPI VI. As a result, OrbiMed Advisors and GP VI share the power to direct the vote and to direct the disposition of the Shares held by OPI VI. 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) Other than as set forth in Item 3, the Reporting Persons have not effected any transactions in the Shares during the past sixty (60) days.
- (d) Not applicable.
- (e) Not applicable.

Item 6. Contracts, Arrangements, Understandings or Relationship 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. 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 purchased by OPI VI. The number of Shares attributable to OPI VI is 3,696,662. OrbiMed Advisors and GP VI may each be considered to hold indirectly 3,696,662 Shares.

Chau Khuong (“Khuong”), an employee at OrbiMed Advisors, has been a member of the Board of Directors of the Issuer since September 2013, and, accordingly, the Reporting Persons may have the ability to affect and influence control of the Issuer. From time to time, Khuong may receive additional stock options or other awards of equity-based compensation pursuant to the Issuer’s compensation arrangements for non-employee directors. Khuong is obligated to transfer any Shares 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 shares or economic benefits are provided to OPI VI.

Lock-Up Agreement

In connection with the Offering, Khuong, and certain other stockholders, entered into Lock-Up Agreements with the Issuer’s underwriters. Pursuant to his Lock-Up Agreement, Khuong agreed that he will not, during the period ending 90 days after the date of the prospectus 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 he has acquired 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 Shares held by Khuong 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 Form of Lock-Up Agreement, which is filed as Exhibit 2 and incorporated herein by reference.

Other than as described in this Amendment No. 5, 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. Materials to Be Filed as Exhibits

Exhibit	Description
1.	Joint Filing Agreement among OrbiMed Advisors LLC and OrbiMed Capital GP VI LLC.
2.	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: April 22, 2021

ORBIMED ADVISORS LLC

By: /s/ Carl L. Gordon
Name: Carl L. Gordon
Title: Member

ORBIMED CAPITAL GP VI LLC

By: ORBIMED ADVISORS LLC, its managing member
Member of OrbiMed Advisors LLC

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>	<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
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 OrbiMed Advisors LLC
David P. Bonita	Member	Member OrbiMed Advisors LLC
Trey Block	Chief Financial Officer	Chief Financial Officer OrbiMed Advisors LLC

SCHEDULE II

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 and OrbiMed Capital GP VI LLC.
2.	Form of Lock-Up Agreement.

JOINT FILING AGREEMENT

The undersigned hereby agree that the Amendment No. 5 to Schedule 13D, dated April 22, 2021, with respect to the ordinary shares of Synlogic, 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 22nd day of April 2021.

ORBIMED ADVISORS LLC

By: /s/ Carl L. Gordon
Name: Carl L. Gordon
Title: Member

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

Form of Lock-Up Agreement

April 15, 2021

SVB Leerink LLC
299 Park Avenue, 21st floor
New York, NY 10171

Re: Proposed Public Offering by Synlogic, Inc.

Ladies and Gentlemen:

The undersigned, a stockholder, officer and/or director of Synlogic, Inc., a Delaware corporation (the "Company"), understands that SVB Leerink LLC ("Leerink"), as representative of the several underwriters listed in the Underwriting Agreement (the "Underwriters"), proposes to enter into an Underwriting Agreement (the "Underwriting Agreement") with the Company providing for the public offering (the "Public Offering") of shares (the "Securities") of the Company's common stock, par value \$0.001 per share (the "Common Stock"). In recognition of the benefit that such an offering will confer upon the undersigned as a stockholder, an officer and/or a director of the Company, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the undersigned agrees with Leerink 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 Leerink, on behalf of the Underwriters, directly or indirectly, (i) 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 for the sale of, or otherwise dispose of or transfer any shares of Common Stock or any securities convertible into or exchangeable or exercisable for 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 or cause to be filed 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 Common Stock or other securities, in cash or otherwise.

Notwithstanding the foregoing, and subject to the conditions below, the undersigned may transfer Lock-Up Securities without the prior written consent of Leerink, provided, in each case, that (1) Leerink receives a signed lock-up agreement for the balance of the Lock-Up Period from each donee, trustee, distributee, or transferee, as the case may be, (2) any such transfer shall not involve a disposition for value, (3) such transfers are not required to be reported with the Securities and Exchange Commission on Form 4 in accordance with Section 16 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and (4) the undersigned does not otherwise voluntarily effect any public filing or report regarding such transfers (other than a filing on a Form 5 made after the expiration of the Lock-Up Period):

- (i) as a *bona fide* gift or gifts;
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- (ii) to any trust 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);
- (iii) as a distribution or other transfer by a partnership to its partners or former partners or by a limited liability company to its members or retired members or by a corporation to its stockholders or former stockholders or to any wholly-owned subsidiary of such corporation;
- (iv) to the undersigned’s affiliates or to any investment fund or other entity controlled or managed by the undersigned;
- (v) pursuant to a qualified domestic relations order or in connection with a divorce settlement;
- (vi) by will or intestate succession upon the death of the undersigned; or
- (vii) to the Company in satisfaction of any tax withholding obligation.

Furthermore, no provision in this letter shall be deemed to restrict or prohibit (1) the transfer of the undersigned’s Lock-Up Securities to the Company in connection with the termination of the undersigned’s services to the Company, provided that any filing under Section 16 of the Exchange Act made in connection with such transfer shall clearly indicate in the footnotes thereto that the filing relates to the circumstances described in this clause (1); (2) the exercise or exchange by the undersigned of any option or warrant to acquire any shares of Common Stock or options to purchase shares of Common Stock or vesting and settlement of any restricted stock awards or units, including the transfers of shares of Common Stock or any security convertible into or exercisable or exchangeable for Common Stock to the Company upon a vesting event of the Company’s securities or upon the exercise or conversion of options or warrants to purchase the Company’s securities, in each case, for cash or on a “cashless” or “net exercise” basis or to cover tax withholding obligations of the undersigned in connection with such vesting or exercise, pursuant to any stock option, stock bonus or other stock plan or arrangement; provided, however, that the underlying shares of Common Stock shall continue to be subject to the restrictions on transfer set forth in this letter and that any filing under Section 16 of the Exchange Act made in connection with such exercise or exchange shall clearly indicate in the footnotes thereto that (a) the filing relates to the circumstances described in this clause (2) and (b) the purpose of such transfer was to cover tax withholding obligations of the undersigned in connection with such vesting or exercise; (3) the transfer of Lock-Up Securities upon the completion of a bona fide third-party tender offer, merger, consolidation or other similar transaction made to all holders of the Company’s securities involving a change of control of the Company; provided, however, that in the event that such tender offer, merger, consolidation or other such transaction is not completed, such securities held by the undersigned shall remain subject to the restrictions on transfer set forth in this letter; (4) sales or transfers of Securities acquired in the Public Offering or on the open market after the date of the Underwriting Agreement, provided that no such transaction is required to be, or is, publicly announced (whether on Form 4, Form 5 or otherwise) during the Lock-Up Period; and (5) transfers of shares of Common Stock pursuant to a trading plan established pursuant to Rule 10b5-1 under the Exchange Act prior to the date hereof, which trading plan shall not be amended during the Lock-Up Period but may be terminated during the Lock-Up Period; provided, that to the extent a public announcement or filing under the Exchange Act, if any, is required of or voluntarily made by or on behalf of the undersigned or the Company regarding sales made under the undersigned’s 10b5-1 Plan, such announcement or filing shall include a statement to the effect that such sales of Common Stock are being made pursuant to the undersigned’s 10b5-1 Plan established prior to the date hereof.

Notwithstanding anything herein to the contrary, nothing herein shall prevent the undersigned from establishing a 10b5-1 trading plan that complies with Rule 10b5-1 under the Exchange Act ("10b5-1 Trading Plan") or from amending an existing 10b5-1 Trading Plan so long as there are no sales of Lock-Up Securities under any such 10b5-1 Trading Plan during the Lock-Up Period; and provided that, the establishment of a 10b5-1 Trading Plan or the amendment of a 10b5-1 Trading Plan shall only be permitted if (i) the establishment or amendment of such plan is not required to be reported in any public report or filing with the Securities Exchange Commission, or otherwise and (ii) the undersigned does not otherwise voluntarily effect any public filing or report regarding the establishment or amendment of such plan.

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. This lock-up agreement shall automatically terminate, and the undersigned shall be released from the undersigned's obligations hereunder, upon the earliest to occur, if any, of (i) prior to the execution of the Underwriting Agreement, the Company advises Leerink in writing that it has determined not to proceed with the Public Offering; (ii) the Underwriting Agreement is executed but is terminated prior to the closing of the Public Offering (other than the provisions thereof which survive termination), or (iii) April 30, 2021, in the event that the Underwriting Agreement has not been executed by such date.

This agreement shall be governed by, and construed in accordance with, the laws of the State of New York.

[SIGNATURE PAGE FOLLOWS]

Very truly yours,

Name of Security Holder (*Print exact name*)

By: _____
Signature

If not signing in an individual capacity:

Name of Authorized Signatory (*Print*)

Title of Authorized Signatory (*Print*)

(indicate capacity of person signing if signing as custodian, trustee, or on behalf of an entity)

[SIGNATURE PAGE TO LOCK-UP AGREEMENT]
