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

**SCHEDULE 13D**  
Under the Securities Exchange Act of 1934  
(Amendment No. 4)\*

**RHYTHM PHARMACEUTICALS, INC.**

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(Name of Issuer)

**COMMON STOCK**

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(Title of Class of Securities)

**76243J105**

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(CUSIP Number)

**OrbiMed Advisors LLC  
OrbiMed Capital GP V LLC**

**601 Lexington Avenue, 54th Floor  
New York, NY 10022  
Telephone: (212) 739-6400**

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(Name, Address and Telephone Number of Person  
Authorized to Receive Notices and Communications)

**August 3, 2018**

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(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).

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CUSIP No. 76243J105	
1	NAME OF REPORTING PERSONS 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 1,629,700
	9 SOLE DISPOSITIVE POWER 0
	10 SHARED DISPOSITIVE POWER 1,629,700
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 1,629,700
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) 4.76% (1)
14	TYPE OF REPORTING PERSON (See Instructions) IA

(1) This percentage is calculated based upon 34,175,137 outstanding shares of common stock, par value \$0.001 per share (the "Shares"), of Rhythm Pharmaceuticals, Inc. (the "Issuer"), as set forth in the Issuer's Form 10-Q, filed with the Securities and Exchange Commission on August 8, 2018.

CUSIP No. 76243J105	
1	NAME OF REPORTING PERSONS OrbiMed Capital GP V 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
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**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 and OrbiMed Capital GP III LLC (the “Statement”) originally filed with the Securities and Exchange Commission (the “SEC”) on October 20, 2017 with Samuel D. Isaly as an additional reporting person, and amended by Amendment No. 1 thereto filed with the SEC on February 7, 2018, Amendment No. 2 thereto filed with the SEC on June 4, 2018 and Amendment No. 3 thereto filed with the SEC on June 27, 2018. The Statement relates to the common stock, par value \$0.001 per share (the “Shares”), of Rhythm Pharmaceuticals, Inc., a corporation organized under the laws of Delaware (the “Issuer”), with its principal executive offices located at 500 Boylston Street, 11<sup>th</sup> floor, Boston, MA 02116. The Shares are listed on the NASDAQ Global Market under the ticker symbol “RYTM”. Information given in response to each item shall be deemed incorporated by reference in all other items, as applicable.

**Item 2. Identity and Background**

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

(b) – (c), (f) Advisors, a registered investment adviser under the Investment Advisers Act of 1940, as amended, is the sole managing member of GP V, which is the sole general partner of OrbiMed Private Investments V, LP (“OPI V”). OPI V holds Shares as described herein. Advisors has their principal offices at 601 Lexington Avenue, 54th Floor, New York, New York 10022.

GP V has its principal offices at 601 Lexington Avenue, 54th Floor, New York, New York 10022.

The directors and executive officers of Advisors and GP V 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;
- (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**

Not applicable.

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

This Amendment No. 4 to the Statement relates to the transactions by the Reporting Persons more fully described in Item 5 below. The Shares initially had been 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 common stock 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 common stock 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 Act, directly or indirectly, including by reason of their mutual affiliation, to be the beneficial owners of 1,629,700 Shares held of record by OPI V. Based upon information contained in the Issuer's Form 10-Q, filed with the SEC on August 8, 2018, such Shares constitutes approximately 4.76% of the issued and outstanding Shares. Advisors, pursuant to its authority as the sole managing member of GP V, which is the sole general partner of OPI V, may be deemed to indirectly beneficially own the Shares held by OPI V. GP V, pursuant to its authority as the general partner of OPI V, may be deemed to indirectly beneficially own the Shares held by OPI V. As a result, Advisors and GP V share the power to direct the vote and the disposition of the Shares held of record by OPI V. 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 V.

In addition, Advisors and GP V, pursuant to their authority under the limited partnership agreement of OPI V, prior to the date of this filing, caused OPI V to enter into the agreements referred to in Item 6 below.

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(c)

Seller	Date of Transaction	Transaction	Number of Shares	Price Per Share*
OPI V	July 2, 2018	Sold	39,800	\$ 33.21
OPI V	July 3, 2018	Sold	35,200	\$ 34.00
OPI V	July 5, 2018	Sold	36,213	\$ 36.04
OPI V	July 6, 2018	Sold	84	\$ 34.95
OPI V	July 6, 2018	Sold	16,103	\$ 36.05
OPI V	July 11, 2018	Sold	24,024	\$ 33.74
OPI V	July 12, 2018	Sold	46,344	\$ 33.04
OPI V	July 16, 2018	Sold	23,600	\$ 32.54
OPI V	July 17, 2018	Sold	2,838	\$ 32.45
OPI V	July 17, 2018	Sold	794	\$ 33.61
OPI V	July 18, 2018	Sold	5,111	\$ 32.27
OPI V	July 20, 2018	Sold	24,300	\$ 32.68
OPI V	July 24, 2018	Sold	1,501	\$ 32.32
OPI V	August 2, 2018	Sold	5,169	\$ 32.14
OPI V	August 3, 2018	Sold	174,219	\$ 32.03

\* The Price Per Share reported above is a weighted average price, except for the Shares sold in a block order at a price of \$34.95 (July 6, 2018) and \$32.54 (July 16, 2018). The Shares were sold in multiple transactions at prices ranging from: \$33.09 to \$33.70 (July 2, 2018); \$33.87 to \$34.49 (July 3, 2018); \$36.00 to \$36.30 (July 5, 2018); \$36.03 to \$36.32 (July 6, 2018); \$33.50 to \$34.10 (July 11, 2018); \$33.00 to \$33.09 (July 12, 2018); \$32.35 to \$33.04 (July 17, 2018); \$33.48 to \$33.75 (July 17, 2018); \$32.10 to \$32.45 (July 18, 2018); \$32.50 to \$32.85 (July 20, 2018); \$32.25 to \$32.54 (July 24, 2018); \$32.00 to \$32.59 (July 2, 2018); and \$32.00 to \$32.17 (August 3, 2018). Upon request, the Reporting Persons undertake to provide the Issuer, any security holder of the Issuer, or the SEC full information regarding the Shares purchased at each separate price within the ranges set forth above.

Except as disclosed above and in Amendment No. 3, the Reporting Persons have not effected any transactions in the Shares during the past sixty (60) days.

(d) Not applicable.

(e) As of August 3, 2018, the Reporting Persons ceased to beneficially own more than 5% of the Shares.

#### **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 V is the sole general partner of OPI V, pursuant to the terms of the limited partnership agreement of OPI V. Advisors is the sole managing member of GP V, pursuant to the terms of the limited liability company agreement of GP V. Pursuant to these agreements and relationships, Advisors and GP V have discretionary investment management authority with respect to the assets of OPI V. Such authority includes the power of GP V and Advisors to vote and otherwise dispose of securities purchased by OPI V. The number of outstanding Shares held of record by OPI V is 1,629,700. Advisors and GP V may be considered to hold indirectly 1,629,700 Shares.

#### ***Investors Rights Agreement***

In addition, OPI V and certain other stockholders of the Issuer entered into an amended and restated investors' rights agreement with the Issuer (the "Investors Rights Agreement"), dated as of August 21, 2017. Pursuant to the Investor Rights Agreement and subject to the terms and conditions therein, the parties agreed that:

#### ***Registration Rights***

Following the closing of the Issuer's initial public offering (the "IPO"), the holders of a certain number of Shares, or their transferees, will be entitled to the registration rights set forth below with respect to registration of the resale of such shares under the Securities Act pursuant to the Investors Rights Agreement.

### *Demand Registration Rights*

At any time after 180 days after the effective date of the IPO, upon the written request of at least a majority of the holders of the registrable securities then outstanding that the Issuer file a registration statement under the Securities Act covering the registration of registrable securities owned by such holder(s) having an anticipated aggregate offering price, net of selling expenses, of at least \$15.0 million, the Issuer will be obligated to notify all holders of registrable securities of such request. As soon as practicable thereafter, and in any event within sixty (60) days after the date such request is received, the Issuer will be required to register the sale on a registration statement on Form S-1 of all registrable securities that holders may request to be registered, subject to specified exceptions, conditions and limitations.

### *Piggyback Registration Rights*

The Investors Rights Agreement further provides that, in the event that the Issuer determines to register any of its securities under the Securities Act, either for its own account or for the account of other security holders, the stockholders who are party to the Investors Rights Agreement, including OPI V, will be entitled to certain “piggyback” registration rights allowing the holders to include their shares in such registration, subject to certain marketing and other limitations. The underwriters of any underwritten offering will have the right to limit the number of registrable securities to be included in the registration statement, but such number may not be below 30% of the total number of Shares included in such registration statement.

### *Form S-3 Registration Rights*

At any time when the Issuer is eligible to use a Form S-3 registration statement, the holders of at least 10% of the registrable securities then outstanding can request that the Issuer register all or a portion of their Shares on Form S-3, so long as the aggregate price to the public of the securities to be sold under the registration statement on Form S-3 is at least \$10.0 million or consists of all the remaining registrable securities, and subject to specified exceptions, conditions and limitations.

### *Expenses of Registration*

Subject to certain limitations, the Issuer will pay the registration expenses of the holders of the shares registered pursuant to the demand, Form S-3 and piggyback registration rights described above.

### *Indemnification*

The Investors Rights Agreement contains customary cross-indemnification provisions, pursuant to which the Issuer is obligated to indemnify the selling stockholders in the event of, among other things, material misstatements or omissions in the registration statement attributable to the Issuer, and the selling stockholders are obligated to indemnify the Issuer for, among other things, material misstatements or omissions attributable to them.

### *Termination of Registration Rights.*

OPI V's demand, Form S-3 and piggyback registration rights described above generally will terminate upon the earlier of: (i) five years following the closing of the IPO or (ii) such time as SEC Rule 144 or another similar exemption under the Securities Act is available for the sale of all Shares held by OPI V during a three-month period without registration and without the requirement for the Issuer to be in compliance with the current public information required under SEC Rule 144(c)(1).

The foregoing description of the Investor Rights Agreement does not purport to be complete and is qualified in its entirety by reference to the full text of the Investor Rights Agreement, a copy of which is filed as Exhibit 2 and incorporated herein by reference.

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**Item 7. Materials to Be Filed as Exhibits**

<b>Exhibit</b>	<b>Description</b>
1.	Joint Filing Agreement among OrbiMed Advisors LLC and OrbiMed Capital GP V LLC.
2.	Amended and Restated Investors' Rights Agreement by and among the Issuer and each of the persons listed on Schedule A thereto, dated as of August 21, 2017 (incorporated by reference to Exhibit 4.2 to the Issuer's Registration Statement on Form S-1 (SEC 333-220337), filed with the SEC on September 5, 2017).

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**SIGNATURE**

After reasonable inquiry and to the best of each of the undersigned's knowledge and belief, each of the undersigned certifies that the information set forth in this statement is true, complete and correct.

Dated: August 10, 2018

OrbiMed Advisors LLC

By: /s/ Jonathan T. Silverstein  
Name: Jonathan T. Silverstein  
Title: Member of OrbiMed Advisors LLC

By: /s/ Sven H. Borho  
Name: Sven H. Borho  
Title: Member of OrbiMed Advisors LLC

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

OrbiMed Capital GP V LLC

By: OrbiMed Advisors LLC  
its Managing Member

By: /s/ Jonathan T. Silverstein  
Name: Jonathan T. Silverstein  
Title: Member of OrbiMed Advisors LLC

By: /s/ Sven H. Borho  
Name: Sven H. Borho  
Title: Member of OrbiMed Advisors LLC

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

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**Schedule I**

The name and present principal occupation of each of the executive officers and directors of OrbiMed Advisors LLC are set forth below. Unless otherwise noted, each of these persons are United States citizens and have as their business address 601 Lexington Avenue, 54th Floor, New York, NY 10022.

Name	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
Evan D. Sotiriou	Chief Financial Officer	Chief Financial Officer OrbiMed Advisors LLC

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**Schedule II**

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

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**EXHIBIT INDEX**

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JOINT FILING AGREEMENT

The undersigned hereby agree that the Statement on this Schedule 13D, dated August 10, 2018 (the "Schedule 13D"), with respect to the Shares of Rhythm Pharmaceuticals, 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, and that this Agreement shall be included as an Exhibit to this Schedule 13D. Each of the undersigned agrees to be responsible for the timely filing of the Schedule 13D, 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 August 2018.

OrbiMed Advisors LLC

By: /s/ Jonathan T. Silverstein  
Name: Jonathan T. Silverstein  
Title: Member of OrbiMed Advisors LLC

By: /s/ Sven H. Borho  
Name: Sven H. Borho  
Title: Member of OrbiMed Advisors LLC

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

OrbiMed Capital GP V LLC

By: OrbiMed Advisors LLC  
its Managing Member

By: /s/ Jonathan T. Silverstein  
Name: Jonathan T. Silverstein  
Title: Member of OrbiMed Advisors LLC

By: /s/ Sven H. Borho  
Name: Sven H. Borho  
Title: Member of OrbiMed Advisors LLC

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

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