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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. 1)\*

**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)

**January 24, 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 PERSON OrbiMed Advisors LLC	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP	(a) <input type="checkbox"/> (b) <input type="checkbox"/>
3	SEC USE ONLY	
4	SOURCE OF FUNDS 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 2,901,295
	9	SOLE DISPOSITIVE POWER 0
	10	SHARED DISPOSITIVE POWER 2,901,295
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 2,901,295	
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) 10.63% (1)	
14	TYPE OF REPORTING PERSON (See Instructions) IA	

(1) This percentage is calculated based upon 27,284,140 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 November 14, 2017.

CUSIP No. 76243J105		
1	NAME OF REPORTING PERSON OrbiMed Capital GP V LLC	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP	(a) <input type="checkbox"/> (b) <input type="checkbox"/>
3	SEC USE ONLY	
4	SOURCE OF FUNDS 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 2,901,295
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## Item 1. Security and Issuer

This Amendment No. 1 (“Amendment No. 1”) to Schedule 13D supplements and amends the Statement on Schedule 13D originally filed by OrbiMed Advisors LLC, OrbiMed Capital GP IV LLC and Samuel D. Isaly with the Securities and Exchange Commission (the “SEC”) on October 20, 2017 (the “Statement”). 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 common stock is 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.

This Amendment No. 1 is being filed to report that Samuel D. Isaly, who was previously identified as a reporting person, has ceased to be the beneficial owner of more than five percent of the outstanding Shares.

Item 2 of the Statement is amended to read in full as set forth below.

## 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.

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Item 5 of the Statement is amended to read in full as set forth below.

**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 2,901,295 Shares held of record by OPI V. Based upon information contained in the Issuer’s Form 10-Q, filed with the Securities and Exchange Commission (the “SEC”) on November 14, 2017, such Shares constitutes approximately 10.63% 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 IV.

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.

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

(d) Not applicable.

(e) As of January 24, 2018, Samuel D. Isaly, who was previously identified as a reporting person, has ceased to be the beneficial owner of more than five percent of the outstanding Shares.

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

Exhibit	Description
1.	Joint Filing Agreement among OrbiMed Advisors LLC and OrbiMed Capital GP V LLC.
2.	Lock-Up Agreement.
3.	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: February 7, 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
Samuel D. Isaly	Managing Member	Managing Member OrbiMed Advisors LLC
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**

<b>Exhibit</b>	<b>Description</b>
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2.	Lock-Up Agreement.
3.	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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## JOINT FILING AGREEMENT

The undersigned hereby agree that the Statement on this Schedule 13D, dated February 7, 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 7<sup>th</sup> day of February 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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**Lock-Up Agreement**

Rhythm Pharmaceuticals, Inc.  
Public Offering of Common Stock

May \_\_\_, 2017

Morgan Stanley & Co. LLC  
Merrill Lynch, Pierce, Fenner & Smith  
Incorporated

As Representatives of the several Underwriters,  
c/o Morgan Stanley & Co. LLC  
1585 Broadway  
New York, NY 10036

Ladies and Gentlemen:

This letter is being delivered to you in connection with the proposed Underwriting Agreement (the "Underwriting Agreement"), between Rhythm Pharmaceuticals, Inc., a Delaware corporation, including any predecessor or successor company, as the case may be (the "Company"), and each of you as representatives of a group of Underwriters named therein (the "Underwriters"), relating to an underwritten public offering of shares of common stock ("Common Stock"), of the Company (the "Offering").

In order to induce you and the other Underwriters to enter into the Underwriting Agreement, the undersigned will not, without the prior written consent of the Representatives, offer, sell, contract to sell, pledge or otherwise dispose of, (or enter into any transaction which is designed to, or might reasonably be expected to, result in the disposition (whether by actual disposition or effective economic disposition due to cash settlement or otherwise) by the undersigned or any affiliate of the undersigned or any person in privity with the undersigned or any affiliate of the undersigned), directly or indirectly, including the filing (or participation in the filing) of a registration statement (other than a registration statement on Form S-8) with the Securities and Exchange Commission (the "SEC") in respect of, or establish or increase a put equivalent position or liquidate or decrease a call equivalent position within the meaning of Section 16 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and the rules and regulations of the SEC promulgated thereunder with respect to, any capital stock of the Company or any securities convertible into, or exercisable or exchangeable for such capital stock, or publicly announce an intention to effect any such transaction, for a period from the date hereof until 180 days after the date of the Underwriting Agreement (the "Lock-up Period"). If the undersigned is an officer or director of the Company, the undersigned further agrees that the foregoing restrictions shall be equally applicable to any issuer-directed shares of Common Stock the undersigned may purchase in the Offering.

The provisions of the immediately preceding paragraph shall not apply to (i) the sale of shares of Common Stock by the undersigned to the Underwriters pursuant to the Underwriting Agreement, (ii) transfers of shares of capital stock of the Company or any securities convertible into, or exercisable or exchangeable for such capital stock as a bona fide gift or gifts, (iii) transfers or dispositions of shares of capital stock of the Company or any securities convertible into, or exercisable or exchangeable for such capital stock to any trust for the direct or indirect benefit of the undersigned or the immediate family of the undersigned in transactions not involving a disposition for value;

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(iv) transfers or dispositions of shares of capital stock of the Company or any securities convertible into, or exercisable or exchangeable for such capital stock to any corporation, partnership, limited liability company or other entity all of the beneficial ownership interests of which are held by the undersigned or the immediate family of the undersigned in a transaction not involving a disposition for value; (v) transfers or dispositions of shares of capital stock of the Company or any securities convertible into, or exercisable or exchangeable for such capital stock by will, other testamentary document or intestate succession to the legal representative, heir, beneficiary or a member of the immediate family of the undersigned; or (vi) distributions of shares of capital stock of the Company or any securities convertible into, or exercisable or exchangeable for such capital stock to partners, members or stockholders of the undersigned; *provided*, that in the case of any transfer, disposition or distribution pursuant to clause (ii), (iii), (iv), (v) or (vi), each transferee, donee or distributee shall execute and deliver to the Representatives a lock-up letter in the form of this letter; *and provided further*, that in the case of any transfer, disposition or distribution pursuant to clause (ii), (iii), (iv) or (vi), no filing by any party (donor, donee, transferor or transferee) under the Exchange Act or other public announcement reporting a reduction in the beneficial ownership of Common Stock held by the undersigned shall be required or shall be made voluntarily in connection with such transfer, disposition or distribution (other than a filing on a Form 5 made after the expiration of the 180-day period referred to in the immediately preceding paragraph). For purposes of this letter, "immediate family" shall mean any relationship by blood, marriage, domestic partnership, or adoption, not more remote than first cousin. Furthermore, notwithstanding the restrictions imposed by this letter, the undersigned may, without the prior written consent of the Representatives, (a) exercise an option to purchase shares of Common Stock granted under any equity incentive plan or equity purchase plan of the Company which is described in the registration statement relating to the Offering, *provided* that the underlying equity securities shall continue to be subject to the restrictions on transfer set forth in this letter, (b) establish a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares of Common Stock, *provided* that such plan does not provide for any transfers of Common Stock, and no filing with the SEC or other public announcement shall be required or voluntarily made by the undersigned or any other person in connection therewith, in each case during the 180-day period referred to in the immediately preceding paragraph, (c) transfer shares of Common Stock to the Company in connection with the termination of the undersigned's employment with the Company, and (d) transfer or dispose of shares of Common Stock purchased in the Offering from the Underwriters (other than any issuer-directed shares of Common Stock purchased in the Offering by an officer or director of the Company) or on the open market following the Offering; *provided* that, in the case of clauses (b), (c) and (d) above, no filing with the SEC or other public announcement shall be required or voluntarily made by the undersigned or any other person in connection therewith, in each case during the 180-day period referred to in the immediately preceding paragraph, other than in the case of clause (c) to the extent such filing is required and the employment termination is footnoted or otherwise disclosed therein.

If the undersigned is an officer or director of the Company, (i) the Representatives agree that, at least three business days before the effective date of any release or waiver of the foregoing restrictions in connection with a transfer of shares of Common Stock, the Representatives will notify the Company of the impending release or waiver, and (ii) the Company has agreed in the Underwriting Agreement to announce the impending release or waiver by press release through a major news service at least two business days before the effective date of the release or waiver. Any release or waiver granted by the Representatives hereunder to any such officer or director shall only be effective two business days after the publication date of such press release. The provisions of this paragraph will not apply if (a) the release or waiver is effected solely to permit a transfer not for consideration and (b) the transferee has agreed in writing to be bound by the same terms described in this letter to the extent and for the duration that such terms remain in effect at the time of the transfer.

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This letter shall automatically terminate and the undersigned shall be released from all obligations under this letter upon the earliest to occur, if any, of (i) either the Company, on the one hand, or the Representatives, on the other hand, advising the other in writing, prior to the execution of the Underwriting Agreement, that they have determined not to proceed with the Offering, (ii) the Underwriting Agreement being terminated prior to the Closing Date (as defined in the Underwriting Agreement), (iii) the registration statement filed with the SEC with respect to the Offering being withdrawn and (iv) December 31, 2017, in the event that the Underwriting Agreement has not been executed by such date.

*[Remainder of the Page Intentionally Left Blank]*

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**OrbiMed Private Investments V, LP**

By: OrbiMed Capital GP V LLC,  
its General Partner

By: OrbiMed Advisors LLC,  
its Managing Member

By: /s/ Jonathan T. Silverstein  
Name: Jonathan T. Silverstein  
Title: Member

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