SECURITIES AND EXCHANGE COMMISSION WASHINGTON, DC 20549

SCHEDULE 13G (Rule 13d-102)

INFORMATION TO BE INCLUDED IN STATEMENTS FILED PURSUANT TO RULES 13d-1(b)(c), AND (d) AND AMENDMENTS THERETO FILED PURSUANT TO RULE 13d-2(b)

(Amendment No. 2) *

Rhythm Pharmaceuticals, Inc.

(Name of Issuer)

Common Stock, par value \$0.001 per share

(Title of Class of Securities)

76243J105

(CUSIP Number)

December 31, 2020

(Date of Event Which Requires Filing of this Statement)

Check the appropriate box to designate the rule pursuant to which this Schedule is filed:

 \Box Rule 13d-1(b)

 \boxtimes Rule 13d-1(c)

 \Box Rule 13d-1(d)

(Page 1 of 11 Pages)

* 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 the disclosures provided in a prior cover page.

The information required in 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 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).

| NAME OF REPORTIN I.R.S. IDENTIFICATIO | | |
|---|---|---|
| Deerfield Mgmt, L.P. | | |
| CHECK THE APPROF | PRIATE BOX IF A MEMBER OF A GROUP* | (a) □ (b) ⊠ |
| SEC USE ONLY CITIZENSHIP OR PLACE OF ORGANIZATION | | |
| | | |
| Delaware | | |
| 5. | SOLE VOTING POWER | |
| | 0 | |
| 6. | SHARED VOTING POWER | |
| | 2.430.198 (1) | |
| 7. | SOLE DISPOSITIVE POWER | |
| | 0 | |
| 8. | SHARED DISPOSITIVE POWER | |
| | 2,430,198 (1) | |
| AGGREGATE AMOU | NT BENEFICIALLY OWNED BY EACH REPORTING PERSON | |
| 2 430 198 (1) | | |
| CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES* | | |
| PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9 | | |
| 5 50% | | |
| | G PERSON* | |
| PN | | |
| | I.R.S. IDENTIFICATIO Deerfield Mgmt, L.P. CHECK THE APPROF SEC USE ONLY CITIZENSHIP OR PLA Delaware Delaware 6. 7. 8. AGGREGATE AMOUT 2,430,198 (1) CHECK BOX IF THE S 9ERCENT OF CLASS 5.50% | I.R.S. IDENTIFICATION NO. OF ABOVE PERSONS (ENTITIES ONLY) Deerfield Mgmt, L.P. CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP* SEC USE ONLY CITIZENSHIP OR PLACE OF ORGANIZATION Delaware 5. SOLE VOTING POWER 0 6. SHARED VOTING POWER 2,430,198 (1) 7. SOLE DISPOSITIVE POWER 0 0 8. SHARED DISPOSITIVE POWER 2,430,198 (1) 0 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 2,430,198 (1) CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES* PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9 5.50% TYPE OF REPORTING PERSON* |

(1) Comprised of Common Stock held by Deerfield Partners, L.P. of which Deerfield Mgmt, L.P. is the general partner.

| 1. | NAME OF REPORTIN | NG PERSONS ON NO. OF ABOVE PERSONS (ENTITIES ONLY) | |
|---|--|---|----------------|
| | Deerfield Management Company, L.P. | | |
| 2. | | PRIATE BOX IF A MEMBER OF A GROUP* | (a) □ (b) ⊠ |
| 3. | SEC USE ONLY | | |
| 4. | CITIZENSHIP OR PLACE OF ORGANIZATION | | |
| | Delaware | | |
| | 5. | SOLE VOTING POWER | |
| NUMBER OF | | 0 | |
| SHARES BENEFICIALLY | 6. | SHARED VOTING POWER | |
| OWNED BY | | 2,721,203 (2) | |
| EACH REPORTING | 7. | SOLE DISPOSITIVE POWER | |
| PERSON | | 0 | |
| WITH | 8. | SHARED DISPOSITIVE POWER | |
| | | 2,721,203 (2) | |
| 9. | AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON | | |
| | 2,721,203 (2) | | |
| 10. | | AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES* | |
| | | | |
| 11. PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9 | | S REPRESENTED BY AMOUNT IN ROW 9 | |
| 6.16% | | | |
| 12. TYPE OF REF | | G PERSON* | |
| | PN | | |

(2) Comprised of Common Stock held by Deerfield Private Design Fund III, L.P. and Deerfield Partners, L.P. of which Deerfield Management Company, L.P. is the investment advisor.

| 1. | | ON NO. OF ABOVE PERSONS (ENTITIES ONLY) | |
|---|---|---|-------|
| 2. | Deerfield Mgmt III, L.P. | | (a) 🗆 |
| 2. | 2. CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP* | | |
| 3. | SEC USE ONLY CITIZENSHIP OR PLACE OF ORGANIZATION | | |
| 4. | | | |
| | Delaware | | |
| | 5. | SOLE VOTING POWER | |
| NUMBER OF | | 0 | |
| SHARES BENEFICIALLY | 6. | SHARED VOTING POWER | |
| OWNED BY | | 291,005 (3) | |
| EACH REPORTING | 7. | SOLE DISPOSITIVE POWER | |
| PERSON WITH | | 0 | |
| WIIII | 8. | SHARED DISPOSITIVE POWER | |
| | | 291,005 (3) | |
| 9. | AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON | | |
| 291,005 (3) | | | |
| 10. | CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES* | | |
| 11. PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9 | | REPRESENTED BY AMOUNT IN ROW 9 | |
| 0.66% | | | |
| 12. | TYPE OF REPORTIN | G PERSON* | |
| | PN | | |

(3) Comprised of Common Stock held by Deerfield Private Design Fund III, L.P. of which Deerfield Mgmt III, L.P. is the general partner.

| 1. | NAME OF REPORTIN I.R.S. IDENTIFICATIO | IG PERSONS ON NO. OF ABOVE PERSONS (ENTITIES ONLY) | |
|--------------------------|--|---|----------------|
| | Deerfield Partners, L.P. | | |
| 2. | CHECK THE APPRO | PRIATE BOX IF A MEMBER OF A GROUP* | (a) □ (b) ⊠ |
| 3. | SEC USE ONLY | | |
| 4. | CITIZENSHIP OR PL | ACE OF ORGANIZATION | |
| | Delaware | | |
| | 5. | SOLE VOTING POWER | |
| NUMBER OF | | 0 | |
| SHARES | 6. | SHARED VOTING POWER | |
| BENEFICIALLY OWNED BY | | 2,430,198 | |
| EACH REPORTING | 7. | SOLE DISPOSITIVE POWER | |
| PERSON | | 0 | |
| WITH | 8. | SHARED DISPOSITIVE POWER | |
| | | 2,430,198 | |
| 9. | AGGREGATE AMOU | NT BENEFICIALLY OWNED BY EACH REPORTING PERSON | |
| | | | |
| 10. | 2,430,198 CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES* | | |
| 10. | | AGGREGATE AMOUNT IN NOW (7) EACLODES CERTAIN STRAKES | |
| 11. | 11. PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9 | | |
| | 5.50% | | |
| 12. | TYPE OF REPORTING PERSON* | | |
| | PN | | |
| | *** | | |

| 1. | NAME OF REPORTIN | NG PERSONS ON NO. OF ABOVE PERSONS (ENTITIES ONLY) | |
|------------------------|---|---|----------------|
| | Deerfield Private Design Fund III, L.P. | | |
| 2. | | PRIATE BOX IF A MEMBER OF A GROUP* | (a) □ (b) ⊠ |
| 3. | SEC USE ONLY | | |
| 4. | CITIZENSHIP OR PL | ACE OF ORGANIZATION | |
| | Delaware | | |
| | 5. | SOLE VOTING POWER | |
| NUMBER OF | | 0 | |
| SHARES BENEFICIALLY | 6. | SHARED VOTING POWER | |
| OWNED BY | | 291,005 | |
| EACH REPORTING | 7. | SOLE DISPOSITIVE POWER | |
| PERSON WITH | | 0 | |
| WIIII | 8. | SHARED DISPOSITIVE POWER | |
| | | 291,005 | |
| 9. | AGGREGATE AMOU | NT BENEFICIALLY OWNED BY EACH REPORTING PERSON | |
| | 291,005 | | |
| 10. | CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES* | | |
| 11. | 11. PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9 | | |
| 0.66% | | | |
| 12. | TYPE OF REPORTING PERSON* | | |
| | PN | | |

| 1. | NAME OF REPORTIN I.R.S. IDENTIFICATIO | IG PERSONS ON NO. OF ABOVE PERSONS (ENTITIES ONLY) | | |
|--|---|---|----------------|--|
| | James E. Flynn | | | |
| 2. | | | (a) □ (b) ⊠ | |
| 3. | SEC USE ONLY | | | |
| 4. | CITIZENSHIP OR PLACE OF ORGANIZATION | | | |
| | United States | | | |
| | 5. | SOLE VOTING POWER | | |
| NUMBER OF | | 0 | | |
| SHARES BENEFICIALLY | 6. | SHARED VOTING POWER | | |
| OWNED BY | | 2,721,203 (4) | | |
| EACH REPORTING | 7. | SOLE DISPOSITIVE POWER | | |
| PERSON WITH | | 0 | | |
| WIIII | 8. | SHARED DISPOSITIVE POWER | | |
| | | 2,721,203 (4) | | |
| 9. AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 2,721,203 (4) | | NT BENEFICIALLY OWNED BY EACH REPORTING PERSON | | |
| | | | | |
| 10. | CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES* | | | |
| 11. | PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9 | | | |
| | 6.16% | | | |
| 12. | TYPE OF REPORTING | G PERSON* | | |
| | IN | | | |

(4) Comprised of Common Stock held by Deerfield Private Design Fund III, L.P. and Deerfield Partners, L.P.

| CUSIP No. | 76243J105 | 13G | Page 8 of 11 |
|------------|--|---|---------------------------------------|
| Item 1(a). | Name of Issuer: | | |
| | Rhythm Pharmaceutica | s, Inc. | |
| Item 1(b). | Address of Issuer's Prin | cipal Executive Offices: | |
| | 222 Berkeley Street, 12 Boston, MA 02116 | h Floor | |
| Item 2(a). | Name of Person Filing: | | |
| | James E. Flynn, Deerfie Private Design Fund III | ld Mgmt, L.P., Deerfield Mgmt III, L.P., Deerfield Management Company, L.P., Dee , L.P. | erfield Partners, L.P. and Deerfield |
| Item 2(b). | Address of Principal Bu | siness Office, or if None, Residence: | |
| | | ld Mgmt, L.P., Deerfield Mgmt III, L.P., Deerfield Management Company, L.P., Dee , L.P., 345 Park Avenue South, 12th Floor, New York, NY 10010 | erfield Partners, L.P., and Deerfield |
| Item 2(c). | Citizenship: | | |
| | Deerfield Mgmt, L.P., D Partners, L.P Delawar | Deerfield Mgmt III, L.P., Deerfield Management Company, L.P., Deerfield Private De e limited partnerships; | sign Fund III, L.P. and Deerfield |
| | James E. Flynn – United | 1 States citizen | |
| Item 2(d). | Title of Class of Securit | ies: | |
| | Common Stock, par val | ue \$0.001 per share | |
| Item 2(e). | CUSIP Number: | | |
| | 76243J105 | | |
| Item 3. | If This Statement is File | ed Pursuant to Rule 13d-1(b), or 13d-2(b) or (c), Check Whether the Person Filing is | a: |
| (a) | □ Broker or dealer | registered under Section 15 of the Exchange Act. | |
| (b) | □ Bank as defined i | n Section 3(a)(6) of the Exchange Act. | |
| (c) | □ Insurance compar | ny as defined in Section 3(a)(19) of the Exchange Act. | |
| (d) | □ Investment comp | any registered under Section 8 of the Investment Company Act. | |
| (e) | □ An investment ad | viser in accordance with Rule 13d-1(b)(1)(ii)(E); | |
| (f) | \Box An employee ben | efit plan or endowment fund in accordance with Rule 13d-1(b)(1)(ii)(F); | |

(g) \Box A parent holding company or control person in accordance with Rule 13d-1(b)(1)(ii)(G);

(h) \Box A savings association as defined in Section 3(b) of the Federal Deposit Insurance Act;

(i) \Box A church plan that is excluded from the definition of an investment company under Section 3(c)(14) of the Investment Company Act;

(j) \Box A non-U.S. institution in accordance with Rule 13d-1(b)(1)(ii)(J);

(k) \Box Group, in accordance with Rule 13d-1(b)(1)(ii)(K).

If filing as a non-U.S. institution in accordance with Rule 13d-1(b)(1)(ii)(J), please specify the type of institution:

Item 4. Ownership.

Provide the following information regarding the aggregate number and percentage of the class of securities of the issuer identified in Item 1.

(a) Amount beneficially owned**:

Deerfield Mgmt, L.P. - 2,430,198 shares Deerfield Mgmt III, L.P. - 291,005 shares Deerfield Management Company, L.P. - 2,721,203 shares Deerfield Partners, L.P. - 2,430,198 shares Deerfield Private Design Fund III, L.P. - 291,005 shares James E. Flynn - 2,721,203 shares

(b) Percent of class**:

Deerfield Mgmt, L.P. - 5.50% Deerfield Mgmt III, L.P. - 0.66% Deerfield Management Company, L.P. - 6.16% Deerfield Partners, L.P. - 5.50% Deerfield Private Design Fund III, L.P. - 0.66% James E. Flynn - 6.16%

(c) Number of shares as to which such person has**:

- (i) Sole power to vote or to direct the vote:
- (ii) Shared power to vote or to direct the vote:

(iii) Sole power to dispose or to direct the disposition of:

(iv) Shared power to dispose or to direct the disposition of:

All Reporting Persons - 0

Deerfield Mgmt, L.P. - 2,430,198 shares Deerfield Mgmt III, L.P. - 291,005 shares Deerfield Management Company, L.P. - 2,721,203 shares Deerfield Partners, L.P. - 2,430,198 shares Deerfield Private Design Fund III, L.P. - 291,005 shares James E. Flynn - 2,721,203 shares

All Reporting Persons - 0

Deerfield Mgmt, L.P. - 2,430,198 shares Deerfield Mgmt III, L.P. - 291,005 shares Deerfield Management Company, L.P. - 2,721,203 shares Deerfield Partners, L.P. - 2,430,198 shares Deerfield Private Design Fund III, L.P. - 291,005 shares James E. Flynn - 2,721,203 shares

**See footnotes on cover pages which are incorporated by reference herein.

Item 7.

13G

Item 5. Ownership of Five Percent or Less of a Class.

If this statement is being filed to report the fact that as of the date hereof the reporting person has ceased to be the beneficial owner of more than five percent of the class of securities check the following \Box .

Item 6. Ownership of More Than Five Percent on Behalf of Another Person.

If any other person is known to have the right to receive or the power to direct the receipt of dividends from, or the proceeds from the sale of, such securities, a statement to that effect should be included in response to this item and, if such interest relates to more than five percent of the class, such person should be identified. A listing of the shareholders of an investment company registered under the Investment Company Act of 1940 or the beneficiaries of employee benefit plan, pension fund or endowment fund is not required.

| N/A | | | | |
|--|--|--|--|--|
| | | | | |
| Identification and Classification of the Subsidiary Which Acquired the Security Being Reported on by the Parent Holding Company or Control | | | | |

If a parent holding company or Control person has filed this schedule, pursuant to Rule 13d-1(b)(1)(ii)(G), so indicate under Item 3(g) and attach an exhibit stating the identity and the Item 3 classification of the relevant subsidiary. If a parent holding company or control person has filed this schedule pursuant to Rule 13d-1(c) or Rule 13d-1(d), attach an exhibit stating the identification of the relevant subsidiary.

Item 8. Identification and Classification of Members of the Group.

If a group has filed this schedule pursuant to ss.240.13d-1(b)(1)(ii)(J), so indicate under Item 3(j) and attach an exhibit stating the identity and Item 3 classification of each member of the group. If a group has filed this schedule pursuant to ss.240.13d-1(c) or ss.240.13d-1(d), attach an exhibit stating the identity of each member of the group.

See Exhibit B

Person.

N/A

Item 9. Notice of Dissolution of Group.

Notice of dissolution of a group may be furnished as an exhibit stating the date of the dissolution and that all further filings with respect to transactions in the security reported on will be filed, if required, by members of the group, in their individual capacity. See Item 5.

N/A

Item 10. Certifications.

"By signing below I certify that, to the best of my knowledge and belief, the securities referred to above were not acquired and are not held for the purpose of or with the effect of changing or influencing the control of the issuer of the securities and were not acquired and are not held in connection with or as a participant in any transaction having that purpose or effect, other than activities solely in connection with a nomination under §240.14a–11."

13G

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.

DEERFIELD MGMT, L.P. By: J.E. Flynn Capital, LLC, General Partner

By: <u>/s/ Jonathan Isler</u> Jonathan Isler, Attorney-In-Fact

DEERFIELD MANAGEMENT COMPANY, L.P. By: Flynn Management LLC, General Partner

By: <u>/s/ Jonathan Isler</u> Jonathan Isler, Attorney-In-Fact

DEERFIELD MGMT III, L.P. By: J.E. Flynn Capital III, LLC, General Partner

By: <u>/s/ Jonathan Isler</u> Jonathan Isler, Attorney-In-Fact

DEERFIELD PARTNERS, L.P. By: Deerfield Mgmt, L.P., General Partner By: J.E. Flynn Capital, LLC, General Partner

By: <u>/s/ Jonathan Isler</u> Jonathan Isler, Attorney-In-Fact

DEERFIELD PRIVATE DESIGN FUND III, L.P. By: Deerfield Mgmt III, L.P., General Partner By: J.E. Flynn Capital III, LLC, General Partner

By: <u>/s/ Jonathan Isler</u> Jonathan Isler, Attorney-In-Fact

JAMES E. FLYNN

<u>/s/ Jonathan Isler</u> Jonathan Isler, Attorney-In-Fact

Date: February 12, 2021

Exhibit A. Joint Filing Agreement.

Exhibit B. Item 8 Statement.

Exhibit C. Power of Attorney (1).

(1) Power of Attorney previously filed as Exhibit 24 to a Form 3 with regard to Proteon Therapeutics, Inc. filed with the Securities and Exchange Commission on August 4, 2017 by Deerfield Special Situations Fund, L.P., Deerfield Partners, L.P., Deerfield International Master Fund, L.P., Deerfield Private Design Fund III, L.P., Deerfield Private Design Fund IV, L.P., Deerfield Mgmt, L.P., Deerfield Mgmt III, L.P., Deerfield Mgmt IV, L.P., Deerfield Mgmt, L.P., Deerfield Mgmt III, L.P., Deerfield Mgmt IV, L.P., Deerfi

Exhibit A

Joint Filing Agreement

The undersigned agree that this Schedule 13G, and all amendments thereto, relating to the Common Stock, par value \$0.001 per share, of Rhythm Pharmaceuticals, Inc. shall be filed on behalf of the undersigned.

DEERFIELD MGMT, L.P. By: J.E. Flynn Capital, LLC, General Partner

By: <u>/s/ Jonathan Isler</u> Jonathan Isler, Attorney-In-Fact

DEERFIELD MANAGEMENT COMPANY, L.P. By: Flynn Management LLC, General Partner

By: <u>/s/ Jonathan Isler</u> Jonathan Isler, Attorney-In-Fact

DEERFIELD MGMT III, L.P. By: J.E. Flynn Capital III, LLC, General Partner

By: <u>/s/ Jonathan Isler</u> Jonathan Isler, Attorney-In-Fact

DEERFIELD PARTNERS, L.P. By: Deerfield Mgmt, L.P., General Partner By: J.E. Flynn Capital, LLC, General Partner

By: <u>/s/ Jonathan Isler</u> Jonathan Isler, Attorney-In-Fact

DEERFIELD PRIVATE DESIGN FUND III, L.P. By: Deerfield Mgmt III, L.P., General Partner By: J.E. Flynn Capital III, LLC, General Partner

By: <u>/s/ Jonathan Isler</u> Jonathan Isler, Attorney-In-Fact

JAMES E. FLYNN

<u>/s/ Jonathan Isler</u> Jonathan Isler, Attorney-In-Fact

Exhibit B

Due to the relationships between them, the reporting persons hereunder may be deemed to constitute a "group" with one another for purposes of Section 13(d)(3) of the Securities Exchange Act of 1934.