UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-1

REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

RHYTHM PHARMACEUTICALS, INC.

(Exact name of Registrant as specified in its charter)

Delaware (State or Other Jurisdiction of Incorporation or Organization)

2834

(Primary Standard Industrial Classification Code Number) **46-2159271** (I.R.S. Employer Identification Number)

500 Boylston Street 11th Floor Boston, MA 02116 (857) 264-4280

(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

Keith M. Gottesdiener, M.D. Chief Executive Officer and President Rhythm Pharmaceuticals, Inc. 500 Boylston Street 11th Floor Boston, MA 02116 (857) 264-4280

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Please send copies of all communications to:

Julio E. Vega Laurie A. Cerveny Morgan, Lewis & Bockius LLP One Federal Street Boston, MA 02110 (617) 951-8000 Patrick O'Brien Thomas J. Danielski Ropes & Gray LLP Prudential Tower 800 Boylston Street Boston, MA 02116 (617) 951-7527

Approximate date of commencement of the proposed sale to the public: As soon as practicable after the effective date of this Registration Statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act, check the following box. o

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. x (File No. 333-225700)

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer" "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer o

Accelerated filer o

Non-accelerated filer x (Do not check if a smaller reporting company) $\begin{array}{c} \text{Smaller reporting company o} \\ \text{Emerging growth company x} \end{array}$

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. x

CALCULATION OF REGISTRATION FEE

- Includes additional shares of common stock which the underwriters have the option to purchase in connection with this offering. The \$1,647,950 proposed maximum aggregate offering price is in addition to the \$172,507,406 proposed maximum aggregate offering price registered pursuant to the Registrant's registration statement on Form S-1 (File No. 333-225700). A registration fee was previously paid in connection with that registration statement.
- (2) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act of 1933, as amended.
- (3) Calculated based on Rule 457(o) based on an estimate of the proposed maximum offering price.

This registration statement shall become effective upon filing with the Securities and Exchange Commission in accordance with Rule 462(b) under the Securities Act of 1933, as amended.

This registration statement is being filed with respect to the registration of additional securities pursuant to Rule 462(b) under the Securities Act of 1933, as amended, and includes the registration statement facing page, this page, the signature page, the exhibit index, and exhibits. Pursuant to Rule 462(b), the contents of the registration statement on Form S-1 (File No. 333-225700), including all amendments and exhibits thereto, which was declared effective by the Commission on June 20, 2018, are incorporated herein by reference into this registration statement and this registration statement is being filed solely for the purpose of registering an increase in the maximum aggregate offering price of \$1,647,950.

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EXHIBIT INDEX

Exhibit Number	Exhibit Description
5.1	Opinion of Morgan, Lewis & Bockius LLP.
23.1	Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm.
23.2	Consent of Morgan, Lewis & Bockius LLP (included in Exhibit 5.1).
24.1	Power of Attorney (incorporated by reference to the signature page of the Registrant's registration statement on Form S-1 (File No. 333-
	225700), filed with the SEC on June 18, 2018).

SIGNATURES

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Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Boston, Commonwealth of Massachusetts on June 20, 2018.

RHYTHM PHARMACEUTICALS, INC. By: /s/ KEITH M. GOTTESDIENER

Keith M. Gottesdiener Chief Executive Officer, President and Director

Pursuant to the requirements of the Securities Act, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

Name	Title	Date
/s/ KEITH M. GOTTESDIENER Keith M. Gottesdiener	Chief Executive Officer, President and Director (Principal Executive Officer)	June 20, 2018
/s/ HUNTER C. SMITH Hunter C. Smith	Chief Financial Officer and Treasurer (Principal Financial and Accounting Officer)	June 20, 2018
* Neil Exter	Director	June 20, 2018
* Todd Foley	Director	June 20, 2018
* Christophe R. Jean	Director	June 20, 2018
* Ed Mathers	Director	June 20, 2018
* David W. J. McGirr	Director	June 20, 2018
* David P. Meeker	Director, Chairman of the Board	June 20, 2018
r: /s/ KEITH M. GOTTESDIENER	<u></u>	
Keith M. Gottesdiener Attorney-in-fact		

June 20, 2018

Rhythm Pharmaceuticals, Inc. 500 Boylston Street, 11th Floor Boston, MA 02116

Re: Form S-1 Registration Statement

Ladies and Gentlemen:

We have acted as counsel to Rhythm Pharmaceuticals, Inc., a Delaware corporation (the "Company"), in connection with the Company's filing of a registration statement on Form S-1 (File No. 333-225700) (the "Initial Registration Statement") filed by the Company with the Securities and Exchange Commission (the "Commission") pursuant to the Securities Act of 1933, as amended (the "Securities Act"), on June 18, 2018 (and amended on June 20, 2018) and declared effective by the Commission on June 20, 2018, as well as this registration statement filed in connection thereto under Rule 462(b) of the Securities Act (the "Rule 462(b) Registration Statement"). The Rule 462(b) Registration Statement was filed by the Company with the Commission pursuant to the Securities Act, for the registration of shares of common stock, \$0.001 par value per share, with a proposed maximum aggregate offering price of \$1,647,950 (the "Shares"), including Shares issuable upon the exercise of an option granted by the Company to the underwriters to purchase additional shares.

This opinion is being furnished in connection with the requirements of Item 601(b)(5) of Regulation S-K under the Act, and no opinion is expressed herein as to any matter pertaining to the contents of the Initial Registration Statement or the related prospectus (the "<u>Prospectus</u>") or the Rule 462(b) Registration Statement, other than as expressly stated herein with respect to the issuance of the Shares.

As such counsel, we have examined such matters of fact and questions of law as we have considered appropriate for purposes of this letter. With your consent, we have relied upon certificates and other assurances of officers of the Company and others as to factual matters without having independently verified such factual matters. We are opining herein as to the General Corporation Law of the State of Delaware (the "<u>DGCL</u>"), and we express no opinion with respect to any other laws.

Subject to the foregoing and the other matters set forth herein, it is our opinion that, as of the date hereof, when the Shares shall have been duly registered on the books of the transfer agent and registrar therefor in the name or on behalf of the purchasers and have been issued by the Company against payment therefor in the circumstances contemplated by the form of underwriting agreement most recently filed as an exhibit to the Initial Registration Statement, the issue and sale of the Shares will have been duly authorized by all necessary corporate action of the Company, and the Shares will be validly issued, fully paid, and nonassessable. In rendering the foregoing opinion, we have assumed that the Company will comply with all applicable notice requirements regarding uncertificated shares provided in the DGCL.

This opinion is for your benefit in connection with the Rule 462(b) Registration Statement and may be relied upon by you and by persons entitled to rely upon it pursuant to the applicable provisions of the Act. We consent to your filing this opinion as an exhibit to the Rule 462(b) Registration Statement and to the reference to our firm in the Prospectus under the heading "Legal Matters." In giving such consent, we do not thereby admit that we are in the category of persons whose consent is required under Section 7 of the Act or the rules and regulations of the Commission thereunder.

Very truly yours,

/s/ MORGAN, LEWIS & BOCKIUS LLP

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the Registration Statement on Form S-1 filed pursuant to Rule 462(b) of the Securities Act of 1933 of the reference to our firm under the caption "Experts" and to the incorporation by reference of our report dated March 12, 2018 (except Note 12, as to which the date is June 11, 2018), with respect to the consolidated financial statements of Rhythm Pharmaceuticals, Inc. included in Amendment No. 1 to the Registration Statement (Form S-1 No. 333-225700) and related Prospectus of Rhythm Pharmaceuticals, Inc. for the registration of its common stock.

/s/ Ernst & Young LLP

Boston, Massachusetts June 18, 2018