

**PROSPECTUS SUPPLEMENT**  
**(To Prospectus dated March 2, 2023)****3,124,995 Shares of Common Stock**

This prospectus supplement relates to the resale or other disposition of up to an aggregate of 3,124,995 shares of our common stock, \$0.001 par value per share, that will become issuable upon conversion of the 150,000 shares of our Series A Convertible Preferred Stock, \$0.001 par value per share, or the Series A Preferred Stock, by the selling stockholders identified in this prospectus supplement. The shares of our Series A Preferred Stock referenced in the preceding sentence were acquired by the selling stockholders on April 15, 2024, in a transaction more fully described in the section entitled "Selling Stockholders." We are not selling any shares of our common stock under this prospectus supplement and will not receive any proceeds from the sale of our common stock by the selling stockholders.

The selling stockholders may offer and sell or otherwise dispose of the shares of common stock described in this prospectus supplement from time to time through public or private transactions at prevailing market prices, at prices related to prevailing market prices, or at privately negotiated prices. The shares of common stock offered by this prospectus supplement may be offered by the selling stockholders directly to purchasers or to or through brokers or dealers or other agents. The selling stockholders will bear all costs, commissions, and discounts, if any, attributable to the sales of shares. We will bear costs, expenses, and fees in connection with the registration of the shares. See "Plan of Distribution" beginning on page S-11 for more information about how the selling stockholders may sell or dispose of their shares of common stock hereunder. No common stock may be sold without delivery of this prospectus supplement and the accompanying prospectus describing the method and terms of the offering of such common stock.

Our common stock is listed on the Nasdaq Global Market under the symbol "RYTM." On July 9, 2024, the last reported sale price of our common stock on the Nasdaq Global Market was \$44.94 per share.

**INVESTING IN OUR SECURITIES INVOLVES RISKS. SEE THE "RISK FACTORS" ON PAGE [S-6](#) OF THIS PROSPECTUS SUPPLEMENT AND IN THE DOCUMENTS INCORPORATED BY REFERENCE IN THIS PROSPECTUS SUPPLEMENT CONCERNING FACTORS YOU SHOULD CONSIDER BEFORE INVESTING IN OUR COMMON STOCK.**

**Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus supplement. Any representation to the contrary is a criminal offense.**

The date of this prospectus supplement is July 10, 2024.

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## Prospectus

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## ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement is part of a registration statement that we have filed with the Securities and Exchange Commission, or SEC, as a “well-known seasoned issuer” as defined in Rule 405 under the Securities Act of 1933, as amended, or the Securities Act, utilizing a “shelf” registration process, and relates to the offering of our common stock. Before buying any of the common stock offered hereunder, we urge you to carefully read this prospectus supplement, the accompanying base prospectus and all of the information incorporated by reference herein and therein, as well as the additional information described under the heading “Where You Can Find More Information; Incorporation by Reference.” These documents contain important information that you should consider when making your investment decision.

We provide information to you about this offering of our common stock in two separate documents that are bound together: (1) this prospectus supplement, which describes the specific details regarding this offering; and (2) the accompanying base prospectus, which provides general information, some of which may not apply to this offering. Generally, when we refer to this “prospectus,” we are referring to both documents combined. If information in this prospectus supplement is inconsistent with the accompanying base prospectus, you should rely on this prospectus supplement. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in any document incorporated by reference in this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement, except as provided in the follow sentence. If any statement in one of these documents is inconsistent with a statement in another document having a later date — for example, a document incorporated by reference in this prospectus supplement — the statement in the document having the later date modifies or supersedes the earlier statement.

You should rely only on the information contained in or incorporated by reference in this prospectus supplement, the accompanying base prospectus and any free writing prospectus that we may authorize for use in connection with this offering. We have not, and the selling stockholders have not, authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and the selling stockholders are not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted or in which the person making that offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make an offer or solicitation. You should assume that the information appearing in this prospectus supplement, the accompanying base prospectus, the documents incorporated by reference herein and therein and any free writing prospectus that we have authorized for use in connection with this offering, is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying base prospectus, the documents incorporated by reference herein and therein and any free writing prospectus that we have authorized for use in connection with this offering, in their entirety before making an investment decision.

When we refer to “Rhythm,” “we,” “our,” “us” and the “Company” in this prospectus supplement, we mean Rhythm Pharmaceuticals, Inc. and its consolidated subsidiaries, unless otherwise specified. When we refer to “you,” we mean the potential holders of our common stock.

We use our trademarks and our logo, in this prospectus supplement and the documents incorporated by reference. This prospectus supplement and the documents incorporated by reference also include trademarks, tradenames and service marks that are the property of other organizations. Solely for convenience, trademarks and tradenames referred to in this prospectus supplement appear without the ® and ™ symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or that the applicable owner will not assert its rights, to these trademarks and tradenames.

## WHERE YOU CAN FIND MORE INFORMATION; INCORPORATION BY REFERENCE

### Available Information

We file reports, proxy statements and other information with the SEC. The SEC maintains a web site that contains reports, proxy and information statements and other information about issuers, such as us, who file electronically with the SEC. The address of that website is <http://www.sec.gov>.

Our web site address is <https://www.rhythmtx.com>. The information on our web site, however, is not, and should not be deemed to be, a part of this prospectus supplement.

This prospectus supplement is part of a registration statement that we filed with the SEC and does not contain all of the information in the registration statement. The full registration statement may be obtained from the SEC or us, as provided below. Documents establishing the terms of this offering are or may be filed as exhibits to the registration statement or documents incorporated by reference in the registration statement. Statements in this prospectus supplement about these documents are summaries and each statement is qualified in all respects by reference to the document to which it refers. You should refer to the actual documents for a more complete description of the relevant matters. You may inspect a copy of the registration statement through the SEC's website, as provided above.

### Incorporation by Reference

The SEC's rules allow us to "incorporate by reference" information into this prospectus supplement, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus supplement, and subsequent information that we file with the SEC will automatically update and supersede that information. Any statement contained in this prospectus supplement or a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus supplement to the extent that a statement contained in this prospectus supplement or a subsequently filed document incorporated by reference modifies or replaces that statement.

This prospectus supplement incorporates by reference the documents set forth below that have previously been filed with the SEC (other than any information therein furnished to, rather than filed with, the SEC):

- [Our Annual Report on Form 10-K for the fiscal year ended December 31, 2023, filed with the SEC on February 29, 2024;](#)
- [Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2024, filed with the SEC on May 7, 2024;](#)
- The information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2023 from our [Definitive Proxy Statement on Schedule 14A](#), filed with the SEC on April 26, 2024;
- Our Current Reports on Form 8-K filed with the SEC on [January 4, 2024](#), [February 22, 2024](#), [February 29, 2024](#), [April 1, 2024](#), [April 16, 2024](#), [May 7, 2024](#) and [June 17, 2024](#); and
- The description of our common stock contained in our registration statement on [Form 8-A](#) filed with the SEC on September 29, 2017 and any amendment or report filed with the SEC for the purpose of updating the description.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, or Exchange Act, prior to the termination of this offering, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus supplement and deemed to be part of this prospectus supplement from the date of the filing of such reports and documents.

You may request a free copy of any of the documents incorporated by reference in this prospectus supplement by writing or telephoning us at the following address:

**Rhythm Pharmaceuticals, Inc.**  
**222 Berkeley Street**  
**12th Floor**  
**Boston, MA 02116**  
**(857) 264-4280**

Exhibits to the filings will not be sent, however, unless those exhibits have specifically been incorporated by reference in this prospectus supplement.

## THE COMPANY

We are a global, commercial-stage biopharmaceutical company dedicated to transforming the lives of patients and their families living with rare neuroendocrine diseases. We are focused on advancing our melanocortin-4 receptor (MC4R) agonists, including our lead asset, IMCIVREE<sup>®</sup> (setmelanotide), as a precision medicine designed to treat hyperphagia and severe obesity caused by rare MC4R pathway diseases. While obesity affects hundreds of millions of people worldwide, we are developing therapies for a subset of individuals who have hyperphagia, a pathological hunger, and severe obesity due to an impaired MC4R pathway, which may be caused by traumatic injury or genetic variants. The MC4R pathway is an endocrine pathway in the brain that is responsible for regulating hunger, caloric intake and energy expenditure, which consequently affect body weight. IMCIVREE, an MC4R agonist for which we hold worldwide rights, is the first-ever therapy developed for patients with certain rare diseases that is approved or authorized in the United States, European Union (EU), Great Britain, Canada and other countries and regions. IMCIVREE is approved by the U.S. Food and Drug Administration (FDA) for chronic weight management in adult and pediatric patients 6 years of age and older with monogenic or syndromic obesity due to: (i) proopiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1) or leptin receptor (LEPR) deficiency as determined by an FDA-approved test demonstrating variants in POMC, PCSK1, or LEPR genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS); or (ii) Bardet-Biedl syndrome (BBS). The European Commission (EC) and Great Britain's Medicines & Healthcare Products Regulatory Agency (MHRA) have authorized IMCIVREE for the treatment of obesity and the control of hunger associated with genetically confirmed BBS or genetically confirmed loss-of-function biallelic POMC, including PCSK1, deficiency or biallelic LEPR deficiency in adults and children 6 years of age and above. Including the United States and Canada, we have achieved market access for IMCIVREE for BBS or POMC and LEPR deficiencies, or both, in 14 countries, and we continue to collaborate with authorities to achieve access in additional markets.

We were incorporated in the State of Delaware in February 2013 under the name Rhythm Metabolic, Inc. In October 2015, we changed our name to Rhythm Pharmaceuticals, Inc.

Our principal executive offices are located at 222 Berkeley Street, 12th Floor, Boston, MA 02116, and our telephone number is (857) 264-4280.

<b>THE OFFERING</b>	
Shares of common stock offered hereby	Up to 3,124,995 shares of common stock issuable upon conversion of our Series A Preferred Stock.
Use of Proceeds	We will not receive any of the proceeds from the sale of shares of our common stock being offered by any of the selling stockholders.
Risk Factors	See “Risk Factors” beginning on page S-6 of this prospectus supplement and the other information included in, or incorporated by reference into, this prospectus supplement for a discussion of certain factors you should carefully consider before deciding to invest in our common stock.
Nasdaq Global Market Symbol	“RYTM”

**RISK FACTORS**

Investment in any common stock offered pursuant to this prospectus supplement and the accompanying prospectus involves risks. Before deciding whether to invest in our common stock, you should carefully read and consider the risks and uncertainties included in and incorporated by reference to our most recent Annual Report on Form 10-K, our most recent Quarterly Report on Form 10-Q, and any subsequent Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q or Current Reports on Form 8-K, and all other information contained or incorporated by reference into this prospectus supplement or the accompanying prospectus, as updated by our subsequent filings under the Exchange Act, and the risk factors and other information contained in any applicable free writing prospectus. The risks and uncertainties described in these reports may not be the only ones we face. The factors discussed in these reports, among others, could cause our actual results to differ materially from historical results and those expressed in forward-looking statements made by us or on our behalf in filings with the SEC, press releases, communications with investors, and oral statements. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered securities.



**CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS**

This prospectus supplement contains forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act, and is subject to the “safe harbor” created by those sections. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. Some of the forward-looking statements can be identified by the use of forward-looking terms such as “anticipates,” “believes,” “could,” “estimates,” “expects,” “intends,” “may,” “might,” “likely,” “plans,” “potential,” “predicts,” “projects,” “seeks,” “should,” “target,” “will,” “would,” or similar expressions and the negatives of those terms include forward-looking statements that involve risks and uncertainties. Forward-looking statements include, but are not limited to, statements regarding the promise or potential of any of our products or product candidates, the marketing and commercialization of IMCIVREE (setmelanotide), and the timing of commercialization, the design, success, cost and timing of our product development activities and clinical trials for setmelanotide and our other product candidates, our ability to obtain regulatory approval for setmelanotide in further indications, as well as for our other product candidates, our financial performance, including our expectations regarding our existing cash, operating losses, expenses and sources of future financing, the sufficiency of our cash, cash equivalents and short-term investments to fund our operations, our ability to hire and retain necessary personnel, patient enrollments and the timing thereof, the timing of announcements regarding results of clinical trials, our ability to protect our intellectual property, ongoing activities under and our ability to negotiate our collaboration and license agreements, if needed, and the impact of termination, our marketing, commercial sales, and revenue generation, expectations surrounding our manufacturing arrangements, the potential financial impact and the ongoing integration process of Xinvento B.V., the impact of the current economic slowdown on our business and operations and our future financial results, and our use of proceeds from this offering.

We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. We cannot guarantee future results, levels of activity, performance or achievements, and you should not place undue reliance on our forward-looking statements. Our actual results may differ significantly from the results discussed in the forward-looking statements. Important factors that might cause such a difference include, but are not limited to, those set forth in filings that are incorporated by reference into this prospectus supplement.

Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. Except as may be required by law, we have no plans to update our forward-looking statements to reflect events or circumstances after the date of this prospectus supplement. We caution readers not to place undue reliance upon any such forward-looking statements, which speak only as of the date made.

### **USE OF PROCEEDS**

We will not receive any of the proceeds from the sale of shares of our common stock being offered by any of the selling stockholders. The selling stockholders will pay any selling commissions and stock transfer taxes or any other expenses incurred by the selling stockholders in connection with the sale of the shares of common stock. We will bear the fees and expenses incurred in effecting the registration of the shares covered by this prospectus supplement, including, without limitation, all registration, filing, and printing fees and expenses, and fees and expenses of our counsel and our independent registered public accounting firm.

## SELLING STOCKHOLDERS

This prospectus supplement relates to the possible resale by certain of the selling stockholders from time to time of up to an aggregate of 3,124,995 shares of common stock.

On April 1, 2024, we entered into an investment agreement with the selling stockholders, pursuant to which we issued 150,000 shares of Series A Preferred Stock for an aggregate purchase price of \$150,000,000 on April 15, 2024. We issued the shares of Series A Preferred Stock in reliance upon the exemption from registration afforded by Section 4(a)(2) of the Securities Act. In accordance with our obligations under a registration rights agreement entered in on April 15, 2024, we agreed to register the resale of the shares of common stock issued or issuable upon conversion of the Series A Preferred Stock which are being offered by the selling stockholders hereby.

This prospectus supplement covers the resale or other disposition by the selling stockholders or their pledgees, donees, transferees or other successors-in-interest of up to the total number of shares of common stock issued or issuable upon conversion of the Series A Preferred Stock issued to the selling stockholders pursuant to the investment agreement, without giving effect to the beneficial ownership limitation described below.

The following table sets forth information concerning the shares of common stock that may be offered from time to time by each selling stockholder. The number of shares beneficially owned by each selling stockholder is determined under rules issued by the SEC. Under these rules, beneficial ownership includes any shares as to which the selling stockholders have sole or shared voting power or investment power. Percentage ownership is based on 60,972,909 shares of common stock outstanding as of May 1, 2024 plus the 3,124,995 shares of common stock issued or issuable upon conversion of the Series A Preferred Stock. For purposes of this table, we have assumed that the selling stockholders will have sold all of the shares of common stock covered by this prospectus supplement upon the completion of the offering. Each of the selling stockholders listed has sole voting and investment power with respect to the shares beneficially owned by the selling stockholders unless noted otherwise.

The information in the following table has been provided to us by or on behalf of the selling stockholders and the selling stockholders may have sold, transferred, or otherwise disposed of all or a portion of the shares of common stock after the date on which they provided us with information regarding their securities. The selling stockholders may sell all, some or none of his, her, or its shares of common stock in this offering. See the section titled “Plan of Distribution.”

Name of Selling Stockholder	Shares of Common Stock Beneficially Owned Prior to Offering	Shares of Common Stock Being Offered	Shares Beneficially Owned After the Offering	
			Number	Percentage
Entities affiliated with Baker Bros. Advisors LP <sup>(1)</sup>	7,648,363	1,249,998	6,398,365	9.98%
Entities affiliated with Perceptive Advisors LLC <sup>(2)</sup>	5,321,576	1,874,997	3,446,579	5.38%

\* less than 1%

- (1) The number of shares disclosed as being beneficially owned prior to the offering consists of (i) 536,697 shares of common stock and 103,437 shares of common stock issuable upon conversion of the Series A Preferred Stock held by 667, L.P. and (ii) 5,861,668 shares of common stock and 1,146,561 shares of common stock issuable upon conversion of the Series A Preferred Stock held by Baker Brothers Life Sciences, L.P. The terms of the Series A Preferred Stock prohibit the conversion thereof to the extent that, upon such conversion, the number of shares of common stock then beneficially owned by the holder and its affiliates would exceed 4.99% of our then-outstanding voting securities. Accordingly, notwithstanding the number of shares reported, each of 667, L.P. and Baker Brothers Life Sciences, L.P. disclaims beneficial ownership of the shares of common stock issuable upon conversion of the Series A Preferred Stock to the extent that upon such conversion, the number of shares beneficially owned by 667, L.P., Baker Brothers Life Sciences, L.P., and their affiliates, in the aggregate, would exceed 4.99% of our then-outstanding voting securities. 667, L.P. and Baker Brothers Life Sciences, L.P. are

under the advisement of Baker Bros. Advisors LP. Baker Bros. Advisors (GP) LLC is the sole general partner of Baker Bros. Advisors LP. Julian C. Baker and Felix. J. Baker are managing members of Baker Bros. Advisors (GP) LLC. The principal business address of the beneficial owners is 860 Washington Street, 3<sup>rd</sup> Floor, New York, NY 10014.

- (2) The number of shares disclosed as being beneficially owned prior to the offering consists of (i) 104,166 shares of common stock issuable upon conversion of the Series A Preferred Stock held by C2 Life Sciences, LLC, (ii) 1,354,165 shares of common stock issuable upon conversion of the Series A Preferred Stock held by Perceptive Discovery ID LP and (iii) 3,446,579 shares of common stock and 416,666 shares of common stock issuable upon conversion of the Series A Preferred Stock held by Perceptive Life Sciences Master Fund, Ltd. The terms of the Series A Preferred Stock prohibit the conversion thereof to the extent that, upon such conversion, the number of shares of common stock then beneficially owned by the holder and its affiliates would exceed 9.99% of our then-outstanding voting securities. Perceptive Advisors LLC serves as the investment advisor to Perceptive Life Sciences Master Fund, Ltd. and C2 Life Sciences LLC. Joseph Edelman is the managing member of Perceptive Advisors LLC. Perceptive Discovery GP LLC is the general partner of Perceptive Discovery ID LP, and is managed by Perceptive Discovery Advisors, a relying advisor of Perceptive Advisors LLC. The principal business address of the beneficial owners is 51 Astor Place, 10th Floor, New York, NY 10003.

## PLAN OF DISTRIBUTION

The selling stockholders and any of their pledgees, donees, transferees, assignees or other successors-in-interest may, from time to time, sell, transfer or otherwise dispose of any or all of their shares of common stock or interests in shares of common stock on any stock exchange, market or trading facility on which the shares are traded or in private transactions under this prospectus supplement. These dispositions may be at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, at varying prices determined at the time of sale, or at negotiated prices. The selling stockholders may use one or more of the following methods when disposing of the shares or interests therein:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- through brokers, dealers or underwriters that may act solely as agents;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- through the writing or settlement of options or other hedging transactions entered into after the effective date of the registration statement of which this prospectus supplement is a part, whether through an options exchange or otherwise;
- broker-dealers may agree with the selling stockholders to sell a specified number of such shares at a stipulated price per share;
- short sales and settlement of short sales entered into after the effective date of the registration statement of which this prospectus supplement is a part;
- a combination of any such methods of disposition; and
- any other method permitted pursuant to applicable law.

The selling stockholders may also sell shares under Rule 144 or Rule 904 under the Securities Act of 1933, as amended, or Securities Act, if available, or Section 4(a)(1) under the Securities Act, rather than under this prospectus supplement.

Broker-dealers engaged by the selling stockholders may arrange for other broker-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the selling stockholders (or, if any broker-dealer acts as agent for the purchaser of shares, from the purchaser) in amounts to be negotiated. The selling stockholders do not expect these commissions and discounts to exceed what is customary in the types of transactions involved.

The selling stockholders may, from time to time, pledge or grant a security interest in some or all of the shares of common stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell shares of common stock from time to time under this prospectus supplement, or under a supplement or amendment to this prospectus supplement under Rule 424(b)(3) or other applicable provision of the Securities Act amending the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus supplement.

Upon being notified in writing by a selling stockholder that any material arrangement has been entered into with a broker-dealer for the sale of common stock through a block trade, special offering, exchange distribution or secondary distribution or a purchase by a broker or dealer, we will file a supplement to this prospectus supplement, if required, pursuant to Rule 424(b) under the Securities Act, disclosing (i) the name of each such selling stockholder and of the participating broker-dealer(s), (ii) the number of shares involved, (iii) the price at which such shares of common stock were sold, (iv) the commissions paid or discounts or concessions allowed to such broker-dealer(s), where applicable, (v) that such broker-dealer(s) did not conduct any investigation to verify the information set out or incorporated by reference in this

prospectus supplement, and (vi) other facts material to the transaction. In addition, upon being notified in writing by a selling stockholder that a donee or pledgee intends to sell more than 500 shares of common stock, we will file a supplement to this prospectus supplement if then required in accordance with applicable securities law.

The selling stockholders also may transfer the shares of common stock in other circumstances, in which case the transferees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus supplement.

In connection with the sale of the shares of common stock or interests in shares of common stock, the selling stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the common stock in the course of hedging the positions they assume. The selling stockholders may also sell shares of common stock short and deliver these securities to close out their short positions, or loan or pledge the common stock to broker-dealers that in turn may sell these securities. The selling stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus supplement, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus supplement (as supplemented or amended to reflect such transaction).

The selling stockholders and any broker-dealers or agents that are involved in selling the shares may be deemed to be “underwriters” within the meaning of the Securities Act in connection with such sales (it being understood that the selling stockholders shall not be deemed to be underwriters solely as a result of their participation in this offering). In such event, any profits realized by such selling stockholders or compensation received by such broker-dealers or agents may be deemed to be underwriting commissions or discounts under the Securities Act. The maximum commission or discount to be received by any member of the Financial Industry Regulatory Authority (FINRA) or independent broker-dealer will not be greater than 8% of the initial gross proceeds from the sale of any security being sold.

We have advised the selling stockholders that they are required to comply with Regulation M promulgated under the Securities Exchange Act of 1934, as amended, during such time as they may be engaged in a distribution of the shares. The foregoing may affect the marketability of the common stock.

The aggregate proceeds to the selling stockholders from the sale of the common stock offered by them will be the purchase price of the common stock less discounts or commissions, if any. Each of the selling stockholders reserves the right to accept and, together with their agents from time to time, to reject, in whole or in part, any proposed purchase of common stock to be made directly or through agents. We will not receive any of the proceeds from this offering.

We are required to pay all fees and expenses incident to the registration of the shares. We have agreed to indemnify the selling stockholders against certain losses, claims, damages and liabilities, including liabilities under the Securities Act or otherwise.

We have agreed with the selling stockholders to keep the registration statement of which this prospectus supplement constitutes a part effective until the earlier of (a) such time as all of the shares covered by this prospectus supplement have been disposed of pursuant to and in accordance with the registration statement and (b) such time as none of the shares covered by this prospectus supplement constitute “registrable securities”, as such term is defined in the registration rights agreement by and among us and the selling stockholders.

**LEGAL MATTERS**

The validity of the shares of common stock being offered by this prospectus supplement will be passed upon for us by Latham & Watkins LLP.

**EXPERTS**

The consolidated financial statements of Rhythm Pharmaceuticals, Inc. appearing in Rhythm Pharmaceuticals, Inc.'s [Annual Report \(Form 10-K\) for the year ended December 31, 2023](#), and the effectiveness of Rhythm Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2023, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their reports thereon, included therein, and incorporated herein by reference. Such financial statements are, and audited financial statements to be included in subsequently filed documents will be, incorporated herein in reliance upon the reports of Ernst & Young LLP pertaining to such financial statements and the effectiveness of our internal control over financial reporting as of the respective dates (to the extent covered by consents filed with the Securities and Exchange Commission) given on the authority of such firm as experts in accounting and auditing.

## PROSPECTUS

**RHYTHM PHARMACEUTICALS, INC.****Common Stock  
Preferred Stock  
Debt Securities  
Warrants  
Units**

We may offer and sell the securities identified above from time to time in one or more offerings. This prospectus provides you with a general description of the securities.

Each time we offer and sell securities, we will provide a supplement to this prospectus that contains specific information about the offering and the amounts, prices and terms of the securities. The supplement may also add, update or change information contained in this prospectus with respect to that offering. You should carefully read this prospectus and the applicable prospectus supplement before you invest in any of our securities.

We may offer and sell the securities described in this prospectus and any prospectus supplement to or through one or more underwriters, dealers and agents, or directly to purchasers, or through a combination of these methods. If any underwriters, dealers or agents are involved in the sale of any of the securities, their names and any applicable purchase price, fee, commission or discount arrangement between or among them will be set forth, or will be calculable from the information set forth, in the applicable prospectus supplement. See the sections of this prospectus entitled "About this Prospectus" and "Plan of Distribution" for more information. No securities may be sold without delivery of this prospectus and the applicable prospectus supplement describing the method and terms of the offering of such securities.

**INVESTING IN OUR SECURITIES INVOLVES RISKS. SEE THE "RISK FACTORS" ON PAGE 4 OF THIS PROSPECTUS AND ANY SIMILAR SECTION CONTAINED IN THE APPLICABLE PROSPECTUS SUPPLEMENT CONCERNING FACTORS YOU SHOULD CONSIDER BEFORE INVESTING IN OUR SECURITIES.**

Our common stock is listed on the Nasdaq Global Market under the symbol "RYTM." On February 27, 2023, the last reported sale price of our common stock on the Nasdaq Global Market was \$24.67 per share.

**Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.**

**The date of this prospectus is March 2, 2023.**

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## ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the U.S. Securities and Exchange Commission, or the SEC, as a “well-known seasoned issuer” as defined in Rule 405 under the Securities Act of 1933, as amended, using a “shelf” registration process. By using a shelf registration statement, we may sell securities from time to time and in one or more offerings as described in this prospectus. Each time that we offer and sell securities, we will provide a prospectus supplement to this prospectus that contains specific information about the securities being offered and sold and the specific terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement or free writing prospectus may also add, update or change information contained in this prospectus with respect to that offering. If there is any inconsistency between the information in this prospectus and the applicable prospectus supplement or free writing prospectus, you should rely on the prospectus supplement or free writing prospectus, as applicable. Before purchasing any securities, you should carefully read both this prospectus and the applicable prospectus supplement (and any applicable free writing prospectuses), together with the additional information described under the heading “Where You Can Find More Information; Incorporation by Reference.”

We have not authorized anyone to provide you with any information or to make any representations other than those contained in this prospectus, any applicable prospectus supplement or any free writing prospectuses prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We will not make an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus and the applicable prospectus supplement to this prospectus is accurate only as of the date on its respective cover, that the information appearing in any applicable free writing prospectus is accurate only as of the date of that free writing prospectus, and that any information incorporated by reference is accurate only as of the date of the document incorporated by reference, unless we indicate otherwise. Our business, financial condition, results of operations and prospects may have changed since those dates. This prospectus incorporates by reference, and any prospectus supplement or free writing prospectus may contain and incorporate by reference, market data and industry statistics and forecasts that are based on independent industry publications and other publicly available information. Although we believe these sources are reliable, we do not guarantee the accuracy or completeness of this information and we have not independently verified this information. In addition, the market and industry data and forecasts that may be included or incorporated by reference in this prospectus, any prospectus supplement or any applicable free writing prospectus may involve estimates, assumptions and other risks and uncertainties and are subject to change based on various factors, including those discussed under the heading “Risk Factors” contained in this prospectus, the applicable prospectus supplement and any applicable free writing prospectus, and under similar headings in other documents that are incorporated by reference into this prospectus. Accordingly, investors should not place undue reliance on this information.

When we refer to “Rhythm,” “we,” “our,” “us” and the “Company” in this prospectus, we mean Rhythm Pharmaceuticals, Inc. and its consolidated subsidiaries, unless otherwise specified. When we refer to “you,” we mean the potential holders of the applicable series of securities.

We use our trademarks and our logo, in this prospectus and the documents incorporated by reference. This prospectus and the documents incorporated by reference also include trademarks, tradenames and service marks that are the property of other organizations. Solely for convenience, trademarks and tradenames referred to in this prospectus appear without the ® and ™ symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or that the applicable owner will not assert its rights, to these trademarks and tradenames.

## WHERE YOU CAN FIND MORE INFORMATION; INCORPORATION BY REFERENCE

### Available Information

We file reports, proxy statements and other information with the SEC. The SEC maintains a web site that contains reports, proxy and information statements and other information about issuers, such as us, who file electronically with the SEC. The address of that website is <http://www.sec.gov>.

Our web site address is <https://www.rhythmtx.com>. The information on our web site, however, is not, and should not be deemed to be, a part of this prospectus.

This prospectus and any prospectus supplement are part of a registration statement that we filed with the SEC and do not contain all of the information in the registration statement. The full registration statement may be obtained from the SEC or us, as provided below. Forms of the indenture and other documents establishing the terms of the offered securities are or may be filed as exhibits to the registration statement or documents incorporated by reference in the registration statement. Statements in this prospectus or any prospectus supplement about these documents are summaries and each statement is qualified in all respects by reference to the document to which it refers. You should refer to the actual documents for a more complete description of the relevant matters. You may inspect a copy of the registration statement through the SEC's website, as provided above.

### Incorporation by Reference

The SEC's rules allow us to "incorporate by reference" information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus, and subsequent information that we file with the SEC will automatically update and supersede that information. Any statement contained in this prospectus or a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or a subsequently filed document incorporated by reference modifies or replaces that statement.

This prospectus and any accompanying prospectus supplement incorporate by reference the documents set forth below that have previously been filed with the SEC:

- [Our Annual Report on Form 10-K for the year ended December 31, 2022, filed with the SEC on March 1, 2023.](#)
- The information specifically incorporated by reference into our Annual Report on Form 10-K from our [Definitive Proxy Statement on Schedule 14A, filed with the SEC on April 28, 2022.](#)
- [The description of our Common Stock contained in our Registration Statement on Form 8-A, filed with the SEC on September 29, 2017 and any amendment or report filed with the SEC for the purpose of updating the description.](#)

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, which we refer to as the "Exchange Act" in this prospectus, prior to the termination of this offering, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus and deemed to be part of this prospectus from the date of the filing of such reports and documents.

You may request a free copy of any of the documents incorporated by reference in this prospectus by writing or telephoning us at the following address:

Rhythm Pharmaceuticals, Inc.  
222 Berkeley Street  
12th Floor  
Boston, MA 02116  
(857) 264-4280

Exhibits to the filings will not be sent, however, unless those exhibits have specifically been incorporated by reference in this prospectus or any accompanying prospectus supplement.

## THE COMPANY

We are a global, commercial-stage biopharmaceutical company dedicated to transforming the lives of patients and their families with rare diseases. We are focused on advancing our lead asset, IMCIVREE<sup>®</sup> (setmelanotide), as a precision medicine designed to treat hyperphagia and severe obesity caused by rare melanocortin-4 receptor (MC4R) pathway diseases. While obesity affects hundreds of millions of people worldwide, we are advancing IMCIVREE<sup>®</sup> (setmelanotide) for a subset of individuals who have hyperphagia, a pathological hunger, and severe obesity due to an impaired MC4R pathway, which may be caused by traumatic injury or genetic variants. The MC4R pathway is an endocrine pathway in the brain that is responsible for regulating hunger, caloric intake and energy expenditure, which consequently affect body weight. IMCIVREE, an MC4R agonist for which we hold worldwide rights, is the first-ever therapy developed for patients with certain ultra-rare diseases that is approved or authorized in the United States, European Union (EU) and Great Britain. IMCIVREE is approved by the U.S. Food and Drug Administration (FDA) for chronic weight management in adult and pediatric patients 6 years of age and older with monogenic or syndromic obesity due to: (i) proopiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1) or leptin receptor (LEPR) deficiency as determined by an FDA-approved test demonstrating variants in POMC, PCSK1, or LEPR genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS); or (ii) Bardet-Biedl syndrome (BBS). The European Commission (EC) and Great Britain's Medicines & Healthcare Products Regulatory Agency (MHRA) have authorized IMCIVREE for the treatment of obesity and the control of hunger associated with genetically confirmed BBS or genetically confirmed loss-of-function biallelic POMC, including PCSK1, deficiency or biallelic LEPR deficiency in adults and children 6 years of age and above. In addition to the United States, we have achieved market access for IMCIVREE for BBS or POMC and LEPR deficiencies, or both, in seven markets in Europe and Argentina, and we continue to collaborate with authorities to achieve access in additional markets.

We were incorporated in the State of Delaware in February 2013 under the name Rhythm Metabolic, Inc. In October 2015, we changed our name to Rhythm Pharmaceuticals, Inc.

Our principal executive offices are located at 222 Berkeley Street, 12th Floor, Boston, MA 02116, and our telephone number is (857) 264-4280.

**RISK FACTORS**

Investment in any securities offered pursuant to this prospectus and the applicable prospectus supplement involves risks. Before deciding whether to invest in our securities, you should carefully consider the risk factors incorporated by reference to our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q or Current Reports on Form 8-K, and all other information contained or incorporated by reference into this prospectus, as updated by our subsequent filings under the Exchange Act, and the risk factors and other information contained in the applicable prospectus supplement and any applicable free writing prospectus. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered securities.

**USE OF PROCEEDS**

We intend to use the net proceeds from the sale of the securities as set forth in the applicable prospectus supplement.

## DESCRIPTION OF CAPITAL STOCK

### General

The following description of our capital stock is a summary, does not purport to be complete and is subject to, and qualified in its entirety by reference to, our amended and restated certificate of incorporation and amended and restated bylaws, copies of which have been filed with the SEC, and the terms and provisions of the Delaware General Corporation Law, or DGCL. For more complete information, you should carefully review our amended and restated certificate of incorporation, amended and restated bylaws and the DGCL.

### Authorized Capital Stock

Our authorized capital stock consists of 120,000,000 shares of common stock, par value \$0.001 per share, and 10,000,000 shares of preferred stock, par value \$0.001 per share.

### Common Stock

Holders of shares of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of stockholders. The holders of a plurality of the shares of our common stock entitled to vote in any election of directors can elect all of the directors standing for election.

Holders of shares of our common stock are entitled to receive dividends when and if declared by our board of directors out of funds legally available therefor, subject to any statutory or contractual restrictions on the payment of dividends and to any restrictions on the payment of dividends imposed by the terms of any outstanding preferred stock.

Upon our dissolution or liquidation or the sale of all or substantially all of our assets, after payment in full of all amounts required to be paid to creditors and to the holders of preferred stock having liquidation preferences, if any, the holders of shares of our common stock will be entitled to receive pro rata our remaining assets available for distribution.

Holders of shares of our common stock do not have preemptive, subscription, redemption or conversion rights.

### Preferred Stock

Our amended and restated certificate of incorporation authorizes our board of directors to establish one or more series of preferred stock (including convertible preferred stock). Unless required by law or by any stock exchange, the authorized shares of preferred stock will be available for issuance without further action by our stockholders. Our board of directors is able to determine, with respect to any series of preferred stock, the terms and rights of that series, including:

- the designation of the series;
- the number of shares of the series, which our board may, except where otherwise provided in the preferred stock designation, increase or decrease, but not below the number of shares then outstanding;
- the voting rights, if any, of the holders of the series;
- whether dividends, if any, will be cumulative or non-cumulative and the dividend rate of the series;
- the dates at which dividends, if any, will be payable;
- the rights of priority and amounts payable, if any, on shares of the series in the event of any voluntary or involuntary liquidation, dissolution or winding-up of the affairs of our company;
- the redemption rights and price or prices, if any, for shares of the series;
- the terms of any purchase, retirement or sinking fund, if any, provided for shares of the series;
- the terms, if any, upon which the shares of the series will be convertible into or exchangeable for shares of any other class, classes or series or other securities, whether or not issued by our company or any other entity;

- restrictions, if any, upon issuance of indebtedness of our company so long as any shares of the series are outstanding; and
- restrictions, if any, on the issuance of shares of the same series or of any other class or series.

We could issue a series of preferred stock that could, depending on the terms of the series, impede or discourage an acquisition attempt or other transaction that some, or a majority, of our stockholders might believe to be in their best interests or in which our stockholders might receive a premium for their shares of common stock over the market price of the shares of common stock.

#### **Authorized but Unissued Capital Stock**

The DGCL does not require stockholder approval for any issuance of authorized shares. However, the listing requirements of the Nasdaq Global Market, which apply so long as our common stock remains listed on the Nasdaq Global Market, require stockholder approval of certain issuances equal to or exceeding 20% of the then outstanding voting power or then outstanding number of shares of common stock. These additional shares may be used for a variety of corporate purposes, including future public offerings, to raise additional capital or to facilitate acquisitions.

One of the effects of the existence of unissued and unreserved common stock or preferred stock may be to enable our board of directors to issue shares to persons friendly to current management, which issuance could render more difficult or discourage an attempt to obtain control of our company by means of a merger, tender offer, proxy contest or otherwise, and thereby protect the continuity of our management and possibly deprive our stockholders of opportunities to sell their shares of common stock at prices higher than prevailing market prices.

#### **Anti-Takeover Effects of Provisions of Delaware Law and Our Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws**

##### ***Undesignated Preferred Stock***

The ability to authorize undesignated preferred stock will make it possible for our board of directors to issue preferred stock with super voting, special approval, dividend or other rights or preferences on a discriminatory basis that could impede the success of any attempt to acquire us or otherwise effect a change in control of us. These and other provisions may have the effect of deferring, delaying or discouraging hostile takeovers, or changes in control or management of our company.

##### ***Requirements for Advance Notification of Stockholder Meetings, Nominations and Proposals***

Our amended and restated certificate of incorporation provides that special meetings of the stockholders may be called only by or at the direction of our board of directors. Our amended and restated bylaws prohibit the conduct of any business at a special meeting other than as specified in the notice for such meeting. These provisions may have the effect of deferring, delaying or discouraging hostile takeovers, or changes in control or management of our company.

Our amended and restated bylaws establish advance notice procedures with respect to stockholder proposals and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee of the board of directors. In order for any matter to be “properly brought” before a meeting, a stockholder will have to comply with advance notice requirements and provide us with certain information. Additionally, vacancies and newly created directorships may be filled only by a vote of a majority of the directors then in office, even though less than a quorum, and not by the stockholders. Our amended and restated bylaws allow the presiding officer at a meeting of the stockholders to adopt rules and regulations for the conduct of meetings which may have the effect of precluding the conduct of certain business at a meeting if the rules and regulations are not followed. These provisions may also defer, delay or discourage a potential acquirer from conducting a solicitation of proxies to elect the acquirer’s own slate of directors or otherwise attempting to obtain control of our company.

Our amended and restated certificate of incorporation provides that the board of directors is expressly authorized to adopt, amend or repeal our amended and restated bylaws.



***No Cumulative Voting***

The DGCL provides that stockholders are not entitled to cumulate votes in the election of directors unless our amended and restated certificate of incorporation provides otherwise. Our amended and restated certificate of incorporation does not expressly provide for cumulative voting.

***Removal of Directors***

In accordance with the terms of our amended and restated certificate of incorporation and amended and restated bylaws, our board of directors are divided into three staggered classes of directors of the same or nearly the same number. At each annual meeting of the stockholders, a class of directors will be elected for a three-year term to succeed the directors of the same class whose terms are then expiring.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that the number of our directors shall be fixed from time to time by a resolution of the majority of our board of directors. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class shall consist of one third of the board of directors.

The division of our board of directors into three classes with staggered three-year terms may delay or prevent stockholder efforts to effect a change of our management or a change in control.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that our directors may be removed only for cause by the affirmative vote of the holders of at least 75% of the outstanding shares of capital stock entitled to vote in the election of directors or class of directors, voting together as a single class, at a meeting of the stockholders called for that purpose. This requirement of a supermajority vote to remove directors could enable a minority of our stockholders to prevent a change in the composition of our board. Any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by the vote of a majority of the remaining directors then in office, although less than a quorum, or by the sole remaining director.

***Amendments to Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws***

The DGCL provides that, unless a corporation's certificate of incorporation provides otherwise, the affirmative vote of holders of shares constituting a majority of the votes of all shares entitled to vote may approve amendments to the certificate of incorporation.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that the affirmative vote of holders of at least 75% of the outstanding shares of capital stock, voting together as a single class, and entitled to vote in the election of directors will be required to amend, alter, change or repeal the amended and restated certificate of incorporation and the amended and restated bylaws. This requirement of a supermajority vote to approve amendments to our amended and restated certificate of incorporation and amended and restated bylaws could enable a minority of our stockholders to exercise veto power over such amendments.

***Stockholder Action by Written Consent***

Pursuant to Section 228 of the DGCL, any action required to be taken at any annual or special meeting of the stockholders may be taken without a meeting, without prior notice and without a vote if a consent or consents in writing, setting forth the action so taken, is signed by the holders of outstanding stock having not less than the minimum number of votes that would be necessary to authorize or take such action at a meeting at which all shares of our stock entitled to vote thereon were present and voted, unless the corporation's certificate of incorporation provides otherwise. Our amended and restated certificate of incorporation prohibits the taking of any action of our stockholders by written consent without a meeting.

***Delaware Anti-Takeover Statute***

We have not opted out of, and therefore are subject to, Section 203 of the DGCL. Section 203 provides that, subject to certain exceptions specified in the law, a publicly-held Delaware corporation shall not engage

in certain “business combinations” with any “interested stockholder” for a three-year period after the date of the transaction in which the person became an interested stockholder unless:

- prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;
- upon completion of the transaction that resulted in the stockholder becoming an interested stockholder, the stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the number of shares outstanding (1) shares owned by persons who are directors and also officers and (2) shares owned under employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- on or subsequent to the date of the transaction, the business combination is approved by the board and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66⅔% of the outstanding voting stock which is not owned by the interested stockholder.

Generally, a business combination includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. An interested stockholder is a person who, together with affiliates and associates, owns or, within three years prior to the determination of interested stockholder status, did own 15% or more of a corporation’s outstanding voting stock. Since Section 203 will apply to us, we expect that it would have an anti-takeover effect with respect to transactions our board of directors does not approve in advance. In such event, we would also anticipate that Section 203 could discourage attempts that might result in a premium over the market price for the shares of common stock held by stockholders.

Under certain circumstances, Section 203 makes it more difficult for a person who would be an “interested stockholder” to effect various business combinations with a corporation for a three-year period. The provisions of Section 203 may encourage companies interested in acquiring our company to negotiate in advance with our board of directors because the stockholder approval requirement would be avoided if our board of directors approves either the business combination or the transaction that results in the stockholder becoming an interested stockholder. These provisions also may make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

#### ***Choice of Forum***

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for: (i) any derivative action or proceeding brought on our behalf; (ii) any action asserting a claim of breach of fiduciary duty; (iii) any action asserting a claim against us arising under the DGCL, our amended and restated certificate of incorporation or our amended and restated bylaws; and (iv) any action asserting a claim against us that is governed by the internal affairs doctrine. In addition, our amended and restated bylaws provide that the federal district courts of the United States are the exclusive forum for any complaint raising a cause of action arising under the Securities Act of 1933, as amended. Any person or entity purchasing or otherwise acquiring any interest in any of our securities shall be deemed to have notice of and consented to the provisions of our amended and restated certificate of incorporation and amended and restated bylaws described above. It is possible that a court of law could find the choice of forum provisions contained in our amended and restated certificate of incorporation or amended and restated bylaws to be inapplicable or unenforceable if challenged in a proceeding or otherwise.

## DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplement or free writing prospectus, summarizes certain general terms and provisions of the debt securities that we may offer under this prospectus. When we offer to sell a particular series of debt securities, we will describe the specific terms of the series in a supplement to this prospectus. We will also indicate in the supplement to what extent the general terms and provisions described in this prospectus apply to a particular series of debt securities.

We may issue debt securities either separately, or together with, or upon the conversion or exercise of or in exchange for, other securities described in this prospectus. Debt securities may be our senior, senior subordinated or subordinated obligations and, unless otherwise specified in a supplement to this prospectus, the debt securities will be our direct, unsecured obligations and may be issued in one or more series.

The debt securities will be issued under an indenture between us and a trustee to be named in the applicable indenture, as trustee. We have summarized select portions of the indenture below. The summary is not complete. The form of the indenture has been filed as an exhibit to the registration statement and you should read the indenture for provisions that may be important to you. In the summary below, we have included references to the section numbers of the indenture so that you can easily locate these provisions. Capitalized terms used in the summary and not defined herein have the meanings specified in the indenture.

As used in this section only, “Rhythm” “we,” “our” or “us” refer to Rhythm Pharmaceuticals, Inc. excluding our subsidiaries, unless expressly stated or the context otherwise requires.

### General

The terms of each series of debt securities will be established by or pursuant to a resolution of our board of directors and set forth or determined in the manner provided in a resolution of our board of directors, in an officer’s certificate or by a supplemental indenture. (Section 2.2) The particular terms of each series of debt securities will be described in a prospectus supplement relating to such series (including any pricing supplement or term sheet).

We can issue an unlimited amount of debt securities under the indenture that may be in one or more series with the same or various maturities, at par, at a premium, or at a discount. (Section 2.1) We will set forth in a prospectus supplement (including any pricing supplement or term sheet) relating to any series of debt securities being offered, the aggregate principal amount and the following terms of the debt securities, if applicable:

- the title and ranking of the debt securities (including the terms of any subordination provisions);
- the price or prices (expressed as a percentage of the principal amount) at which we will sell the debt securities;
- any limit on the aggregate principal amount of the debt securities;
- the date or dates on which the principal of the securities of the series is payable;
- the rate or rates (which may be fixed or variable) per annum or the method used to determine the rate or rates (including any commodity, commodity index, stock exchange index or financial index) at which the debt securities will bear interest, the date or dates from which interest will accrue, the date or dates on which interest will commence and be payable and any regular record date for the interest payable on any interest payment date;
- the place or places where principal of, and interest, if any, on the debt securities will be payable (and the method of such payment), where the securities of such series may be surrendered for registration of transfer or exchange, and where notices and demands to us in respect of the debt securities may be delivered;
- the period or periods within which, the price or prices at which and the terms and conditions upon which we may redeem the debt securities;

- any obligation we have to redeem or purchase the debt securities pursuant to any sinking fund or analogous provisions or at the option of a holder of debt securities and the period or periods within which, the price or prices at which and in the terms and conditions upon which securities of the series shall be redeemed or purchased, in whole or in part, pursuant to such obligation;
- the dates on which and the price or prices at which we will repurchase debt securities at the option of the holders of debt securities and other detailed terms and provisions of these repurchase obligations;
- the denominations in which the debt securities will be issued, if other than denominations of \$1,000 and any integral multiple thereof;
- whether the debt securities will be issued in the form of certificated debt securities or global debt securities;
- the portion of principal amount of the debt securities payable upon declaration of acceleration of the maturity date, if other than the principal amount;
- the currency of denomination of the debt securities, which may be United States Dollars or any foreign currency, and if such currency of denomination is a composite currency, the agency or organization, if any, responsible for overseeing such composite currency;
- the designation of the currency, currencies or currency units in which payment of principal of, premium and interest on the debt securities will be made;
- if payments of principal of, premium or interest on the debt securities will be made in one or more currencies or currency units other than that or those in which the debt securities are denominated, the manner in which the exchange rate with respect to these payments will be determined;
- the manner in which the amounts of payment of principal of, premium, if any, or interest on the debt securities will be determined, if these amounts may be determined by reference to an index based on a currency or currencies or by reference to a commodity, commodity index, stock exchange index or financial index;
- any provisions relating to any security provided for the debt securities;
- any addition to, deletion of or change in the Events of Default described in this prospectus or in the indenture with respect to the debt securities and any change in the acceleration provisions described in this prospectus or in the indenture with respect to the debt securities;
- any addition to, deletion of or change in the covenants described in this prospectus or in the indenture with respect to the debt securities;
- any depositaries, interest rate calculation agents, exchange rate calculation agents or other agents with respect to the debt securities;
- the provisions, if any, relating to conversion or exchange of any debt securities of such series, including if applicable, the conversion or exchange price and period, provisions as to whether conversion or exchange will be mandatory, the events requiring an adjustment of the conversion or exchange price and provisions affecting conversion or exchange;
- any other terms of the debt securities, which may supplement, modify or delete any provision of the indenture as it applies to that series, including any terms that may be required under applicable law or regulations or advisable in connection with the marketing of the securities; and
- whether any of our direct or indirect subsidiaries will guarantee the debt securities of that series, including the terms of subordination, if any, of such guarantees. (Section 2.2)

We may issue debt securities that provide for an amount less than their stated principal amount to be due and payable upon declaration of acceleration of their maturity pursuant to the terms of the indenture. We will provide you with information on the federal income tax considerations and other special considerations applicable to any of these debt securities in the applicable prospectus supplement.

If we denominate the purchase price of any of the debt securities in a foreign currency or currencies or a foreign currency unit or units, or if the principal of and any premium and interest on any series of debt

securities is payable in a foreign currency or currencies or a foreign currency unit or units, we will provide you with information on the restrictions, elections, general tax considerations, specific terms and other information with respect to that issue of debt securities and such foreign currency or currencies or foreign currency unit or units in the applicable prospectus supplement.

### **Transfer and Exchange**

Each debt security will be represented by either one or more global securities registered in the name of The Depository Trust Company, or the Depository, or a nominee of the Depository (we will refer to any debt security represented by a global debt security as a “book-entry debt security”), or a certificate issued in definitive registered form (we will refer to any debt security represented by a certificated security as a “certificated debt security”) as set forth in the applicable prospectus supplement. Except as set forth under the heading “Global Debt Securities and Book-Entry System” below, book-entry debt securities will not be issuable in certificated form.

**Certificated Debt Securities.** You may transfer or exchange certificated debt securities at any office we maintain for this purpose in accordance with the terms of the indenture. (Section 2.4) No service charge will be made for any transfer or exchange of certificated debt securities, but we may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection with a transfer or exchange. (Section 2.7)

You may effect the transfer of certificated debt securities and the right to receive the principal of, premium and interest on certificated debt securities only by surrendering the certificate representing those certificated debt securities and either reissuance by us or the trustee of the certificate to the new holder or the issuance by us or the trustee of a new certificate to the new holder.

**Global Debt Securities and Book-Entry System.** Each global debt security representing book-entry debt securities will be deposited with, or on behalf of, the Depository, and registered in the name of the Depository or a nominee of the Depository. Please see “Global Securities.”

### **Covenants**

We will set forth in the applicable prospectus supplement any restrictive covenants applicable to any issue of debt securities. (Article IV)

### **No Protection in the Event of a Change of Control**

Unless we state otherwise in the applicable prospectus supplement, the debt securities will not contain any provisions which may afford holders of the debt securities protection in the event we have a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control) which could adversely affect holders of debt securities.

### **Consolidation, Merger and Sale of Assets**

We may not consolidate with or merge with or into, or convey, transfer or lease all or substantially all of our properties and assets to any person (a “successor person”) unless:

- we are the surviving entity or the successor person (if other than Rhythm) is a corporation, partnership, trust or other entity organized and validly existing under the laws of any U.S. domestic jurisdiction and expressly assumes our obligations on the debt securities and under the indenture; and
- immediately after giving effect to the transaction, no Default or Event of Default, shall have occurred and be continuing.

Notwithstanding the above, any of our subsidiaries may consolidate with, merge into or transfer all or part of its properties to us. (Section 5.1)

### **Events of Default**

“Event of Default” means with respect to any series of debt securities, any of the following:

- default in the payment of any interest upon any debt security of that series when it becomes due and payable, and continuance of such default for a period of 30 days (unless the entire amount of the payment is deposited by us with the trustee or with a paying agent prior to the expiration of the 30-day period);

- default in the payment of principal of any security of that series at its maturity;
- default in the performance or breach of any other covenant or warranty by us in the indenture (other than a covenant or warranty that has been included in the indenture solely for the benefit of a series of debt securities other than that series), which default continues uncured for a period of 60 days after we receive written notice from the trustee or Rhythm and the trustee receive written notice from the holders of not less than 25% in principal amount of the outstanding debt securities of that series as provided in the indenture;
- certain voluntary or involuntary events of bankruptcy, insolvency or reorganization of Rhythm;
- any other Event of Default provided with respect to debt securities of that series that is described in the applicable prospectus supplement. (Section 6.1)

No Event of Default with respect to a particular series of debt securities (except as to certain events of bankruptcy, insolvency or reorganization) necessarily constitutes an Event of Default with respect to any other series of debt securities. (Section 6.1) The occurrence of certain Events of Default or an acceleration under the indenture may constitute an event of default under certain indebtedness of ours or our subsidiaries outstanding from time to time.

We will provide the trustee written notice of any Default or Event of Default within 30 days of becoming aware of the occurrence of such Default or Event of Default, which notice will describe in reasonable detail the status of such Default or Event of Default and what action we are taking or propose to take in respect thereof. (Section 6.1)

If an Event of Default with respect to debt securities of any series at the time outstanding occurs and is continuing, then the trustee or the holders of not less than 25% in principal amount of the outstanding debt securities of that series may, by a notice in writing to us (and to the trustee if given by the holders), declare to be due and payable immediately the principal of (or, if the debt securities of that series are discount securities, that portion of the principal amount as may be specified in the terms of that series) and accrued and unpaid interest, if any, on all debt securities of that series. In the case of an Event of Default resulting from certain events of bankruptcy, insolvency or reorganization, the principal (or such specified amount) of and accrued and unpaid interest, if any, on all outstanding debt securities will become and be immediately due and payable without any declaration or other act on the part of the trustee or any holder of outstanding debt securities. At any time after a declaration of acceleration with respect to debt securities of any series has been made, but before a judgment or decree for payment of the money due has been obtained by the trustee, the holders of a majority in principal amount of the outstanding debt securities of that series may rescind and annul the acceleration if all Events of Default, other than the non-payment of accelerated principal and interest, if any, with respect to debt securities of that series, have been cured or waived as provided in the indenture. (Section 6.2) We refer you to the prospectus supplement relating to any series of debt securities that are discount securities for the particular provisions relating to acceleration of a portion of the principal amount of such discount securities upon the occurrence of an Event of Default.

The indenture provides that the trustee may refuse to perform any duty or exercise any of its rights or powers under the indenture unless the trustee receives indemnity satisfactory to it against any cost, liability or expense which might be incurred by it in performing such duty or exercising such right or power. (Section 7.1(e)) Subject to certain rights of the trustee, the holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee with respect to the debt securities of that series. (Section 6.12)

No holder of any debt security of any series will have any right to institute any proceeding, judicial or otherwise, with respect to the indenture or for the appointment of a receiver or trustee, or for any remedy under the indenture, unless:

- that holder has previously given to the trustee written notice of a continuing Event of Default with respect to debt securities of that series; and
- the holders of not less than 25% in principal amount of the outstanding debt securities of that series have made written request, and offered indemnity or security satisfactory to the trustee, to the

trustee to institute the proceeding as trustee, and the trustee has not received from the holders of not less than a majority in principal amount of the outstanding debt securities of that series a direction inconsistent with that request and has failed to institute the proceeding within 60 days. (Section 6.7)

Notwithstanding any other provision in the indenture, the holder of any debt security will have an absolute and unconditional right to receive payment of the principal of, premium and any interest on that debt security on or after the due dates expressed in that debt security and to institute suit for the enforcement of payment. (Section 6.8)

The indenture requires us, within 120 days after the end of our fiscal year, to furnish to the trustee a statement as to compliance with the indenture. (Section 4.3) If a Default or Event of Default occurs and is continuing with respect to the securities of any series and if it is known to a responsible officer of the trustee, the trustee shall mail to each Securityholder of the securities of that series notice of a Default or Event of Default within 90 days after it occurs or, if later, after a responsible officer of the trustee has knowledge of such Default or Event of Default. The indenture provides that the trustee may withhold notice to the holders of debt securities of any series of any Default or Event of Default (except in payment on any debt securities of that series) with respect to debt securities of that series if the trustee determines in good faith that withholding notice is in the interest of the holders of those debt securities. (Section 7.5)

### **Modification and Waiver**

We and the trustee may modify, amend or supplement the indenture or the debt securities of any series without the consent of any holder of any debt security:

- to cure any ambiguity, defect or inconsistency;
- to comply with covenants in the indenture described above under the heading “Consolidation, Merger and Sale of Assets”;
- to provide for uncertificated securities in addition to or in place of certificated securities;
- to add guarantees with respect to debt securities of any series or secure debt securities of any series;
- to surrender any of our rights or powers under the indenture;
- to add covenants or events of default for the benefit of the holders of debt securities of any series;
- to comply with the applicable procedures of the applicable depository;
- to make any change that does not adversely affect the rights of any holder of debt securities;
- to provide for the issuance of and establish the form and terms and conditions of debt securities of any series as permitted by the indenture;
- to effect the appointment of a successor trustee with respect to the debt securities of any series and to add to or change any of the provisions of the indenture to provide for or facilitate administration by more than one trustee; or
- to comply with requirements of the SEC in order to effect or maintain the qualification of the indenture under the Trust Indenture Act. (Section 9.1)

We may also modify and amend the indenture with the consent of the holders of at least a majority in principal amount of the outstanding debt securities of each series affected by the modifications or amendments. We may not make any modification or amendment without the consent of the holders of each affected debt security then outstanding if that amendment will:

- reduce the amount of debt securities whose holders must consent to an amendment, supplement or waiver;
- reduce the rate of or extend the time for payment of interest (including default interest) on any debt security;
- reduce the principal of or premium on or change the fixed maturity of any debt security or reduce the amount of, or postpone the date fixed for, the payment of any sinking fund or analogous obligation with respect to any series of debt securities;



- reduce the principal amount of discount securities payable upon acceleration of maturity;
- waive a default in the payment of the principal of, premium or interest on any debt security (except a rescission of acceleration of the debt securities of any series by the holders of at least a majority in aggregate principal amount of the then outstanding debt securities of that series and a waiver of the payment default that resulted from such acceleration);
- make the principal of or premium or interest on any debt security payable in currency other than that stated in the debt security;
- make any change to certain provisions of the indenture relating to, among other things, the right of holders of debt securities to receive payment of the principal of, premium and interest on those debt securities and to institute suit for the enforcement of any such payment and to waivers or amendments; or
- waive a redemption payment with respect to any debt security. (Section 9.3)

Except for certain specified provisions, the holders of at least a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all debt securities of that series waive our compliance with provisions of the indenture. (Section 9.2) The holders of a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all the debt securities of such series waive any past default under the indenture with respect to that series and its consequences, except a default in the payment of the principal of, premium or any interest on any debt security of that series; provided, however, that the holders of a majority in principal amount of the outstanding debt securities of any series may rescind an acceleration and its consequences, including any related payment default that resulted from the acceleration. (Section 6.13)

#### **Defeasance of Debt Securities and Certain Covenants in Certain Circumstances**

*Legal Defeasance.* The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, we may be discharged from any and all obligations in respect of the debt securities of any series (subject to certain exceptions). We will be so discharged upon the irrevocable deposit with the trustee, in trust, of money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. Dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money or U.S. government obligations in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities.

This discharge may occur only if, among other things, we have delivered to the trustee an opinion of counsel stating that we have received from, or there has been published by, the United States Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable United States federal income tax law, in either case to the effect that, and based thereon such opinion shall confirm that, the holders of the debt securities of that series will not recognize income, gain or loss for United States federal income tax purposes as a result of the deposit, defeasance and discharge and will be subject to United States federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit, defeasance and discharge had not occurred. (Section 8.3)

*Defeasance of Certain Covenants.* The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, upon compliance with certain conditions:

- we may omit to comply with the covenant described under the heading “Consolidation, Merger and Sale of Assets” and certain other covenants set forth in the indenture, as well as any additional covenants which may be set forth in the applicable prospectus supplement; and
- any omission to comply with those covenants will not constitute a Default or an Event of Default with respect to the debt securities of that series (“covenant defeasance”).

The conditions include:

- depositing with the trustee money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. Dollars, government obligations of the



government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal of, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities; and

- delivering to the trustee an opinion of counsel to the effect that the holders of the debt securities of that series will not recognize income, gain or loss for United States federal income tax purposes as a result of the deposit and related covenant defeasance and will be subject to United States federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit and related covenant defeasance had not occurred. (Section 8.4)

#### **No Personal Liability of Directors, Officers, Employees or Securityholders**

None of our past, present or future directors, officers, employees or securityholders, as such, will have any liability for any of our obligations under the debt securities or the indenture or for any claim based on, or in respect of or by reason of, such obligations or their creation. By accepting a debt security, each holder waives and releases all such liability. This waiver and release is part of the consideration for the issue of the debt securities. However, this waiver and release may not be effective to waive liabilities under U.S. federal securities laws, and it is the view of the SEC that such a waiver is against public policy.

#### **Governing Law**

The indenture and the debt securities, including any claim or controversy arising out of or relating to the indenture or the securities, will be governed by the laws of the State of New York.

The indenture will provide that we, the trustee and the holders of the debt securities (by their acceptance of the debt securities) irrevocably waive, to the fullest extent permitted by applicable law, any and all right to trial by jury in any legal proceeding arising out of or relating to the indenture, the debt securities or the transactions contemplated thereby.

The indenture will provide that any legal suit, action or proceeding arising out of or based upon the indenture or the transactions contemplated thereby may be instituted in the federal courts of the United States of America located in the City of New York or the courts of the State of New York in each case located in the City of New York, and we, the trustee and the holder of the debt securities (by their acceptance of the debt securities) irrevocably submit to the non-exclusive jurisdiction of such courts in any such suit, action or proceeding. The indenture will further provide that service of any process, summons, notice or document by mail (to the extent allowed under any applicable statute or rule of court) to such party's address set forth in the indenture will be effective service of process for any suit, action or other proceeding brought in any such court. The indenture will further provide that we, the trustee and the holders of the debt securities (by their acceptance of the debt securities) irrevocably and unconditionally waive any objection to the laying of venue of any suit, action or other proceeding in the courts specified above and irrevocably and unconditionally waive and agree not to plead or claim any such suit, action or other proceeding has been brought in an inconvenient forum. (Section 10.10)

**DESCRIPTION OF OTHER SECURITIES**

We will set forth in the applicable prospectus supplement a description of any warrants or units issued by us that may be offered and sold pursuant to this prospectus.

## GLOBAL SECURITIES

### Book-Entry, Delivery and Form

Unless we indicate differently in any applicable prospectus supplement or free writing prospectus, the securities initially will be issued in book-entry form and represented by one or more global notes or global securities, or, collectively, global securities. The global securities will be deposited with, or on behalf of, The Depository Trust Company, New York, New York, as depository, or DTC, and registered in the name of Cede & Co., the nominee of DTC. Unless and until it is exchanged for individual certificates evidencing securities under the limited circumstances described below, a global security may not be transferred except as a whole by the depository to its nominee or by the nominee to the depository, or by the depository or its nominee to a successor depository or to a nominee of the successor depository.

DTC has advised us that it is:

- a limited-purpose trust company organized under the New York Banking Law;
- a “banking organization” within the meaning of the New York Banking Law;
- a member of the Federal Reserve System;
- a “clearing corporation” within the meaning of the New York Uniform Commercial Code; and
- a “clearing agency” registered pursuant to the provisions of Section 17A of the Exchange Act.

DTC holds securities that its participants deposit with DTC. DTC also facilitates the settlement among its participants of securities transactions, such as transfers and pledges, in deposited securities through electronic computerized book-entry changes in participants’ accounts, thereby eliminating the need for physical movement of securities certificates. “Direct participants” in DTC include securities brokers and dealers, including underwriters, banks, trust companies, clearing corporations and other organizations. DTC is a wholly-owned subsidiary of The Depository Trust & Clearing Corporation, or DTCC. DTCC is the holding company for DTC, National Securities Clearing Corporation and Fixed Income Clearing Corporation, all of which are registered clearing agencies. DTCC is owned by the users of its regulated subsidiaries. Access to the DTC system is also available to others, which we sometimes refer to as indirect participants, that clear through or maintain a custodial relationship with a direct participant, either directly or indirectly. The rules applicable to DTC and its participants are on file with the SEC.

Purchases of securities under the DTC system must be made by or through direct participants, which will receive a credit for the securities on DTC’s records. The ownership interest of the actual purchaser of a security, which we sometimes refer to as a beneficial owner, is in turn recorded on the direct and indirect participants’ records. Beneficial owners of securities will not receive written confirmation from DTC of their purchases. However, beneficial owners are expected to receive written confirmations providing details of their transactions, as well as periodic statements of their holdings, from the direct or indirect participants through which they purchased securities. Transfers of ownership interests in global securities are to be accomplished by entries made on the books of participants acting on behalf of beneficial owners. Beneficial owners will not receive certificates representing their ownership interests in the global securities, except under the limited circumstances described below.

To facilitate subsequent transfers, all global securities deposited by direct participants with DTC will be registered in the name of DTC’s partnership nominee, Cede & Co., or such other name as may be requested by an authorized representative of DTC. The deposit of securities with DTC and their registration in the name of Cede & Co. or such other nominee will not change the beneficial ownership of the securities. DTC has no knowledge of the actual beneficial owners of the securities. DTC’s records reflect only the identity of the direct participants to whose accounts the securities are credited, which may or may not be the beneficial owners. The participants are responsible for keeping account of their holdings on behalf of their customers.

So long as the securities are in book-entry form, you will receive payments and may transfer securities only through the facilities of the depository and its direct and indirect participants. We will maintain an office or agency in the location specified in the prospectus supplement for the applicable securities, where notices and demands in respect of the securities and the indenture may be delivered to us and where certificated securities may be surrendered for payment, registration of transfer or exchange.

Conveyance of notices and other communications by DTC to direct participants, by direct participants to indirect participants and by direct participants and indirect participants to beneficial owners will be governed by arrangements among them, subject to any legal requirements in effect from time to time.

Redemption notices will be sent to DTC. If less than all of the securities of a particular series are being redeemed, DTC's practice is to determine by lot the amount of the interest of each direct participant in the securities of such series to be redeemed.

Neither DTC nor Cede & Co. (or such other DTC nominee) will consent or vote with respect to the securities. Under its usual procedures, DTC will mail an omnibus proxy to us as soon as possible after the record date. The omnibus proxy assigns the consenting or voting rights of Cede & Co. to those direct participants to whose accounts the securities of such series are credited on the record date, identified in a listing attached to the omnibus proxy.

So long as securities are in book-entry form, we will make payments on those securities to the depository or its nominee, as the registered owner of such securities, by wire transfer of immediately available funds. If securities are issued in definitive certificated form under the limited circumstances described below and unless if otherwise provided in the description of the applicable securities herein or in the applicable prospectus supplement, we will have the option of making payments by check mailed to the addresses of the persons entitled to payment or by wire transfer to bank accounts in the United States designated in writing to the applicable trustee or other designated party at least 15 days before the applicable payment date by the persons entitled to payment, unless a shorter period is satisfactory to the applicable trustee or other designated party.

Redemption proceeds, distributions and dividend payments on the securities will be made to Cede & Co., or such other nominee as may be requested by an authorized representative of DTC. DTC's practice is to credit direct participants' accounts upon DTC's receipt of funds and corresponding detail information from us on the payment date in accordance with their respective holdings shown on DTC records. Payments by participants to beneficial owners will be governed by standing instructions and customary practices, as is the case with securities held for the account of customers in bearer form or registered in "street name." Those payments will be the responsibility of participants and not of DTC or us, subject to any statutory or regulatory requirements in effect from time to time. Payment of redemption proceeds, distributions and dividend payments to Cede & Co., or such other nominee as may be requested by an authorized representative of DTC, is our responsibility, disbursement of payments to direct participants is the responsibility of DTC, and disbursement of payments to the beneficial owners is the responsibility of direct and indirect participants.

Except under the limited circumstances described below, purchasers of securities will not be entitled to have securities registered in their names and will not receive physical delivery of securities. Accordingly, each beneficial owner must rely on the procedures of DTC and its participants to exercise any rights under the securities and the indenture.

The laws of some jurisdictions may require that some purchasers of securities take physical delivery of securities in definitive form. Those laws may impair the ability to transfer or pledge beneficial interests in securities.

DTC may discontinue providing its services as securities depository with respect to the securities at any time by giving reasonable notice to us. Under such circumstances, in the event that a successor depository is not obtained, securities certificates are required to be printed and delivered.

As noted above, beneficial owners of a particular series of securities generally will not receive certificates representing their ownership interests in those securities. However, if:

- DTC notifies us that it is unwilling or unable to continue as a depository for the global security or securities representing such series of securities or if DTC ceases to be a clearing agency registered under the Exchange Act at a time when it is required to be registered and a successor depository is not appointed within 90 days of the notification to us or of our becoming aware of DTC's ceasing to be so registered, as the case may be;

- we determine, in our sole discretion, not to have such securities represented by one or more global securities; or
- an Event of Default has occurred and is continuing with respect to such series of securities,

we will prepare and deliver certificates for such securities in exchange for beneficial interests in the global securities. Any beneficial interest in a global security that is exchangeable under the circumstances described in the preceding sentence will be exchangeable for securities in definitive certificated form registered in the names that the depository directs. It is expected that these directions will be based upon directions received by the depository from its participants with respect to ownership of beneficial interests in the global securities.

#### ***Euroclear and Clearstream***

If so provided in the applicable prospectus supplement, you may hold interests in a global security through Clearstream Banking S.A., which we refer to as “Clearstream,” or Euroclear Bank S.A./N.V., as operator of the Euroclear System, which we refer to as “Euroclear,” either directly if you are a participant in Clearstream or Euroclear or indirectly through organizations which are participants in Clearstream or Euroclear. Clearstream and Euroclear will hold interests on behalf of their respective participants through customers’ securities accounts in the names of Clearstream and Euroclear, respectively, on the books of their respective U.S. depositories, which in turn will hold such interests in customers’ securities accounts in such depositories’ names on DTC’s books.

Clearstream and Euroclear are securities clearance systems in Europe. Clearstream and Euroclear hold securities for their respective participating organizations and facilitate the clearance and settlement of securities transactions between those participants through electronic book-entry changes in their accounts, thereby eliminating the need for physical movement of certificates.

Payments, deliveries, transfers, exchanges, notices and other matters relating to beneficial interests in global securities owned through Euroclear or Clearstream must comply with the rules and procedures of those systems. Transactions between participants in Euroclear or Clearstream, on one hand, and other participants in DTC, on the other hand, are also subject to DTC’s rules and procedures.

Investors will be able to make and receive through Euroclear and Clearstream payments, deliveries, transfers and other transactions involving any beneficial interests in global securities held through those systems only on days when those systems are open for business. Those systems may not be open for business on days when banks, brokers and other institutions are open for business in the United States.

Cross-market transfers between participants in DTC, on the one hand, and participants in Euroclear or Clearstream, on the other hand, will be effected through DTC in accordance with the DTC’s rules on behalf of Euroclear or Clearstream, as the case may be, by their respective U.S. depositories; however, such cross-market transactions will require delivery of instructions to Euroclear or Clearstream, as the case may be, by the counterparty in such system in accordance with the rules and procedures and within the established deadlines (European time) of such system. Euroclear or Clearstream, as the case may be, will, if the transaction meets its settlement requirements, deliver instructions to its U.S. depository to take action to effect final settlement on its behalf by delivering or receiving interests in the global securities through DTC, and making or receiving payment in accordance with normal procedures for same-day fund settlement. Participants in Euroclear or Clearstream may not deliver instructions directly to their respective U.S. depositories.

Due to time zone differences, the securities accounts of a participant in Euroclear or Clearstream purchasing an interest in a global security from a direct participant in DTC will be credited, and any such crediting will be reported to the relevant participant in Euroclear or Clearstream, during the securities settlement processing day (which must be a business day for Euroclear or Clearstream) immediately following the settlement date of DTC. Cash received in Euroclear or Clearstream as a result of sales of interests in a global security by or through a participant in Euroclear or Clearstream to a direct participant in DTC will be received with value on the settlement date of DTC but will be available in the relevant Euroclear or Clearstream cash account only as of the business day for Euroclear or Clearstream following DTC’s settlement date.

***Other***

The information in this section of this prospectus concerning DTC, Clearstream, Euroclear and their respective book-entry systems has been obtained from sources that we believe to be reliable, but we do not take responsibility for this information. This information has been provided solely as a matter of convenience. The rules and procedures of DTC, Clearstream and Euroclear are solely within the control of those organizations and could change at any time. Neither we nor the trustee nor any agent of ours or of the trustee has any control over those entities and none of us takes any responsibility for their activities. You are urged to contact DTC, Clearstream and Euroclear or their respective participants directly to discuss those matters. In addition, although we expect that DTC, Clearstream and Euroclear will perform the foregoing procedures, none of them is under any obligation to perform or continue to perform such procedures and such procedures may be discontinued at any time. Neither we nor any agent of ours will have any responsibility for the performance or nonperformance by DTC, Clearstream and Euroclear or their respective participants of these or any other rules or procedures governing their respective operations.

**PLAN OF DISTRIBUTION**

We may sell the offered securities from time to time:

- through underwriters or dealers;
- through agents;
- directly to one or more purchasers; or
- through a combination of any of these methods of sale.

We will identify the specific plan of distribution, including any underwriters, dealers, agents or direct purchasers and their compensation in the applicable prospectus supplement.

**LEGAL MATTERS**

Latham & Watkins LLP will pass upon certain legal matters relating to the issuance and sale of the securities offered hereby on behalf of Rhythm Pharmaceuticals, Inc. Additional legal matters may be passed upon for us or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

**EXPERTS**

The consolidated financial statements of Rhythm Pharmaceuticals, Inc. appearing in Rhythm Pharmaceuticals, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2022, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon included therein, and incorporated herein by reference. Such financial statements are, and audited financial statements to be included in subsequently filed documents will be, incorporated herein in reliance upon the reports of Ernst & Young LLP pertaining to such financial statements (to the extent covered by consents filed with the Securities and Exchange Commission) given on the authority of such firm as experts in accounting and auditing.



## Calculation of Filing Fee Tables

**424(b)(7)**  
(Form Type)

**Rhythm Pharmaceuticals, Inc.**

(Exact Name of Registrant as Specified in its Charter)

Table 1: Newly Registered and Carry Forward Securities

	Security Type	Security Class Title	Fee Calculation or Carry Forward Rule	Amount Registered	Proposed Maximum Offering Price Per Unit	Maximum Aggregate Offering Price	Fee Rate	Amount of Registration Fee	Carry Forward Form Type	Carry Forward File Number	Carry Forward Initial effective date	Filing Fee Previously Paid In Connection with Unsold Securities to be Carried Forward
Newly Registered Securities												
Fees to Be Paid	Equity	Common Stock, par value \$0.001 per share	Rule 457(c)	3,124,995 (1)	\$41.62(2)	\$130,062,292	0.00014760	\$19,198				
Fees Previously Paid	—	—	—	—	—	—	—	—	—	—	—	—
Carry Forward Securities												
Carry Forward Securities	—	—	—	—	—	—	—	—	—	—	—	—
	Total Offering Amounts					\$130,062,292		\$19,198				
	Total Fees Previously Paid							—				
	Total Fee Offsets(3)							—				
	Net Fee Due							\$19,198				

- (1) Consists of 3,124,995 shares of common stock registered pursuant to this prospectus supplement to be offered by the selling stockholders named herein. Pursuant to Rule 416 under the Securities Act of 1933, as amended (the "Securities Act"), the shares of common stock being registered hereunder include such indeterminate number of shares of common stock as may be issuable with respect to the shares of common stock being registered hereunder as a result of any stock dividend, stock split, recapitalization or similar transaction. Separate consideration may or may not be received for shares of common stock that are issuable upon conversion, exercise, or exchange of other securities.
- (2) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(c) of the Securities Act, on the basis of the average of the high and low prices for a share of the Registrant's common stock as reported on the Nasdaq Global Market on July 5, 2024, which date is within five business days prior to the filing of this prospectus supplement.
- (3) The Registrant does not have any fee offsets.