UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

SCHEDULE 14A

Proxy Statement Pursuant to Section 14(a) of the Securities Exchange Act of 1934 (Amendment No.

)

Filed by the Registrant ⊠

Filed by a Party other than the Registrant \Box

Check the appropriate box:

- □ Preliminary Proxy Statement
- □ Confidential, for Use of the Commission Only (as permitted by Rule 14a-6(e)(2))
- ☑ Definitive Proxy Statement
- □ Definitive Additional Materials
- □ Soliciting Material under §240.14a-12

RHYTHM PHARMACEUTICALS, INC.

(Name of Registrant as Specified In Its Charter)

(Name of Person(s) Filing Proxy Statement, if other than the Registrant)

Payment of Filing Fee (Check the appropriate box):

- ⊠ No fee required.
- □ Fee paid previously with preliminary materials.
- □ Fee computed on table in exhibit required by Item 25(b) per Exchange Act Rules 14a-6(i)(1) and 0-11.

Rhythm[®]

Rhythm Pharmaceuticals, Inc.

222 Berkeley Street, 12th Floor Boston, MA 02116

April 28, 2022

Dear Stockholder:

On behalf of the Board of Directors of Rhythm Pharmaceuticals, Inc. (the "Company," "we" or "Rhythm"), I invite you to attend the Annual Meeting of Stockholders (the "Annual Meeting") that will be held on Wednesday, June 8, 2022, at 2:00 p.m., Eastern Time. The Annual Meeting will be held entirely online. You will be able to attend the Annual Meeting online and submit your questions during the meeting by visiting *www.meetnow.global/M6NM5QJ*. The matters to be voted upon at the Annual Meeting are listed in the Notice of Annual Meeting of Stockholders and more fully described in the proxy statement accompanying this letter (the "Proxy Statement").

All stockholders of record of our common stock at the close of business on April 13, 2022, the record date, are entitled to notice of and to vote at the Annual Meeting and any continuation, postponement, or adjournment thereof. We know that certain of our stockholders will be unable to attend the Annual Meeting electronically. We, therefore, are soliciting proxies so that each stockholder has an opportunity to vote on the matters that are scheduled to come before the stockholders at the Annual Meeting. If you have previously received our Notice of Internet Availability of Proxy Materials (the "Internet Notice"), then instructions regarding how you can vote are contained in that notice. If you have received a proxy card, then instructions regarding how you can vote are contained on the proxy card. Submitting your vote via the Internet or by telephone or proxy card will not affect your right to vote electronically if you decide to attend the Annual Meeting. If your shares are held in street name (held for your account by a broker or other nominee), you will receive instructions from your broker or other nominee explaining how to vote your shares. Whether or not you expect to attend the Annual Meeting electronically, we urge you to vote your shares as promptly as possible to ensure your representation and the presence of a quorum at the Annual Meeting. Your proxy is revocable in accordance with the procedures set forth in the Proxy Statement.

Thank you for your continuing interest in the Company.

Sincerely,

/s/ DAVID P. MEEKER, M.D. David P. Meeker, M.D. Chairman of the Board, President and Chief Executive Officer TABLE OF CONTENTS

Rhythm[®]

Rhythm Pharmaceuticals, Inc.

222 Berkeley Street, 12th Floor Boston, MA 02116

NOTICE OF ANNUAL MEETING OF STOCKHOLDERS

The Annual Meeting of Stockholders (the "Annual Meeting") of Rhythm Pharmaceuticals, Inc. (the "Company," "we" or "Rhythm") will be held on Wednesday, June 8, 2022, at 2:00 p.m., Eastern Time. The Annual Meeting will be a completely virtual meeting, which will be conducted via live webcast. You will be able to attend the Annual Meeting online and submit your questions during the meeting by visiting *www. meetnow.global/M6NM5QJ* and entering your 15-digit control number included in your Notice of Internet Availability of Proxy Materials (the "Internet Notice"), on any proxy card that you received or on the instructions that accompanied your proxy materials. The Annual Meeting will be held for the following purposes:

- 1. To elect Jennifer Good and Edward T. Mathers as Class II directors, each to serve for a three-year term until the 2025 Annual Meeting of Stockholders and until their respective successors are duly elected and qualified;
- 2. To ratify the appointment of Ernst & Young LLP as the independent registered public accounting firm for the Company for the fiscal year ending December 31, 2022;
- 3. To approve, on an advisory (non-binding) basis, the compensation of our named executive officers ("Say-on-Pay Vote"); and
- 4. To transact such other business as may properly come before the Annual Meeting or any continuation, postponement, or adjournment of the Annual Meeting.

The Board has fixed the close of business on April 13, 2022 as the record date for determining stockholders entitled to notice of and to vote at the Annual Meeting. Therefore, each outstanding share of Rhythm's common stock entitles the holder of record of such shares at the close of business on April 13, 2022 to receive notice of, and to vote at, the Annual Meeting or any continuation, adjournment or postponement thereof. To participate in the Annual Meeting, including to vote via the Internet or telephone, you will need the 15-digit control number included in your Internet Notice, on any proxy card that you received or on the instructions that accompanied your proxy materials. A complete list of such stockholders will be open to the examination of any stockholder for a period of ten days prior to the Annual Meeting for a purpose germane to the meeting by sending an email to David Connolly, Head of Investor Relations and Corporate Communications, at dconnolly@rhythmtx.com, stating the purpose of the request and providing proof of ownership of Company stock. The list of these stockholders will also be available on the bottom of your screen during the Annual Meeting after entering the 15-digit control number included in your Internet Notice, on any proxy card that you received or on the materials provided by your bank or broker. The Annual Meeting may be continued or adjourned from time to time without notice other than by announcement at the Annual Meeting.

Whether or not you expect to attend the Annual Meeting electronically, we urge you to vote your shares as promptly as possible to ensure your representation and the presence of a quorum at the Annual Meeting. If you choose to attend the Annual Meeting, you may still vote your shares electronically, even if you have previously voted or returned your proxy by any of the methods described in the Proxy Statement. If your shares are held in street name in a bank or brokerage account, please refer to the materials provided by your bank, broker or other nominee for voting instructions. Your proxy is revocable in accordance with the procedures set forth in the Proxy Statement. All stockholders are extended a cordial invitation to attend the meeting online.

By Order of the Board of Directors,

/s/ DAVID P. MEEKER, M.D.

David P. Meeker, M.D. Chairman of the Board, President and Chief Executive Officer April 28, 2022

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Rhythm Pharmaceuticals, Inc.

222 Berkeley Street, 12th Floor Boston, MA 02116

PROXY STATEMENT

GENERAL INFORMATION

This proxy statement ("Proxy Statement") is furnished in connection with the solicitation by the Board of Directors (the "Board") of Rhythm Pharmaceuticals, Inc., a Delaware corporation ("Rhythm," "we," "our," "us" or the "Company"), of proxies in the accompanying form to be used at our annual meeting of stockholders to be held on June 8, 2022 at 2:00 p.m., Eastern Time, and any continuation, postponement or adjournment thereof (the "Annual Meeting"). The Annual Meeting will be a completely virtual meeting, which will be conducted via live webcast. You will be able to attend the Annual Meeting online and submit your questions during the meeting by visiting www.meetnow.global/M6NM5QJ and entering your 15-digit control number included in your Notice of Internet Availability of Proxy Materials (the "Internet Notice"), on any proxy card you received or on the instructions that accompanied your proxy materials.

Holders of record of shares of our common stock, \$0.001 par value per share, as of the close of business on April 13, 2022 (the "Record Date"), will be entitled to notice of and to vote at the Annual Meeting and any continuation, postponement, or adjournment of the Annual Meeting.

When are this Proxy Statement and the accompanying materials scheduled to be sent to stockholders?

This Proxy Statement and the Company's Annual Report to Stockholders for the year ended December 31, 2021 (the "2021 Annual Report") will be released on or about April 28, 2022 to our stockholders on the Record Date.

Notice of Internet Availability of Proxy Materials.

As permitted by Securities and Exchange Commission ("SEC") rules, Rhythm is making this Proxy Statement and its 2021 Annual Report available to its stockholders electronically via the Internet. On or about April 28, 2022, we mailed to our stockholders a Notice of Internet Availability of Proxy Materials (the "Internet Notice") containing instructions on how to access this Proxy Statement and our 2021 Annual Report and vote online. If you received an Internet Notice by mail, you will not receive a printed copy of the proxy materials in the mail unless you specifically request them, by following the instructions for requesting such materials contained on the Internet Notice.

The Internet Notice instructs you on how to access and review all of the important information contained in the Proxy Statement and 2021 Annual Report. The Internet Notice also instructs you on how you may submit your proxy over the Internet.

Who can vote at the Annual Meeting?

The Record Date for the Annual Meeting is April 13, 2022. You are entitled to vote at the Annual Meeting only if you were a stockholder of record at the close of business on that date, or if you hold a valid proxy for the Annual Meeting. As of the close of business on the Record Date, we had 50,393,731 shares of common stock outstanding. Each share of common stock entitles the holder to one vote on each matter presented at the Annual Meeting. There is no cumulative voting.

Who can attend the Annual Meeting?

The Annual Meeting will be held entirely online this year. You may attend the Annual Meeting online only if you are a stockholder who is entitled to vote at the Annual Meeting, or if you hold a valid proxy for the Annual Meeting. You may attend and participate in the Annual Meeting by visiting the following

website: www.meetnow.global/M6NM5QJ. To attend and participate in the Annual Meeting, you will need the 15-digit control number included in your Internet Notice, on any proxy card you received or on the instructions that accompanied your proxy materials. If you lose your 15-digit control number, you may join the Annual Meeting as a "Guest" but you will not be able to vote, ask questions or access the list of stockholders as of the Record Date.

If your shares are held in "street name," as described below, you must register in advance to attend the Annual Meeting online or attend the Annual Meeting online using the control number provided by your bank or broker by following the instructions found under the caption "*How do I vote*?" below. You will need to obtain your own Internet access if you choose to attend the Annual Meeting online and/or vote over the Internet.

The meeting webcast will begin promptly at 2:00 p.m. Eastern Time. We encourage you to access the meeting prior to the start time, leaving ample time for check-in procedures.

What is the difference between a stockholder of record and beneficial owner of shares held in "street name"?

Stockholder of Record. If your shares are registered directly in your name with our transfer agent, Computershare Trust Company, N.A. ("Computershare"), you are considered the stockholder of record with respect to those shares, and the Notice of Annual Meeting and Proxy Statement were sent directly to you by the Company.

Beneficial Owner of Shares Held in "Street Name." If your shares are held in an account at a brokerage firm, bank, broker-dealer, or other similar organization, then you are the beneficial owner of shares held in "street name," and the Notice and Proxy Statement were forwarded to you by that organization. The organization holding your account is considered the stockholder of record for purposes of voting at the Annual Meeting. As a beneficial owner, you have the right to direct that organization on how to vote the shares held in your account.

How do I vote?

Stockholders of Record. If you are a stockholder of record, you may vote:

- **By Internet.** You may vote by proxy via the Internet at *www.investorvote.com/RYTM* by following the instructions provided on the Internet Notice or any proxy card you received.
- **By Telephone.** If you live in the United States or Canada, you may vote by proxy by calling tollfree 1-800-579-1639 and by following the instructions provided on the Internet Notice or any proxy card you received. You must have the control number that is included on the Internet Notice or proxy card when voting.
- **By Mail.** Complete and mail any proxy card you may have received in the accompanying postage prepaid envelope, and return the proxy card to Computershare Investor Services, P.O. Box 505008, Louisville, KY, 40233-9814. Your proxy will be voted in accordance with your instructions. If you have received printed copies of these proxy materials and sign and return the enclosed proxy but do not otherwise specify how you want your shares voted, they will be voted "FOR" the election of the Class II director nominees named herein to the Board, "FOR" the ratification of the selection of Ernst & Young LLP as Rhythm's independent registered public accounting firm for the fiscal year ending December 31, 2022 and "FOR" the approval, on an advisory basis, of the compensation of our named executive officers (the "Say-on-Pay Vote"), and will be voted according to the discretion of the proxy holder named in the proxy card upon any other business that may properly be brought before the meeting and at all continuations, adjournments and postponements thereof.
- **Electronically at the Meeting.** If you attend the meeting online, you will need the 15-digit control number included in your Internet Notice or any proxy card you received or on the instructions that accompanied your proxy materials to vote electronically during the meeting.

Whether or not you expect to attend the Annual Meeting electronically, we urge you to vote your shares as promptly as possible to ensure your representation and the presence of a quorum at the Annual Meeting. If you submit your proxy, you may still decide to attend the Annual Meeting and vote your shares electronically.

Beneficial Owners of Shares Held in "Street Name." If your shares are held in a brokerage account, by a bank, by a trustee, or by another nominee (also referred to as held in "street name"), you may:

- Vote in Advance. You may vote in advance of the Annual Meeting by following the voting instructions provided by your broker or other nominee and, if desired, attend the Annual Meeting webcast as a "Guest." Most brokers or other nominees permit their customers to vote by telephone or by Internet, in addition to voting by signing, dating and returning the voting instruction form provided by the broker or other nominee.
- **Register to Attend the Annual Meeting in Advance.** You may register to attend the Annual Meeting webcast as a stockholder in advance (allowing you to both vote and ask questions during the Annual Meeting). To register to attend the Annual Meeting online in advance, you must submit proof of your proxy power (legal proxy) reflecting your holdings in the Company along with your name and email address to Computershare. Requests for registration must be labeled as "Legal Proxy" and be received no later than 5:00 p.m., Eastern daylight time, on June 3, 2022. You will receive a confirmation of your registration by email after Computershare receives your registration materials. Requests for registration should be directed to Computershare in the following manner: (1) by email: Forward the email from your broker, or attach an image of your legal proxy, to legalproxy@computershare.com; or (2) by mail: Computershare, Rhythm Therapeutics, Inc. Legal Proxy, P.O. Box 43001, Providence, RI 02940-3001.
- Attend the Annual Meeting Using a Control Number. We expect that the vast majority of beneficial holders will be able to attend and participate in the Annual Meeting by logging into the Annual Meeting using the control number received with the voting instruction form provided by your broker or other nominee. However, some beneficial holders may need to request a legal proxy and register in advance of the Annual Meeting pursuant to the instructions above under "Register to Attend the Annual Meeting in Advance." Please contact your broker or other nominee to confirm whether your control number will allow you to access the Annual Meeting or whether you will need to obtain a legal proxy and register in advance.

You will need to obtain your own Internet access if you choose to attend the Annual Meeting online and/or vote over the Internet.

What are the Board's recommendations on how to vote my shares?

The Board recommends a vote:

- *Proposal 1:* "FOR" the election of each of Jennifer Good and Edward T. Mathers as Class II directors.
- *Proposal 2:* **"FOR"** the ratification of the selection of Ernst & Young LLP as Rhythm's independent registered public accounting firm for the fiscal year ending December 31, 2022.
- Proposal 3: "FOR" the approval, on an advisory basis, of the Say-on-Pay Vote.

Who pays the cost for soliciting proxies?

Rhythm will bear the cost of solicitation of proxies. This includes the charges and expenses of brokerage firms and others for forwarding solicitation material to beneficial owners of our outstanding common stock. Rhythm may solicit proxies by mail, personal interview, telephone or via the Internet through its officers, directors and other management employees, who will receive no additional compensation for their services. We will also request that brokers, nominees, custodians and other fiduciaries forward soliciting materials to the beneficial owners of shares held by the brokers, nominees, custodians and other fiduciaries. We will reimburse these persons for their reasonable expenses in connection with these activities.

Can I change or revoke my vote?

You may revoke your proxy at any time before it is voted by notifying the Secretary of Rhythm in writing at our principal executive offices, by returning a signed proxy with a later date, by transmitting a subsequent vote over the Internet or by telephone prior to the close of the Internet voting facility or the

telephone voting facility, or by attending the meeting and voting electronically. If your stock is held in street name, you must contact your broker or nominee for instructions as to how to change or revoke your vote.

How is a quorum reached?

The presence, online or by proxy, of holders of at least a majority of the issued and outstanding shares entitled to vote is necessary to constitute a quorum for the transaction of business at the Annual Meeting. Abstentions and "broker non-votes," if any, will be counted as present and entitled to vote for purposes of determining whether a quorum is present for the transaction of business at the meeting.

What are broker non-votes?

"Broker non-votes" are shares represented at the Annual Meeting held by brokers, banks or other nominees (i.e., in "street name") which do not vote on a particular proposal because the nominee does not have discretionary voting power with respect to that item and has not received instructions from the beneficial owner. Generally, nominees may vote to ratify the selection of independent auditors and on other "discretionary" or "routine" items. In contrast, nominees may not vote to elect directors, because those proposals are considered "non-discretionary" items. Accordingly, if you do not instruct your broker, bank or other nominee how to vote your shares on "non-discretionary" matters, your broker, bank or other nominee will not be permitted to vote your shares on these matters. This is a "broker non-vote."

What vote is required to approve each item?

Election of Directors (Proposal No. 1). Directors will be elected by a plurality of the votes cast, present online or represented by proxy at the Annual Meeting and entitled to vote on the election of directors. This means that the two individuals receiving the highest number of "FOR" votes will be elected as directors. Abstentions and broker non-votes will not be treated as votes cast for this purpose and, therefore, will not affect the outcome of the election.

Ratification of the Selection of Independent Registered Public Accounting Firm (Proposal No. 2). The affirmative vote of a majority of shares of our common stock, present online or represented by proxy at the Annual Meeting and entitled to vote, is required to ratify the selection of our independent auditors. An abstention is treated as present and entitled to vote and, therefore, has the effect of a vote "against" the proposal. Because the ratification of the selection of the independent auditors is a routine matter, a nominee holding shares in street name may vote on this proposal in the absence of instructions from the beneficial owner and, therefore, we do not expect any broker non-votes on this proposal.

Approval, on an Advisory (Non-Binding) Basis, of the Compensation of Our Named Executive Officers ("Say-on-Pay Vote") (Proposal No. 3). The affirmative vote of a majority of shares of our common stock, present online or represented by proxy at the Annual Meeting and entitled to vote, is required to approve the compensation of our named executive officers. An abstention is treated as present and entitled to vote and, therefore, has the effect of a vote "against" the proposal. Broker non-votes will have no effect on the outcome of the vote on this proposal.

If the Annual Meeting is adjourned or postponed for any purpose, at any subsequent reconvening of the meeting, your proxy will be voted in the same manner as it would have been voted at the original convening of the Annual Meeting unless you withdraw or revoke your proxy.

What if a quorum is not present at the Annual Meeting?

If a quorum is not present or represented at the scheduled time of the Annual Meeting, the presiding officer of the Annual Meeting may adjourn the Annual Meeting without notice other than announcement at the meeting.

Could other matters be decided at the Annual Meeting?

Stockholders at an annual meeting will only be able to consider proposals or nominations specified in the Notice of Annual Meeting or brought before the meeting by or at the direction of our Board or by a stockholder of record on the Record Date for the meeting who is entitled to vote at the meeting and who has

delivered timely written notice in proper form to our Corporate Secretary of the stockholder's intention to bring such business before the meeting. As of the date of this Proxy Statement, Rhythm does not know of any other matters that may be presented for action at the Annual Meeting. Should any other business properly come before the meeting, the persons named on the enclosed proxy will have discretionary authority to vote the shares represented by such proxies in accordance with their best judgment to the same extent as the person signing the proxy would be entitled to vote. If you hold your shares through a broker, bank or other nominee as described above, the broker, bank or other nominee will not be able to vote your shares on any other business that comes before the Annual Meeting unless they receive instructions from you with respect to such matter.

Why hold a virtual meeting?

We believe that hosting a virtual meeting this year is in the best interest of the Company and its stockholders. A virtual meeting enables increased stockholder attendance and participation because stockholders can participate from any location around the world. You will be able to attend the Annual Meeting online and submit your questions by visiting *www.meetnow.global/M6NM5QJ*. You also will be able to vote your shares electronically at the Annual Meeting by following the instructions above.

What if during the check-in time or during the Annual Meeting I have technical difficulties or trouble accessing the virtual meeting website?

We will have technicians ready to assist you with any technical difficulties you may have accessing the virtual meeting website. Please call 888-724-2416 (local) or +1 781-575-2748 (international) for assistance.

Will there be a question and answer session during the Annual Meeting?

As part of the Annual Meeting, we will hold a live Q&A session, during which we intend to answer questions submitted online during the meeting that are pertinent to the Company and the meeting matters, as time permits. Only stockholders that have accessed the Annual Meeting as a stockholder (rather than a "Guest") by following the procedures outlined above in "Who can attend the Annual Meeting?" will be permitted to submit questions during the Annual Meeting. Each stockholder is limited to no more than two questions. Questions should be succinct and only cover a single topic. We will not address questions that are, among other things:

- irrelevant to the business of the Company or to the business of the Annual Meeting;
- related to material non-public information of the Company, including the status or results of our business since our last Quarterly Report on Form 10-Q;
- related to any pending, threatened or ongoing litigation;
- related to personal grievances;
- · derogatory references to individuals or that are otherwise in bad taste;
- substantially repetitious of questions already made by another stockholder;
- in excess of the two question limit;
- in furtherance of the stockholder's personal or business interests; or
- out of order or not otherwise suitable for the conduct of the Annual Meeting as determined by the Chair or Secretary in their reasonable judgment.

Additional information regarding the Q&A session will be available in the "Rules of Conduct" available on the Annual Meeting webpage for stockholders that have accessed the Annual Meeting as a stockholder (rather than a "Guest") by following the procedures outlined above in "Who can attend the Annual Meeting?".

What happens if the meeting is continued, postponed or adjourned?

Your proxy may be voted at the continued, postponed or adjourned meeting. You will still be able to change your proxy until it is voted.



What does it mean if I receive more than one Internet Notice, proxy card or voting instruction form?

It means that you have multiple accounts at the transfer agent or with brokers. Please complete and return all proxy cards or voting instruction forms to ensure that all of your shares are voted.

Where can I find the voting results of the meeting?

The preliminary voting results will be announced at the Annual Meeting. The final results will be disclosed in a Current Report on Form 8-K within four business days after the Annual Meeting date.

IMPORTANT NOTICE REGARDING THE AVAILABILITY OF PROXY MATERIALS FOR THE 2022 ANNUAL MEETING OF STOCKHOLDERS TO BE HELD ON JUNE 8, 2022

The Notice of Annual Meeting of Stockholders, this Proxy Statement and our Annual Report on Form 10-K for the fiscal year ended December 31, 2021 are available free of charge at *www.edocumentview.com/RYTM* or *www.rhythmtx.com* under "Investors & Media" at "SEC Filings."



PROPOSAL NO. 1—ELECTION OF DIRECTORS

In accordance with Rhythm's certificate of incorporation and bylaws, each as currently amended and in effect, the Board is divided into three classes of directors of approximately equal size. The members of each class of directors are elected to serve a three-year term with the term of office of each class ending in successive years. Jennifer Good and Edward T. Mathers are the Class II directors whose terms expire at the Annual Meeting. Each of Jennifer Good and Edward T. Mathers has been nominated for, and has agreed to stand for, election to the Board to serve as a Class II director of Rhythm for three years until the 2025 Annual Meeting of Stockholders and until her or his successor is duly elected and qualified or until her or his earlier death, incapacity, resignation or removal.

It is intended that, unless you give contrary instructions, shares represented by proxies will be voted for the election of each of the two nominees listed above as director nominees. Rhythm has no reason to believe that any nominee will be unable to serve. In the event that one or more nominees is unexpectedly not available to serve, proxies may be voted for another person nominated as a substitute by the Board, or the Board may reduce the number of directors to be elected at the Annual Meeting. Proxies cannot be voted for a greater number of persons than the number of nominees named in this proposal. Information relating to each nominee for election as director and for each continuing director, including his or her period of service as a director of Rhythm, principal occupation and other biographical material, is included under "Director Biographies" below.

Vote Required

A plurality of the votes cast at the meeting will be required for the election of the Class II director nominees. The two nominees for director with the highest number of affirmative votes will be elected as directors. Broker non-votes and abstentions will not be treated as votes cast for this purpose and, therefore, will not affect the outcome of the election.

THE BOARD OF DIRECTORS UNANIMOUSLY RECOMMENDS THAT YOU VOTE "FOR" EACH OF THE CLASS II DIRECTOR NOMINEES NAMED IN THIS PROXY STATEMENT.

(PROPOSAL NO. 1)

BOARD OF DIRECTORS

Board Composition and Structure

Our certificate of incorporation and bylaws, each as currently amended and in effect, state that our Board shall consist of a number of directors that shall be fixed exclusively by the Board from time to time in accordance with the bylaws of the Company. Each director holds office until his or her successor is duly elected and qualified or until his or her death, incapacity, resignation or removal. Our certificate of incorporation provides that our directors may be removed only for cause by the affirmative vote of the holders of at least 75% of the voting power of the outstanding shares of capital stock of Rhythm entitled to vote in the election of directors, voting together as a single class, at a meeting of the stockholders called for that purpose. Any vacancy in the Board, including a vacancy that results from an increase in the number 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.

Our certificate of incorporation, as currently amended and in effect, provides that our Board is divided into three classes of directors, with the classes as nearly equal in number as possible. Each of our directors identified below serves in the class indicated. Subject to any earlier resignation or removal in accordance with the terms of our certificate of incorporation and bylaws, our current Class I directors, will serve until the 2024 Annual Meeting of Stockholders; our current Class II directors, if elected at the Annual Meeting, will serve until the 2025 Annual Meeting of Stockholders; and our current Class III directors will serve until the 2023 Annual Meeting of Stockholders. Any additional directorships resulting from an increase in the number of directors will be apportioned by our Board among the three classes as equally as possible.

The current size of our Board is fixed at nine directors. Proxies cannot be voted for a greater number of persons than the number of director nominees named in this proposal.

Below is a list of the names, ages as of April 28, 2022 and classification of the individuals who currently serve as our directors, two of whom are also nominees to be re-elected at the Annual Meeting.

Name	Age	Position(s)	Class	Term Expires
Stuart A. Arbuckle(1)(2)	56	Director	Ι	2024
Camille L. Bedrosian, M.D.(3)	69	Director	III	2023
Jennifer Good	57	Director	II	2022
Christophe R. Jean(2)	66	Director	Ι	2024
Edward T. Mathers(3)	62	Lead Director	II	2022
David W. J. McGirr(2)(3)	67	Director	III	2023
David P. Meeker, M.D.	67	Director, Chairman of the Board	III	2023
Lynn A. Tetrault, J.D.(1)	59	Director	Ι	2024

(1) Member of the Compensation Committee.

(2) Member of the Audit Committee.

(3) Member of the Governance and Nominating Committee.

In consultation with the Governance and Nominating Committee, the Board has determined that the classified board structure remains appropriate for us at this time. A classified board provides for stability, continuity and experience among our Board. Further, the Board believes that building a cohesive board is an important goal. In our industry in particular, long-term focus is critical. The time horizon required for successful development of pharmaceuticals makes it vital that we have a board that understands the implications of this process and has the ability to develop and implement long-term strategies while benefiting from an in-depth knowledge of Rhythm's business and operations. A classified board structure helps to ensure that there will be the continuity and stability of leadership required to navigate a challenging economic environment while resisting the pressure to focus on short-term results at the expense of our long-term value and success. The future success of Rhythm depends in significant part on the ability to attract and

retain capable and experienced directors. In this regard, we believe that longer terms for our directors will enhance director independence from both management and stockholder special interest groups.

Director Biographies

Information concerning our continuing directors and director nominees is set forth below. The biographical description of each continuing director and director nominee includes the specific experience, qualifications, attributes and skills that led the Board to conclude that such person should serve as a director.

Class II Directors (Nominees Standing for Re-Election)

Jennifer Good

Ms. Good has served as a member of our Board since June 2019. She is a co-founder of Trevi Therapeutics, Inc., a clinical-stage biopharmaceutical company, and has served as a member of the board of directors and as the President and Chief Executive Officer of Trevi Therapeutics, Inc. since its inception in 2011. Previously, Ms. Good served at Penwest Pharmaceuticals Co. from 1997 to 2010, where she held various positions including President and Chief Executive Officer, Chief Operating Officer and Chief Financial Officer. Ms. Good served on the board of Juniper Pharmaceuticals, Inc. from September 2017 until it was acquired by Catalent, Inc. in August 2018. Ms. Good received a Bachelor of Business Administration degree with a concentration in accounting from Pacific Lutheran University in 1987 and is a Certified Public Accountant (inactive).

The Board considered the role Ms. Good played in the founding and growth of Trevi Therapeutics, Inc. and her senior executive roles at publicly traded life sciences companies, as well as her service on the boards of directors of biotechnology companies and organizations, in concluding that she is qualified to serve as a director.

Edward T. Mathers

Mr. Mathers has served as a member of our Board since 2013 and as Lead Director since December 2020. He has been a Partner at New Enterprise Associates, a venture capital firm, since 2008, and has also served as General Partner since October 2019. Mr. Mathers currently serves on the boards of directors of Akouos, Inc., Inozyme Pharma, Inc., ObsEva SA, Trevi Therapeutics, Inc., Mirum Pharmaceuticals, Inc., Reneo Pharmaceuticals, Inc. and Synlogic, Inc. Mr. Mathers also serves on the boards of directors of numerous private companies. Mr. Mathers previously served on the board of directors of Ra Pharmaceuticals, Inc. until its acquisition by UCB in April 2020 and Liquidia Technologies, Inc. until May 2019. Prior to joining New Enterprise Associates, Mr. Mathers served in various corporate development roles at MedImmune, Inc., a biotechnology company that was acquired by AstraZeneca PLC in 2007, culminating in the position of Executive Vice President, Corporate Development and Venture. In this role, he also led the company's venture capital subsidiary, MedImmune Ventures, Inc. Prior to that, Mr. Mathers was Vice President, Marketing and Corporate Licensing and Acquisitions at Inhale Therapeutic Systems, Inc., a biopharmaceutical company, which is now known as Nektar Therapeutics, Inc. Previously, for 15 years, Mr. Mathers was at Glaxo Wellcome, Inc., where he held sales and marketing positions of increasing responsibility. Mr. Mathers received a B.S. in chemistry from North Carolina State University.

The Board considered Mr. Mathers' senior executive roles in publicly traded life sciences companies, his extensive experience as a venture capitalist, as well as his service on the boards of directors of numerous biotechnology companies, in concluding that he is qualified to serve as a director.

Continuing Directors Not Standing for Re-Election at the 2022 Annual Meeting

Stuart A. Arbuckle

Mr. Arbuckle has served as a member of our Board since July 2019. He currently serves as Executive Vice President and Chief Operating Officer at Vertex Pharmaceuticals Incorporated, a biopharmaceutical company, a role he has held since August 2021, where he is responsible for the company's global commercial team, including reimbursement and access, sales, marketing, patient support, market research, commercial



manufacturing, supply chain and other activities that support the approved use of Vertex's cystic fibrosis medicines. Mr. Arbuckle also oversees the Human Resources, Corporate Communications and Program and Portfolio Management functions. Prior to assuming his current role, he served as Executive Vice President and Chief Commercial Officer at Vertex from September 2012 to March 2021. Prior to joining Vertex, Mr. Arbuckle held several commercial leadership positions at Amgen Inc., including leading sales and marketing efforts for Amgen Inc.'s portfolio of cancer medicines, such as Aranesp[®], Neulasta[®] injection and NEUPOGEN[®], and leading the successful launches of XGEVA[®] injection and Nplate[®] injection. Most recently, he served as Vice President and Regional General Manager at Amgen Inc., where he led efforts to expand the company's presence in Asia, the Middle East, and Africa. Prior to these roles, Mr. Arbuckle spent 15 years at GlaxoSmithKline plc, where he held sales and marketing roles for medicines aimed at treating metabolic, respiratory, musculoskeletal, cardiovascular and other diseases. Mr. Arbuckle currently serves as a board member of ImmunoGen, Inc. Mr. Arbuckle holds a B.S. in Pharmacology and Physiology from the University of Leeds in the United Kingdom.

The Board considered Mr. Arbuckle's senior executive roles at publicly-held life sciences companies, as well as his service on the boards of directors of biotechnology companies and organizations, in concluding that he is qualified to serve as a director.

Camille L. Bedrosian, M.D.

Dr. Bedrosian has served as a member of our Board since December 2020. Since January 2018, Dr. Bedrosian has served as Executive Vice President and Chief Medical Officer at Ultragenyx Pharmaceutical, a rare disease company with a diverse portfolio of approved therapies and product candidates, where she provides strategic leadership to the clinical development and translational research programs and oversees Medical Affairs, Global Development, Clinical Operations and Drug Safety. Previously, Dr. Bedrosian served as Senior Vice President and Chief Medical Officer at Alexion Pharmaceuticals, Inc., a biopharmaceutical company, from May 2008 to December 2017, where she provided leadership for the development of drugs and drug candidates including those designed to address devastating rare diseases such as Soliris(r) (eculizumab). Prior to this, she served as Chief Medical Officer at ARIAD Pharmaceuticals, as well as in the Clinical Research and Development Department of Genetics Institute, Inc. Before transitioning to the biotechnology industry, Dr. Bedrosian was an Assistant Professor of Medicine at Duke University Medical Center where she was a member of the Duke Comprehensive Cancer Center. Dr. Bedrosian holds an A.B. from Harvard University, M.D. from Harvard Medical School, and M.S. in Biophysics from the Massachusetts Institute of Technology.

The Board considered Dr. Bedrosian's scientific expertise and extensive experience serving as a Chief Medical Officer at companies engaged in the development of drugs for the treatment of rare diseases in concluding that she is qualified to serve as a director.

Christophe R. Jean

Mr. Jean has served as a member of our Board since 2015. He is currently a Strategic Advisor for Oraxys S.A., a private equity firm, a role he has held since June 2019. Mr. Jean also served as a Senior Advisor for JSB Partners, LLC, a specialized biotechnology and pharmaceutical investment banking and advisory services firm, from November 2018 until December 2019. Previously, Mr. Jean served as Executive Vice President of Corporate Strategy, Business Development, Alliances and M&A for Ipsen S.A., a pharmaceutical company, from 2013 until his retirement in July 2018, after serving for 11 years in the position of Executive Vice President, Chief Operating Officer, with responsibility for all commercial operations and medical affairs worldwide as well as Ipsen S.A.'s therapeutic area franchises. Prior to joining Ipsen S.A., Mr. Jean was President and CEO for the pharmaceutical activities of the Pierre Fabre Group and President of Europe, Middle East, and Africa for Novartis Pharma AG's Pharmaceutical Division. Prior to the merger of Ciba-Geigy AG and Sandoz Inc. that formed Novartis Pharma AG, he held a number of marketing and management positions in Europe and Latin America for Ciba-Geigy AG, culminating as Head of Finance and IT Worldwide and Member of the Pharma Executive Committee. Mr. Jean also serves on the boards of directors of multiple private companies. He holds an M.B.A. from Harvard Business School.

The Board considered Mr. Jean's international business experience and executive leadership at several of the world's leading pharmaceutical companies and his long career in commercial leadership roles in

concluding that he is qualified to serve as a director. The Board also considered Mr. Jean's extensive experience in commercializing therapeutics outside of the United States.

David W.J. McGirr

Mr. McGirr has served as a member of our Board since 2015. Mr. McGirr serves as a director of X4 Pharmaceuticals, Inc., a clinical-stage biopharmaceutical company focused on the discovery and development of novel therapeutics designed to improve immune cell trafficking to treat rare diseases and cancer, and Insmed Incorporated, a pharmaceutical company devoted to the treatment of rare diseases. Mr. McGirr previously served on the boards of directors of Menlo Therapeutics, Inc. until March 2020, Roka Bioscience until January 2018 and Relypsa Inc. until September 2016. Previously, Mr. McGirr held various roles at Cubist Pharmaceuticals, including Senior Advisor to the chief executive officer and Senior Vice President and Chief Financial Officer. Prior to joining Cubist, Mr. McGirr was the President and Chief Operating Officer of Hippo Inc., an internet technology, venture-financed company. Before that, he held roles of increasing responsibility at GAB Robins North America, Inc., a risk management company, including as Chief Executive Officer. Earlier in his career, Mr. McGirr served in various positions within the S.G. Warburg Group, ultimately as Chief Financial Officer, Chief Administrative Officer and Managing Director of S.G. Warburg & Co., Inc. Mr. McGirr received a B.Sc. in Civil Engineering from the University of Glasgow and received an M.B.A. from The Wharton School at the University of Pennsylvania. Mr. McGirr has been designated an audit committee financial expert as defined in applicable SEC rules.

In concluding that he is qualified to serve as a director, the Board considered Mr. McGirr's deep experience in corporate finance and financial reporting, as well as his knowledge, perspective and corporate governance expertise. The Board also considered that his expertise in financial and accounting matters, his prior experience as Chief Financial Officer of a leading biotechnology company, and his service on other public company boards and committees would significantly benefit the Company.

David P. Meeker, M.D.

Dr. Meeker has served as a member of our Board since 2015 and became Chairman of the Board in April 2017. Dr. Meeker has served as our President and Chief Executive Officer since July 2020. Previously, Dr. Meeker served as CEO of KSQ Therapeutics, Inc., a biotechnology company, from October 2017 to July 2020. From October 2011 until June 2017, Dr. Meeker served as President and CEO of Genzyme Corporation and subsequently as EVP, Head Sanofi Genzyme, a unit of Sanofi S.A., a global pharmaceutical company. Dr. Meeker oversaw the company's specialty business units-Rare Diseases, Multiple Sclerosis, Oncology and Immunology. As an Executive Vice President of Sanofi S.A., he was a member of Sanofi S.A.'s Executive Committee. Dr. Meeker joined Genzyme Corporation in 1994 as Medical Director to work on the Cystic Fibrosis Gene Therapy program. Subsequently, as Vice President, Medical Affairs, he was responsible for the development of rare disease therapies that today represent transformative and life-saving advancements in medicine for patients. Prior to Genzyme Corporation's merger with Sanofi S.A. in 2011, Dr. Meeker was Genzyme Corporation's Chief Operating Officer, responsible for its commercial organization, overseeing its business units, country management organization and global market access functions. He played an important role in the integration with Sanofi S.A. Prior to joining Genzyme Corporation, Dr. Meeker was the director of the Pulmonary Critical Care Fellowship at the Cleveland Clinic and an assistant professor of medicine at Ohio State University. Dr. Meeker is currently Chairman of the board of directors of Pharvaris GmbH and the Chairman of the board of directors of Trevi Therapeutics, Inc. He has authored more than 40 articles and multiple book chapters. Dr. Meeker received his M.D. from the University of Vermont Medical School. He completed the Advanced Management Program at Harvard Business School in 2000.

In concluding that he is qualified to serve as a director, the Board considered Dr. Meeker's deep experience as a senior executive at leading global pharmaceutical companies, including his experience serving as our President and Chief Executive Officer, and his involvement in the development and commercialization of pharmaceutical product candidates for the treatment of rare and ultra-rare diseases. The Board also considered the integral role he played in the growth of Genzyme during its period of rapid growth. The Board also noted Dr. Meeker's extensive scientific and clinical experience, both in academia and as part of one of the world's leading medical institutions.

Lynn A. Tetrault, J.D.

Ms. Tetrault has served as a member of our Board since December 2020. Ms. Tetrault currently serves as a board member and Lead Independent Director of NeoGenomics, Inc. Ms. Tetrault spent over 21 years at AstraZeneca PLC, serving in a variety of senior positions, including most recently as EVP of Human Resources and Corporate Affairs from May 2007 to March 2014. In May 2017, Ms. Tetrault founded Anahata Leadership, Inc., an advisory firm focused on supporting the leadership and development of executive women, and continues to serve as a principal. Ms. Tetrault also is a Fellow of Simmons University's Institute for Inclusive Leadership and is a Director of Paradigm for Parity, a non-profit organization whose mission is to close the gender parity gap in corporate leadership by 2030. Ms. Tetrault began her career as a lawyer in private healthcare practice in Boston. Ms. Tetrault holds a B.A. from Princeton University and a J.D. from the University of Virginia.

In connection with her nomination to the Board, the Board considered Ms. Tetrault's significant experience as a senior executive at a global biopharmaceutical company and her strong background in executive leadership.

BOARD DIVERSITY MATRIX				
Board Diversity Matrix (As of April 28, 2022)				

Board Diversity Matrix (As of April 28, 2022)						
8						
Female	Male	Non-Binary	Did Not Disclose Gender			
3	5	0	0			
0	0	0	0			
0	0	0	0			
0	0	0	0			
0	0	0	0			
0	0	0	0			
3	5	0	0			
0	0	0	0			
	0					
	0					
	Female 3 0 0 0 0 0 0 0 3	Female Male 3 5 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	Female Male Non-Binary 3 5 0 3 5 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0			

CORPORATE GOVERNANCE

Director Independence

Under the rules of The Nasdaq Stock Market LLC, or Nasdaq, a majority of a listed company's board of directors must be comprised of independent directors. In addition, Nasdaq rules require that, subject to specified exceptions, each member of a listed company's audit committee and compensation committee be independent and satisfy additional independence criteria set forth in Rules 10A-3 and 10C-1, respectively, under the Securities Exchange Act of 1934, as amended, or the Exchange Act. Under Nasdaq rules, a director will only qualify as an "independent director" if, in the opinion of that company's board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director.

Based upon information requested from and provided by our directors and nominees concerning their background, employment and affiliations, including family relationships, our Board has determined, upon the recommendation of our Governance and Nominating Committee, that each of Stuart A. Arbuckle, Camille L. Bedrosian, M.D., Christophe R. Jean, Edward T. Mathers, David W. J. McGirr and Lynn A. Tetrault, J.D. has no relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and is independent within the meaning of the director independence standards of Nasdaq and the Securities and Exchange Commission, or SEC. The Board also determined that Todd Foley was independent during the time he served on our Board in 2021. Our Board has also determined that each of the current members of our Audit Committee and our Compensation Committee as set forth in the "Board Committees" section below satisfies the heightened independence standards for such committee. In making such determination, our Board considered the relationships that each non-employee director has with Rhythm and all other facts and circumstances deemed relevant in determining their independence.

There are no family relationships among any of our directors, nominees or executive officers.

Board Meetings, Attendance and Executive Sessions

The Board held five meetings during the year ended December 31, 2021. All board members attended at least 75% of the meetings of the Board and the committees of the Board on which they served.

Executive sessions without management present are held regularly.

Rhythm encourages its directors to attend the Annual Meeting. All members of the Board then-serving attended the 2021 Annual Meeting of Stockholders.

Board of Directors Leadership Structure

Our Corporate Governance Guidelines provide our Board with flexibility to combine or separate the positions of Chairman of the Board and Chief Executive Officer in accordance with its determination that utilizing one or the other structure would be in the best interests of our Company. At the current time, David P. Meeker, M.D., our President and Chief Executive Officer, serves as Chairman of the Board. Our Board has determined that combining the roles of Chairman of the Board and Chief Executive Officer is best for our company and our stockholders at this time because it promotes unified leadership by Dr. Meeker and allows for a single, clear focus for management to execute the Company's strategy and business plans. If the Chairman of the Board is a member of management or does not otherwise qualify as independent, our Corporate Governance Guidelines provide for the appointment by the independent directors of a Lead Director. The independent directors have appointed Edward T. Mathers as the Lead Director. The Lead Director's responsibilities include, but are not limited to, presiding over all meetings of the Board of Directors at which the Chairman of the Board is not present, including any executive sessions of the independent directors, and acting as liaison between the independent directors of the Board and the Chief Executive Officer and the Chairman of the Board. Our Board is comprised of individuals with extensive experience with the biotechnology and pharmaceutical industries and a majority of our directors meet the independence standards of Nasdaq. For these reasons and because of the strong leadership of Dr. Meeker as Chairman of the Board and Chief Executive Officer and the counterbalancing role of the Lead Director, our Board has

concluded that our current leadership structure is appropriate at this time. However, our Board will continue to periodically review our leadership structure and may make such changes in the future as it deems appropriate.

Board of Directors' Role in Risk Oversight

The Audit Committee of the Board is primarily responsible for overseeing our risk management processes on behalf of the Board. The Audit Committee receives reports from management regarding our assessment of risks. In addition, the Audit Committee reports regularly to the Board, which also considers our risk profile. The Audit Committee and the Board focus on the most significant risks we face and our general risk management strategies, including business continuity risks, such as risks relating to the COVID-19 pandemic, and our major financial and cybersecurity risk exposures and the steps our management has taken to monitor and control these exposures. The Audit Committee and the Board also monitor compliance with legal and regulatory requirements. In addition, our Compensation Committee assesses and monitors whether any of our compensation policies and programs has the potential to encourage excessive risk-taking, and the Governance and Nominating Committee oversees risks associated with the independence of the Board and also considers and approves or disapproves any related person transactions and monitors the effectiveness of our corporate governance guidelines.

While the Board oversees our risk management, management is responsible for day-to-day risk management processes. Our Board expects management to consider risk and risk management in each business decision, to proactively develop and monitor risk management strategies and processes for day-to-day activities and to effectively implement risk management strategies adopted by the Audit Committee and the Board. Management discusses strategic and operational risks at regular management meetings and conducts specific strategic planning and review sessions during the year that include a focused discussion and analysis of the risks facing us. Throughout the year, senior management reviews these risks with the Board of Directors at regular Board meetings as part of management presentations that focus on particular business functions, operations or strategies, and presents the steps taken by management to mitigate or eliminate such risks. We believe this division of responsibilities is the most effective approach for addressing the risks we face and that the leadership structure of our Board, which also emphasizes the independence of the Board in its oversight of its business and affairs, supports this approach.

Board Committees

Our Board has established the following standing committees: an Audit Committee, a Compensation Committee, and a Governance and Nominating Committee. The composition and responsibilities of each committee are described below. Members serve on these committees until their resignation or until otherwise determined by our Board. Each of the Audit Committee, Compensation Committee and Governance and Nominating Committee operates pursuant to a written charter and each committee reviews and assesses the adequacy of its charter annually and recommends any proposed changes to the Board for approval. The charters for the Audit Committee, Compensation Committee, and Governance and Nominating Committee are all available on our website at *www.rhythmtx.com* under "Investors & Media" at "Corporate Governance."

The following table describes which directors serve on each of the Board committees.

Name:	Governance and Nominating Committee	Compensation Committee	Audit Committee
Stuart A. Arbuckle		Х	Х
Camille L. Bedrosian, M.D.	Х		
Jennifer Good			
Christophe R. Jean			Х
Edward T. Mathers	X*		
David W. J. McGirr	Х		X*
Lynn A. Tetrault, J.D.		X*	

* Denotes chair of committee.

Audit Committee

Our Audit Committee provides oversight of our accounting and financial reporting process, the audit of our financial statements and our internal control function. Among other matters, the Audit Committee is responsible for the following: assisting the Board in oversight of the independent auditors' qualifications, independence and performance; the engagement, retention and compensation of the independent auditors; reviewing the scope of the annual audit; reviewing and discussing with management and the independent auditors the results of the annual audit and the review of our quarterly financial statements, including the disclosures in our annual and quarterly reports filed with the SEC; reviewing our risk assessment and risk management processes; establishing procedures for receiving, retaining and investigating complaints received by us regarding accounting, internal accounting controls or audit matters; and approving audit and permissible non-audit services provided by our independent auditor.

The current members of our Audit Committee are David W.J. McGirr, who is the chair of the Audit Committee, Stuart Arbuckle and Christophe R. Jean. All members of our Audit Committee meet the requirements for financial literacy under the applicable rules and regulations of the SEC and Nasdaq. Our Board has determined that Mr. McGirr is an audit committee financial expert as defined under SEC rules and has the requisite financial sophistication under applicable rules and regulations of Nasdaq as a result of, among other things, his senior-level executive experience, including his service as Chief Financial Officer of Cubist Pharmaceuticals, Inc. from November 2002 to March 2013. All of the members of our Audit Committee are independent directors as defined under the applicable rules and regulations of the SEC and Nasdaq.

During the year ended December 31, 2021, the Audit Committee met four times. The report of the Audit Committee is included in this Proxy Statement under "Audit Committee Report."

Compensation Committee

Our Compensation Committee adopts and administers the compensation policies, plans and benefit programs for our executive officers and all other members of our executive team. Our Compensation Committee is also responsible for making recommendations to the full Board regarding non-employee director compensation. In addition, among other things, our Compensation Committee evaluates annually, in consultation with the Board, the performance of our chief executive officer, reviews and approves corporate goals and objectives relevant to compensation of our chief executive officer and other executives and evaluates the performance of these executives in light of those goals and objectives. Although our chief executive officer does not participate in decisions involving his own compensation, his recommendations and input, along with input from other executive officers, are often taken into consideration by the Compensation Committee when making compensation decisions.

Our Compensation Committee also administers our equity compensation plans, including approving, or recommending to our Board for approval, issuances of stock options and other awards under such plans. The Compensation Committee may delegate its authority under its charter to one or more subcommittees as it deems appropriate from time to time as further described in its charter. The Compensation Committee may also delegate, or recommend to our Board that it delegate, to our chief executive officer the authority to approve equity awards under our equity plans, as further described in its charter and to the extent permitted under our equity plans.

The Compensation Committee has the authority to retain or obtain the advice of compensation consultants, legal counsel and other advisors to assist in carrying out its responsibilities. For discussion of the role of compensation consultants in determining executive and non-employee director compensation, please refer to "Executive Compensation" and "Director Compensation" below.

The current members of our Compensation Committee are Lynn A. Tetrault, J.D., who is the chair of the Compensation Committee and Stuart Arbuckle. Before his resignation on June 9, 2021, Todd Foley also

served on the Compensation Committee. All members of our Compensation Committee, as well as Todd Foley, are independent under applicable rules and regulations of the SEC and Nasdaq.

During the year ended December 31, 2021, the Compensation Committee met six times.

Governance and Nominating Committee

Our Governance and Nominating Committee is responsible for, among other things, making recommendations regarding corporate governance, the composition of our Board, the identification, evaluation and nomination of director candidates and the structure and composition of committees of our Board. In addition, our Governance and Nominating Committee oversees our corporate governance guidelines, oversees our strategy, initiatives and policies concerning corporate social responsibility, including environmental, social and governance matters, reviews and assesses the adequacy of our committee charters, oversees compliance with our code of business conduct and ethics, contributes to succession planning, reviews policies and procedures with respect to any related party transactions and oversees our Board self-evaluation process.

The current members of our Governance and Nominating Committee are Edward T. Mathers, who is the chair of the Governance and Nominating Committee, Camille Bedrosian, M.D. and David W.J. McGirr. All of the members of our Governance and Nominating Committee are independent under applicable rules and regulations of Nasdaq.

During the year ended December 31, 2021, the Governance and Nominating Committee met one time.

Policies Governing Director Nominations

Director Nomination Process

Our Board is responsible for selecting its own members. The Board delegates the selection and nomination process to the Governance and Nominating Committee, with the expectation that other members of the Board and of management will be requested to take part in the process as appropriate. The Governance and Nominating Committee makes recommendations to the Board regarding the size and composition of the Board. The Governance and Nominating Committee reviews annually with the Board the composition of the Board as a whole and recommends, if necessary, measures to be taken so that the Board reflects the appropriate balance of knowledge, experience, skills, expertise and diversity required for the Board as a whole and contains at least the minimum number of independent directors required by applicable laws and regulations. The Governance and Nominating Committee is responsible for ensuring that the composition of the Board accurately reflects the needs of Rhythm's business and, in furtherance of this goal, for proposing the resignation of members for purposes of ensuring the appropriate members and skills. The Governance and Nominating Committee recommends, and the Board nominates, candidates to stand for election as directors.

Generally, our Governance and Nominating Committee identifies candidates for director nominees in consultation with management, through the use of search firms or other advisors, through recommendations submitted by stockholders or through such other methods as the Governance and Nominating Committee deems to be helpful to identify candidates. Once candidates have been identified, our Governance and Nominating Committee confirms that the candidates meet all of the minimum qualifications for director nominees established by the Governance and Nominating Committee. The Governance and Nominating Committee may gather information about the candidates through interviews, detailed questionnaires, background checks or any other means that the Governance and Nominating Committee then meets as a group to discuss and evaluate the qualifications and skills of each candidate, both on an individual basis and taking into account the overall composition and needs of the Board. Based on the results of the evaluation process, the Governance and Nominating Committee recommends to the Board for approval candidates as director nominees for election to the Board.

Stockholders may also recommend potential director candidates by submitting the names of the recommended individuals, together with appropriate biographical information and background materials,

to the Governance and Nominating Committee, c/o Secretary, 222 Berkeley Street, 12th Floor, Boston, MA 02116. In the event there is a vacancy, and assuming that appropriate biographical and background material has been provided on a timely basis, the Governance and Nominating Committee will evaluate stockholderrecommended candidates by following substantially the same process described above, and applying substantially the same criteria set forth below under "Minimum Qualifications," as it follows for candidates submitted by others.

To nominate a person to stand for election as a director, a stockholder must provide our Secretary with timely notice of the nomination and the notice must include the information required by Section 2.12(b) of our bylaws. Nominations must also comply with the requirements of Rule 14a-19 under the Exchange Act. Additional information regarding requirements for stockholder nominations of director candidates for next year's annual meeting is described in this Proxy Statement under "General Matters-Stockholder Proposals and Nominations."

Minimum Qualifications

Our Governance and Nominating Committee will consider, among other things, the following qualifications, skills and attributes when recommending candidates for the Board's selection as nominees for the Board and as candidates for appointment to the Board's committees. The nominee shall have the highest personal and professional integrity, shall have demonstrated exceptional ability and judgment, and shall be most effective, in conjunction with the other members of the Board, in collectively serving the long-term interests of our stockholders. Board members should possess such attributes and experience as are necessary to provide a broad range of personal characteristics including diversity, management skills and business experience. Directors should be able to commit the requisite time for preparation and attendance at regularly scheduled Board and committee meetings, as well as be able to participate in other matters necessary to ensure that good corporate governance is practiced.

In evaluating the suitability of individual candidates (both proposed director candidates and current Board members), our Governance and Nominating Committee may consider, in addition to the minimum qualifications and other criteria for board membership approved by the Board from time to time, all facts and circumstances that it deems appropriate or advisable, including, among other things, diversity, not limited to race, gender or national origin, the skills of the proposed director candidate, his or her depth and breadth of professional experience or other background characteristics, his or her independence and the needs of the Board. Although we have no formal policy regarding board diversity, we consider diversity in our Board's makeup, and our Governance and Nominating Committee's priority in selecting Board members is the identification of persons who will further the interests of Rhythm through an established record of professional accomplishment, the ability to contribute positively to the collaborative culture among Board members, and professional and personal experiences and expertise relevant to our growth strategy. The Governance and Nominating Committee will consider candidates recommended by stockholders. See "Director Nomination Process" above.

Stockholder Engagement and Communications

Members of the Rhythm management team actively engaged with stockholders during 2021, consistent with our commitment to enabling open and ongoing dialogue with stockholders and potential investors. Due to continued restrictions on travel and face-to-face meetings due to the COVID-19 pandemic, these meetings were primarily held via video conference. According to internal records, we participated in approximately 175 meetings with representatives of more than 65 institutional stockholders or prospective investors in 2021, representing the holders of approximately 67 percent of our outstanding common stock as of February 14, 2022. In addition, members of our management team participated in 10 financial conferences or sponsored "bus" tours and executed two non-deal roadshows.

This active engagement enables us to better understand the perspectives of our stockholders. Through our active stockholder engagement, we provided regular business updates relative to the advancement of setmelanotide through clinical development, disclosures relative to clinical and safety data, U.S. and EU regulatory strategy and milestones including FDA approval of IMCIVREE, and guidance on financial resources. Our robust engagement also enables feedback channels that provide a valuable way to receive ongoing input from our stockholders.

Stockholders wishing to communicate with our Board may do so by writing to the Board or to the nonemployee members of the Board as a group, at:

Rhythm Pharmaceuticals, Inc. 222 Berkeley Street, 12th Floor Boston, MA 02116 Attention: Secretary

The communication must prominently display the legend "BOARD COMMUNICATION" in order to indicate to the Secretary that it is a communication for the Board. Upon receiving such a communication, the Secretary will promptly forward the communication to the relevant individual or group to which it is addressed. Certain items that are unrelated to the Board's duties and responsibilities may be excluded, such as spam, junk mail and mass mailings, resumes and other forms of job inquiries, surveys and business solicitations or advertisements. The Secretary will not forward any communication determined in good faith belief to be frivolous, unduly hostile, threatening, illegal or similarly unsuitable.

Code of Business Conduct and Ethics and Corporate Governance Guidelines

We have a code of business conduct and ethics that applies to all of our employees, including our executive officers and those employees responsible for financial reporting, and directors. The code of business conduct and ethics is available on our website at *www.rhythmtx.com* under "Investors & Media" at "Corporate Governance"; or by requesting a copy, free of charge, in writing from our Secretary at Rhythm Pharmaceuticals, Inc., 222 Berkeley Street, 12th Floor, Boston, MA 02116. We intend to satisfy the disclosure requirement under Item 5.05 of Form 8-K regarding any amendment to, or waiver under, a provision of the code of business conduct and ethics, as well as Nasdaq's requirement to disclose waivers with respect to directors and executive officers, by posting such information on our website at the address specified above within four business days following the date of such amendment or waiver.

A copy of our corporate governance guidelines may also be accessed free of charge by visiting our website at *www.rhythmtx.com* under "Investors & Media" at "Corporate Governance" or by requesting a copy from our Secretary at our principal executive offices above.

Anti-Hedging and Pledging Policy

Pursuant to our Insider Trading Policy, we prohibit our employees and members of the Board from engaging in any hedging or monetization transactions relating to our equity securities, including through the use of financial instruments such as prepaid variable forwards contracts, equity swaps, collars and exchange funds. We also prohibit our employees and members of the Board from holding our equity securities in a margin account or otherwise pledging our equity securities as collateral for a loan.

ESG Overview

Social Impact

Rhythm believes that its core mission will have a significantly positive impact on society. Obesity is an epidemic affecting hundreds of millions of people worldwide, and current treatment approaches have demonstrated limited long-term success for most obese patients. Addressing early-onset obesity, even among rare disease populations, confronts one of the most pernicious aspects of one of the world's most impactful public health problems. While we are focused on a rare subset of people with severe obesity, those who suffer from early-onset, severe obesity and hyperphagia caused by certain genetic variants, we are focused on advancing the understanding of the biology and genetics of obesity and expanding genetic testing to improve diagnosis of rare genetic diseases of obesity. As part of these efforts, we have launched Uncovering Rare Obesity (URO) in order to increase access to genetic testing. URO is a free genetic test that physicians may order from us for individuals who qualify based on their body index. This program raises awareness and brings access to genetic testing into the community setting. Currently available physician-ordered genetic testing panels are often cost prohibitive, while many consumer genetic tests are incomplete when it comes to genetic disorders of obesity. As of December 31, 2021, 2,758 United States health care providers have requested 28,171 Uncovering Rare Obesity kits, and 13,029 sequencing tests have been ordered and patient

samples collected. We believe the program marks an important step in the understanding of these disorders that might help patients and their families find new diagnosis and treatment strategies in the years ahead.

In 2021, Rhythm participated in a number of charitable efforts either by a direct donation or through a partnership in order to enable our employees to support non-profit organizations. For example, we facilitated participation on the Wonderful Christmas gifts program that provides holiday presents to children in foster care who are supported by the Massachusetts Department of Children and Family Services and a program in collaboration with our building management and neighbors to support the Boys and Girls Clubs of Boston. Additionally, we participated in a program through the non-profit group Love Your Melon to support programs for families living with pediatric cancer, and the Together We Rise program, providing skateboards to children in Boston associated with the Communities for People, a residential program for troubled youth that teaches independent living skills. We also donated to the Biomedical Science Careers program, which supports minority students in their pursuit of a career in science, and the Dimock Center—a community health center serving Roxbury, a lower-income community in Boston populated primarily by Black and Latino residents.

Integrating Sustainability

In the context of being a mission-driven organization, we are incorporating our existing approach to environmental, social and governance (ESG) matters into our governance mechanisms. The Board amended the Nominating Committee charter and delegated to the Nominating Committee oversight responsibility with respect to our strategy, initiatives and policies concerning corporate social responsibility, including ESG matters.

Response to COVID-19

As we continue work to address the unprecedented challenges introduced by the COVID-19 pandemic, our primary focus remains on the health and safety of those who participate in our ongoing studies, as well as our employees and their families. To that end, we implemented precautionary measures to support patient well-being, ensure consistent and appropriate clinical trial conduct, and enable our ongoing studies to continue with minimal interruption. We ensured that patients enrolled in our studies continued to be able to access their study drug and be monitored as scheduled throughout the duration of the pandemic, and that COVID-19 does not delay our ability to deliver setmelanotide to people living with rare genetic diseases of obesity.

In addition, in 2021 we continued to provide our employees with the resources and flexibility to work from home. With a focus on mental health and work-life balance, we encouraged our employees to take the time needed to care for family and loved ones, as necessary, and leverage our Employee Assistance Program for confidential support. To further promote wellbeing, we also provided paid summer and winter breaks for the entire employee population. Employees were not required but for those who wished to return to our Boston office, we instituted protocols related to limiting capacity, minimizing face-to-face interactions and instituted vaccination requirements to promote the safety of all employees. In March 2021, we executed a virtual "Wellness Week," with a series of events designed to encourage physical activity, exercise, nutrition and mental wellness. Moving forward, we are engaging with employees to evaluate the "future of the office" to provide employees with the flexibility and resources to work both in-office and remotely, collaborating effectively for the benefit of patients.

Human Capital

We believe that our future success largely depends upon our continued ability to attract and retain highly skilled employees. We emphasize a number of measures and objectives in managing our human capital assets, including, among others, employee engagement, development and training, talent acquisition and retention, employee wellness, diversity, inclusion, and compensation and pay equity. As of March 31, 2022, we had 137 employees and active recruitment efforts to grow further. Approximately 60 percent of our employees are female, including 45 percent of our vice president/senior vice president/executive level employees; and approximately 20 percent of our positions are filled by employees of minority backgrounds. We also work with consultants and contractors to provide both specific expertise and flexibility for our business needs. At the board level, three of our directors are female.

We believe that developing a diverse and inclusive culture is critical to continuing to attract and retain the top talent necessary to deliver on our growth strategy. As such, we are investing in a work environment where our employees feel inspired and included. We continue to focus on extending our diversity and inclusion initiatives across our entire workforce. In addition, we work to ensure our employees understand and embrace our commitment to our patient community and our focus on changing the paradigm for treatment of rare genetic diseases of obesity. We value our employees' courage to ask bold questions and their commitment to learning and collaboration, as each person brings a unique contribution to furthering our mission. Grounded in these guiding principles, we believe we have developed a collaborative environment where our colleagues feel respected, valued, and can contribute to their fullest potential.

DIRECTOR COMPENSATION

We maintain a non-employee director compensation program that is intended to provide a total compensation package that enables us to attract and retain qualified and experienced individuals to serve as directors and to align our directors' interests with those of our stockholders. Our Compensation Committee periodically reviews the compensation of our non-employee directors and, as applicable, makes recommendations to the Board for its consideration of changes to our non-employee director compensation program. Our Compensation Committee compares the compensation of our Board to compensation paid to non-employee directors of similarly sized public companies. Our Compensation Committee also considers the responsibilities we ask of the members of our Board along with the amount of time required to perform those responsibilities.

Under our director compensation program, we provide our non-employee directors with cash retainers and stock options. We do not pay any compensation to our President and Chief Executive Officer in connection with his service on our Board. The compensation that we pay to our President and Chief Executive Officer is discussed in the "Executive Compensation" section of this Proxy Statement. For 2021, each non-employee director received an annual retainer fee of \$45,000 paid in arrears. In addition, in 2021 non-employee directors received the following, as applicable:

Non-Employee Director	Annual Fee
Lead Director	\$25,000
Non-Executive Chair	\$30,000
Chair of the Audit Committee	\$20,000
Member of the Audit Committee (other than chair)	\$10,000
Chair of the Compensation Committee	\$15,000
Member of the Compensation Committee (other than chair)	\$ 7,500
Chair of the Governance and Nominating Committee	\$10,000
Member of the Governance and Nominating Committee (other than chair)	\$ 5,000

We also reimburse our non-employee directors for reasonable travel and out-of-pocket expenses incurred in connection with attending Board and committee meetings.

Under the non-employee director compensation program for 2021, each individual who is initially appointed or elected to the Board is also eligible to receive an option to purchase up to 30,000 shares of our common stock under our 2017 Equity Incentive Plan on the date he or she first becomes a non-employee director. These option grants vest annually over a three-year period from the date of grant, subject to continued service as a non-employee director through the vesting date. In addition, on the date of the annual meeting of stockholders, each continuing non-employee director who has served on the Board for a minimum of six months is eligible to receive an option grant to purchase 15,000 shares of our common stock, which will vest in full upon the earlier of the first anniversary of the date of grant or the date of the next annual meeting of stockholders. The exercise price for each of these option grants is equal to the fair market value of our common stock on the date of grant. These initial grants and annual grants are subject to approval by our Board at the time of grant.

In February 2022, upon the recommendation of the Compensation Committee and following a competitive market review prepared by Radford, the Compensation Committee's independent compensation

consultant, the Board approved amending our director compensation policy, effective January 1, 2022, to provide that each non-employee director would receive an annual retainer fee of \$47,500, as well as the additional following cash fees:

Non-Employee Director	Annual Fee
Lead Director	\$35,000
Non-Executive Chair	\$30,000
Chair of the Audit Committee	\$20,000
Member of the Audit Committee (other than chair)	\$10,000
Chair of the Compensation Committee	\$15,000
Member of the Compensation Committee (other than chair)	\$ 7,500
Chair of the Governance and Nominating Committee	\$10,000
Member of the Governance and Nominating Committee (other than chair)	\$ 5,000

In addition, under the amended policy, the initial option granted to a non-employee director first joining the Board will cover 40,000 shares of our common stock, and the annual option granted to our non-employees will cover 20,000 shares of our common stock. Such changes were intended to position both the cash and equity components of our non-employee director compensation closer to the median of market.

The following table sets forth information regarding compensation earned by our non-employee directors during fiscal year 2021. Dr. Meeker did not receive any compensation for his service on our Board while employed as our President and Chief Executive Officer during 2021.

Name	Fees Earned or Paid in Cash (\$)(1)	Option Awards (\$)(2)	Total (\$)
Stuart Arbuckle	62,500	176,550	239,050
Camille Bedrosian, M.D.	50,000	176,550	226,550
Todd Foley	28,125		28,125
Jennifer Good	45,000	176,550	221,550
Christophe R. Jean	55,000	176,550	231,550
Edward T. Mathers	80,000	176,550	256,550
David W. J. McGirr	70,000	176,550	246,550
Lynn A. Tetrault	56,250	176,550	232,800

⁽¹⁾ Amounts represent annual cash compensation earned for services rendered by each member of the Board.

⁽²⁾ Amounts reflect the full grant-date fair value of stock options granted during 2021 computed in accordance with ASC Topic 718, rather than the amounts paid to or realized by the named individual. We provide information regarding the assumptions used to calculate the value of all stock awards and option awards made to our directors in Note 8 to the consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2021.

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The following table sets forth, as of December 31, 2021, the aggregate numbers of option awards (exercisable and unexercisable) and unvested stock awards held by each non-employee director at that time.

Name	Option Awards Outstanding at 2021 Fiscal Year End	Unvested Stock Awards Outstanding at 2021 Fiscal Year End
Stuart Arbuckle	63,500	25,000
Camille Bedrosian, M.D.	52,000	39,420
Jennifer Good	63,500	25,000
Christophe R. Jean	58,500	15,000
Edward T. Mathers	58,500	15,000
David W. J. McGirr	145,741	15,000
Lynn A. Tetrault	52,000	39,420

EXECUTIVE OFFICERS

Below is a list of the names, ages as of April 28, 2022, positions, and a brief account of the business experience of the individuals who serve as our executive officers.

Name	Age	Position(s)
David P. Meeker, M.D.	67	Chairman of the Board, President and Chief Executive Officer
Hunter C. Smith	54	Chief Financial Officer and Treasurer
Pamela Cramer	48	Chief Human Resources Officer
Linda Shapiro, M.D., Ph.D.	51	Chief Medical Officer
Joseph Shulman	47	Chief Technical Officer
Jennifer Chien	47	Executive Vice President, Head of North America
Yann Mazabraud	49	Executive Vice President, Head of International

Executive Officer Biographies

David P. Meeker, M.D. | Chairman of the Board, President and Chief Executive Officer

Dr. Meeker's biography is included on page 11 of this Proxy Statement.

Hunter C. Smith | Chief Financial Officer and Treasurer

Mr. Smith has served as our Chief Financial Officer since July 2017 and Treasurer since August 2017. Mr. Smith also served as our Interim President and Chief Executive Officer from March 2020 to July 2020 and as our Secretary from April 2020 to March 2021. He has more than 25 years of global finance and management experience across multiple industries and financial disciplines, including expertise in business analysis and planning, mergers and acquisitions, treasury, capital raising and investor relations. Previously, he was Vice President, Finance and Chief Financial Officer of the Inflammation and Immunology Business Unit at Celgene Corporation, or Celgene, a global biopharmaceutical company, from 2013 to July 2017. In this role, Mr. Smith provided finance leadership for the global launch of Otezla[®] and led global business planning and analysis for commercial affiliates and clinical study activities in over 16 countries. Before joining Celgene, Mr. Smith worked in roles of increasing responsibility at Bunge Limited from 1999 to 2013, including Director of Investor Relations, Chief Financial Officer-Asia, Chief Risk Officer, Corporate Treasurer, and Chief Financial Officer of Bunge's Sugar and Bioenergy Segment. Mr. Smith has served as an independent director of Aeglea Biotherapeutics Inc. since November 2021, and serves as Chair of its Audit Committee. Mr. Smith previously served as an independent director of Genesee & Wyoming Inc. and as a member of its compensation and governance committees. Mr. Smith holds an M.B.A. in Finance from New York University's Stern School of Business and a B.A. in History, with honors, from Northwestern University.

Pamela Cramer | Chief Human Resources Officer

Ms. Cramer has served as our Chief Human Resources Officer since July 2021. She brings 20 years of leadership experience in organizational effectiveness, talent development and human resources transformation with globally diverse life sciences and financial services companies. She joined Rhythm from Foundation Medicine, where she most recently served as Head of People Solutions from March 2020 to June 2021, and held a variety of human resources positions since January 2018. Prior to that, Ms. Cramer held senior human resources positions at Cambridge Associates from October 2015 to 2018, and at PAREXEL International and Epsilon Data Management. Earlier in her career, Ms. Cramer served in a wide range of positions at Bank of America Merrill Lynch and General Electric, where she began her career as a graduate of the Human Resources Leadership Program. She holds an M.B.A. from Georgetown University.

Linda Shapiro, M.D., Ph.D. | Chief Medical Officer

Dr. Shapiro has served as our Chief Medical Officer since September 2021, and prior to that served as our Senior Vice President—Clinical from July 2021. Prior to joining Rhythm, Dr. Shapiro served as Director,

Clinical Development and Medical Affairs at Boehringer Ingelheim from September 2017 to October 2020, as Director, Scientific Affairs at Merck & Co., Inc. from August 2016 to July 2017, and as International Medical Director, Global Clinical Development at Novo Nordisk A/S from April 2014 to July 2016, as well as other roles in the pharmaceutical industry in medical affairs and scientific affairs since February 2011. In these roles, she led clinical development for assets in obesity, NASH, type 2 diabetes and cardiometabolic conditions. Prior to joining industry, Dr. Shapiro practiced medicine for 10 years in Colorado, obtaining certification and specializing in obesity medicine. She holds a Ph.D. and completed a post-doctoral research fellowship in kinesiology and applied physiology from the University of Colorado, an M.D. from Tulane University School of Medicine, and a B.S. in exercise science from the University of Southern California.

Joseph Shulman | Chief Technical Officer

Mr. Shulman has served as our Chief Technical Officer since February 2022 and is responsible for chemistry, manufacturing, and controls (CMC), clinical and commercial supply chains, and GMP/GDP quality assurance and quality control, and program management. Prior to his current role, he served as our Senior Vice President, Technical Operations since July 2020. Prior to joining Rhythm, Mr. Shulman served as Senior Vice President of Technical Operations at Ra Pharmaceuticals, acquired by UCB in 2020, from July 2019 to July 2020. Before that, he was Senior Vice President of Global Technical Operations at Novelion Therapeutics, from September 2014 to July 2019. Earlier in his career, Mr. Shulman held roles of increasing responsibility at biotechnology companies in the areas of CMC, technical operations, and program and alliance management. He holds an M.B.A. from Boston University and earned a B.S. in chemical engineering from Miami University.

Jennifer Chien | Executive Vice President, Head of North America

Ms. Chien has served as our Executive Vice President, Head of North America since November 2020. Prior to joining Rhythm, Ms. Chien served as Chief Commercial Officer at Krystal Biotech, Inc., a biopharmaceutical company, from January 2020 to October 2020. From November 2014 to January 2020, Ms. Chien held a variety of roles with increasing responsibility Sanofi Genzyme, a biotechnology company, including Vice President, Head of Genetic Diseases from January 2017 to January 2020 (where she was responsible for the U.S. commercial strategy and implementation for seven brands and launch presentation with rare diseases) and Vice President, Global Head of Rare Nephrological Diseases from November 2014 to January 2017. Ms. Chien holds a B.S. from the Massachusetts Institute of Technology and an M.P.H. from Harvard University.

Yann Mazabraud | Executive Vice President, Head of International

Mr. Mazabraud has served as our Executive Vice President, Head of International, since October 2020. Prior to joining Rhythm, Mr. Mazabraud served as Chief Commercial Officer and Head of International of Trevi Therapeutics, Inc., a pharmaceutical company, from November 2017 to October 2020. Prior to that, he held several leadership positions at Sanofi Genzyme, including as U.S. General Manager and North America Head, Rare Diseases from January 2016 to October 2017 and Vice President and Head of Latin America from March 2014 to December 2015. He also served as a member of the Sanofi Genzyme Executive Leadership Team. While at Genzyme and Sanofi Genzyme, he led and managed several product launches for rare genetic diseases in Europe, Latin America and the United States across multiple areas including genetics, pediatrics, nephrology, neurology and endocrinology. Mr. Mazabraud holds a master's degree in management from Ecole Supérieure de Commerce de La Rochelle.

EXECUTIVE COMPENSATION

COMPENSATION DISCUSSION AND ANALYSIS

General

In this Compensation Discussion and Analysis ("<u>CD&A</u>"), we provide an overview and analysis of the compensation awarded to or earned by our named executive officers identified in the Summary Compensation Table below (each, an "<u>NEO</u>") during fiscal 2021, including the elements of our compensation program for NEOs, material compensation decisions made under that program for fiscal 2021 and the material factors considered in making those decisions. Our NEOs for the year ended December 31, 2021 are:

- David P. Meeker, M.D., Chairman, President and Chief Executive Officer;
- Hunter C. Smith, Chief Financial Officer;
- · Jennifer Chien, Executive Vice President, Head of North America
- Yann Mazabraud, Executive Vice President, Head of International
- · Joseph Shulman, Chief Technical Officer; and
- · Murray Stewart, our former Chief Medical Officer.

Effective as of September 10, 2021, Dr. Stewart resigned from his position as our Chief Medical Officer and transitioned to a consultant position as our Senior Medical Advisor.

Executive Summary

2021 Performance Highlights and Pay for Performance.

Our executive compensation programs are designed to deliver pay in accordance with corporate and individual performance, rewarding superior performance and providing consequences for underperformance. We believe that the compensation of our NEOs for fiscal year 2021 was aligned with the Company's performance during 2021. Highlights of that performance include:

- Expanded clinical development efforts through development of proof-of-concept Daybreak and registration-enabling Emanate study designs with the FDA and EMA, and enrollment of the first patients in the Daybreak study.
- Laid groundwork for successful execution of those studies through the expansion of its genetic testing panel and exceeded targets for the identification of priority sites and patients for enrollment.
- Filed its New Drug Applications with the FDA and MAA ahead of stretch goal timelines, and both applications were accepted by the respective regulatory agencies.
- Made significant progress in patient identification for an eventual BBS launch and for its smaller POMC-LEPR indication, completing submission of its Companion Diagnostic as well as its MAA applications.
- Exceeded internal targets for patients on commercial therapy during the year. The Company made additional progress on its Weekly Formulation, Pediatric indication, Hypothalamic Obesity study and development of a new formulation with the potential for improved safety, tolerability and efficacy.
- Made significant progress in business development, negotiating a license for Setmelanotide in China with RareStone Ltd.
- Built out its North American field team and expanded its International footprint. Significantly increased its female representation among leadership roles and conducted its first employee engagement survey.

In order to align pay with performance, a significant portion of our NEOs' compensation is delivered in the form of equity awards and annual cash incentives, including awards that are contingent on Company performance relative to our key performance metrics. For fiscal year 2021, approximately 84% of the total

target compensation opportunity for our NEOs (defined as the sum of base salary, target short-term cash incentives and the grant date fair value of long-term equity incentives) was "at risk" compensation. We consider pay to be "at risk" if it is subject to performance- or time-based payment conditions or has a value dependent upon the price per share of our common stock.

2021 *Compensation Highlights.* Consistent with our compensation philosophy, key compensation decisions for 2021 included the following:

- *Base Salaries and Target Annual Cash Incentive Opportunities*. The 2021 base salaries and target bonuses for our NEOs remained level or were increased in order to position base salaries and target bonuses at the median of market, based on the market analysis of our independent compensation consultant, as described further below.
- *Annual Cash Incentives*. For 2021, our Compensation Committee selected performance goals for our performance-based annual bonus program that were intended to promote our business plan and short-term goals. In line with our employee annual bonus program, these corporate performance goals represent 70% of each NEO's annual bonus target, with 30% representing individual achievement. In light of our achievement of our corporate goals, the Compensation Committee determined to pay out annual bonuses for all employees, including NEOs at 119% of target for the corporate performance component.
- *Equity-Based Long Term Incentives*. In 2021, we granted approximately 76% of our NEOs' target direct compensation as equity-based compensation in the form of stock options, restricted stock units ("RSUs") and performance stock units ("PSUs"). We believe that these equity incentive awards effectively align the interests of our executives with those of our stockholders by directly linking compensation to the value of our common stock.
- *Performance-Based Long-Term Incentives*. In November 2021, our Compensation Committee granted Performance Stock Units (PSUs) to all employees, including our NEO's which are intended to align and unite the entire organization around achieving key development, regulatory and commercial milestones during 2022 and 2023. Each PSU represents a right to receive one share of the Company's common stock upon vesting upon completion of the 2023 performance year, subject to achievement of performance milestones and approval of the Compensation Committee.

Compensation Governance and Best Practices. We are committed to having strong governance standards with respect to our compensation programs, procedures and practices. Our key compensation practices include the following:

	What We Do		What We Do Not Do
1	Emphasize performance-based, at risk compensation.	X	Do not grant guaranteed equity compensation.
1	Emphasize the use of equity compensation to promote executive retention and reward long-term value creation.	Х	Do not provide significant perquisites.
1	Weight the overall pay mix towards incentive compensation for senior executives.	Х	Do not provide any compensation-related tax gross-ups.
1	Engage an independent compensation consultant to advise our Compensation Committee.	Х	Do not reprice our stock option awards and our equity incentive plan expressly forbids exchanging underwater options for cash without stockholder approval.

Stockholder Advisory Vote on Executive Compensation

At our 2021 annual meeting of stockholders, our stockholders voted in a non-binding, advisory vote to approve the compensation of our NEOs. Our Compensation Committee reviewed the result of this vote, and, in light of the approval by a substantial majority of our stockholders of the compensation programs described in our 2021 proxy statement (representing over 90% of the votes cast), did not implement any significant changes to our executive compensation program as a result of the vote. At our 2021 annual meeting

of stockholders, our stockholders voted in a non-binding, advisory vote in favor of having a non-binding stockholder vote on executive compensation once every year. Consistent with the stated preference of a majority of our stockholders, our next advisory vote on our NEOs' compensation will be held at this 2022 annual meeting, pursuant to Proposal No. 3.

Executive Compensation Objectives and Philosophy

The key objective in our executive compensation program is to attract, motivate, and reward leaders who create an inclusive and diverse environment and have with the skills and experience necessary to successfully execute on our strategic plan to maximize stockholder value. Our executive compensation program is designed to:

- Attract and retain talented and experienced executives in a competitive and dynamic market;
- Motivate our NEOs to help our company achieve the best possible financial and operational results;
- Provide reward opportunities consistent with our performance on both a short-term and long-term basis; and
- Align the long-term interests of our NEOs with those of our stockholders.

We strive to set our overall total compensation at a competitive level. Executives may be compensated above or below the targeted market position based on factors such as experience, performance, scope of position and the competitive demand for proven executive talent, as described further below under "Determination of Executive Compensation".

Determination of Executive Compensation

Role of Board of Directors, Compensation Committee and Executive Officers

The Compensation Committee is responsible for establishing and overseeing our executive compensation programs and annually reviews and determines the compensation to be provided to our NEOs, other than with respect to our Chief Executive Officer, whose compensation is determined by the Board.

In setting executive compensation, the Compensation Committee considers a number of factors, including the recommendations of our Chief Executive Officer (other than with respect to the Chief Executive Officer's own compensation), current and past total compensation, competitive market data and analysis provided by the Compensation Committee's independent compensation consultant, Company performance and each executive's impact on performance, each executive's relative scope of responsibility and potential, each executive's individual performance and demonstrated leadership, and internal equity pay considerations. Our Chief Executive Officer's recommendations are based on his evaluation of each executive's individual performance and contributions, of which our Chief Executive Officer has direct knowledge. Our Board makes decisions regarding our Chief Executive Officer's compensation, following recommendation from the Compensation Committee which is informed by market data provided by our independent compensation consultant.

Role of Compensation Consultant

In order to design a competitive executive compensation program that will continue to attract top executive talent and reflect our compensation philosophy, our Compensation Committee has retained Radford, a business unit of Aon plc ("Radford"), as an independent compensation consultant to provide executive compensation advisory services, help evaluate our compensation philosophy and objectives and provide guidance in administering our executive compensation program. The Compensation Committee has evaluated Radford's independence pursuant to the requirements of Nasdaq and SEC rules and has determined that Radford does not have any conflicts of interest in advising the Compensation Committee. Radford did not provide any other services to the Company in 2021 for which the amount of fees exceeded \$120,000.

The Compensation Committee retained Radford to evaluate its executive and board compensation programs and recommend a course of action for fiscal year 2021. Radford determined a group of peer companies using the following parameters:



- Operates in the biopharmaceutical industry and, to the degree possible, having a rare disease focus
- · Comparable in terms of market capitalization, clinical stage of development, headcount, and revenue
- · Allows for sufficient room to grow without over-or under-extending
- Considers the criteria proxy advisors will apply when determining their own comparator groups for purposes of pay for performance and Say on Pay analyses

In consultation with Radford, in October 2020, our Compensation Committee selected our 2021 peer group as follows, focusing on sector, market cap, stage of development, revenue and headcount.

Akebia Therapeutics	ChemoCentryx	Global Blood Therapeutics	Magenta Therapeutics	Zongenix
Apellis Pharmaceuticals	Deciphera Pharmaceuticals	Insmed	Odonate Therapeutics	
Atara Biotherapeutics	Dicerna Pharmaceuticals	Intra-Cellular Therapeutics	Rigel Pharmaceuticals	
Biohaven Pharmaceutical	Epizyme	Iovance Biotherapeutics	Syros Pharmaceuticals	
Cara Therapeutics	Esperion Therapeutics	Karyopharm Therapeutics	TG Therapeutics	

As of September 2020, as compared to such peer group, we were at the 0 percentile for revenue for the preceding four quarters, the 17th percentile for 30 day average market cap, and the 16th percentile for headcount. The 2021 peer group reflected the following changes from our 2020 peer group:

The following companies were removed from the peer group as market value relative to Rhythm was significantly above the targeted range.

- · Acceleron Pharma;
- Audentes Therapeutics;
- MyoKardia;
- Ra Pharmaceuticals; and
- · Reata Pharmaceuticals

The following companies were added to the peer group to ensure Rhythm remains within a reasonable range of peer median in terms of market value and headcount

- Apellis Pharmaceuticals;
- Epizyme;
- Magenta Therapeutics; and
- Rigel Pharmaceuticals

In November 2020, Radford provided an analysis of data derived from (i) members of our peer group and (ii) the Radford Global Life Sciences survey, the constituent companies of which were not provided to the Compensation Committee. For 2021, the Compensation Committee used Radford's analysis to help structure a competitive executive compensation program, position executive compensation by considering market data, and make individual compensation decisions based on comparable positions at companies with which we compete for talent. While the Compensation Committee does not establish compensation levels solely based on a review of competitive data or benchmark to any particular level, it believes such data is a useful tool in its deliberations as our compensation policies and practices must be competitive in the marketplace for us to be able to attract, motivate and retain qualified executive officers.

Elements of Compensation

The primary elements of our NEOs' compensation and the main objectives of each are:

- *Base Salary*. Base salary attracts and retains talented executives, recognizes individual roles and responsibilities, and provides stable income;
- Annual Performance-Based Incentive Compensation. Annual performance bonuses promote shortterm performance objectives and reward executives for their contributions toward achieving those objectives;
- *Equity Based Long-Term Incentive Compensation*. Equity compensation, provided in the form of stock options, RSUs and PSUs, aligns executives' interests with our stockholders' interests, emphasizes long-term financial and operational performance, and helps retain executive talent.

In addition, our executives are eligible to participate in our health and welfare programs and our 401(k) plan on the same basis as our other employees. We also maintain severance and change in control arrangements, which aid in attracting and retaining executive talent and help executives to remain focused and dedicated during potential transition periods due to a change in control. Each of these elements of compensation for 2021 is described further below.

Base Salary

The base salaries of our NEOs are an important part of their total compensation package, and are intended to reflect their respective positions, duties and responsibilities. Base salary is a visible and stable fixed component of our compensation program. Base salaries provide our NEOs with a reasonable degree of financial certainty and stability. Our Compensation Committee, and with respect to our Chief Executive Officer, the Board, annually reviews and determines the base salaries of our executives and evaluates the base salaries of new hires at the time of hire. In February 2021, our Compensation Committee, and with respect to our Chief Executive Officer, the Board, approved the following base salary increases for 2021: 1.6% for Dr. Meeker; 4% for Mr. Smith; 4% for Dr. Stewart and 3% for Mr. Shulman. Such increases were intended to position our NEOs' base salaries closer to the market median, as well as to reflect additional considerations set forth above under "Determination of Executive Compensation." Following such determinations, our NEOs' base salaries were as set forth below:

Name	2021 Annualized Base Salary (\$)
David P. Meeker	630,000
Hunter C. Smith	435,937
Jennifer Chien	395,000
Yann Mazabraud	395,000
Joseph Shulman	386,250
Murray Stewart	471,328

Cash Incentive Compensation

We consider annual cash incentive bonuses to be an important component of our total compensation program that provides incentives necessary to retain executive officers. Each NEO is eligible to receive an annual performance-based cash bonus based on a specified target annual bonus award amount expressed as a percentage of the named NEO's base salary. Actual bonuses are calculated based on these target bonus amounts multiplied by a weighted achievement score determined by the Compensation Committee and the Board based on overall achievement of the annual corporate goals and each named executive officer's achievement of his or her individual goals. In 2021, achievement of the corporate goals accounted for 70% of the overall achievement score and achievement of each named executive officer's individual goals accounted for 30% of the overall achievement score. At the beginning of each year, the Compensation Committee and the Board reviews and approves the annual corporate goals. There is no minimum bonus percentage or amount established for the named executive officers and, as a result, the bonus amounts vary from year to year

based on corporate and individual performance. The Compensation Committee and the Board retain discretion to increase or decrease individual awards in their discretion.

For the 2021 annual bonus program, the corporate goals were designed to measure our commercial growth and the development of our product candidates, including the progression and enrollment of our clinical programs, announcement of clinical trial results, achievement of product candidate development and regulatory milestones, expansion of genetic disease and patient identification programs, and progression of our commercial capabilities through establishment of infrastructure and facilities. The individual goals were designed to measure each officer's individual contribution to the corporate goals and his or her individual performance.

For 2021, the corporate performance goals as well as their relative weightings and levels of actual achievement are set out in the table below. The threshold, target and maximum payouts for each corporate performance category was 50%, 100% and 150%, respectively, of the applicable portion of target bonus opportunity.

Performance Category	Weight	Objectives	Weight	Achievement
MC4R Pathway	35%	 Advance MC4R pathway clinical development 	20%	20%
		Build the RGDO community and identify patients for pathway clinical studies	15%	22.5%
BBS/AS	30%	3. Product registration for BBS integration	20%	30%
		4. Commercial readiness for IMCIVREE launch in BBS/AS	10%	10%
POMC/PCSK1/LEPR	10%	 Product and diagnostic registration for POMC/LEPR indication 	5%	7.5%
		6. IMCIVREE availability for POMC/ LEPR patients	5%	6.25%
Science and Pipeline	20%	7. Advance once weekly, pediatric and hypothalamic obesity programs	10%	7.5%
		 Advance next generation (CV safe MCIR sparing) compounds 	5%	5%
		9. Create and execute on business development strategy	5%	2.5%
People & Organization	5%	10. Develop Talent and Engagement Strategy	5%	5%
		Achieveme	nt Level	116%
		Adjustment for QW/PEI	DS 3 of 4	119%

The 2021 individual goals for each NEO were aligned with and based on each NEO's ability to influence the company's attainment of the corporate objectives. No specified weightings were assigned to the 2021 individual goals.

Our NEOs' 2021 target bonuses as a percentage of base salary were as follows:

Name	2021 Target Bonus (as a percentage of base salary)
David P. Meeker	60%
Hunter C. Smith	40%
Jennifer Chien	40%
Yann Mazabraud	40%
Joseph Shulman(1)	35%
Murray Stewart	40%

(1) Mr. Shulman's target bonus increased from 30% to 35% of base salary effective January 2021 as a result of market data obtained from Radford.

After the end of 2021, the Compensation Committee and the Board determined that the Company had achieved the 2021 corporate goals at 119% of target, reflecting the significant progress on key objectives made during 2021. In addition, based on its subjective review of the executives' individual performance in 2021, the Compensation Committee approved individual performance modifiers for 2021. The table also shows each executive's target award and actual payout under the Program.

Named Executive Officer	2021 Target Bonus	Actual 2021 Bonus Payout
David P. Meeker	\$378,000	\$450,954
Hunter C. Smith	\$174,375	\$210,654
Jennifer Chien	\$158,000	\$190,864
Yann Mazabraud	\$158,000	\$190,864
Joseph Shulman	\$135,188	\$157,223
Murray Stewart	\$188,531	\$187,890(1)

(1) The bonus paid to Dr. Stewart was prorated to reflect his partial period of service during 2021.

Equity-Based Long-Term Incentive Awards

We maintain the 2017 Equity Incentive Plan (the "2017 Plan"), under which we may grant equity incentive awards to directors, employees and consultants of our Company and our affiliates, to enable us to attract and retain services, skills and experience of these individuals, which we believe are essential to our long-term success. We do not currently have any formal policy for determining the number of equity-based awards to grant to NEOs.

February 2021 Awards

In February 2021, our Compensation Committee approved grants of stock options and RSUs to our NEOs. With the exception of Dr. Meeker who was awarded 100% of equity in options, our NEO's were awarded a blend of stock options and RSUs similar to other commercial stage life sciences companies in the market. The mix of options and RSUs is 75/25. In determining the number of awards to issue, RSUs are considered to have a target grant date value of twice the value of an option covering the same number of shares. Annual equity awards are designed as long-term incentive and retention tools, determined by the Compensation Committee and based on a number of factors including equity value, equity as a portion of total direct compensation, and relevant external market data. The stock options are scheduled to vest and become exercisable in sixteen substantially equal quarterly installments following the applicable vesting commencement date. Vesting of the stock options and RSUs is subject to continued service through each applicable vesting date.

Introduction of PSUs in 2021

We maintain an ongoing commitment to good corporate governance principles and strong performance orientation in our compensation program by proactively reviewing our policies and program design. In 2021, this included an evaluation of our incentive compensation program.

In November 2021, our Compensation Committee approved grants of PSUs to all employees, including our NEOs (collectively, the "2021 PSU Awards"). Forty percent (40%) of the PSUs underlying the 2021 PSU Awards are eligible to vest based on the achievement of certain specific clinical development, regulatory and commercial performance events, as determined by our Compensation Committee, during the performance period beginning on January 1, 2022 and ending on December 31, 2022. The remaining 60% of the PSUs underlying the 2021 PSU Awards are eligible to vest based on the achievement of certain specific clinical

development, regulatory and commercial performance events, as determined by our Compensation Committee, during the performance period beginning on January 1, 2023 and ending on December 31, 2023. Vesting of the PSUs is subject to continued service through each applicable vesting date. In the event of a "change in control" (as defined in the 2017 Plan), the 2021 PSU Awards will vest at 100% of target levels unless our Compensation Committee determines otherwise.

The following table contains a summary of grants of stock options, RSUs and PSUs to our NEOs in 2021:

	Number of Shares Underlying Stock		
Name	Options	Number of RSUs	Number of PSU's
David P. Meeker	220,000	—	87,979
Hunter C. Smith	56,250	9,375	29,993
Murray Stewart	56,250	9,375	
Jennifer Chien	48,750	8,125	29,993
Yann Mazabraud	48,750	8,125	29,993
Joseph Shulman	37,500	6,250	29,993

Retirement Savings, Health and Welfare Benefits

We maintain a 401(k) retirement savings plan for our employees, including our NEOs, who satisfy certain eligibility requirements. Our NEOs are eligible to participate in the 401(k) plan on the same terms as other full-time employees. The Internal Revenue Code (the "<u>Code</u>") allows eligible employees to defer a portion of their compensation, within prescribed limits, on a pre-tax basis through contributions to the 401(k) plan. Currently, we match contributions made by participants in the 401(k) plan up to a specified percentage of the employee contributions, and these matching contributions are fully vested as of the date on which the contribution is made. We believe that providing a vehicle for tax-deferred retirement savings through our 401(k) plan, and making fully vested matching contributions, adds to the overall desirability of our executive compensation package and further incentivizes our employees, including our NEOs, in accordance with our compensation policies.

Employee Benefits

All of our full-time employees, including our NEOs, are eligible to participate in our health and welfare plans, including medical, dental and vision benefits, medical and dependent care flexible spending accounts, short-term and long-term disability insurance, and life insurance. Employees also have the option to participate in our Employee Stock Purchase Plan which allows for discounted purchase of Rhythm stock. We believe the benefits described above are necessary and appropriate to provide a competitive compensation package to our named executive officers.

Under his employment agreement, Mr. Mazabraud is entitled to an annual allowance of &8,000 to compensate him for expenses incurred while working remotely.

We do not generally provide any tax "gross ups" to our named executive officers.

Severance and Change in Control Arrangements

We are party to employment letter agreements with each of our NEOs. The employment letter agreements for our NEOs that are based in the United States provide for severance benefits and payments upon a termination without cause or for good reason, whereas Mr. Mazabraud's employment letter agreement provides for a three-month notice period in the event of a termination of his employment other than a termination due to serious or gross misconduct. Our Compensation Committee believes that these types of arrangements are necessary to attract and retain executive talent and are a customary component of executive compensation. In particular, such arrangements can mitigate a potential disincentive for our NEOs when they are evaluating a potential acquisition of the Company and can encourage retention through the conclusion of the transaction. The payments and benefits provided under our severance and change in

control arrangements are designed to be competitive with market practices. A description of these arrangements, as well as information on the estimated payments and benefits that our NEOs would have been eligible to receive as of December 31, 2021, are set forth in *"Potential Payments Upon Termination or Change in Control"* below.

Following Dr. Stewart's termination of employment in September 2021, Dr. Stewart has continued to provide services to the Company as Senior Medical Advisor. He did not receive cash severance payments in connection with the termination of his employment, and the portion of his stock options which were unvested as of the date of termination were forfeited without consideration. The Compensation Committee decided to extend the post-termination exercisability period of his vested stock options until the date that is three months following the termination of his engagement as Senior Medical Advisor. Moreover, Dr. Stewart's RSUs remained outstanding and eligible to vest in accordance with their terms, subject to Dr. Stewart's continued services through each applicable vesting date. Dr. Stewart remained eligible to receive an annual performance bonus for 2021, pro-rated based on his employment and consulting services during 2021.

Other Policies and Considerations

Derivatives Trading, Hedging, and Pledging Policies. Our Insider Trading Policy provides that no employee, officer, or director may acquire, sell, or trade in any interest or position relating to the future price of Company securities, such as a put option, a call option or a short sale, or engage in hedging transactions. In addition, our Insider Trading Policy provides that no employee, officer, or director to may pledge Company securities as collateral to secure loans. This prohibition means, among other things, that these individuals may not hold Company securities in a "margin" account, which would allow the individual to borrow against their holdings to buy securities.

Section 409A. The Compensation Committee takes into account whether components of the compensation for our executive officers will be adversely impacted by the penalty tax imposed by Section 409A of the Code, and aims to structure these components to be compliant with or exempt from Section 409A to avoid such potential adverse tax consequences.

"Golden Parachute" Payments. Sections 280G and 4999 of the Code provide that certain executive officers and other service providers who are highly compensated or hold significant equity interests may be subject to an excise tax if they receive payments or benefits in connection with a change in control of the Company that exceeds certain prescribed limits, and that we, or a successor, may forfeit a tax deduction on the amounts subject to this additional tax. While the Compensation Committee may take the potential forfeiture of such tax deduction into account when making compensation decisions, it will award compensation that it determines to be consistent with the goals of our executive compensation program even if such compensation is not deductible by us. We do not provide any tax gross-ups to cover excise taxes under Section 4999 in connection with a change in control.

Accounting for Share-Based Compensation. We follow Financial Accounting Standard Board Accounting Standards Codification Topic 718, ("ASC Topic 718"), for our share-based compensation awards. ASC Topic 718 requires companies to measure the compensation expense for all share-based payment awards made to employees and directors, including stock options and RSUs, based on the grant date "fair value" of these awards. This calculation is performed for accounting purposes and reported in the compensation tables below, even though our NEOs may never realize any value from their awards.

COMPENSATION COMMITTEE REPORT

The compensation committee has reviewed and discussed with management the Compensation Discussion and Analysis set forth above. Based on such review and discussions, the compensation committee has recommended to the board of directors that the Compensation Discussion and Analysis be included in this proxy statement and in the Annual Report on Form 10-K for the year ended December 31, 2021, filed by us with the SEC.

This report of the compensation committee is not "soliciting material," shall not be deemed "filed" with the SEC and shall not be incorporated by reference by any general statement incorporating by reference

this proxy statement into any filing under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing, except to the extent that we specifically incorporate this information by reference, and shall not otherwise be deemed filed under such acts.

The foregoing report has been furnished by the compensation committee.

Respectfully submitted,

The Compensation Committee of the Board of Directors

Lynn A. Tetrault, J.D. (Chairperson) Stuart A. Arbuckle

EXECUTIVE COMPENSATION TABLES

2021 Summary Compensation Table

The following table contains information about the compensation earned by each of our NEOs during the fiscal years indicated.

Name and Principal Position	Year	Salary (\$)	Bonus (\$)	Stock Awards (\$)(1)	Option Awards (\$)(2)	Non-Equity Incentive Plan Compensation (\$)(3)	All Other Compensation (\$)(4)	Total
David P. Meeker	2021	630,000	_	1,164,842	4,204,200	450,954	8,364	6,458,360
Chief Executive Officer	2020	262,308	—	918,500	12,844,897	207,958	43,704	14,277,367
Hunter C. Smith	2021	435,957	_	576,264	1,074,938	210,654	11,600	2,309,412
Chief Financial Officer	2020	416,118	60,000	132,000	1,837,630	209,595	7,125	2,530,468
	2019	393,992	—	—	1,286,061	153,224	86,576	1,922,853
Murray Stewart	2021	365,837	—	320,487	1,074,938	187,890	41,600(5)	1,990,752
Former Chief Medical Officer(6)	2020	451,169	60,000	113,000	1,555,420	226,600	7,125	2,300,314
Jennifer Chien	2021	395,000	—	552,376	931,613	190,864	11,600	2,081,452
Executive Vice President, Head of North America	2020	45,577	100,000	100,000	1,517,540	49,375	7,125	1,712,492
Yann Mazabraud(7)	2021	384,250	—	552,376	931,613	190,864	118,502(8)	2,177,605
Executive Vice President, Head of International								
Joseph Shulman	2021	386,837	—	516,545	716,625	157,223	11,600	1,788,243
Chief Technical Officer								

- (1) Amounts reflect the full grant-date fair value of stock awards granted during fiscal 2021 computed in accordance with ASC Topic 718, rather than the amounts paid to or realized by the named individual. We provide information regarding the assumptions used to calculate the value of all stock awards made to our NEOs in Note 8 to the consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2021. As required pursuant to SEC disclosure rules, the grant-date fair values of the PSUs awarded to Dr. Meeker, Mr. Smith, Ms. Chien, Mr. Mazabraud and Mr. Shulman were computed based on the probable outcomes of the performance conditions as of the grant date. Assuming maximum achievement of the performance conditions, the value of the PSUs as of the grant date is \$1,675,006 for Dr. Meeker, \$571,001 for Mr. Smith, \$571,001 for Ms. Chien, \$571,001 for Mr. Mazabraud and \$571,001 for Mr. Shulman.
- (2) Amounts reflect the full grant-date fair value of stock options granted during fiscal 2021 computed in accordance with ASC Topic 718, rather than the amounts paid to or realized by the named individual. We provide information regarding the assumptions used to calculate the value of all stock options granted to our NEOs in Note 8 to the consolidated financial statements included in in our Annual Report on Form 10-K for the year ended December 31, 2021. The amount for Dr. Stuart includes the incremental fair value attributable to the extended exercisability of certain of his options pursuant to his separation agreement with the Company.
- (3) Amounts for fiscal 2021 represent payments earned by our NEOs based upon the achievement of certain company and individual performance objectives for fiscal 2021. Please see the description of the annual bonus program under "*Cash Incentive Compensation*" in the CD&A above.
- (4) Other than for Mr. Mazabraud and Dr. Stewart, amounts for fiscal 2021 represent employer matching contributions to our 401(k) plan.
- (5) Amount includes consulting fees paid to Dr. Stewart pursuant to his consulting agreement (\$30,000).
- (6) Dr. Stewart ceased to serve as our Chief Medical Officer effective as of September 11, 2021.
- (7) Amounts shown for Mr. Mazabraud have been converted from euros to U.S. dollars based on the average exchange rate (1.1833) during 2021.

(8) Amount includes the aggregate amount of payments made in respect of Mr. Mazabraud's work-fromhome allowance (\$9,467) and employer contributions to statutory pension and social security schemes on his behalf (\$109,035).

Grants of Plan-Based Awards in Fiscal 2021

The following table provides supplemental information relating to grants of plan-based awards made during fiscal 2021 to help explain information provided above in our Summary Compensation Table. This table presents information regarding all grants of plan-based awards occurring during fiscal 2021.

	Grant	Non-Eq	Future Pay uity Incen Awards(1 Target			entive Pla	youts Under n Awards(2) Maximum	All Other Stock Awards: Number of Shares of Stock or	All Other Option Awards: Number of Securities Underlying	Exercise or Base Price of Option Awards	Grant Date Fair Value of Stock and Option Awards
Name	Date	(\$)	(\$)	(\$)	(#)	(#)	(#)	Units (#)	Options (#)	(\$/Sh)	(\$)(3)
David P. Meeker			378,000								
	2/11/2021								220,000	30.66	4,204,200
	11/9/2021				4,399	87,979	126,511				1,164,842
Hunter C. Smith			174,383								
	2/11/2021								56,250	30.66	1,074,938
	2/11/2021							9,375			179,156
	11/9/2021				1,500	29,993	43,127				397,107
Murray Stewart			188,531								
	2/11/2021								56,250	30.66	1,074,938
	2/11/2021							9,375			179,156
	9/11/2021										141,331(4)
Jennifer Chien			158,000								
	2/11/2021								48,750	30.66	911,613
	2/11/2021							8,125			155,269
	11/9/2021				1,500	29,993	43,127	29,993			397,107
Yann Mazabraud			158,000								
	2/11/2021								48,750	30.66	911,613
	2/11/201							8,125			155,269
	11/9/2021				1,500	29,993	43,127	29,993			397,107
Joseph Shulman			154,500								
	2/11/2021								37,500	30.66	911,613
	2/11/2021							6,250			119,438
	11/9/2021				1,500	29,993	43,127	29,993			397,107

- (1) Amounts reflect potential payouts under our 2021 annual bonus program. The target amount is based on a percentage of the individual's fiscal year 2021 base salary. Please see the description of the annual bonus program under "*Cash Incentive Compensation*" in the CD&A above.
- (2) PSUs are eligible to vest based on the achievement of specific clinical development and regulatory performance events over a performance period ending on December 31, 2023, subject to continued service through December 31, 2023.
- (3) Amounts reflect the full grant-date fair value of stock options, RSUs and PSUs granted during fiscal 2021 computed in accordance with ASC Topic 718, rather than the amounts paid to or realized by the named individual. We provide information regarding the assumptions used to calculate the value of all stock awards made to our NEOs in Note 8 to the consolidated financial statements included in in our Annual Report on Form 10-K for the year ended December 31, 2021.
- (4) Amount represents the incremental fair value attributable to the extended exercisability of certain of their options pursuant to their separation agreement with the Company.

NARRATIVE TO SUMMARY COMPENSATION TABLE AND GRANTS OF PLAN-BASED AWARDS TABLE

Summary of Executive Compensation Arrangements

Named Executive Officer Employment Agreements

David P. Meeker, M.D. Letter Agreement

On July 16, 2020, we entered into a letter agreement with Dr. Meeker, which sets forth the terms and conditions of his employment as President and Chief Executive Officer. Dr. Meeker's service pursuant to the letter agreement will continue until terminated in accordance with its terms.

Under the letter agreement, Dr. Meeker is entitled to receive an initial annual base salary of \$620,000, subject to periodic review and adjustment by the Board, and is eligible to receive an annual performance bonus initially targeted at 60% of his then-current annual base salary. The actual amount of any annual bonus will be determined by reference to the attainment of applicable Company and/or individual performance objectives, as determined by the Compensation Committee. In addition, in connection with joining our Company, we granted to Dr. Meeker a stock option to purchase 900,000 shares.

Dr. Meeker's letter agreement also contains a parachute payment "best pay" provision, under which payments and benefits pursuant to the letter agreement or otherwise will either be made to him in full or as to such lesser amount as which would result in no portion of the payments and benefits being subject to an excise tax under Section 4999 of the Code, whichever of the foregoing amounts is greater on an after-tax basis.

Hunter C. Smith Letter Agreement

On December 17, 2017, we entered into an amended and restated letter agreement with Mr. Smith, which sets forth the terms and conditions of his employment as Chief Financial Officer. Mr. Smith's service pursuant to the letter agreement will continue until terminated in accordance with its terms.

Under the letter agreement, Mr. Smith is entitled to receive an initial annual base salary of \$380,000, subject to periodic review and adjustment, and is eligible to receive an annual performance bonus initially targeted at 35% of his then-current annual base salary. The actual amount of any annual bonus will be determined by reference to the attainment of applicable Company and/or individual performance objectives, as determined by the Compensation Committee. In addition, in connection with joining our Company, we granted to Mr. Smith \$27,000 signing bonus.

Mr. Smith's letter agreement also contains a parachute payment "best pay" provision, under which payments and benefits pursuant to the letter agreement or otherwise will either be made to him in full or as

to such lesser amount as which would result in no portion of the payments and benefits being subject to an excise tax under Section 4999 of the Code, whichever of the foregoing amounts is greater on an after-tax basis.

Murray Stewart, M.D. Letter Agreement

On September 14, 2018, we entered into a letter agreement with Dr. Stewart, which sets forth the terms and conditions of his employment as Chief Medical Officer. Dr. Stewart's service pursuant to the letter agreement terminated effective as of September 10, 2021.

Under the letter agreement, Dr. Stewart was entitled to receive an initial annual base salary of \$440,000, subject to periodic review and adjustment, and is eligible to receive an annual performance bonus initially targeted at 35% of his then-current annual base salary.

Dr. Stewart's letter agreement also contained a parachute payment "best pay" provision, under which payments and benefits pursuant to the letter agreement or otherwise will either be made to him in full or as to such lesser amount as which would result in no portion of the payments and benefits being subject to an excise tax under Section 4999 of the Code, whichever of the foregoing amounts is greater on an after-tax basis.

Murray Stewart, M.D. Consulting Agreement

Following Dr. Stewart's termination of employment on September 10, 2021, we entered into a consulting agreement with Dr. Stewart on September 11, 2021, pursuant to which Dr. Stewart agreed to continue to provide services to the Company as Senior Medical Advisor for a \$12,000 monthly consulting fee.

Jennifer Chien Letter Agreement

On September 25, 2020, we entered into a letter agreement with Ms. Chien, which sets forth the terms and conditions of her employment as Executive Vice President, Head of North America. Ms. Chien's service pursuant to the letter agreement will continue until terminated in accordance with its terms.

Under the letter agreement, Ms. Chien is entitled to receive an initial annual base salary of \$395,000, subject to periodic review and adjustment, and is eligible to receive an annual performance bonus initially targeted at 40% of her then-current annual base salary.

Ms. Chien's letter agreement also contains a parachute payment "best pay" provision, under which payments and benefits pursuant to the letter agreement or otherwise will either be made to him in full or as to such lesser amount as which would result in no portion of the payments and benefits being subject to an excise tax under Section 4999 of the Code, whichever of the foregoing amounts is greater on an after-tax basis.

Yann Mazabraud Employment Contract

On October 5, 2020, we entered into an employment agreement with Mr. Mazabraud, which sets forth the terms and conditions of his employment as Executive Vice President, Head of International. Mr. Mazabraud's service pursuant to the employment contract will continue until terminated in accordance with its terms.

Under the employment contract, Mr. Mazabraud is entitled to receive an initial annual base salary of €333,000, which includes an annual allowance of €8,000 for expenses incurred while working remotely. Mr. Mazabraud is also eligible to receive an annual performance bonus initially targeted at 40% of his thencurrent annual base salary.

Joseph Shulman Letter Agreement

On June 23, 2020, we entered into a letter agreement with Mr. Shulman, which sets forth the terms and conditions of his employment as Senior Vice President, Technical Operations and continued to govern the

terms and conditions of his employment as Chief Technical Officer. Mr. Shulman's service pursuant to the letter agreement will continue until terminated in accordance with its terms.

Under the letter agreement, Mr. Shulman is entitled to receive an initial annual base salary of \$375,000, subject to periodic review and adjustment, and is eligible to receive an annual performance bonus initially targeted at 30% of his then-current annual base salary.

Mr. Shulman's letter agreement also contains a parachute payment "best pay" provision, under which payments and benefits pursuant to the letter agreement or otherwise will either be made to him in full or as to such lesser amount as which would result in no portion of the payments and benefits being subject to an excise tax under Section 4999 of the Code, whichever of the foregoing amounts is greater on an after-tax basis.

Outstanding Equity Awards at 2021 Fiscal Year-End Table

The following table summarizes the number of shares of common stock underlying outstanding equity incentive plan awards for each NEO as of December 31, 2021.

	Option Awards				Stock Awards				
Name	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price (\$)	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (#)	Market Value of Shares or Units of Stock That Have Not Vested (\$)(1)	Equity Incentive Plan Awards: Number of Unearned Shares, Units or Other Rights That Have Not Vested (#)	Equity Incentive Plan Awards: Market or Payout Value of Unearned Shares, Units or Other Rights That Have Not Vested (\$)(1)	
David P. Meeker	43,661(2)		4.59	11/16/2025					
	65,430(2)		6.05	2/7/2027					
	10,000(3)		34.89	6/5/2028					
	15,000(3)		22.93	6/18/2029					
	18,500(3)		21.37	6/16/2030					
	281,250(4)	618,750	22.53	7/16/2030					
	41,250(5)	178,750	30.66	2/10/2031					
	-,(_)						87,979(6)	878,030	
Hunter C. Smith	163,094(4)		6.88	8/8/2027			0,0,0,0(0)	,	
	61,000(5)		25.79	2/13/2028					
	48,125(5)	21,875	29.78	2/12/2029					
	35,875(5)	46,125	17.87	2/12/2023					
	7812(5)	17,188	22.53	7/16/2030					
	10,546(5)	45,704	30.66	2/10/2031					
	10,540(5)	43,704	30.00	2/10/2031	25,000(7)	249,500			
					25,000(7)	249,500	20,002(0)	200 220	
					0.275(0)	02 502	29,993(6)	299,330	
N 0	60 550(4)	24.050	06 5 4	10/11/2020	9,375(8)	93,563			
Murray Stewart	68,750(4)	31,250	26.54	10/14/2028					
	37,500(5)	22,500	29.78	2/12/2029					
	33,000(5)	55,000	17.87	2/13/2030					
	7,031(5)	49,219	30,66	2/10/2031					
					25,000(7)	249,500			
					9,375(8)	93,563			
Jennifer Chien	25,000(9)	75,000	24.29	11/8/2030					
	9,140(5)	39,610	30.66	2/10/2031					
					8,125(8)	81,088			
							29,993(6)	299,330	
Yann Mazabraud	25,000(9)	75,000	22.28	10/4/2030					
	9,140(5)	39,610	30.66	2/10/2031					
					8,125(8)	81,088			
							29,993(6)	299,330	
Joseph Shulman	26,563(9)	58,437	21.38	7/26/2030					
	7,031(5)	30,469	30.66	2/10/2031					
					6,250(8)	62,375			
							29,993(6)	299,330	

- (1) Amounts are calculated based on multiplying the number of shares shown in the table by the per share closing price of our common stock on December 31, 2021, which was \$9.98.
- (2) These options vest in 48 equal monthly installments following the vesting commencement date, except that the last installment, if necessary, may be smaller.
- (3) These options vest in full upon the earlier of the first anniversary of the date of grant or the date of the next annual meeting of stockholders.
- (4) 25% of the shares subject to these options vest on the first anniversary of the vesting commencement date, and the remaining shares vest in 36 monthly installments thereafter, except that the last installment, if necessary, may be smaller.
- (5) These options vest in 16 equal quarterly installments following the vesting commencement date, except that the last installment, if necessary, may be smaller.
- (6) These PSUs vest at the end of each applicable performance period ending on December 31, 2022 and December 31, 2023. For additional information about the PSUs, see the section titled *"Equity Compensation"* above.
- (7) These RSUs will vest in full on June 30, 2022, provided that the RSUs will vest in full in the event of a "qualifying termination" (as such term or a term of similar effect is defined in offer letter or employment agreement between the named executive officer and the Company).
- (8) These RSUs will vest in 4 equal annual installments following the vesting commencement date, except that the last installment, if necessary, may be smaller.
- (9) 25% of the shares subject to this option vests on the first anniversary of the vesting commencement date, and the remaining shares vest in 12 quarterly installments thereafter, except that the last installment, if necessary, may be smaller.

Option Exercises and Stock Vested in Fiscal 2021

During 2021, our NEOs did not exercise any stock options and did not have any stock awards vest.

Potential Payments Upon Termination or Change in Control

In accordance with SEC rules, the following table summarizes the payments that would be made to certain of our NEOs upon the occurrence of certain qualifying terminations of employment, assuming such NEO's termination of employment with the Company occurred on December 31, 2021 and, where relevant, that a change of control of the Company occurred on December 31, 2021. Amounts shown in the table below do not include (1) accrued but unpaid salary and (2) other benefits earned or accrued by the named executive officers during his employment that are available to all salaried employees, such as accrued vacation.

We have entered into certain letter agreements with each of our NEOs that provide our NEOs with severance protections. The letter agreements provide that the NEOs will be eligible for severance benefits in certain circumstances following a termination of employment without cause or with good reason, whether or not in connection with a change in control. In connection with Dr. Stewart's departure from the Company in September 2021, his employment agreement terminated.

Under the employment letter agreements for the NEOs, other than Mr. Mazabraud, in the event that such executive's employment is terminated by the Company without "cause," or by the executive for "good reason" (each, as defined in the applicable agreement, and referred to herein as a qualifying termination), then such executive will be entitled to the severance payments and benefits described below.

If Dr. Meeker experiences a qualifying termination of employment, then, in addition to any accrued amounts, he will be entitled to receive 12 months of continued base salary, paid in substantially equal installments over a period of 12 months, and reimbursement for continued healthcare benefits for up to 9 months following the date of termination. However, in the event that Dr. Meeker experiences a qualifying termination of employment within three months prior to, or within 12 months following a change in control of the Company (referred to herein as the change of control protection period), then Dr. Meeker will be entitled to receive (i) 18 months of continued base salary, paid in substantially equal installments over

a period of 18 months (unless the Company elects to pay such amount in lump sum), (ii) reimbursement for continued healthcare benefits for up to 12 months following the date of termination and (iii) full accelerated vesting of the option granted pursuant to his letter agreement.

If Mr. Smith experiences a qualifying termination of employment, then, in addition to any accrued amounts, he will be entitled to receive 9 months of continued base salary, paid in substantially equal installments over a period of 9 months, and reimbursement for continued healthcare benefits for up to 9 months following the date of termination. However, in the event that Mr. Smith experiences a qualifying termination of employment within the change of control period, Mr. Smith will be entitled to receive (i) a cash severance amount equal to (A) 12 months of his then-current base salary and (B) 100% of his then-current target bonus, payable over 12 months following such termination (unless the Company elects to pay such amount in lump sum) and (ii) reimbursement for continued healthcare benefits for up to 12 months following the date of termination. In addition, pursuant to the award agreement evidencing Mr. Smith's 2021 PSU Award, in the event that Mr. Smith experiences a qualifying termination prior to a change of control of the Company, his PSUs will remain outstanding and eligible to vest in connection with a change of control that occurs within three months following such termination.

If Dr. Stewart, Ms. Chien or Mr. Shulman experiences a qualifying termination of employment, then, in addition to any accrued amounts, the executive will be entitled to receive 9 months of continued base salary, paid in substantially equal installments over a period of 9 months, and reimbursement for continued healthcare benefits for up to 9 months following the date of termination. However, in the event that the applicable executive experiences a qualifying termination of employment within the change of control period, the executive will be entitled to receive (i) a cash severance amount equal to (A) 12 months of the executive's then-current base salary and (B) 100% of the executive's then-current target bonus, payable over 12 months following such termination (unless the Company elects to pay such amount in lump sum), (ii) reimbursement for continued healthcare benefits for up to 12 months following the date of termination and (iii) full accelerated vesting of the option granted pursuant to the applicable letter agreement. In addition, pursuant to the award agreement evidencing each of the 2021 PSU Awards granted to Ms. Chien and Mr. Shulman, in the event that the executive experiences a qualifying termination prior to a change of control of the Company, their PSUs will remain outstanding and eligible to vest in connection with a change of control that occurs within three months following such termination.

If Mr. Mazabraud experiences a termination of employment that is not due to serious misconduct ("faute grave") or gross misconduct ("faute lourde"), Mr. Mazabraud is entitled to a three-month notice period or three months' compensation in lieu of notice.

Dr. Stewart did not receive cash severance payments or benefits in connection with his termination of employment in September 2021. Pursuant to the consulting agreement between the Company and Dr. Stewart entered into on September 11, 2021, the portion of Dr. Stewart's stock options which were vested as of the date of his termination will remain outstanding and exercisable until the three-month anniversary of the termination of his services as Senior Medical Advisor. The shares underlying the unvested portion of Dr. Stewart's stock options were forfeited without consideration. In addition, any RSUs held by Dr. Stewart as of the date of his termination remained outstanding and eligible to vest in accordance with their terms, subject to his continued service through each applicable vesting date. Dr. Stewart remained eligible to receive an annual performance bonus for 2021, pro-rated based on his employment and consulting services during 2021.

All severance payments and benefits under the letter agreements are subject to the NEO's execution of a release of claims against us and continued compliance with certain restrictive covenants. The letter agreements also include a Section 280G "best pay" provision, which provides that if any amount received by the NEO pursuant to the agreement or otherwise that would be subject to the excise tax imposed by Section 4999 of the Code, the NEO would receive the full amount of the payments and benefits or an amount reduced so that no portion would be subject to the excise tax, whichever would result in the largest payment to the NEO on an after-tax basis.

Name	Benefit	Termination Without Cause or for Good Reason / Cause (no Change in Control) (\$)	Change in Control (no Termination) (\$) (1)	Termination Without Cause or for Good Reason / Cause in Connection with a <u>Change in Control (\$)</u>
David P. Meeker	Cash	630,000	N/A	945,000
	Equity Acceleration(2)	0	878,030	878,030
	Continued Healthcare	24,421	N/A	45,789
	Total(3)	654,421	1,262,580	2,253,369
Hunter C. Smith	Cash	326,968	N/A	610,340
	Equity Acceleration(2)	0	642,393	642,393
	Continued Healthcare	15,132	N/A	25,220
	Total(3)	342,100	773,470	1,409,030
Murray Stewart	Cash	N/A	N/A	N/A
	Equity Acceleration(2)	0	343,063	343,063
	Continued Healthcare	N/A	N/A	N/A
	Total(3)	N/A	343,063	343,063
Jennifer Chien	Cash	296,250	N/A	553,000
	Equity Acceleration(2)	0	380,418	380,418
	Continued Healthcare	N/A	N/A	N/A
	Total(3)	296,250	511,495	1,064,495
Yann Mazabraud	Cash	98,750	N/A	98,750
	Equity Acceleration(2)	0	380,418	380,418
	All Other Payments or Benefits		N/A	
	Total(3)	98,750	511,495	610,245
Joseph Shulman	Cash	290,203	N/A	522,365
	Equity Acceleration	0	361,605	361,605
	Continued Healthcare	22,894	N/A	24,421
	Total(3)	313,098	492,782	1,039,568

Estimated Potential Payments

(1) Assumes awards are not assumed or substituted in connection with the change in control.

(2) With respect to options, the value of equity acceleration was calculated by multiplying (i) the number of accelerated shares of common stock underlying the options by (ii) the excess, if any, of \$9.98, the closing trading price of our common stock on December 31, 2021, over the exercise price for the options. With respect to RSUs and PSUs, the value of equity acceleration was calculated by multiplying the number of accelerated RSUs and/or PSUs, as applicable, by \$9.98, the closing trading price of our common stock on December 31, 2021.

(3) Amounts shown are the maximum potential payment the NEO would have received as of December 31, 2021. Amounts of any reduction pursuant to the 280G best pay provision, if any, would be calculated upon actual termination of employment.

* * * * *

CEO Pay Ratio

As required by Section 953(b) of the Dodd-Frank Wall Street Reform and Consumer Protection Act and Item 402(u) of Regulation S-K, we are providing the following information regarding the ratio of our Chief Executive Officer's annual total compensation to the annual total compensation of our median employee.

⁴⁴

The annual total compensation for 2021 for our Chief Executive Officer was \$6,458,360, as reported in the Summary Compensation Table. The annual total compensation for 2021 for our median employee, identified as discussed below, was \$351,479, calculated using the methodology below. Based on this information, for 2021, the ratio of the annual total cash compensation of our Chief Executive Officer to the median of the annual total compensation of our other employees was approximately 18 to 1.

Methodology, Assumptions and Estimates Used in Determining our Pay Ratio Disclosure

We identified the median employee from our entire employee population (other than our Chief Executive Officer), whether employed on a full-time or part-time basis, as of December 31, 2021, which consisted of 134 employees. Within this group, the median employee was identified using a consistently applied compensation measure ("CACM") of target total direct compensation, which we calculated by aggregating, for each employee as of December 31, 2021: (1) annual base pay, (2) annual target cash incentive opportunity, and (3) the grant date fair value for equity awards granted in 2021. In identifying the median employee, we converted compensation amounts paid in foreign currencies based on the applicable year-to-date average exchange rate as of December 31, 2021 and annualized the compensation values of individuals that joined our Company during 2021. We did not exclude workers in non-U.S. countries and did not make any cost-of-living adjustments.

Once the median employee was identified, we calculated the median employee's annual target total direct compensation in accordance with the requirements of the Summary Compensation Table.

This information is being provided for compliance purposes and should be viewed as a reasonable estimate calculated in a manner consistent with the SEC rules, based on our internal records and the methodology described above. The SEC rules for identifying the median compensated employee allow companies to adopt a variety of methodologies, to apply certain exclusions and to make reasonable estimates and assumptions that reflect their employee populations and compensation practices. Accordingly, the pay ratio reported by other companies may not be comparable to the pay ratio reported above, as other companies have different employee populations and compensation practices and may use different methodologies, exclusions, estimates and assumptions in calculating their own pay ratios. Neither the Compensation Committee nor management of the Company used the CEO Pay Ratio measure in making compensation decisions for 2021.

Compensation Risk Assessment

We have assessed our compensation programs for all employees and concluded that our compensation policies and practices do not create risks that are reasonably likely to have a material adverse effect on us. Management has evaluated our executive and employee compensation and benefits programs to determine if these programs' provisions and operations create undesired or unintentional risk of a material nature. The risk assessment process includes a review of program policies and practices; analysis to identify risks and risk controls related to our compensation programs; and determinations as to the sufficiency of risk identification, the balance of potential risk to potential reward, the effectiveness of our risk controls and the impacts of our compensation programs and their risks to our strategy. Although we periodically review all compensation programs, we focus on the programs with variability of payout, with the ability of a participant to directly affect payout and the controls on participant action and payout. In relation to this, we believe that our incentive compensation arrangements provide incentives that do not encourage risk taking beyond our ability to effectively identify and manage significant risks and are compatible with effective internal controls and our risk management practices.

The Compensation Committee monitors our compensation programs on an annual basis and expects to make modifications as necessary to address any changes in our business or risk profile.

AUDIT COMMITTEE REPORT

The Audit Committee has reviewed the audited consolidated financial statements of the Company for the fiscal year ended December 31, 2021 and has discussed these financial statements with management and the Company's independent registered public accounting firm. The Audit Committee has also received from, and discussed with, Rhythm Pharmaceuticals, Inc.'s independent registered public accounting firm the matters that they are required to provide to the Audit Committee, including the matters required to be discussed by the Public Company Accounting Oversight Board ("PCAOB") and the SEC.

The Company's independent registered public accounting firm also provided the Audit Committee with a formal written statement required by the applicable requirements of the PCAOB describing all relationships between the independent registered public accounting firm and the Company, including the disclosures required by the applicable requirements of the PCAOB regarding the independent registered public accounting firm's communications with the Audit Committee concerning independence. In addition, the Audit Committee discussed with the independent registered public accounting firm its independence from the Company.

Based on its discussions with management and the independent registered public accounting firm, and its review of the representations and information provided by management and the independent registered public accounting firm, the Audit Committee recommended to the Board of Directors that the audited consolidated financial statements be included in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2021.

David W.J. McGirr, *Chair* Stuart A. Arbuckle Christophe R. Jean

PROPOSAL NO. 2—RATIFICATION OF SELECTION OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We are asking our stockholders to ratify the Audit Committee's selection of Ernst & Young LLP, or Ernst & Young, as our independent registered public accounting firm for the fiscal year ending December 31, 2022. Ernst & Young has served as our independent registered public accounting firm since 2015.

The Audit Committee annually reviews the independent registered public accounting firm's independence, including reviewing all relationships between the independent registered public accounting firm and us and any disclosed relationships or services that may impact the objectivity and independence of the independent registered public accounting firm, and the independent registered public accounting firm's performance.

Although stockholder ratification is not required by our bylaws or otherwise, the Board believes it is advisable to provide stockholders an opportunity to ratify this selection and is submitting the selection of Ernst & Young to our stockholders for ratification as a matter of good corporate practice. If the selection is not ratified, the Audit Committee will consider whether it is appropriate to select another independent registered public accounting firm, but is not required to do so. Even if the selection is ratified, the Audit Committee a different registered public accounting firm at any time during the year if the Audit Committee determines that such a change would be in the best interests of Rhythm and its stockholders.

We expect that a representative of Ernst & Young will attend the Annual Meeting and will have an opportunity to make a statement if he or she so chooses and will be available to respond to appropriate questions from stockholders.

Policy on Audit Committee Pre-Approval of Audit and Permissible Non-Audit Services of Independent Registered Public Accounting Firm

The Audit Committee pre-approves all audit services, and permitted non-audit services (including the fees and terms thereof) to be performed by Ernst & Young, subject to the de minimis exception for non-audit services that are approved by the Audit Committee prior to the completion of an audit. The Audit Committee may delegate pre-approval authority to one or more members of the Audit Committee consistent with applicable law and listing standards, provided that the decisions of such Audit Committee member or members must be presented to the full Audit Committee at its next scheduled meeting.

Principal Accountant Fees and Services

We regularly review the services and fees of Ernst & Young LLP. These services and fees are also reviewed by the Audit Committee on an annual basis. The following table sets forth all fees paid or accrued by us for professional audit services and other services rendered by Ernst & Young LLP during the years ended December 31, 2021 and 2020:

Fee Category	2020	2021
Audit Fees	\$813,700	\$903,571
Audit Related Fees	—	_
Tax Fees	\$ 22,500	\$ 53,600
All Other Fees	\$ 3,600	\$ 3,600
Total Fees	\$839,800	\$960,771

Audit Fees. Consist of aggregate fees for professional services provided in connection with the annual audit of our consolidated financial statements, the review of our quarterly condensed consolidated financial statements, consultations on accounting matters directly related to the audit, and comfort letters, consents and assistance with and review of documents filed with the SEC.

Tax Fees. Consist of aggregate fees for tax compliance, tax advice and tax planning services including the review and preparation of our federal and state income tax returns.

All Other Fees. Consist of aggregate fees billed for products and services provided by the independent registered public accounting firm other than those fees disclosed above. For the years ended December 31, 2020 and, 2021, the other fees consist of fees billed related to our Ernst & Young research website membership.

The Audit Committee pre-approved all services performed since the pre-approval policy was adopted.

Vote Required

The affirmative vote of a majority of shares of our common stock, present online or represented by proxy at the Annual Meeting and entitled to vote, is required to ratify the selection of our independent auditors. An abstention is treated as present and entitled to vote and, therefore, has the effect of a vote "against" the proposal. Because the ratification of the selection of the independent auditors is a routine matter, a nominee holding shares in street name may vote on this proposal in the absence of instructions from the beneficial owner and, therefore, we do not expect any broker non-votes on this proposal.

THE BOARD OF DIRECTORS UNANIMOUSLY RECOMMENDS THAT YOU VOTE "FOR" THE RATIFICATION OF THE SELECTION OF ERNST & YOUNG AS THE COMPANY'S INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM.

(PROPOSAL NO. 2)

PROPOSAL NO. 3—APPROVAL, ON AN ADVISORY (NON-BINDING) BASIS, OF THE COMPENSATION OF OUR NAMED EXECUTIVE OFFICERS

As required by Section 14A(a)(1) of the Exchange Act, the below resolution enables our stockholders to vote to approve, on an advisory (non-binding) basis, the compensation of our named executive officers as disclosed in this Proxy Statement. This proposal, commonly known as a "Say-on-Pay Vote", gives our stockholders the opportunity to express their views on our named executive officers' compensation. The Say-on-Pay Vote is not intended to address any specific item of compensation, but rather the overall compensation of our named executive officers described in this Proxy Statement.

We encourage our stockholders to review the "Executive Compensation" section of this Proxy Statement for more information.

As an advisory approval, this proposal is not binding upon us or our Board or the Compensation Committee, which is responsible for the design and administration of our executive compensation program. However, the Board and Compensation Committee value the opinions of our stockholders expressed through your vote on this proposal. The Board and Compensation Committee will consider the outcome of this vote in making future compensation decisions for our named executive officers. Accordingly, we ask our stockholders to vote "FOR" the following resolution at the Annual Meeting:

"**RESOLVED**, that the Company's stockholders approve, by a non-binding advisory vote, the compensation of the named executive officers, as disclosed in the Company's Proxy Statement for the 2022 Annual Meeting of Stockholders pursuant to the compensation disclosure rules of the Securities and Exchange Commission, including the Compensation Discussion and Analysis, the compensation tables and narrative discussion."

The Board has determined that the next advisory Say-on-Pay Vote will be held in 2023, following consideration of the outcome of the advisory vote on the frequency of future Say-on-Pay Votes at the 2021 Annual Meeting of Stockholders.

Vote Required

The affirmative vote of a majority of shares of our common stock, present online or represented by proxy at the Annual Meeting and entitled to vote, is required to approve the compensation of our named executive officers. An abstention is treated as present and entitled to vote and, therefore, has the effect of a vote "against" the proposal. Broker non-votes will have no effect on the outcome of the vote on this proposal.

THE BOARD OF DIRECTORS UNANIMOUSLY RECOMMENDS THAT YOU VOTE "FOR" THE APPROVAL, ON AN ADVISORY (NON-BINDING) BASIS, OF THE COMPENSATION OF OUR NAMED EXECUTIVE OFFICERS.

(PROPOSAL NO. 3)

BENEFICIAL OWNERSHIP OF COMMON STOCK

The following table sets forth certain information as of April 13, 2022 (unless otherwise specified), with respect to the beneficial ownership of our common stock by each person who is known to own beneficially more than 5% of the outstanding shares of common stock, each person currently serving as a director, each director nominee, each named executive officer, and all directors and executive officers as a group).

Shares of common stock subject to options or other rights to purchase which are now exercisable or are exercisable within 60 days after April 13, 2022, are to be considered outstanding for purposes of computing the number of shares beneficially owned and the percentage ownership of the persons holding these options or other rights, but are not to be considered outstanding for the purpose of computing the number of shares beneficially owned or the percentage ownership of any other person. As of April 13, 2022, there were 50,393,731 shares of common stock outstanding. Unless otherwise indicated, the address for each beneficial owner is c/o Rhythm Pharmaceuticals, Inc., 222 Berkeley Street, 12th Floor, Boston, MA 02116.

Name and Address of Beneficial Owner	Number of Shares Beneficially Owned†	Percentage of Shares Beneficially Owned
5% or Greater Stockholders:		
Entities affiliated with PRIMECAP Management Company(1) 77 E. Colorado Blvd., 11th Floor Pasadena, CA 91105	6,256,991	12.4
Entities affiliated with Federated Hermes, Inc.(2) 1001 Liberty Avenue Pittsburgh, PA 15222-3779	5,065,113	10.1
Entities affiliated with New Enterprise Associates 13, L.P.(3) New Enterprise Associates 1954 Greenspring Drive, Suite 600 Timonium, MD 21093	4,912,306	9.8
Entities affiliated with RA Capital Management, LLC(4) c/o RA Capital Management, LLC 200 Berkeley Street, 18th Floor, Boston, MA 02116	4,871,067	9.7
Entities affiliated with Baker Bros. Advisors LP(5) c/o Baker Bros. Advisors LP 860 Washington Street, 3rd Floor New York, NY 10014	3,863,239	7.7
BlackRock, Inc.(6) 55 East 52nd Street New York, NY 10055	3,328,061	6.6
Janus Henderson Group plc(7) 201 Bishopsgate EC2M 3AE United Kingdom	3,133,935	6.2
The Goldman Sachs Group, Inc.(8) 200 West Street New York, NY 10282	3,057,449	6.1
Directors and Named Executive Officers:		
David P. Meeker, M.D.(9)	758,261	1.5
Hunter C. Smith(10)	401,863	*
Murray Stewart, D.M., F.R.C.P.(11)	146,281	*
Jennifer Chien(12)	59,200	*
Yann Mazabraud(13)	58,988	*
Joseph Shulman(14)	53,896	*
Stuart A. Arbuckle(15)	53,500	*

Name and Address of Beneficial Owner	Number of Shares Beneficially Owned†	Percentage of Shares Beneficially Owned
Camille L. Bedrosian, M.D. (16)	27,580	*
Jennifer Good(17)	53,500	*
Christophe R. Jean(18)	58,500	*
Edward T. Mathers(19)	58,500	*
David W.J. McGirr(20)	145,741	*
Lynn A. Tetrault, J.D. (21)	27,580	*
All executive officers and directors as a group (15 persons)(22)	1,911,592	3.8

* Represents beneficial ownership of less than 1%.

- † None of the shares are pledged as security.
- (1) Based solely on a Schedule 13G/A filed on February 10, 2022. PRIMECAP Management Company has sole voting and dispositive power over 6,256,991 shares.
- (2) Based solely on a Schedule 13G/A filed on April 11, 2022. All of the outstanding voting stock of Federated Hermes, Inc., or Federated, is held in the Voting Shares Irrevocable Trust, or the Trust, for which Thomas R. Donahue, Rhodora J. Donahue and J. Christopher Donahue act as trustees, or collectively, the Trustees. The Trustees exercise collective voting control over Federated. Federated is the parent holding company of Federated Equity Management Company of Pennsylvania and Federated Global Investment Management Corp., or the Investment Advisers, which act as investment advisers to registered investment companies and separate accounts that own shares Common Stock. The Investment Advisers are wholly owned subsidiaries of FII Holdings, Inc., which is wholly owned subsidiary of Federated. According to the cover page of the Schedule 13G/A, each of Federated and the Trust have sole voting and investment power over the shares reflected in the table. Federated, the Trust, and each of the Trustees expressly disclaim beneficial ownership of the shares reflected in the table.
- (3) Based on a Schedule 13D filed on October 13, 2017 and other information known to the Company. Consists of shares held directly by New Enterprise Associates 13, L.P., or NEA 13. Includes 2,350 shares held directly by NEA Ventures 2009, L.P. The shares held directly by NEA 13 are indirectly held by NEA Partners 13, L.P., or Partners 13, which is the sole general partner of NEA 13, NEA 13 GP, LTD, or NEA 13 LTD, which is the sole general partner of Partners 13, and each of the individual directors of NEA 13 LTD. The individual directors of NEA 13 LTD, or the NEA 13 Directors, are M. James Barrett, Peter J. Barris, Forest Baskett, Patrick J. Kerins, David M. Mott, Scott D. Sandell and Ravi Viswanathan. NEA Partners 13, NEA 13 LTD, and the NEA 13 Directors share voting and dispositive power over the shares held directly by NEA 13. All indirect holders of the above referenced shares disclaim beneficial ownership of the shares. The address of the principal business office of NEA 13, Partners 13 and NEA 13 LTD is referenced above. The address of the principal business office of each of Mr. Barrett, Mr. Barris, Mr. Kerins and Mr. Mott is New Enterprise Associates, 5425 Wisconsin Avenue, Suite 800, Chevy Chase, MD 20815. The address of the principal business office of Mr. Baskett, Mr. Sandell, and Mr. Viswanathan is New Enterprise Associates, 2855 Sand Hill Road, Menlo Park, California 94025.
- (4) Based solely on a Schedule 13G/A filed on February 14, 2022. Consists of 4,871,067 shares held directly by RA Capital Healthcare Fund, L.P., or RAC Healthcare. The general partner of RA Capital Management, L.P., or RA Capital, is RA Capital Management GP, LLC, of which Peter Kolchinsky and Rajeev Shah are the controlling persons. RA Capital serves as investment adviser for RAC Healthcare and the Account and may be deemed a beneficial owner of the shares directly owned by RA Capital and the Account. As managers of RA Capital, Dr. Kolchinsky and Mr. Shah may be deemed beneficial owners of the shares beneficially owned by RA Capital. RAC Healthcare has delegated to RA Capital the sole power to vote and dispose of all securities held by RAC Healthcare and may not revoke that delegation on less than 61 days' notice. RA Capital, Dr. Kolchinsky and Mr. Shah each disclaim beneficial ownership of all shares held by RAC Healthcare or the Account. According to the cover page of the Schedule 13G/A, each of RA Capital, Dr. Kolchinsky, Mr. Shah and RAC Healthcare has shared voting and dispositive power over 4,871,067 shares.

- (5) Based solely on a Schedule 13G/A filed with the SEC on February 14, 2022. Pursuant to management agreements among Baker Bros. Advisors LP (the "Adviser"), the Funds and their respective general partners, the Funds' respective general partners relinquished to the Adviser all discretion and authority with respect to the investment and voting power of the securities held by the Funds, and thus the Adviser has complete and unlimited discretion and authority with respect to the Funds' investments. Baker Bros. Advisors (GP) LLC (the "Adviser GP"), Felix J. Baker and Julian C. Baker as managing members of the Adviser GP, and the Adviser may be deemed to be beneficial owners of the common shares directly held by the Funds.
- (6) Based solely on a Schedule 13G/A filed on February 3, 2022. BlackRock, Inc. has sole voting power over 3,248,859 shares and sole dispositive power over 3,328,061 shares.
- (7) Based solely on a Schedule 13G/A filed on February 10, 2022. Janus Henderson Group plc, or Janus Group, has a 100% ownership stake in Janus Capital Management LLC, or Janus Capital. Janus Capital is an investment advisor furnishing investment advice to various fund, individual, and institutional clients, or the Managed Portfolios, and may be deemed to be the beneficial owners of the shares held by the Managed Portfolios. Janus Capital does not have the right to receive any dividends from, or the proceeds from the sale of, the securities held in the Managed Portfolios and disclaims any ownership associated with such rights. According to the cover page of the Schedule 13G/A, Janus Group has shared voting and dispositive power over the shares.
- (8) Based solely on a Schedule 13G jointly filed with the SEC on January 19, 2022 by The Goldman Sachs Group, Inc. and Goldman Sachs & Co. LLC. The Goldman Sachs Group, Inc. and Goldman Sachs & Co. LLC share voting and dispositve power over 3,057,559 shares of common stock. The address of the principal business office of each of the Goldman Sachs Group, Inc. and Goldman Sachs & Co. LLC is 200 West Street, New York, NY 10282.
- (9) Consists of (i) 111,335 shares of common stock and (ii) 646,926 shares of common stock underlying options that are exercisable within 60 days of April 13, 2022.
- (10) Consists of (i) 40,161 shares of common stock and (ii) 361,702 shares of common stock underlying options that are exercisable within 60 days of April 13, 2022.
- (11) Based on information known to the Company on September 10, 2021, the date of Dr. Stewart's departure. Consists of 146,281 shares of common stock underlying options that are exercisable within 60 days of April 13, 2022.
- (12) Consists of (i) 1,310 shares of common stock and (ii) 57,890 shares of common stock underlying options that are exercisable within 60 days of April 13, 2022.
- (13) Consists of (i) 1,098 shares of common stock and (ii) 57,890 shares of common stock underlying options that are exercisable within 60 days of April 13, 2022.
- (14) Consists of (i) 1,006 shares of common stock and (ii) 52,890 shares of common stock underlying options that are exercisable within 60 days of April 13, 2022.
- (15) Consists of 53,500 shares of common stock underlying options that are exercisable within 60 days of April 13, 2022.
- (16) Consists of 27,580 shares of common stock underlying options that are exercisable within 60 days of April 13, 2022.
- (17) Consists of 53,500 shares of common stock underlying options that are exercisable within 60 days of April 13, 2022.
- (18) Consists of 58,500 shares of common stock underlying options that are exercisable within 60 days of April 13, 2022.
- (19) Consists of 58,500 shares of common stock underlying options that are exercisable within 60 days of April 13, 2022. Mr. Mathers is a partner of New Enterprise Associates, Inc. Mr. Mathers does not have voting or dispositive power over any of the shares directly held by NEA 13 referenced in footnote (2) above.

- (20) Consists of 145,741 shares of common stock underlying options that are exercisable within 60 days of April 13, 2022.
- (21) Consists of 27,580 shares of common stock underlying options that are exercisable within 60 days of April 13, 2022.
- (22) Consists of (i) 154,910 shares of common stock, and (ii) 1,756,682 shares of common stock underlying options that are exercisable within 60 days of April 13, 2022.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

Related Party Transactions Policy

Our Board has adopted a policy that our executive officers, directors, nominees for election as a director, beneficial owners of more than 5% of any class of our common stock and any members of the immediate family of any of the foregoing persons are not permitted to enter into a related person transaction with us without the prior review and approval of our Governance and Nominating Committee. Any request for us to enter into a transaction with an executive officer, director, nominee for election as a director, beneficial owner of more than 5% of any class of our common stock or any member of the immediate family of any of the foregoing persons in which the amount involved exceeds \$120,000 and such person would have a direct or indirect material interest must first be presented to our Governance and Nominating Committee for review, consideration and approval. In approving or rejecting any such proposal, our Governance and Nominating Committee is to consider the material facts of the transaction, including, but not limited to, whether the transaction is on terms no less favorable than terms generally available to an unaffiliated third party under the same or similar circumstances and the extent of the related person's interest in the transaction.

Since January 1, 2021, we have been a party to the following transactions or series of similar transactions, in which:

- the amounts involved exceeded or will exceed \$120,000; and
- any of the directors, nominees for election as a director, executive officers or holders of more than 5% of our voting equity, or any member of the immediate family of the foregoing persons, had or will have a direct or indirect material interest.

Compensation termination, change in control and other arrangements for our directors and named executive officers are described under "Executive Compensation."

Director and Officer Indemnification and Insurance

We have entered into indemnification agreements with each of our directors and executive officers. These agreements, among other things, require us or will require us to indemnify each director (and in certain cases their related venture capital funds) and executive officer to the fullest extent permitted by Delaware law, including indemnification of expenses such as attorneys' fees, judgments, fines and settlement amounts incurred by the director or executive officer in any action or proceeding, including any action or proceeding by or in right of us, arising out of the person's services as a director or executive officer.

OTHER MATTERS

Delinquent Section 16(a) Reports

Section 16(a) of the Exchange Act requires our directors, officers (as defined under Rule 16a-1(f) under the Exchange Act) and stockholders who beneficially own more than 10% of any class of our equity securities registered pursuant to Section 12 of the Exchange Act (collectively, the "Reporting Persons") to file initial statements of beneficial ownership of securities and statements of changes in beneficial ownership of securities with respect to our equity securities with the SEC. To our knowledge, based solely on our review of the copies of such forms filed with the SEC and upon written representations of the Reporting Persons received by us, we believe that there has been compliance with all Section 16(a) filing requirements applicable to such Reporting Persons with respect to the fiscal year ended December 31, 2021, except for a late Form 3 filing for Linda Shapiro, and a late Form 4 filing for Linda Shapiro reporting two transactions.

GENERAL MATTERS

Availability of Certain Documents

A copy of our Annual Report on Form 10-K for the year ended December 31, 2021 (the "2021 Annual Report on Form 10-K") has been posted on our website along with this Proxy Statement at *www.edocumentview.com/RYTM* or *www.rhythmtx.com* under "Investors & Media" at "SEC Filings." We will mail without charge, upon written request, a copy of our 2021 Annual Report on Form 10-K including financial statements and schedules thereto but excluding exhibits. A reasonable fee will be charged for copies of exhibits. Please send a written request to our Secretary at:

Rhythm Pharmaceuticals, Inc. 222 Berkeley Street, 12th Floor Boston, MA 02116 Attention: Secretary

You may also find a copy of this Proxy Statement and our 2021 Annual Report on Form 10-K (with exhibits) on the SEC's website at *www.sec.gov*.

Stockholders Sharing an Address / Householding

The SEC has adopted rules that permit companies and intermediaries (such as banks and brokers) to satisfy the delivery requirements for proxy statements and annual reports with respect to two or more stockholders sharing the same address by delivering a single proxy statement addressed to those stockholders. This process, which is commonly referred to as "householding," potentially means extra convenience for stockholders and cost savings for companies.

Only one copy of our 2021 Annual Report and this Proxy Statement is being delivered to multiple stockholders sharing an address, unless we have received contrary instructions from one or more of the stockholders.

We will undertake to deliver promptly, upon written or oral request, a separate copy to a stockholder at a shared address to which a single copy of the 2021 Annual Report and this Proxy Statement was delivered. To receive a separate copy of our 2021 Annual Report or Proxy Statement, or to receive separate copies in the future, or if two stockholders sharing an address have received two copies of any of these documents and desire to only receive one, you may write the Secretary of Rhythm Pharmaceuticals, Inc. at our principal executive offices at 222 Berkeley Street, 12th Floor, Boston, MA 02116 or call the Secretary at (857) 264-4280.

Stockholder Proposals and Nominations

Stockholder Proposals to be Considered for Inclusion in our Proxy Materials. Under Rule 14a-8 of the Exchange Act, to submit a proposal for inclusion in our Proxy Statement for the 2023 Annual Meeting of Stockholders, stockholder proposals must be received no later than close of business on December 29, 2022, by our Secretary at our principal executive offices at 222 Berkeley Street, 12th Floor, Boston, MA 02116.

Other Proposals or Nominees for Presentation at the 2023 Annual Meeting. Our bylaws provide that, for stockholder nominations to the Board or other business to be considered at the 2023 Annual Meeting of Stockholders, the stockholder must have given timely notice thereof in writing to the Secretary at Rhythm Pharmaceuticals, Inc., 222 Berkeley Street, 12th Floor, Boston, MA 02116 between February 8, 2023 and March 10, 2023 (assuming the date of the 2023 Annual Meeting of Stockholders is not so advanced or delayed as described in our bylaws). To be timely for the 2023 Annual Meeting of Stockholders, the stockholder's notice must be delivered to or mailed and received by us not earlier than the close of business on the 120th day nor later than the close of business on the 90th day prior to the anniversary date of the previous year's annual meeting, except that if the annual meeting is scheduled more than 30 days before or 60 days after such anniversary date, we must receive the notice not later than the close of business on the 10th day following the day on which we first provide notice or public disclosure of the date of the meeting. Such notice must provide the information required by Section 2.12 of our bylaws with respect to each nomination or matter the stockholder proposes to bring before the 2023 Annual Meeting of Stockholders.

In addition to satisfying the foregoing requirements under the Amended and Restated Bylaws, to comply with the universal proxy rules, stockholders who intend to solicit proxies in support of director nominees other than the Company's nominees must provide notice that sets forth the information required by Rule 14a-19 under the Exchange Act no later than April 10, 2023.

We intend to file a Proxy Statement and WHITE proxy card with the SEC in connection with the solicitation of proxies for our 2023 Annual Meeting of Stockholders. Stockholders may obtain our Proxy Statement (and any amendments and supplements thereto) and other documents as and when filed by us with the SEC without charge from the SEC's website at: *www.sec.gov*.

Other Matters

As of the date of this Proxy Statement, the Board does not intend to present any matters other than those described herein at the Annual Meeting and is unaware of any matters to be presented by other parties. If other matters are properly brought before the meeting for action by the stockholders, proxies will be voted in accordance with the recommendation of the Board or, in the absence of such a recommendation, in accordance with the judgment of the proxy holder.

Whether or not you plan to attend the Annual Meeting virtually, we urge you to vote your shares promptly.

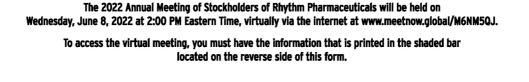
By Order of the Board of Directors

/s/ DAVID P. MEEKER, M.D.

David P. Meeker, M.D. Chairman of the Board, President and Chief Executive Officer April 28, 2022



	Your vote matters - here's how to vote! You may vote online or by phone instead of mailing this card. Online - During the Meeting Go to www.meetnow.global/M6NM5QJ. To access the virtual meeting, you must have the information that is printed in the shaded bar located below. Online - Before the Meeting Go to www.investorvote.com/RYTM or scan the QR code – login details are located in the shaded bar below. Phone Call toll free 1-800-652-VOTE (8683) within the USA, US territories and Canada Save paper, time and money! Sign up for electronic delivery at www.investorvote.com/RYTM
2022 Annual Meeting Proxy Card	
FOR all nominees L_J vote from all nominees L_J "For All Except" and write	A Proposal 2 and 3. If their respective successors are duly elected and qualified.
	dministrator, corporate officer, trustee, guardian, or custodian, please give
DOSMZHA 1 U P X	+



Important notice regarding the Internet availability of proxy materials for the Annual Meeting of Stockholders. The Notice & Proxy Statement and Annual Report is available at: www.investorvote.com/RYTM



Small steps make an impact.

Help the environment by consenting to receive electronic delivery, sign up at www.investorvote.com/RYTM

▼ IF VOTING BY MAIL, SIGN, DETACH AND RETURN THE BOTTOM PORTION IN THE ENCLOSED ENVELOPE. ▼

Rhythm Pharmaceuticals, Inc.

2022 Annual Meeting of Stockholders

Proxy Solicited by Board of Directors for Annual Meeting – June 8, 2022, 2:00 PM Eastern Time

The undersigned stockholder(s) of Rhythm Pharmaceuticals, Inc. hereby appoint(s) David P. Meeker, M.D. and Hunter C. Smith, or either of them, as proxies, each with the power to appoint his substitute, and hereby authorize(s) them to represent and to vote, as designated on the reverse side of this proxy card, all of the shares of Common stock of RHYTHM PHARMACEUTICALS, INC. that the stockholder(s) is/are entitled to vote at the Annual Meeting of Stockholders to be held at 2:00 PM, ET on June 8, 2022, via a live webcast at www.meetnow.global/M6NM5QJ, and any adjournment, continuation or postponement thereof.

Such proxies are authorized to vote in their discretion (x) for the election of any person to the Board of Directors if any nominee named herein becomes unable to serve or for good cause will not serve, (y) on any matter that the Board of Directors did not know would be presented at the Annual Meeting by a reasonable time before the proxy solicitation was made, and (z) on such other business as may properly be brought before the meeting or any adjournment, continuation or postponement thereof.

This proxy, when properly executed, will be voted in the manner directed herein by the undersigned stockholder(s).

If no such direction is made, this proxy will be voted in accordance with the Board of Directors' recommendations.

(Items to be voted appear on reverse side)

C Non-Voting Items	
Change of Address – Please print new address below.	Comments – Please print your comments below.
	+