
**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

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

Karyopharm Therapeutics 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 computed on table below per Exchange Act Rules 14a-6(i)(1) and 0-11.

(1) Title of each class of securities to which transaction applies:

(2) Aggregate number of securities to which transaction applies:

(3) Per unit price or other underlying value of transaction computed pursuant to Exchange Act Rule 0-11 (set forth the amount on which the filing fee is calculated and state how it was determined):

(4) Proposed maximum aggregate value of transaction:

(5) Total fee paid:

Fee paid previously with preliminary materials.

Check box if any part of the fee is offset as provided by Exchange Act Rule 0-11(a)(2) and identify the filing for which the offsetting fee was paid previously. Identify the previous filing by registration statement number, or the Form or Schedule and the date of its filing.

(1) Amount previously paid:

(2) Form, Schedule or Registration Statement No.:

(3) Filing party:

(4) Date Filed:



**NOTICE OF ANNUAL MEETING OF STOCKHOLDERS
TO BE HELD ON FRIDAY, MAY 21, 2021**

Dear Stockholder:

You are cordially invited to our 2021 Annual Meeting of Stockholders (the "Annual Meeting") to be held on Friday, May 21, 2021, beginning at 9:00 a.m. Eastern Time, exclusively online via the Internet as a virtual web conference at www.virtualshareholdermeeting.com/KPTI2021 to consider and act upon the following matters:

- (1) To elect the following three Class II directors nominated by our Board of Directors to serve as directors, each to hold office for a three-year term to expire at the 2024 annual meeting of stockholders and until their resignation or removal or until their successors are duly elected and qualified: Deepika R. Pakianathan, Ph.D., Richard Paulson, M.B.A., and Chen Schor, M.B.A., C.P.A.;
- (2) To approve, on an advisory basis, the compensation of our named executive officers, as described in this proxy statement;
- (3) To ratify the appointment of Ernst & Young LLP as our independent registered public accounting firm for the year ending December 31, 2021; and
- (4) To consider and vote upon such other business as may be properly brought before the meeting or any adjournments or postponements thereof.

To support the health and well-being of our stockholders, employees and directors in light of the coronavirus ("COVID-19") pandemic, our Annual Meeting will be a "virtual meeting" of stockholders, which will be conducted exclusively online via the Internet as a virtual web conference. There will not be a physical meeting location, and stockholders will not be able to attend the Annual Meeting in person. This means that you can attend the Annual Meeting online, vote your shares during the online meeting and submit questions during the online meeting by visiting the above-mentioned Internet site. In light of the public health and safety concerns related to COVID-19, we believe that hosting a virtual meeting will enable greater stockholder attendance and participation from any location around the world. We intend to resume our historical practice of holding an in-person meeting next year, if, taking into account public health and safety concerns related to COVID-19, our Board determines that holding a physical meeting is in the best interest of the Company and its stockholders.

Instead of mailing a printed copy of our proxy materials to all of our stockholders, we are providing access to these materials via the Internet. This reduces the amount of paper necessary to produce these materials as well as the costs associated with mailing these materials to all stockholders. Accordingly, on or about April 7, 2021, we will begin mailing a Notice of Internet Availability of Proxy Materials ("Notice") to stockholders and will post our proxy materials on the website referenced in the Notice. As more fully described in the Notice, stockholders may choose to access our proxy materials on the website referred to in the Notice or may request to receive a printed set of our proxy materials. In addition, the Notice and website provide information regarding how you may request to receive proxy materials in printed form by mail, or electronically by email, on an ongoing basis.

If you are a stockholder of record, you may vote in one of the following ways:

- **Vote over the Internet prior to the virtual Annual Meeting**, by visiting www.proxyvote.com (have your Notice or proxy card in hand to access the website).
- **Vote by Telephone**, by calling the toll-free number 1-800-690-6903 (have your Notice or proxy card in hand when you call);

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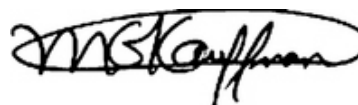
- **Vote by Mail**, if you received a printed copy of the proxy materials, by returning the enclosed proxy card (signed and dated) in the envelope provided; or
- **Vote online at the virtual Annual Meeting**, by using the Notice or proxy card to access the Annual Meeting website, www.virtualshareholdermeeting.com/KPTI2021.

If your shares are held in “street name,” meaning that they are held for your account by a broker or other nominee, you will receive instructions from the holder of record that you must follow to vote your shares.

Only stockholders of record at the close of business on March 26, 2021, the record date for the Annual Meeting, are entitled to notice of, and will be entitled to vote at, the Annual Meeting, or any adjournments or postponements thereof.

Whether or not you plan to attend the Annual Meeting online, we urge you to take the time to vote your shares. Further information about how to attend the Annual Meeting online, vote your shares online during the meeting and submit your questions online during the Annual Meeting is included in the accompanying proxy statement.

By Order of the Board of Directors,

A handwritten signature in black ink, appearing to read "M. G. Kauffman", enclosed within a hand-drawn oval.

Michael G. Kauffman, M.D., Ph.D.
Chief Executive Officer

Newton, Massachusetts
April 7, 2021

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PROXY STATEMENT FOR THE 2021 ANNUAL MEETING OF STOCKHOLDERS

TO BE HELD ON FRIDAY, MAY 21, 2021

The Board of Directors (the "Board") of Karyopharm Therapeutics Inc. (which we also refer to as "Karyopharm," "the Company," "we," "us," or "our") is soliciting proxies for use at the 2021 Annual Meeting of Stockholders (the "Annual Meeting"), to be held exclusively online via the Internet as a virtual web conference at www.virtualshareholdermeeting.com/KPTI2021 on Friday, May 21, 2021 at 9:00 a.m. Eastern Time. In light of the COVID-19 pandemic, to support the health and well-being of our stockholders, employees and directors, we have determined that the Annual Meeting will be held in a virtual meeting format only, via the Internet, with no physical in-person meeting. At our virtual Annual Meeting, stockholders will be able to attend, vote and submit questions by visiting www.virtualshareholdermeeting.com/KPTI2021. Further information about how to attend the Annual Meeting online, vote your shares online during the meeting and submit questions during the meeting is included in this proxy statement.

Important Notice Regarding the Availability of Proxy Materials for the Annual Meeting of Stockholders to be Held on Friday, May 21, 2021:

This proxy statement and our annual report are available electronically at www.proxyvote.com.

On or about April 7, 2021, we will begin mailing a Notice of Internet Availability of Proxy Materials ("Notice") to our stockholders (other than those who previously requested electronic or paper delivery of proxy materials), directing stockholders to a website where they can access our proxy materials, including this proxy statement and our Annual Report on Form 10-K for the year ended December 31, 2020, which we filed with the Securities and Exchange Commission (the "SEC") on February 24, 2021 (the "2020 Annual Report") and view instructions on how to vote online or by telephone. If you would prefer to receive a paper copy of our proxy materials, please follow the instructions included in the Notice. If you have previously elected to receive our proxy materials electronically, you will continue to receive access to those materials via e-mail unless you elect otherwise.

EXPLANATORY NOTE

We qualify as a "smaller reporting company" as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), for the fiscal year ended December 31, 2020, and have elected to provide in this proxy statement certain scaled disclosures permitted under the Exchange Act for smaller reporting companies.

GENERAL INFORMATION ABOUT THIS PROXY STATEMENT, THE ANNUAL MEETING AND VOTING

How do I attend the virtual Annual Meeting?

This year's Annual Meeting will be conducted as a virtual meeting of stockholders. We will host the Annual Meeting exclusively online via the Internet as a virtual web conference. You will be able to attend the Annual Meeting online, vote your shares online during the Annual Meeting and submit your questions online during the Annual Meeting by visiting www.virtualshareholdermeeting.com/KPTI2021. There will not be a physical meeting location, and you will not be able to attend the Annual Meeting in person. The webcast will start at 9:00 a.m. Eastern Time on Friday, May 21, 2021. You will need the control number included on your proxy card or in the instructions from your broker in order to be able to enter the Annual Meeting online. Information contained on this website is not incorporated by reference into this proxy statement or any other report we file with the SEC.

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Online check-in will begin at 8:45 a.m. Eastern Time on Friday, May 21, 2021, and you should allow ample time for the online check-in proceedings. If you encounter any difficulties accessing the virtual Annual Meeting during the check-in or meeting time, please call the technical support number that will be posted on the virtual Annual Meeting log-in page. Technical support will be available starting at 8:45 a.m. on the day of the meeting.

Why is the Annual Meeting a virtual, online meeting?

In light of the public health and safety concerns related to COVID-19, we believe that hosting a virtual meeting will facilitate stockholder attendance and participation at the Annual Meeting by enabling stockholders to participate remotely from any location around the world. Our virtual meeting will be governed by our Rules of Conduct and Procedures, which will be posted on the virtual meeting platform on the date of the Annual Meeting. We have designed the virtual Annual Meeting to provide the same rights and opportunities to participate as stockholders would have at an in-person meeting, including the right to vote and ask questions through the virtual meeting platform. There will not be a physical meeting location, and stockholders will not be able to attend the Annual Meeting in person. We intend to return to holding an in-person annual meeting in 2022, if, taking into account public health and safety concerns related to COVID-19, our Board determines that holding a physical meeting is in the best interest of the Company and its stockholders.

Why did you send me these proxy materials?

We are providing these proxy materials because our Board is soliciting your proxy to vote at the Annual Meeting. This proxy statement summarizes information related to your vote at the Annual Meeting. All stockholders who find it convenient to do so are cordially invited to attend the Annual Meeting online. However, you do not need to attend the meeting virtually to vote your shares. Instead, you may vote your shares as described in further detail in the answer to the question “How do I vote?” below.

The Notice of Annual Meeting, proxy statement, and voting instructions, together with our 2020 Annual Report, will be made available to each stockholder entitled to vote starting on or about April 7, 2021. These materials are available for viewing, printing and downloading on the Internet at www.proxyvote.com.

Who can vote at the Annual Meeting and what are the voting rights of such stockholders?

Only stockholders of record at the close of business on March 26, 2021 (the “Record Date”) are entitled to vote at the Annual Meeting. On the Record Date, there were 75,061,474 shares of our common stock outstanding and entitled to vote (each share entitles its holder to one vote). Common stock is our only class of stock outstanding.

May I see a list of stockholders entitled to vote as of the Record Date?

A list of registered stockholders as of the close of business on the Record Date will be available for examination by any stockholder for any purpose germane to the Annual Meeting for a period of at least 10 days prior to the Annual Meeting. If you wish to view this list, please contact our Corporate Secretary at Karyopharm Therapeutics Inc., 85 Wells Avenue, Newton, Massachusetts 02459, Attention: Corporate Secretary, (617) 658-0600. This list will also be available for examination by the stockholders during the Annual Meeting at www.virtualshareholdermeeting.com/KPTI2021.

What is the purpose of the Annual Meeting?

At the Annual Meeting, stockholders will consider and vote on the following matters:

- (1) To elect the following three Class II directors nominated by our Board to serve as directors, each to hold office for a three-year term to expire at the 2024 annual meeting of stockholders and until their resignation or removal or until their successors are duly elected and qualified: Deepika R. Pakianathan, Ph.D., Richard Paulson, M.B.A., and Chen Schor, M.B.A., C.P.A.;

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- (2) To approve, on an advisory basis, the compensation of our named executive officers (“NEOs”), as described in this proxy statement;
- (3) To ratify the appointment of Ernst & Young LLP as our independent registered public accounting firm for the year ending December 31, 2021; and
- (4) To consider and vote upon such other business as may be properly brought before the Annual Meeting or any adjournments or postponements thereof.

How many votes do I have?

Each stockholder is entitled to one vote for each share of our common stock held by such stockholder on the Record Date.

How do I vote?

If you are the “record holder” of your shares, meaning that you own your shares in your own name and not through a bank, brokerage firm or other nominee (each a “Nominee”), you may vote:

- (1) **Over the Internet prior to the Annual Meeting:** Go to the website of our tabulator at www.proxyvote.com. Use the vote control number printed on the Notice (or your proxy card) to access your account and vote your shares. You must specify how you want your shares voted or your Internet vote cannot be completed and you will receive an error message. Your shares will be voted according to your instructions. You must submit your Internet proxy before 11:59 p.m. Eastern Time on May 20, 2021, the day before the Annual Meeting, for your proxy to be validly submitted over the Internet and for your vote to count.
- (2) **By Telephone:** Call 1-800-690-6903, toll free from the United States, Canada and Puerto Rico, and follow the recorded instructions. You will need to have the Notice (or your proxy card) in hand when you call. You must specify how you want your shares voted and confirm your vote at the end of the call or your telephone vote cannot be completed. Your shares will be voted according to your instructions. You must submit your telephonic proxy before 11:59 p.m. Eastern Time on May 20, 2021, the day before the Annual Meeting, for your telephonic proxy to be valid and your vote to count.
- (3) **By Mail:** If you received a printed copy of the proxy materials, complete and sign the enclosed proxy card and mail it in the enclosed envelope, postage prepaid, to Vote Processing, c/o Broadridge, 51 Mercedes Way, Edgewood, NY 11717, where the proxy card must be received no later than May 20, 2021, the day before the Annual Meeting, for it to be valid and your vote to count. Your shares will be voted according to your instructions. If you return your proxy card but do not specify how you want your shares voted on any particular matter, they will be voted in accordance with the recommendations of our Board.
- (4) **Online while virtually attending the Annual Meeting:** You may vote your shares online while virtually attending the Annual Meeting by visiting www.virtualshareholdermeeting.com/KPTI2021. You will need your control number included on your notice or proxy card in order to be able to vote during the Annual Meeting.

If your shares are held in “street name,” meaning they are held for your account by a Nominee, you may vote:

- (1) **Over the Internet prior to the Annual Meeting or by Telephone:** You will receive instructions from your Nominee if they permit Internet or telephone voting. You should follow those instructions.
- (2) **By Mail:** You will receive instructions from your Nominee explaining how you can vote your shares by mail. You should follow those instructions.
- (3) **Online while virtually attending the Annual Meeting:** You will receive instructions from your Nominee explaining how you can vote your shares online during the Annual Meeting. You will need your

control number included on the Notice or voting instruction form in order to demonstrate proof of beneficial ownership and to be able to vote during the Annual Meeting.

If you hold your shares of our common stock in multiple accounts, you should vote your shares as described above for each account.

Can I revoke or change my vote?

If your shares are registered directly in your name, you may revoke your proxy and change your vote at any time before the Annual Meeting. To do so, you must do one of the following:

- (1) Vote over the Internet or by telephone prior to the Annual Meeting as instructed above. Only your latest Internet or telephone vote submitted prior to the Annual Meeting is counted. You may not revoke or change your vote over the Internet or by telephone after 11:59 p.m. Eastern Time on May 20, 2021.
- (2) Sign a new proxy card and submit it by mail to Vote Processing, c/o Broadridge, 51 Mercedes Way, Edgewood, NY 11717, where the proxy card must be received no later than May 20, 2021. Only your latest dated proxy will be counted.
- (3) Attend the virtual Annual Meeting and vote online as instructed above. Attending the virtual Annual Meeting alone will not revoke your Internet vote, telephone vote, or proxy submitted by mail, as the case may be.
- (4) Provide our Corporate Secretary written notice before or at the Annual Meeting that you want to revoke your proxy.

If your shares are held in “street name,” you may submit new voting instructions with a later date by contacting your Nominee. You may also vote your shares online while virtually attending the Annual Meeting, which will have the effect of revoking any previously submitted voting instructions.

Will my shares be voted if I do not return my proxy or do not provide specific voting instructions on the proxy card or voting instruction form that I submit?

If your shares are registered directly in your name, your shares will not be voted if you do not vote over the Internet prior to the Annual Meeting, by telephone, by returning your proxy by mail, or online at the virtual Annual Meeting. If you submit a proxy card without giving specific voting instructions on one or more matters listed in the Notice, your shares will be voted as recommended by our Board on such matters, and as the proxyholders may determine in their discretion how to vote with respect to any other matters properly presented for a vote at the Annual Meeting.

If your shares are held in “street name,” your brokerage firm may under certain circumstances vote your shares if you do not timely return your voting instructions. **Brokers can vote their customers’ unvoted shares on discretionary matters but cannot vote such shares on non-discretionary matters.** If you do not timely return voting instructions to your brokerage firm to vote your shares, your brokerage firm may, on discretionary matters, either vote your shares or leave your shares unvoted.

Proposal 1 (election of directors) and Proposal 2 (advisory vote on the compensation of our NEOs) are non-discretionary matters. If you do not instruct your Nominee how to vote with respect to either or both of these proposals, your Nominee may not vote with respect to such proposal or proposals, and those shares that would have otherwise been entitled to be voted will be counted as “broker non-votes.” “Broker non-votes” are shares that are held in “street name” by a Nominee that indicates on its proxy that it does not have or did not exercise discretionary authority to vote on a particular matter.

Proposal 3 (ratification of the appointment of our independent registered public accounting firm) is considered a discretionary matter, and your Nominee will be able to vote on this proposal even if it does not timely

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receive instructions from you, so long as it holds your shares in its name. We encourage you to timely provide voting instructions to your Nominee. This ensures that your shares will be voted at the Annual Meeting according to your instructions. You should receive directions from your Nominee about how to submit your voting instructions to them.

What constitutes a quorum at the Annual Meeting?

A quorum is needed to hold a valid meeting. A quorum will be present if the holders of at least a majority of the shares of common stock issued and outstanding and entitled to vote on the Record Date are present at the virtual Annual Meeting either “in person” virtually or as represented by proxy. For purposes of establishing a quorum, abstentions and broker non-votes are counted as present or represented. If a quorum is not present, we expect to adjourn the Annual Meeting until we obtain a quorum. The presence at the Annual Meeting, in person or by proxy, of holders representing a majority of our outstanding common stock as of the Record Date, or 37,530,738 shares, constitutes a quorum at the Annual Meeting, permitting us to conduct the business of the Annual Meeting. Shares present virtually during the Annual Meeting will be considered shares of common stock represented in person at the meeting.

What vote is required to approve each matter and how are votes counted?

Proposal 1—Election of Directors

The three nominees for director to receive the highest number of votes FOR election will be elected as Class II directors. This is called a plurality. **Proposal 1 is a non-discretionary matter.** Therefore, if your shares are held by your Nominee in “street name” and you do not timely provide voting instructions with respect to your shares, your Nominee cannot vote your shares on Proposal 1. Broker non-votes will not be counted as votes FOR or WITHHELD from the nominee. As a result, such “broker non-votes” will have no effect on the voting on Proposal 1. You may:

- vote FOR the nominees;
- vote FOR one or more nominees and WITHHOLD your vote from the other nominee or nominees; or
- WITHHOLD your vote from the nominees.

Votes that are withheld will not be included in the vote tally for the election of directors and will not affect the vote results.

Proposal 2—Advisory Vote on the Compensation of Our Named Executive Officers

To approve Proposal 2, stockholders holding a majority of the votes cast on the matter must vote FOR the approval of the compensation of our NEOs, as described in this proxy statement. **Proposal 2 is a non-discretionary matter.** Therefore, if your shares are held by your Nominee in “street name” and you do not timely provide voting instructions with respect to your shares, your Nominee cannot vote your shares on Proposal 2. Broker non-votes will have no effect on the outcome of this proposal. If you vote to ABSTAIN on Proposal 2, your shares will not be voted FOR or AGAINST the proposal and will also not be counted as votes cast or shares voting on Proposal 2. As a result, voting to ABSTAIN will have no effect on the voting on Proposal 2.

As an advisory vote, this proposal is not binding. The outcome of this advisory vote will not overrule any decision by us or our Board (or any committee thereof). However, our Compensation Committee and our Board value the opinions expressed by our stockholders in their vote on this proposal and will consider the outcome of the vote when making future compensation decisions for our NEOs.

Proposal 3—Ratification of the Appointment of our Independent Registered Public Accounting Firm

To approve Proposal 3, stockholders holding a majority of the votes cast on the matter must vote FOR the proposal. **Proposal 3 is a discretionary matter.** If your shares are held by your Nominee in “street name” and you do

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not timely provide voting instructions with respect to your shares, your Nominee may vote your unvoted shares on Proposal 3. If you ABSTAIN from voting on Proposal 3, your shares will not be voted FOR or AGAINST the proposal and will also not be counted as votes cast or shares voting on the proposal. As a result, voting to ABSTAIN will have no effect on the outcome of Proposal 3.

Although stockholder ratification of our Audit Committee's appointment of Ernst & Young LLP as our independent registered public accounting firm for the year ending December 31, 2021 is not required, we believe that it is advisable to give stockholders an opportunity to ratify this appointment. If this proposal is not approved at the Annual Meeting, our Audit Committee and Board will reconsider the appointment of Ernst & Young LLP as our independent registered public accounting firm for future service.

How does the Board recommend that I vote on the proposals?

Our Board recommends that you vote:

- **FOR** the election of each of the three nominees to serve as Class II directors on our Board for a three-year term to expire at the 2024 annual meeting of stockholders and until their resignation or removal or until their successors are duly elected and qualified;
- **FOR** the approval of the compensation of our NEOs; and
- **FOR** the ratification of the appointment of Ernst & Young LLP as our independent registered public accounting firm for the year ending December 31, 2021.

Are there other matters to be voted on at the Annual Meeting?

We do not know of any matters that may come before the Annual Meeting other than Proposals 1, 2, and 3. If any other matters are properly presented at the Annual Meeting, the persons named in the accompanying proxy intend to vote, or otherwise act, in accordance with their judgment on the matter.

How do I submit a question at the virtual Annual Meeting?

If you wish to submit a question on the day of the Annual Meeting, beginning at 8:45 a.m. Eastern Time, you may log into the virtual meeting platform at www.virtualshareholdermeeting.com/KPTI2021, select "Q & A" at the bottom right hand side of the screen, type your question into the "Submit a Question" field, and click "Submit." Our virtual meeting will be governed by our Rules of Conduct and Procedures, which will be posted at www.virtualshareholdermeeting.com/KPTI2021 during the Annual Meeting. The Rules of Conduct and Procedures will address the ability of stockholders to ask questions during the meeting, including rules on permissible topics, and rules for how questions and comments will be recognized. We will answer appropriate questions that are pertinent to the Company and the matters to be voted on by the stockholders at the Annual Meeting. Because time is limited at the Annual Meeting, we may not be able to answer all questions that are submitted. If there are any matters of individual concern to a stockholder and not of general concern to all stockholders, or if a question was not otherwise answered, such matters may be raised separately after the Annual Meeting by contacting Investor Relations at <https://investors.karyopharm.com/contact-us>. To promote fairness, efficiently use the Company's resources and address all shareholder questions, we will limit each stockholder to two questions, which should each be succinct and should cover only one topic. Questions from multiple stockholders on the same topic or that are otherwise related may be grouped, summarized and answered together.

How are we soliciting proxies and tabulating votes?

We will pay all of the costs of soliciting proxies. In addition to these proxy materials, our directors, officers, and other employees may also solicit proxies in person or by mail, telephone, fax or email without additional compensation. We do not currently plan to hire a proxy solicitor to help us solicit proxies, although we reserve the right to do so. We will ask Nominees to forward these proxy materials to beneficial owners and to obtain authority to execute proxies. We will then reimburse them for their expenses, which we do not expect to be significant. Votes will be tabulated by Broadridge.

How do I obtain an Annual Report on Form 10-K?

If you would like a copy of our 2020 Annual Report, we will send you one without charge. Please write to:

Karyopharm Therapeutics Inc.
85 Wells Avenue
Newton, Massachusetts 02459
Attn: Investor Relations

All of our SEC filings are also available free of charge under the heading “*Financial Information—SEC Filings*” in the “*Investors*” section of our website at www.karyopharm.com.

How can I find out the results of the voting at the virtual Annual Meeting?

Preliminary voting results will be announced at the Annual Meeting. Final voting results will be published in a current report on Form 8-K that we expect to file with the SEC within four business days after the Annual Meeting. If final voting results are not available to us in time to file a Form 8-K within four business days after the Annual Meeting, we intend to file a Form 8-K to publish preliminary results and, within four business days after the final results are known to us, file an amended Form 8-K to publish the final results.

**PROPOSAL 1:
ELECTION OF DIRECTORS**

Our Board is divided into three classes, with one class of our directors standing for election each year to serve for a three-year term. Directors for each class are elected at the annual meeting of stockholders held in the year in which the term for their class expires and hold office until their resignation or removal or until their successors are duly elected and qualified. In accordance with our certificate of incorporation and bylaws, our Board may fill existing vacancies on the Board by appointment.

The term of office of our Class II directors, Deepika R. Pakianathan, Ph.D., Richard Paulson, M.B.A., and Chen Schor, M.B.A., C.P.A., will expire at the Annual Meeting. Accordingly, the nominees for Class II director for election at the Annual Meeting are Dr. Pakianathan and Messrs. Paulson and Schor. If Dr. Pakianathan and Messrs. Paulson and Schor are elected at the Annual Meeting, each such individual will be elected to serve for a three-year term that will expire at our 2024 annual meeting of stockholders and until such individual's successor is duly elected and qualified.

If no contrary indication is made, proxies are to be voted for Dr. Pakianathan and Messrs. Paulson and Schor, or in the event that any of Dr. Pakianathan and Messrs. Paulson and Schor is not a candidate or is unable to serve as a director at the time of the election (which is not currently expected), for any nominee who is designated by our Board to fill the vacancy.

Our Board currently consists of nine members. We have no formal policy regarding board diversity, but our Corporate Governance Guidelines provide that the background and qualifications of the members of our Board considered as a group should provide a significant breadth of experience, knowledge, and ability to assist our Board in fulfilling its responsibilities. Our priority in selection of board members is: (a) identification of members who will further the interests of our stockholders through his or her established record of professional accomplishment; (b) ability to contribute positively to the collaborative culture among board members; (c) knowledge of our business; (d) understanding of the competitive landscape; and (e) adherence to high ethical standards. Certain individual qualifications and skills of our directors that contribute to our Board's effectiveness as a whole are described below.

Information Regarding Directors

The information set forth below as to the directors and nominees for directors has been furnished to us by the directors and nominees for directors:

Nominees for Election to the Board

**For a Three-Year Term Expiring at the
2024 Annual Meeting of Stockholders (Class II)**

<u>Name</u>	<u>Age</u>	<u>Present Position with Karyopharm Therapeutics Inc.</u>
Deepika R. Pakianathan, Ph.D.	56	Director
Richard Paulson, M.B.A.	53	Director
Chen Schor, M.B.A., C.P.A.	48	Director

Deepika R. Pakianathan, Ph.D. Dr. Pakianathan has served as a member of our Board since April 2013. Since 2001, Dr. Pakianathan has been a Managing Member at Delphi Ventures, a venture capital firm focused on biotechnology and medical device investments, where she leads the firm's biotechnology investment activities. From 1998 to 2001, Dr. Pakianathan was a senior biotechnology banker at JPMorgan, a global investment bank, from 1997 to 1998, she was a research analyst covering biotech at Genesis Merchant Group and from 1993 to 1997 she was a post-doctoral research scientist at Genentech. Dr. Pakianathan has served on the board of directors of Theravance

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Biopharma, Inc., a public biopharmaceutical company, since July 2020, where she also serves on the audit committee and scientific technology committee; Mereo Biopharma Group PLC, a public biopharmaceutical company, since April 2019, where she also serves as chair of its remuneration committee; Calithera Biosciences, Inc., a public biopharmaceutical company, since 2010, where she also serves as the lead independent director, chair of the nominating and governance committee and member of the compensation committee; and Foresite Development Corp II, a special purpose acquisition company, since February 2021. In December 2020, Dr. Pakianathan was also appointed to the board of directors of Palleon Pharmaceuticals, Inc., a biotechnology company, where she serves as lead director and chair of the compensation committee. From 2004 to 2016, Dr. Pakianathan served on the board of directors of Alexza Pharmaceuticals, Inc., a public biopharmaceutical company. Dr. Pakianathan holds a M.S. and Ph.D. from Wake Forest University, a B.Sc. from the University of Bombay, India and a M.Sc. from The Cancer Research Institute at the University of Bombay, India. We believe Dr. Pakianathan's qualifications to serve on our Board include her experience as a venture capital investor and director of multiple biotechnology companies, as well as her experience as a biotechnology investment banker, research analyst and research scientist.

Richard Paulson, M.B.A. Mr. Paulson has served as a member of our Board since February 2020. Mr. Paulson has been the Executive Vice President of Ipsen Pharmaceuticals, Inc. and Chief Executive Officer of Ipsen North America, a biopharmaceutical company focused on innovation and specialty care in areas of oncology, neuroscience and rare diseases, since February 2018. Mr. Paulson serves as a member of Ipsen's Executive Leadership Team. Mr. Paulson was Vice President and General Manager, U.S. Oncology Business Unit at Amgen Inc., a public biotechnology company, from 2015 to February 2018 and prior to that was Vice President, Marketing for Amgen's U.S. Oncology Business, General Manager, Amgen Germany and General Manager of Amgen Central & Eastern. Prior to Amgen, Mr. Paulson held a number of global leadership positions at Pfizer Inc. ("Pfizer"), including serving as General Manager of Pfizer South Africa and Pfizer Czech Republic. Mr. Paulson also previously held a variety of sales, marketing, and market access roles with increasing seniority at GlaxoWellcome plc in Canada. Mr. Paulson has an M.B.A. from the University of Toronto, Canada and an undergraduate degree in commerce from the University of Saskatchewan, Canada. We believe Mr. Paulson's qualifications to serve on our Board include his more than 25 years of global biopharmaceutical industry experience, as well as his achievements in leading and growing businesses, both in the U.S. and internationally.

Chen Schor, M.B.A., C.P.A. Mr. Schor has served as a member of our Board since November 2020. Mr. Schor has served as the President, Chief Executive Officer and Director of Adicet Bio, Inc. ("Adicet Bio"), a public biotechnology company, since September 2020. He held the role of President and Chief Executive Officer at resTORbio, Inc. ("resTORbio") since co-founding the company in July 2016 until its merger with Adicet Bio, Inc. in September 2020. Prior to co-founding resTORbio, Mr. Schor served as President, Chief Executive Officer and Director of Synta Pharmaceuticals Corporation from 2014 until July 2016. Previously, he served as Vice President, Global Branded Business Development and Pipeline Management at Teva Pharmaceuticals Industries Ltd. and held leadership positions at several emerging private and public companies. Before that, Mr. Schor was a Partner at Yozma Venture Capital, where he led the foundation and growth of multiple therapeutic companies from inception to commercial success. Mr. Schor has served on the board of directors of resTORbio/Adicet Bio since July 2016 and also served on the board of directors and audit committee of Brainstorm Cell Therapeutics Inc. from 2011 until March 2020. Mr. Schor has led strategic transactions valued at over \$8 billion with companies such as GlaxoSmithKline plc, Amgen Inc., Pfizer, Merck KGaA (co-led) and Cephalon, Inc. (co-led). Mr. Schor holds a B.A. in Biology and an M.B.A. from Tel Aviv University, a B.A. in Economics and Accounting from Haifa University and is a Certified Public Accountant. We believe Mr. Schor's qualifications to serve on our Board include his substantial transactional experience and extensive experience leading biotech companies across all stages, from formation and early stage discovery to a publicly traded multi-product company.

Recommendation of the Board of Directors:

OUR BOARD OF DIRECTORS UNANIMOUSLY RECOMMENDS THAT THE STOCKHOLDERS VOTE FOR THE ELECTION OF EACH OF DR. PAKIANATHAN AND MESSRS. PAULSON AND SCHOR AS A CLASS II DIRECTOR.

Members of the Board of Directors Continuing in Office**Term Expiring at the
2022 Annual Meeting of Stockholders (Class III)**

<u>Name</u>	<u>Age</u>	<u>Present Position with Karyopharm Therapeutics Inc.</u>
Garen G. Bohlin	73	Director
Mikael Dolsten, M.D., Ph.D.	62	Director
Michael G. Kauffman, M.D., Ph.D.	57	Chief Executive Officer and Director

Garen G. Bohlin. Mr. Bohlin has served as a member of our Board since October 2013. Since 2012, Mr. Bohlin has focused exclusively on service on boards of directors and consulting. From 2010 until his retirement in 2012, he served as Executive Vice President of Constellation Pharmaceuticals, Inc. (“Constellation”), a public biopharmaceutical company, where he served as a part-time business partner with the Chief Executive Officer. Prior to Constellation, Mr. Bohlin served as Chief Operating Officer of Sirtris Pharmaceuticals, Inc. (“Sirtris”), a biotechnology company, from 2006 to 2009, where he played key roles in the overall management of Sirtris, its initial public offering and the sale of the company to GlaxoSmithKline plc. Mr. Bohlin was the founding Chief Executive Officer of Syntonix Pharmaceuticals, Inc. (“Syntonix”), a biopharmaceutical company, from 1999 through 2008, where he played a key role in the overall management of Syntonix, positioning it for an eventual sale to Biogen Idec. Prior to Syntonix, Mr. Bohlin was Executive Vice President of Genetics Institute, Inc., a biotechnology company, where he played a key role in overall management, its initial public offering and its sale to American Home Products/Wyeth, and a partner at Arthur Andersen & Co., a public accounting and consulting organization. Mr. Bohlin has served on the board of directors and audit committee of Collegium Pharmaceutical, Inc., a public biopharmaceutical company, since 2015 and on the board of directors of Curadel Surgical Innovations, Inc., a private biopharmaceutical company, since March 2020. Mr. Bohlin previously served on the board of directors and audit committee of Tetrphase Pharmaceuticals, Inc., from 2010 through July 2020, and as a director of several other private and public biotechnology companies. Mr. Bohlin holds a B.S. in Accounting from the University of Illinois. We believe Mr. Bohlin’s qualifications to serve on our Board include his extensive industry and board experience, including his audit committee experience, with publicly traded and privately held biotechnology companies.

Mikael Dolsten, M.D., Ph.D. Dr. Dolsten has served as a member of our Board since March 2015. Dr. Dolsten has served as President of Worldwide Research, Development and Medical, Chief Scientific Officer and Executive Vice President of Pfizer, one of the largest public pharmaceutical companies in the world, since 2010. Dr. Dolsten served as President of Worldwide Research and Development and Senior Vice President of Pfizer from May 2010 until December 2010 and President of Pfizer BioTherapeutics Research & Development Group and Senior Vice President of Pfizer from 2009 until 2010. From 2008 to 2009, Dr. Dolsten served as Senior Vice President of Wyeth Pharmaceuticals, Inc., a public biopharmaceutical company that was acquired by Pfizer in 2009, and President of Wyeth Research from 2008 to 2009. Prior to joining Wyeth, Dr. Dolsten was a Private Equity Partner at Orbimed Advisors, LLC and Executive Vice President, Head of Pharma Research at Boehringer Ingelheim, a pharmaceutical company. Dr. Dolsten also previously held research leadership positions at AstraZeneca plc, Pharmacia and Upjohn Company. We believe Dr. Dolsten’s qualifications to serve on our Board include his depth of experience leading pharmaceutical research and development teams at large public companies. He is widely recognized as a leader within the medical research and drug development community and this level of expertise is significant to our Board as we continue to advance our clinical development pipeline and initiate additional clinical trials.

Michael G. Kauffman, M.D., Ph.D. Dr. Kauffman has served as Karyopharm’s Chief Executive Officer since 2011 and has been one of our directors since 2008. Dr. Kauffman co-founded Karyopharm with Dr. Sharon Shacham in 2008 and served as our President from 2011 to 2013 and as Chief Medical Officer from 2012 to 2013. Prior to joining Karyopharm, he was Chief Medical Officer of Onyx Pharmaceuticals Inc. (“Onyx”), a public biopharmaceutical company, from 2009 to 2010. From 2008 to 2009, Dr. Kauffman was Chief Medical Officer of Proteolix Inc.

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(“Proteolix”), which was acquired by Onyx. At Proteolix, he led the development of Kyprolis® (carfilzomib), a novel proteasome inhibitor approved in refractory myeloma by the U.S. Food and Drug Administration (“FDA”) in 2012. Dr. Kauffman was an operating partner at Bessemer Venture Partners from 2006 to 2008, where he led investments in biotechnology companies. From 2006 to 2008, he was President and Chief Executive Officer of Epix Pharmaceuticals, Inc. (“Epix”), a public biopharmaceutical company that underwent liquidation proceedings through an assignment for the benefit of creditors under Massachusetts law in 2009. Dr. Kauffman was President and Chief Executive Officer of Predix Pharmaceuticals, Inc. (“Predix”), a private biopharmaceutical company focused on G protein-coupled receptors, from 2002 until its merger into Epix in 2006. In that role, he led the merger of Predix and Epix, oversaw the discovery and development of four new clinical candidates and led collaboration transactions with Amgen and GlaxoSmithKline plc. From 2000 to 2002, Dr. Kauffman was Vice President, Clinical at Millennium Pharmaceuticals, Inc. (“Millennium”), a biopharmaceutical company, where he led the Velcade® development program. From 1997 to 2000, Dr. Kauffman held a number of senior positions at Millennium Predictive Medicine, Inc., a biopharmaceutical company and a subsidiary of Millennium, where he led the discovery and development of novel molecular diagnostics for major cancers, including melanoma and led transactions with Becton-Dickenson and Bristol Myers Squibb. From 1995 to 1997, Dr. Kauffman held a number of senior positions at Biogen Idec, Inc., a biopharmaceutical company, where he led the clinical development of anti-CD40L antibodies in autoimmune and inflammatory diseases, and acted as the main medical advisor to the Biogen business development group. Dr. Kauffman has served on the board of directors, the audit committee and as chairman of the compensation committee of Kezar Life Sciences, Inc., a public biopharmaceutical company, since December 2016 and has been the lead director and a member of the compensation committee of Verastem Inc., a public biopharmaceutical company, since 2012. Dr. Kauffman previously served on the board of directors, nominating and governance committee and research and development committee of Infinity Pharmaceuticals, Inc., a public biopharmaceutical company, from April 2017 to March 2020. Dr. Kauffman received his B.A. in Biochemistry from Amherst College and his M.D. and Ph.D. from Johns Hopkins Medical School, and he trained in internal medicine and rheumatology at Beth Israel Hospital (now Beth Israel Deaconess Medical Center) and Massachusetts General Hospital. He is board certified in internal medicine. We believe Dr. Kauffman’s qualifications to serve on our Board include his extensive experience in the healthcare industry as well his extensive knowledge of the Company and its business since inception through service in multiple executive leadership positions and as a member of our Board.

Term Expiring at the 2023 Annual Meeting of Stockholders (Class I)

<u>Name</u>	<u>Age</u>	<u>Present Position with Karyopharm Therapeutics Inc.</u>
Christy J. Oliger	51	Director
Barry E. Greene	57	Director
Mansoor Raza Mirza, M.D.	60	Director and Clinical Consultant

Christy J. Oliger. Ms. Oliger has served as a member of our Board since August 2020. Until August 2020, Ms. Oliger served in numerous leadership roles over twenty years at Genentech, Inc. (“Genentech”), a biotechnology company, including most recently as Senior Vice President of the Oncology Business Unit from January 2017 to August 2020, where she managed a portfolio of 15 products and approximately \$13.0 billion revenue, and Senior Vice President, Neuroscience and Rare Disease Business Unit at Genentech from 2014 to January 2017. During her tenure with Genentech, Ms. Oliger also held a number of senior leadership roles across a variety of therapeutic areas, including oncology, neurology, rare disease, respiratory, dermatology and immunology in hospital and specialty settings. Prior to Genentech, Ms. Oliger held management positions at Schering-Plough. Ms. Oliger holds a bachelor’s degree in Economics from the University of California at Santa Barbara. We believe Ms. Oliger’s qualifications to serve on our Board include her nearly thirty years of strategic and operational experience in the biopharmaceutical industry with broad commercial, portfolio management and leadership expertise, including in the oncology field.

Barry E. Greene. Mr. Greene has served as a member of our Board since 2013 and as our Lead Independent Director since 2015. Mr. Greene has served as Chief Executive Officer of Sage Therapeutics, Inc. (“Sage”), a public

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biopharmaceutical company, since December 2020. Mr. Greene served as President of Alnylam Pharmaceuticals, Inc. (“Alnylam”), a public biopharmaceutical company, from 2007 to September 2020, and as its Chief Operating Officer from 2003 to September 2016. Prior to Alnylam, he was General Manager of Oncology at Millennium Pharmaceuticals, Inc., a public biopharmaceutical company, where he led the company’s global strategy and execution for its oncology business, including strategic business direction and execution, culminating in the successful FDA approval and launch of Velcade® (bortezomib) in 2003. Prior to joining Millennium in 2001, Mr. Greene served as Executive Vice President and Chief Business Officer for Mediconsult.com, a healthcare consulting company. Prior to Mediconsult.com, Mr. Greene’s experience included serving as Vice President of Marketing and Customer Services for AstraZeneca (formerly AstraMerck), a public biopharmaceutical company; Vice President, Strategic Integration with responsibility for the AstraZeneca North American post-merger integration; and a partner of Andersen Consulting, a consulting company, where he was responsible for the pharmaceutical/biotechnology marketing and sales practice. Mr. Greene has served as a member of the board of directors of Sage since October 2020 and has served as a member of the board of directors of Acorda Therapeutics, Inc., a public biopharmaceutical company, since 2007, where he also serves as a member of its compensation committee. Mr. Greene received his B.S. in Industrial Engineering from the University of Pittsburgh and served as a Senior Scholar at Duke University’s Fuqua School of Business. We believe Mr. Greene’s qualifications to serve on our Board and as our Lead Independent Director include his extensive experience in the healthcare and consulting industries as well as his practical experience with business and product aspects of the biopharmaceutical industry, including guiding new drugs through research, development, and the commercialization process.

Mansoor Raza Mirza, M.D. Dr. Mirza has served as a member of our Board since October 2010. He has also served as a clinical consultant to us since 2010. Dr. Mirza has served as Chief Oncologist at the Department of Oncology, Rigshospitalet—the Copenhagen University Hospital, Denmark since 2009 and as Medical Director of the Nordic Society of Gynaecological Oncology since 2012. Dr. Mirza is Chairman and Executive Founding Member of the European Network of Gynaecological Oncological Trial groups. Dr. Mirza is both a medical and radiation oncologist, with a primary focus in non-surgical treatment of gynecologic cancers. His key academic goals are to promote clinical research, international trial collaboration and education, and he has broad experience in clinical protocol development, trial conduct and clinical trial regulations. Dr. Mirza is the author of several phase 1, 2 and 3 studies. Several of those studies led to FDA and European Medicines Agency registrations. He serves on several Independent Data Safety Monitoring Committees of international studies. He is an invited speaker at several international conferences, such as “Meet the Professor” at American Society of Clinical Oncology and “Presidential Symposium” at European Society for Medical Oncology. He is the author of global consensus guidelines for the management of ovarian cancer and of European guidelines for the management of several gynecological malignancies. His other current appointments include service as ESGO Council Member (European Society of Gynaecological Oncology), Executive Director of GCIG (Gynecologic Cancer InterGroup), Vice-Chairman of the Danish Gynecological Cancer Society, faculty member of the European Society of Medical Oncology and of ESGO. He also serves on the board of directors of Sera Prognostics, Inc., a private biopharmaceutical company. He has over 100 publications in high-impact journals, including several publications in the New England Journal of Medicine and the Lancet. He holds an M.D., Diploma in Surgery and Diploma in Clinical Oncology from the Pirogov Moscow State Medical Institute as well as post-graduate education and certification in radiation and medical oncology from the University of Southern Denmark. We believe Dr. Mirza’s qualifications to serve on our Board include his expertise in the non-surgical treatment of cancer, and gynecologic cancers in particular, and his knowledge of the Company and its business through service on our Board since 2010.

CORPORATE GOVERNANCE

General

We believe that good corporate governance is important to ensure the long-term benefit of our stockholders. This section describes key corporate governance practices that we have adopted, including a Code of Business Conduct and Ethics, which applies to all of our officers, directors and employees, Corporate Governance Guidelines, and charters for our Audit Committee, Compensation Committee, and Nominating, Corporate Governance & Compliance Committee. We have posted copies of our Code of Business Conduct and Ethics and the Corporate Governance Guidelines, as well as each of our committee charters, under the heading “*Corporate Governance*” in the “*Investors*” section of our website, www.karyopharm.com, which you can access free of charge. Information contained on the website is not incorporated by reference in, or considered part of, this proxy statement. We intend to disclose on our website any amendments to, or waivers from, our Code of Business Conduct and Ethics that are required to be disclosed by law or the Listing Rules of the Nasdaq Stock Market (“Nasdaq”). We will also provide copies of these documents as well as our other corporate governance documents, free of charge, to any stockholder upon written request to Karyopharm Therapeutics Inc., 85 Wells Avenue, Newton, Massachusetts 02459, Attention: Investor Relations.

Director Independence

Rule 5605 of the Nasdaq Listing Rules requires a majority of a listed company’s board of directors to be comprised of independent directors. In addition, the Nasdaq Listing Rules require that, subject to specified exceptions, each member of a listed company’s audit, compensation and nominations committees be independent and that audit and compensation committee members also satisfy independence criteria set forth in Rule 10A-3 and Rule 10C-1, respectively, under the Exchange Act.

Under Rule 5605(a)(2) of the Nasdaq Listing Rules, a director will only qualify as an “independent director” if, in the opinion of our Board, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In order to be considered independent for purposes of Rule 10A-3 of the Exchange Act, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee, accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries or otherwise be an affiliated person of the listed company or any of its subsidiaries.

In addition, in affirmatively determining the independence of any director who will serve on a company’s compensation committee, Rule 10C-1 under the Exchange Act requires that a company’s board of directors consider all factors specifically relevant to determining whether a director has a relationship to such company which is material to that director’s ability to be independent from management in connection with the duties of a compensation committee member, including, but not limited to: (a) the source of compensation of the director, including any consulting, advisory or other compensatory fee paid by such company to the director; and (b) whether the director is affiliated with the company or any of its subsidiaries or affiliates.

Our Board has reviewed the composition of our Board and its committees and the independence of each director. Based upon information requested from and provided by each director concerning his background, employment and affiliations, including family relationships, our Board has determined that each of our directors, with the exception of Dr. Kauffman, is an “independent director” as defined under Rule 5605(a)(2) of the Nasdaq Listing Rules. In making this determination, our Board considered the consulting agreements we have in place with each of Dr. Mirza and Ms. Oliger and concluded that neither constitutes a relationship that would interfere with such director’s exercise of independent judgment in carrying out his or her responsibilities as a director. Our Board also determined that Messrs. Bohlin and Paulson and Dr. Pakianathan, who currently comprise our Audit Committee; Dr. Pakianathan, Mr. Greene and Ms. Oliger, who comprise our Compensation Committee; and Messrs. Greene and Bohlin and Dr. Dolsten, who currently comprise our Nominating, Corporate Governance & Compliance Committee, satisfy the independence standards for such committees established by the SEC and the Nasdaq Listing Rules, as applicable.

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There are no family relationships among any of our directors or executive officers, except that Dr. Kauffman, our Chief Executive Officer and a director, is married to Dr. Shacham, our President and Chief Scientific Officer.

Board Leadership Structure

Our bylaws and Corporate Governance Guidelines provide our Board with flexibility to combine or separate the positions of Chairman of the Board and Chief Executive Officer and/or to implement the role of Lead Independent Director in accordance with its determination that utilizing one or the other structure would be in the best interests of the Company.

At this time, we do not have a Chairman of the Board, though our Board appointed Mr. Greene to serve as Lead Independent Director in 2015. While our Board believes that oversight of the Company is the responsibility of our Board as a whole, and this responsibility can be properly discharged without a Chairman or Lead Independent Director, our Board determined that appointing Mr. Greene as Lead Independent Director would facilitate interactions between Dr. Kauffman, our Chief Executive Officer, and the other independent directors and would enable the Board and the Company to utilize Mr. Greene's breadth of experience across many strategic and operational matters in biotechnology companies.

Mr. Greene serves as a liaison between our Chief Executive Officer and our independent directors. He meets regularly and communicates directly with the independent directors outside the presence of management and reports any comments and concerns of the independent directors to our Chief Executive Officer. He also meets regularly with our senior management to discuss operational and strategic matters. Mr. Greene presides over executive sessions of the Board and provides our Chief Executive Officer with an annual review, as well as regular feedback, based on the consensus views collected from members of our Board.

While Dr. Kauffman facilitates communications between members of our Board and works with management in the preparation of the agenda for each meeting of the Board, Mr. Greene also has an important role in establishing the agenda, determining what information is provided to our Board and coordinating with management to ensure that sufficient meeting time is allocated to each agenda item. Additionally, all of our directors are encouraged to make suggestions for agenda items or pre-meeting materials for meetings of our Board.

Our Board has concluded that the current leadership structure described above 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.

The Board's Role in Risk Oversight

Our Board has responsibility for the oversight of the Company's risk management processes and, either as a whole or through its committees, regularly discusses with management our major risk exposures, the potential impact of these risks on our business and the steps we take to manage them. The risk oversight process includes receiving regular reports from Board committees and members of senior management to enable our Board to understand the Company's risk identification, risk management and risk mitigation strategies with respect to areas of potential material risk, including the Company's corporate strategy, business objectives, compliance, financial condition, legal, regulatory, commercial and reputational risk. The committees of the Board execute their risk oversight responsibility for risk management as follows:

- The Audit Committee reviews information regarding liquidity and operations and oversees our management of financial risks as well as risks associated with cybersecurity. Periodically, the Audit Committee reviews our policies with respect to risk assessment, risk management, loss prevention and financial-related regulatory compliance. Oversight by the Audit Committee includes direct communication with our external auditors, and discussions with management regarding significant risk exposures and the actions management has taken to limit, monitor or control such exposures.

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- The Compensation Committee is responsible for the design and oversight of our executive compensation philosophy, policies, plans and practices, including ensuring that our overall executive compensation program appropriately links pay to performance and aligns the interests of our executives with our stockholders and that the elements of our compensation programs mitigate excessive risk-taking.
- The Nominating, Corporate Governance & Compliance Committee manages risks associated with the independence of members of our Board, corporate disclosure practices, potential conflicts of interest and corporate responsibility and sustainability efforts, including the impact of environmental and social issues on the Company. In July 2020, the Board disbanded its Compliance Committee, and delegated its roles and responsibilities to the Nominating, Corporate Governance & Compliance Committee, including oversight of our non-financial compliance program by monitoring our compliance policies, standards, procedures, systems and initiatives as well as our information technology systems dedicated to quality, regulatory and commercial compliance.
- The Commercialization Committee assists our Board with oversight of risks associated with our commercial and medical affairs strategies, plans and programs.

While each committee is responsible for evaluating certain risks and overseeing the management of such risks, the entire Board is regularly informed through committee reports about such risks. Matters of significant risk are considered by our Board as a whole.

Corporate Responsibility

We are highly committed to policies and practices focused on environmental, social and corporate governance (“ESG”) matters, positively impacting our communities and maintaining and cultivating good corporate governance. By focusing on such policies and practices, we believe we can affect a meaningful and positive change in our communities and maintain our open, collaborative corporate culture. Some of the initiatives that we were most proud of in 2020 included working with advocacy groups to donate thousands of personal protection equipment items to hospitals, cancer centers, veterans organizations, and various community groups across the U.S. and around the globe in response to the COVID-19 pandemic. We also actively support a number of scholarship and mentoring programs for students in underserved communities as well as those interested in pursuing degrees in science and technology. We strive to bring together employees with a wide variety of backgrounds, skills and culture and encourage all of our employees to maintain a work environment in which our differences are respected, including by providing diversity and inclusion training programs to our employees throughout the year. We continue to advance our efforts related to sustainability, including initiatives such as the addition of electric vehicle charging stations to be available to our employees in 2021 at our corporate headquarters. With the support and oversight of our Board, primarily through its Nominating, Corporate Governance & Compliance Committee, we plan to continue to advance our efforts related to corporate responsibility and sustainability initiatives.

Board of Directors Meetings

Our Board met ten times during the year ended December 31, 2020, including telephonic meetings. During 2020, each of our incumbent directors attended or participated telephonically in 75% or more of the aggregate of (a) the total number of meetings of the Board held during the period for which he or she served as a director and (b) the total number of meetings of all committees on which the director served during the periods that he or she served. We do not have a formal policy regarding attendance by members of our Board at our annual meeting of stockholders. Four members of our Board serving at the time attended our 2020 annual meeting of stockholders held on May 21, 2020 by teleconference.

Committees of the Board of Directors

Our Board currently has three standing committees: the Audit Committee, the Compensation Committee, and the Nominating, Corporate Governance & Compliance Committee. Each of these committees has a written charter

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approved by our Board. A copy of each charter can be found under the heading “*Corporate Governance*” in the “*Investors*” section of our website at www.karyopharm.com. In addition, the Board had a Compliance Committee until it was disbanded in July 2020 and also established an ad hoc Commercialization Committee in late 2020.

Audit Committee

The members of our Audit Committee currently include Messrs. Bohlin (Chair) and Paulson and Dr. Pakianathan. Mr. Garland previously served as a member of our Audit Committee until May 2020, at which time Mr. Paulson was appointed a member of the Audit Committee. Our Board has determined that Mr. Bohlin qualifies as an “audit committee financial expert” within the meaning of SEC regulations and the Nasdaq Listing Rules. In making this determination, our Board considered the formal education and nature and scope of Mr. Bohlin’s previous experience, coupled with past and present service on various audit committees. Our Audit Committee assists our Board in its oversight of our accounting and financial reporting process and the audits of our financial statements. The Audit Committee met nine times during 2020, including telephonic meetings. Pursuant to its charter, the Audit Committee’s general responsibilities currently include, among other things, the following:

- appointing, approving the compensation of, and assessing the independence of our registered public accounting firm;
- overseeing the work of our registered public accounting firm, including through the receipt and consideration of reports from such firm;
- reviewing and discussing with management and the registered public accounting firm our annual and quarterly financial statements and related disclosures;
- recommending to our Board whether the audited financial statements should be included in our annual report;
- monitoring our internal control over financial reporting, disclosure controls and procedures and Code of Business Conduct and Ethics;
- discussing our risk assessment and risk management policies;
- overseeing our information technology strategy and matters related to the security and risks related to information technology systems;
- establishing policies regarding hiring employees from the registered public accounting firm and procedures for the receipt, retention and treatment of accounting related complaints and concerns;
- meeting independently with our registered public accounting firm and management;
- reviewing and approving or ratifying any related person transactions; and
- preparing an annual audit committee report required by SEC rules.

Compensation Committee

The members of our Compensation Committee currently include Dr. Pakianathan (Chair), Mr. Greene and Ms. Oliger. Mr. Paulson served as a member of our Compensation Committee until August 2020, at which time Ms. Oliger was appointed a member of the Compensation Committee. Our Compensation Committee assists our Board in the discharge of its responsibilities relating to the compensation of our executive officers and Board members. The Compensation Committee met five times during 2020. Pursuant to its charter, the Compensation Committee’s general responsibilities currently include, among other things, the following:

- reviewing and approving, or recommending for approval by the Board, the compensation of our chief executive officer and our other executive officers;
- overseeing an evaluation of our senior executives;

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- overseeing and administering our incentive compensation and equity-based plans;
- reviewing and making recommendations to our Board with respect to non-employee director compensation; and
- reviewing and discussing with management our compensation disclosure required by SEC rules.

The Compensation Committee generally meets at least four times annually and with greater frequency if necessary. The agenda for each meeting is usually developed by the chair of the Compensation Committee, in consultation with our Chief Executive Officer, Chief People & Corporate Engagement Officer and/or our General Counsel. The Compensation Committee meets regularly in executive session. However, from time to time, various members of management and other employees, as well as outside advisors or consultants, may be invited by the Compensation Committee to make presentations, to provide financial or other background information or advice or to otherwise participate in Compensation Committee meetings. No officer may participate in, or be present during, any deliberations or determinations of the Compensation Committee regarding the compensation for such officer or any immediate family member of such officer. The charter of the Compensation Committee grants the Compensation Committee full access to all of our books, records, facilities, and personnel, as well as authority to obtain, at our expense, advice and assistance from internal and external legal, accounting, or other advisors and consultants, and other external resources that the Compensation Committee considers necessary or appropriate in the performance of its duties. In particular, the Compensation Committee has the sole authority to retain compensation consultants to assist in its evaluation of executive and director compensation, including the authority to approve the consultant's reasonable fees and other retention terms. In addition, under its charter, the Compensation Committee may form, and delegate authority to, subcommittees, consisting of independent directors, as it deems appropriate.

Historically, the Compensation Committee has approved (and, in the case of Drs. Kauffman and Shacham, the Compensation Committee has recommended to the Board and the Board has approved) significant adjustments to executives' annual compensation, determined variable cash compensation and equity awards, and established new performance objectives at one or more meetings held during the last quarter of the year and the first quarter of the following year. However, the Compensation Committee also considers matters related to individual compensation, such as compensation for new executive hires, as well as high-level strategic issues, such as the efficacy of our compensation strategy, potential modifications to that strategy, and new trends, plans, or approaches to compensation, at various meetings throughout the year. The Compensation Committee is responsible for making determinations, or making recommendations to our Board, regarding compensation of executive officers, making changes to pre-approved salary ranges, salary increase budgets, equity award budgets, variable cash compensation targets, incentive payments, and pre-approved equity ranges for new hires and high performers, and making material changes to benefits offered to our employees. In determining compensation of executive officers other than our Chief Executive Officer and President and Chief Scientific Officer, the Compensation Committee, with input from its compensation consultant, also considers the recommendations of our Chief Executive Officer and President and Chief Scientific Officer. In addition, the Compensation Committee, with input from its compensation consultant, makes recommendations to our Board regarding the compensation of non-employee directors. The Compensation Committee also administers our equity-based plans and determines whether to approve the maximum increases or smaller increases permitted to the number of shares reserved under our 2013 Stock Incentive Plan (the "2013 Plan") and 2013 Employee Stock Purchase Plan (the "2013 ESPP") that automatically occur each year pursuant to the "evergreen" provisions of such plans.

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Nominating, Corporate Governance & Compliance Committee

The members of our Nominating, Corporate Governance & Compliance Committee currently include Messrs. Greene (Chair) and Bohlin and Dr. Dolsten. The Nominating, Corporate Governance & Compliance Committee met seven times during 2020. As of July 2020, following the disbandment of the Compliance Committee, the Nominating, Corporate Governance & Compliance Committee assumed oversight of the Company's compliance-related duties and responsibilities. Pursuant to its charter, the Nominating, Corporate Governance & Compliance Committee's general responsibilities currently include, among other things, the following:

- identifying individuals qualified to become Board members consistent with the criteria approved by the Board;
- recommending to our Board the persons to be nominated for election as directors and to each committee of our Board;
- reviewing and making recommendations to our Board with respect to management succession planning;
- developing and recommending corporate governance guidelines to the Board;
- developing and overseeing periodic self-evaluations, which are generally conducted annually, to assess the effectiveness of our Board and its committees;
- overseeing the implementation of and monitoring the Company's non-financial compliance program, including policies, standards, procedures, systems and initiatives, with a focus on quality, regulatory and commercial compliance matters;
- evaluating, monitoring and discussing with senior management the adequacy and effectiveness of the Company's non-financial compliance program and compliance assurance systems and initiatives and considering recommendations for improvement thereof;
- making findings and recommendations to the Board regarding the adequacy of the Company's non-financial compliance program;
- assisting the Audit Committee in assessing financial risk arising from non-financial compliance matters;
- developing and overseeing an orientation program for new directors and a continuing education program for current directors; and
- reviewing the Company's corporate responsibility and sustainability efforts, including the impact of ESG issues on the Company.

Compliance Committee

Prior to its disbandment in July 2020, the members of the Compliance Committee, which met one time during 2020, were Messrs. Garland and Greene and Drs. Mirza and Dolsten.

Commercialization Committee

In late 2020, the Board established an ad hoc Commercialization Committee to provide advice and support to management and the commercial and medical affairs teams on our strategies, tactics, practices and policies that relate to commercial and medical affairs activities. Ms. Oliger and Messrs. Greene and Paulson serve on the Commercialization Committee, which generally meets on a monthly basis.

The responsibilities of the Commercialization Committee currently include:

- ensuring commercial and medical plans are consistent with our goals and objectives;
- ensuring that proper compliance measures are built into planning activities;

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- periodically conducting in-depth reviews of the commercial strategies for our currently marketed indications of XPOVIO and evaluating the resulting sales performance;
- reviewing commercial and medical launch strategies prior to regulatory approval of new products or indications; and
- providing other support as requested by the Board in maximizing the value of our products to patients.

Code of Business Conduct and Ethics

We have adopted a written Code of Business Conduct and Ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. We have posted on our website, www.karyopharm.com, a current copy of the Code of Business Conduct and Ethics and all disclosures that are required by law or Nasdaq listing rules concerning any amendments to, or waivers from, any provision of the Code of Business Conduct and Ethics. Information contained on the website is not incorporated by reference in, or considered part of, this proxy statement.

Director Nomination Process

Director Qualifications

In evaluating director nominees, the Nominating, Corporate Governance & Compliance Committee considers, among other things, the following factors:

- reputation for personal and professional integrity, honesty and adherence to high ethical standards;
- demonstrated business acumen, experience and ability to exercise sound judgments in matters that relate to the current and long-term objectives of the Company;
- commitment to understand the Company and its industry and to regularly attend and participate in meetings of the Board and its committees;
- interest and ability to understand the sometimes-conflicting interests of the various constituencies of the Company, which include stockholders, employees, customers, governmental units, creditors and the general public, and to act in the interests of all stockholders;
- diversity of expertise and experience in substantive matters pertaining to our business relative to other Board members;
- diversity of background and perspective, including with respect to age, gender, race, place of residence and specialized experience; and
- practical and mature business judgment, including the ability to make independent analytical inquiries.

The Nominating, Corporate Governance & Compliance Committee's goal is to assemble a Board that brings to the Company a variety of perspectives and skills derived from high quality business and professional experience. Moreover, the Nominating, Corporate Governance & Compliance Committee believes that the background and qualifications of the members of our Board, considered as a group, should provide a significant breadth of experience, knowledge and abilities to assist the Board in fulfilling its responsibilities. Nominees are not discriminated against on the basis of race, religion, national origin, sex, sexual orientation, disability, or any other basis proscribed by law.

The Nominating, Corporate Governance & Compliance Committee has not adopted a formal policy with respect to a fixed set of specific minimum qualifications for its candidates for membership on the Board. The committee considers such factors, including those set forth above, as it may deem are in the best interests of the Company and its stockholders. The committee further believes it is appropriate for at least one member of our Board to meet the criteria for an "audit committee financial expert" as that phrase is defined under the regulations promulgated by the SEC, and

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that a majority of the members of our Board be independent as required under the Nasdaq qualification standards. The Nominating, Corporate Governance & Compliance Committee believes it is appropriate for our Chief Executive Officer to serve as a member of our Board. Our directors' performance and qualification criteria are reviewed periodically by the Nominating, Corporate Governance & Compliance Committee.

Identification and Evaluation of Nominees for Directors

The Nominating, Corporate Governance & Compliance Committee identifies nominees for director by first evaluating the current members of our Board willing to continue in service. Current members with qualifications and skills that are consistent with the Nominating, Corporate Governance & Compliance Committee's criteria for service on the Board and who are willing to continue in service are considered for re-nomination, balancing the value of continuity of service by existing members of our Board with that of obtaining a new perspective or expertise. The Nominating, Corporate Governance & Compliance Committee reviews the overall service provided by these directors to the Company during their terms, including the number of meetings attended, level of participation, quality of performance and any other relationships and transactions that might impair the directors' independence, as well as the results of the Board's self-evaluation, which is generally conducted annually, to determine whether to recommend them to the Board for nomination for a new term.

If any member of our Board does not wish to continue to serve on the Board or if our Board decides not to re-nominate a member for re-election, and our Board seeks to fill such vacancy, the Nominating, Corporate Governance & Compliance Committee identifies a new nominee that meets the criteria above. The Nominating, Corporate Governance & Compliance Committee generally inquires of our Board and members of management for their recommendations, such as in the case of Chen Schor who was appointed to the Board in December 2020, and may also review the composition and qualification of the boards of directors of our competitors or seek input from industry experts or analysts. The Nominating, Corporate Governance & Compliance Committee then reviews the qualifications, experience, and background of suggested candidates. Final candidates, if other than our current directors, are interviewed by the members of the Nominating, Corporate Governance & Compliance Committee and by certain of our other independent directors and executive management. In making its determinations, the Nominating, Corporate Governance & Compliance Committee evaluates each individual in the context of our Board as a whole, with the objective of assembling a group that can best contribute to the success of the Company and represent stockholder interests through the exercise of sound judgment. After review and deliberation of all feedback and data, the Nominating, Corporate Governance & Compliance Committee makes its recommendation to our Board. The Nominating, Corporate Governance & Compliance Committee has previously engaged a search firm to conduct a search for additional directors with extensive development or commercialization expertise to join our Board. In 2020, the Nominating, Corporate Governance & Compliance Committee retained Spencer Stuart to conduct two searches to identify new candidates to serve on the Board. The searches resulted in the appointment of Richard Paulson in February 2020 and Christy Olinger in August 2020. The Nominating, Corporate Governance & Compliance Committee may in the future engage additional third-party search firms in those situations where particular qualifications are required or where existing contacts are not sufficient to identify an appropriate candidate.

We have not received director candidate recommendations from our stockholders and do not have a formal policy regarding consideration of such recommendations. However, any recommendations received from stockholders will be evaluated in the same manner that potential nominees suggested by board members, management, or other parties are evaluated. Stockholders wishing to recommend a director candidate for consideration by our Nominating, Corporate Governance & Compliance Committee must submit such recommendation in writing to our principal executive offices at Karyopharm Therapeutics Inc., 85 Wells Avenue, Newton, Massachusetts 02459, Attention: Corporate Secretary. Such recommendation must be received by us no later than February 20, 2022. Such submissions must state the nominee's name, together with appropriate biographical information and background materials, and information with respect to the stockholder or group of stockholders making the recommendation, including the number of shares of common stock owned by such stockholder or group of stockholders. We may require any proposed nominee to furnish such other information as we may reasonably require to determine the eligibility of the proposed nominee to serve as an independent director or that could be material to a reasonable stockholder's understanding of the independence, or lack thereof, of such proposed nominee.

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Stockholders also have the right under our bylaws to directly nominate director candidates, without any action or recommendation on the part of the Nominating, Corporate Governance & Compliance Committee or the Board, by following the procedures set forth below under “*Stockholder Proposals*.” If our Board determines to nominate a stockholder-recommended candidate and recommends his or her election, then his or her name will be included in our proxy statement and proxy card for the next annual meeting of stockholders. Otherwise, candidates nominated by stockholders in accordance with the procedures set forth in the bylaws will not be included in our proxy statement and proxy card for the next annual meeting.

Limits on Director Service on Other Company Boards

We have a highly effective and engaged Board, and we believe that our directors’ service on other companies’ boards enable them to contribute valuable knowledge and perspective to our Board activities. Nonetheless, the Board is sensitive to the external obligations of its directors and the potential for overboarding to compromise their ability to effectively serve the Company. Our Corporate Governance Guidelines limit each director’s service on other boards of public companies to a number that permits them, given their individual circumstances, to responsibly perform all director duties. Directors who serve as chief executive officers of a public company may not serve on more than two public company boards other than the board of the company of which he or she is chief executive officer. All other directors may not serve on more than five public company boards.

Communications with Our Board of Directors

Stockholders seeking to communicate with our Board must submit their written comments to Karyopharm Therapeutics Inc., 85 Wells Avenue, Newton, Massachusetts 02459, Attention: Corporate Secretary. The Corporate Secretary will forward such communications to each member of our Board; provided that, if in the opinion of our Corporate Secretary it would be inappropriate to send a particular stockholder communication to a specific director, such communication will only be sent to the remaining directors (subject to the remaining directors concurring with such opinion).

Director Compensation

We compensate non-employee members of our Board for their service using a combination of cash and equity compensation. Directors who are also employees, such as Dr. Kauffman, do not receive any compensation for service on the Board in addition to compensation payable for their service as our employees. The non-employee members of our Board are also reimbursed for travel, lodging, and other reasonable expenses incurred in attending Board or committee meetings.

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The Compensation Committee, based on an evaluation of our peer group conducted by Compensia, Inc. (“Compensia”) in 2019 and 2020, recommended, and the Board approved, the following changes to our non-employee director compensation in order to align our director compensation to the median of our respective peer group.

Compensation Type	January - May 2020	May 2020 – August 2020	August 2020 - May 2021	Post May 2021
Annual Cash Retainers				
Board				
All non-employee directors	\$ 40,000	\$ 50,000	\$ 50,000	\$ 50,000
Additional retainer—Lead Independent Director or independent Chairman	\$ 35,000	\$ 35,000	\$ 35,000	\$ 35,000
Audit Committee				
Chair	\$ 20,000	\$ 20,000	\$ 20,000	\$ 20,000
Non-chair members	\$ 10,000	\$ 10,000	\$ 10,000	\$ 10,000
Compensation Committee				
Chair	\$ 15,000	\$ 15,000	\$ 15,000	\$ 20,000
Non-chair members	\$ 7,500	\$ 7,500	\$ 7,500	\$ 10,000
Nominating, Corporate Governance & Compliance Committee(1)				
Chair	\$ 10,000	\$ 10,000	\$ 20,000	\$ 20,000
Non-chair members	\$ 5,000	\$ 5,000	\$ 10,000	\$ 10,000
Compliance Committee(1)				
Chair	\$ 17,000	\$ 17,000	\$ —	\$ —
Non-chair members	\$ 8,000	\$ 8,000	\$ —	\$ —
Commercialization Committee(2)				
Chair	\$ —	\$ —	\$ 20,000	\$ 20,000
Non-chair members	\$ —	\$ —	\$ 10,000	\$ 10,000
Initial Stock Option Award (Shares)(3)				
	50,000	32,800	32,800	47,800
Annual Stock Option Award (Shares)(4)				
	25,000	16,400	16,400	23,900

- (1) The Compliance Committee of the Board was disbanded in July 2020 and its duties and responsibilities were assumed by the Nominating, Corporate Governance & Compliance Committee. In August 2020, the Board amended the director compensation program to increase the annual cash retainer for the members of the Nominating, Corporate Governance & Compliance Committee and its Chair to \$10,000 and \$20,000, respectively, as a result of the additional compliance-related responsibilities.
- (2) In November 2020, the Board amended the director compensation program to provide for an annual cash retainer of \$10,000 for the members of the Commercialization Committee effective October 1, 2020 and in April 2021 approved an annual cash retainer for its Chair of \$20,000, effective March 18, 2021.
- (3) This is a one-time non-qualified stock option award granted upon initial election to our Board. The stock option vests with respect to one-third of the shares on the first anniversary of the grant date and with respect to an additional 1/36th of the total number of shares underlying the grant at the end of each successive month following the first anniversary of the grant date until the third anniversary of the grant date.
- (4) This non-qualified stock option award is granted after each annual meeting of stockholders and vests in full on the first anniversary of the grant date. Beginning on May 21, 2021, if a non-employee director is elected or appointed to our Board at a time other than at our annual meeting of stockholders, the number of shares of our common stock subject to such annual grant will be pro-rated based on the number of days served by such director through the date immediately preceding the date of the annual meeting of stockholders.

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The stock options granted to our non-employee directors for service on our Board have an exercise price equal to the fair market value of our common stock on the date of grant, expire ten years after the date of grant, and are subject to the director's continued service on our Board.

To the extent that a non-employee director has other responsibilities to the Company in addition to service on our Board, such director may receive additional compensation as deemed appropriate by our Board, or any Board committee delegated authority in such respect.

In April 2021, our Board, upon the recommendation of our Compensation Committee, revised the compensation guidelines for non-employee directors, to become effective upon the adjournment of the Annual Meeting. The changes to the compensation guidelines are shown in the table above and are as follows:

- annual cash retainers for the Compensation Committee Chair and its non-chair members will increase to \$20,000 and \$10,000, respectively;
- the Chair of the Commercialization Committee will receive an annual cash retainer of \$20,000, effective March 18, 2021;
- the annual stock option award, granted after each annual meeting of stockholders to each non-employee director, will be an option to purchase 23,900 shares, which vests in full on the first anniversary of the grant date, subject to the director's continued service (for directors who joined the Board in the prior 12 months, this award will be pro-rated as described above); and
- new non-employee directors joining our Board will receive a non-qualified stock option to purchase a number of shares of our common stock equal to two times the number of shares of our common stock underlying the most recent annual stock option award, which vests with respect to one-third of the shares on the first anniversary of the grant date and with respect to an additional 1/36th of the total number of shares underlying the grant at the end of each successive month following the first anniversary of the grant date until the third anniversary of the grant date, subject to the director's continued service.

All other elements of the compensation guidelines for non-employee directors remain unchanged.

The following table sets forth the compensation paid to or earned by our non-employee directors during the year ended December 31, 2020.

2020 Director Compensation

<u>Name(1)</u>	<u>Fees Earned or Paid In Cash \$(2)</u>	<u>Option Awards \$(3)</u>	<u>All Other Compensation (\$)</u>	<u>Total (\$)</u>
Garen G. Bohlin(4)	73,327	208,679	—	282,006
Mikael Dolsten, M.D.(5)	57,806	208,679	—	266,485
Scott Garland(6)	25,953	—	—	25,953
Barry E. Greene(7)	110,007	208,679	—	318,686
Mansoor Raza Mirza, M.D.(8)	50,605	208,679	90,000(9)	349,284
Christy J. Oliger(10)	22,188	321,834	9,016(11)	353,038
Deepika R. Pakianathan, Ph.D.(12)	71,126	208,679	—	279,805
Richard Paulson, M.B.A.(13)	52,377	1,079,219	—	1,131,596
Chen Schor, M.B.A., C.P.A.(14)	5,027	320,305	—	325,332

(1) Dr. Kauffman, one of our directors who also serves as our Chief Executive Officer, does not receive any compensation for his service as a director.

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- (2) Represents cash compensation earned or paid for services rendered by each non-employee member of our Board for their services on our Board or a committee thereof.
- (3) Amounts listed represent the aggregate grant date fair value of stock options awarded to our non-employee directors calculated in accordance with Financial Accounting Standards Board Accounting Standards Codification Topic 718 (“ASC 718”). Assumptions used in the calculation of these amounts are described in Note 12, *Stock-based Compensation*, to our consolidated financial statements included in our 2020 Annual Report. Pursuant to the terms of the non-employee director compensation policy in effect on the date of grant and in connection with each director’s initial election to the Board: Mr. Paulson was awarded a stock option to purchase 50,000 shares of our common stock on March 5, 2020, with a grant date fair value of \$870,540; Ms. Oliger was awarded a stock option to purchase 32,800 shares of our common stock on August 28, 2020, with a grant date fair value of \$321,834; and Mr. Schor was awarded a stock option to purchase 32,800 shares of our common stock on November 25, 2020, with a grant date fair value of \$320,305. Further, each non-employee director serving on the Board on May 21, 2020, the date of our 2020 annual meeting of stockholders, was awarded a stock option to purchase 16,400 shares of our common stock, with a grant date fair value of \$208,679.
- (4) As of December 31, 2020, Mr. Bohlin held outstanding stock options to purchase 116,006 shares of our common stock.
- (5) As of December 31, 2020, Dr. Dolsten held outstanding stock options to purchase 115,400 shares of our common stock.
- (6) Mr. Garland did not stand for re-election at our 2020 annual meeting of stockholders. Amount reflects fees earned by Mr. Garland during 2020 prior to the annual meeting of stockholders. As of December 31, 2020, Mr. Garland held outstanding stock options to purchase 99,000 shares of our common stock.
- (7) As of December 31, 2020, Mr. Greene held outstanding stock options to purchase 116,006 shares of our common stock.
- (8) As of December 31, 2020, Dr. Mirza held outstanding stock options to purchase 85,400 shares of our common stock.
- (9) Represents \$90,000 earned by Mirza Consulting, an entity wholly-owned by Dr. Mirza, for consulting and advisory services provided to us by Dr. Mirza in 2020 pursuant to a consulting agreement between the Company and Dr. Mirza.
- (10) Ms. Oliger joined the Board in August 2020. As of December 31, 2020, Ms. Oliger held outstanding stock options to purchase 32,800 shares of our common stock.
- (11) Represents \$9,016 earned by Ms. Oliger in 2020 for consulting and advisory services provided to us pursuant to a consulting agreement between the Company and Ms. Oliger.
- (12) As of December 31, 2020, Dr. Pakianathan held outstanding stock options to purchase 125,400 shares of our common stock.
- (13) Mr. Paulson joined the Board in February 2020. As of December 31, 2020, Mr. Paulson held outstanding stock options to purchase 66,400 shares of our common stock.
- (14) Mr. Schor joined the Board in November 2020. As of December 31, 2020, Mr. Schor held outstanding stock options to purchase 32,800 shares of our common stock.

Limitation of Liability and Indemnification

Our certificate of incorporation limits the personal liability of directors for breach of fiduciary duty to the maximum extent permitted by the Delaware General Corporation Law and provides that no director will have personal liability to us or to our stockholders for monetary damages for any breach of fiduciary duty as a director. However, these provisions do not eliminate or limit the liability of any of our directors:

- for any breach of the director’s duty of loyalty to us or our stockholders;

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- for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law;
- for voting or assenting to unlawful payments of dividends, stock repurchases, or other distributions; or
- for any transaction from which the director derived an improper personal benefit.

Any amendment to or repeal of these provisions will not eliminate or reduce the effect of these provisions in respect of any act, omission or claim that occurred or arose prior to such amendment or repeal. If the Delaware General Corporation Law is amended to provide for further limitations on the personal liability of directors of corporations, then the personal liability of our directors will be further limited to the greatest extent permitted by the Delaware General Corporation Law.

In addition, our certificate of incorporation provides that we must indemnify our directors and officers, and we must advance expenses, including attorneys' fees, to our directors and officers in connection with legal proceedings, subject to very limited exceptions.

We maintain an insurance policy that covers certain liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers. In addition, we have entered into indemnification agreements with our directors. These indemnification agreements require us, among other things, to indemnify each such director for some expenses, including attorneys' fees, judgments, fines, and settlement amounts incurred by him in any action or proceeding arising out of his service as one of our directors.

Certain of our non-employee directors may, through their relationships with their employers, be insured and/or indemnified against certain liabilities incurred in their capacity as members of our Board.

Insofar as indemnification for liabilities arising under the Securities Act of 1933, as amended (the "Securities Act") may be permitted to directors, executive officers or persons controlling us, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Report of the Audit Committee of the Board of Directors

The Audit Committee oversees the Company's financial reporting process on behalf of the Board of Directors. We have reviewed the Company's audited consolidated financial statements for the year ended December 31, 2020 and discussed them with Company management and Ernst & Young LLP, the Company's independent registered public accounting firm for the year ended December 31, 2020.

We have received from, and discussed with, Ernst & Young LLP, which is responsible for expressing an opinion on the conformity of the Company's audited consolidated financial statements with accounting principles generally accepted in the United States, its judgments as to the quality, not just the acceptability, of the Company's accounting principles and such other matters as are required to be discussed with the Audit Committee under generally accepted auditing standards, including the matters required to be discussed by the applicable requirements of the Public Company Accounting Oversight Board ("the "PCAOB") and the SEC. In addition, we have discussed with Ernst & Young LLP its independence from management and the Company, have received from Ernst & Young LLP the written disclosures and the letter required by applicable requirements of the PCAOB regarding its communications with us concerning independence, and have considered the compatibility of non-audit services with the auditors' independence.

Based on the review and discussions referred to above, we 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 year ended December 31, 2020.

This report of the Audit 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 Audit Committee.

Respectfully submitted,
The Audit Committee of the Board of Directors
Garen G. Bohlin (Chair)
Deepika R. Pakianathan
Richard Paulson

**PROPOSAL 2:
ADVISORY VOTE ON THE COMPENSATION OF OUR NAMED EXECUTIVE OFFICERS**

We are providing our stockholders the opportunity to vote to approve, on an advisory basis, the compensation of our NEOs as disclosed in this proxy statement in accordance with the SEC's rules. This proposal, which is commonly referred to as "say-on-pay," is required by the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010, which added Section 14A to the Exchange Act.

We encourage stockholders to read closely the "*Executive Compensation*" section of this proxy statement beginning on page 28, which describes in detail our executive compensation programs and the decisions made by our Compensation Committee and our Board with respect to the year ended December 31, 2020.

As we describe in the "*Narrative Disclosure to Summary Compensation Table*," we maintain straightforward executive compensation programs that consist almost entirely of base salary, an annual cash incentive bonus and annual equity awards. These elements of compensation have been selected by our Compensation Committee because the committee believes that they effectively achieve the fundamental goals of our compensation program, which are to attract, motivate and retain qualified and talented executives who are critical to our success, motivating them to achieve our business goals and rewarding them for superior short- and long-term performance. One of the goals of our Compensation Committee is to ensure that our compensation programs are aligned with the interests of our stockholders and our business goals in order to attain our ultimate objective of increasing stockholder value. We believe that, consistent with these goals, the total compensation paid to each of our NEOs is fair, reasonable and competitive. Further, we believe our programs do not encourage excessive risk-taking by management.

We do not provide any compensation or benefit plans to executive officers that are not also available to other employees. We differentiate among executive officers primarily based on size of annual cash incentive awards and annual equity awards and, to a lesser extent, base salary. Annual compensation decisions for executive officers are made by our Compensation Committee and Board based on the achievement of specified corporate performance goals as described under "*Narrative Disclosure to Summary Compensation Table*."

Our Board is asking stockholders to approve, on an advisory basis, the following resolution:

RESOLVED, that the compensation paid to Karyopharm Therapeutics Inc.'s named executive officers, as disclosed pursuant to the compensation disclosure rules of the SEC, including the compensation tables and any related material disclosed in this proxy statement, is hereby approved.

As an advisory vote, this proposal is not binding. The outcome of this advisory vote does not overrule any decision by the Company or the Board (or any committee thereof), create or imply any change to the fiduciary duties of the Company or the Board (or any committee thereof), or create or imply any additional fiduciary duties for the Company or the Board (or any committee thereof). However, our Compensation Committee and Board value the opinions expressed by our stockholders in their vote on this proposal and will consider the outcome of the vote when making future compensation decisions for NEOs.

THE BOARD UNANIMOUSLY RECOMMENDS THAT STOCKHOLDERS VOTE "FOR" THE APPROVAL OF THE COMPENSATION OF OUR NAMED EXECUTIVE OFFICERS.

EXECUTIVE COMPENSATION

This section discusses the material elements of our executive compensation policies and important factors relevant to an analysis of these policies. It provides qualitative information regarding the manner and context in which compensation is awarded to and earned by our NEOs named in the “*Summary Compensation Table*” below and is intended to place in perspective the information presented in the following tables and the corresponding narrative.

Summary Compensation Table

The following table sets forth information regarding compensation earned by each of our NEOs during the years ended December 31, 2020 and 2019. Our NEOs include Dr. Michael Kauffman, our Chief Executive Officer; Dr. Sharon Shacham, our President and Chief Scientific Officer; and Mr. Michael Mason, our Senior Vice President, Chief Financial Officer, and Treasurer.

Summary Compensation Table

Name and Principal Position	Year	Salary (\$)	Stock Awards \$(1)	Option Awards \$(1)	Non-Equity Incentive Plan Compensation \$(2)	All Other Compensation \$(3)	Total (\$)
Michael G. Kauffman, M.D., Ph.D. <i>Chief Executive Officer</i>	2020	625,624	1,029,886	1,920,899	348,750	11,880	3,937,039
	2019	566,500	803,112	1,486,339	363,693	11,860	3,231,504
Sharon Shacham, Ph.D., M.B.A. <i>President and Chief Scientific Officer</i>	2020	483,624	1,029,886	1,920,899	224,595	11,880	3,670,884
	2019	468,500	803,112	1,486,339	250,648	11,860	3,020,459
Michael Mason, M.B.A., C.P.A.(4) <i>Senior Vice President, Chief Financial Officer and Treasurer</i>	2020	415,624	586,963	1,096,226	156,123	11,880	2,266,816
	2019	340,332	—	529,935(5)	75,000	11,430	956,697

- (1) Amounts listed represent the aggregate grant date fair value of restricted stock units (“RSUs”) (with respect to the “Stock Awards” column) and stock options (with respect to the “Option Awards” column) granted to our NEOs during 2020 and 2019, calculated in accordance with ASC 718. Stock option awards are valued using a Black-Scholes option-pricing model and RSUs are valued by multiplying the closing market price of a share of our common stock on the grant date by the number of RSUs granted. Assumptions used in the calculation of these amounts are set forth in Note 12, *Stock-based Compensation*, included in our 2020 Annual Report.
- (2) Represents awards to our NEOs under our annual performance-based cash incentive program. See “*Narrative Disclosure to Summary Compensation Table—Components of Executive Compensation -Annual Performance-Based Cash Incentives*” for a description of that program. Annual bonus compensation for 2019 was earned in 2019 and paid in 2020 and annual bonus compensation for 2020 was earned in 2020 and paid in 2021.
- (3) For 2020, “all other compensation” includes the following: (a) life and accidental death and dismemberment insurance premiums in the amount of \$480 paid by us on behalf of each of Drs. Kauffman and Shacham and Mr. Mason and (b) 401(k) plan matching contributions in the amount of \$11,400 for each of Drs. Kauffman and Shacham and Mr. Mason. For 2019, “all other compensation” includes the following: (a) life and accidental death and dismemberment insurance premiums in the amounts of \$660 paid by us on behalf of each of Drs. Kauffman and Shacham and \$550 paid by us on behalf of Mr. Mason and (b) 401(k) plan matching contributions in the amount of \$11,200 for each of Drs. Kauffman and Shacham and \$10,880 for Mr. Mason.

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- (4) Mr. Mason's 2019 salary and bonus payment each reflect a pro-rated amount for the time he was employed by the Company in 2019.
- (5) This stock option was granted to Mr. Mason as a new hire award in connection with the commencement of his employment with the Company in February 2019. This grant was made outside of our stockholder approved equity plan in reliance on NASDAQ Listing Rule 5635(c)(4).

Narrative Disclosure to Summary Compensation Table

Our Compensation Committee is responsible for overseeing the total compensation of our senior management team, which is comprised of our executive officers and certain other senior managers. In this capacity, our Compensation Committee designs, implements, reviews and approves all compensation for our executive officers, except that in the case of Drs. Kauffman and Shacham, the Board approves all compensation-related matters based on the review and recommendation of the Compensation Committee. In addition, the Compensation Committee seeks to ensure that our compensation programs are aligned with the interests of our stockholders and our business goals and that the total compensation paid to each of our NEOs is fair, reasonable and competitive. Key elements of our 2020 compensation programs included:

Compensation Element	Purpose	Features
Base salary	To attract, retain and reward talented executives needed to drive our business.	Fixed component of compensation to provide financial stability, based on responsibilities, experience, internal equity, performance and peer company data.
Annual cash incentive program	To promote and reward the achievement of key short-term objectives and align executive and stockholder interests.	Variable component of compensation tied to the achievement of pre-determined quantitative and qualitative corporate performance goals.
Equity incentive compensation	To encourage executives to deliver long-term Company performance, align executive and stockholder interests and promote retention.	Variable component of compensation in the form of stock options and RSUs typically subject to multi-year vesting based on continued service with value tied to the performance of our common stock price.

Executive Compensation Program Best Practices

Our Compensation Committee believes that a strong foundation for our compensation program is necessary to execute our executive compensation philosophy effectively. The following best practices serve as the foundation for our executive compensation program:

What We Do

- | | |
|---|---|
| ✓ | Use a mix of short- and long-term incentive compensation, with an emphasis on long-term compensation. |
| ✓ | Use a mix of fixed and variable compensation, with an emphasis on variable, at-risk performance-based compensation. |
| ✓ | Compare against peer companies. |
| ✓ | Require a “double-trigger” (both a change in control and termination without cause or for good reason) for cash payments and accelerated vesting of equity awards. |
| ✓ | Engage independent consultants to advise our Compensation Committee on topics related to board and executive compensation. |
| ✓ | Assess risk of incentive compensation policies and programs. |
| ✓ | Certain of our executive officers, including our NEOs, are subject to a clawback policy under which we can recover incentive compensation in the event that we are required to prepare an accounting restatement due to material noncompliance with financial statement requirements. |

What We Don't Do

- | | |
|---|---|
| × | Offer our executive team substantially enhanced benefits or perquisites when compared to our employee population. |
| × | Provide our executive officers with guaranteed annual salary increases or guaranteed bonuses. |
| × | Provide any excise or income tax gross-ups on severance or other payments in the event of a change in control. |
| × | Permit repricing of underwater stock options without stockholder approval under the 2013 Plan. |
| × | Permit hedging transactions by our directors, officers or other employees with our securities and we restrict pledging of our securities. |

Determining and Setting Executive Compensation

We develop our compensation programs after reviewing publicly available compensation data and subscription survey data for our peer group, provided by an independent compensation consulting firm engaged by our Compensation Committee. For setting 2020 compensation, our Compensation Committee engaged Compensia as its independent compensation consultant, to advise on executive compensation matters including: executive compensation philosophy, overall compensation program design, peer group development and updates, and benchmarking executive officer and director compensation programs. Our Compensation Committee assessed the independence of Compensia consistent with Nasdaq Listing Rules and concluded that the engagement of Compensia did not raise any conflict of interest. The Company paid the cost for Compensia's services; however, the Compensation Committee retained the sole authority to direct, terminate, or engage Compensia's services and Compensia reported directly to the Compensation Committee. Compensation paid to Compensia for services not related to executive and director compensation and provided during 2020 was less than \$120,000.

Defining and Comparing Compensation to Market Benchmarks

In evaluating the total compensation of our NEOs, our Compensation Committee, using information provided by Compensia, established a peer group comprised of 18 companies selected primarily on the basis of the following criteria:

- Publicly-traded;
- Primary operations in the biotechnology and pharmaceuticals industry;

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- Commercial-stage or with product candidates pending approval; and
- Comparable market capitalization.

With input from senior management, in late 2019 the Compensation Committee discussed, reviewed and approved the updated peer group based on the above criteria. Accordingly, the Compensation Committee conducted its 2020 executive compensation review utilizing the following peer group.

2020 Peer Group		
Aerie Pharmaceuticals, Inc.	Blueprint Medicines Corporation	ImmunoGen, Inc.
Agenus Inc.	ChemoCentryx, Inc.	Ironwood Pharmaceuticals, Inc.
Agios Pharmaceuticals, Inc.	Collegium Pharmaceutical, Inc.	Progenics Pharmaceuticals Inc.*
Aimmune Therapeutics, Inc.*	Corcept Therapeutics, Inc.	Radius Health, Inc.
Akebia Therapeutics, Inc.	Deciphera Pharmaceuticals, Inc.	Spectrum Pharmaceuticals, Inc.
BioCryst Pharmaceuticals, Inc.	Epizyme, Inc.	ZIOPHARM Oncology Inc.

* Progenics Pharmaceuticals Inc. and Aimmune Therapeutics, Inc. were each acquired by another company in June 2020 and October 2020, respectively.

We believe that the compensation practices of our 2020 peer group provided us with appropriate compensation benchmarks for evaluating the compensation of our NEOs during 2020. We strive to ensure that the total compensation levels for our executives are competitive with peer companies so that we can attract and retain high performing key executive talent. Notwithstanding the similarities of the 2020 peer group to our company, due to the nature of our business, we compete for executive talent with larger public companies across our industry that are more established than we are or that possess greater resources than we do, and with smaller private companies that may be able to offer greater equity compensation potential. Therefore, in evaluating the compensation of our executives, the Compensation Committee utilizes the companies in our peer group primarily as reference points to determine the 50th percentile of our peers and then assesses each individual executive's compensation using subjective measures, such as individual and Company performance levels, uniqueness of skillsets and demand for particular talent to make adjustments as needed.

Components of Executive Compensation

The primary elements of our executive compensation program include:

- base salaries;
- annual performance-based cash incentive awards;
- equity incentive awards;
- health and welfare benefits and other employee benefits; and
- severance and change in control benefits.

The value of our variable, performance-based compensation is allocated between short-term compensation in the form of a cash bonus and long-term compensation in the form of stock option and RSU awards that vest over time from the date of grant. The annual cash bonus is intended to provide an incentive to our executives to achieve short-term operational objectives. The stock option and RSU awards are intended to provide an incentive for our executives to achieve longer-term strategic business goals, which should lead to higher stock prices and increased stockholder value. We have not had any formal or informal policy or target for allocating compensation between long-term and short-term compensation, between cash and non-cash compensation, or among the different forms of non-cash compensation. Instead, the Compensation Committee, after reviewing industry information and our cash and equity resources, determines subjectively what it believes to be the appropriate level and mix of the various compensation components.

We do not have any defined benefit pension plans or any non-qualified deferred compensation plans.

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We are party to employment arrangements with each of our NEOs, which are described below under the caption “*Executive Compensation—Employment, Severance and Change in Control Arrangements.*”

Base Salaries

We provide base salaries to our NEOs to compensate them with a fair and competitive base level of compensation for services rendered during the year. Base salaries for our NEOs typically are established through arm’s-length negotiation at the time the executive is hired, taking into account responsibilities, experience, internal equity and peer company data. On an annual basis, our Compensation Committee reviews and evaluates, with input from our Chief Executive Officer and President and Chief Scientific Officer, for executives other than themselves, the need for adjustment of the base salaries of our NEOs based on changes and expected changes in the scope of an NEO’s responsibilities.

The Compensation Committee also considers promotions, the individual contributions made by, and performance of, the executive during the prior year, the executive’s performance over a period of years, overall labor market conditions, the relative ease or difficulty of replacing the executive with a well-qualified person, our overall growth and development as a company, general salary trends in our industry and among our peer group and where the executive’s salary falls in the salary range presented by that data. We do not provide for any formulaic base salary increases for our NEOs and none of our executive officers is currently party to an employment agreement that provides for automatic or scheduled increases in base salary.

Merit-based increases in base salary for all of our executive officers (other than Drs. Kauffman and Shacham) are determined by our Compensation Committee and merit-based increases in base salary for Drs. Kauffman and Shacham are determined by our Board based on the recommendation of our Compensation Committee.

As part of our annual compensation review, in February 2020 the Compensation Committee approved Mr. Mason’s annual base salary and recommended to the Board, and the Board approved, the annual base salaries for Drs. Kauffman and Shacham for 2020. In determining and recommending these annual base salaries, the Compensation Committee reviewed the market compensation data presented by Compensia and considered each executive officer’s performance. Accordingly, the base salaries, on an annualized basis, of our NEOs for 2019 and 2020 were as follows:

<u>Name</u>	<u>2019 Base Salary</u>	<u>2020 Base Salary</u>
Michael G. Kauffman, M.D., Ph.D.	\$ 566,500	\$ 625,000
Sharon Shacham, Ph.D., M.B.A.	\$ 468,500	\$ 483,000
Michael Mason, M.B.A., C.P.A.	\$ 400,000	\$ 415,000

Annual Performance-Based Cash Incentives

Our Compensation Committee aims to determine an appropriate mix of cash payments and equity incentive awards to meet short- and long-term goals and objectives. Annual performance-based cash incentive awards are paid to our executive officers under the Karyopharm Annual Bonus Plan (the “Bonus Plan”), which was established in August 2019 to attract, motivate, and retain employees by promoting and rewarding the achievement of key short-term corporate objectives as well as individual performance and to align the interests of employees and stockholders. The target amount for the annual bonus opportunity for all of our executive officers (other than Drs. Kauffman and Shacham) is generally determined at the outset of the year by the Compensation Committee (and, in the case of Drs. Kauffman and Shacham, the Compensation Committee recommends to the Board and the Board approves the target bonus amount). Pursuant to the terms of the Bonus Plan, the amount of each executive officer’s annual bonus is based on the level of achievement of pre-established corporate goals, as described below, in combination with the level of achievement of the executive officer’s individual goals, with higher weighting to Company performance as an executive’s level of responsibility increases. Following the end of a plan year, the Compensation Committee determines the Company’s overall actual corporate performance for that plan year as a cumulative percentage of the

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Company's corporate goals achieved and in combination with the executive officer's individual score, as applicable. Partial or excess achievement as compared to the original goal weighting may be determined for each goal, at the discretion of the Compensation Committee.

In making its determination regarding the 2020 annual performance-based cash incentive awards, in February 2021, the Compensation Committee scored the 2020 corporate goals and awarded the Company 93% based on the following conclusions:

<u>2020 Corporate Goals</u>	<u>Relative Weighting</u>	<u>Award Value</u>	<u>Weighted Performance</u>
Submit a supplemental New Drug Application ("sNDA") and receive FDA approval of XPOVIO based on the BOSTON Study and submit a Marketing Authorization Application based on the BOSTON Study	30%	125%	37.5%
Secure FDA approval of XPOVIO based on the SADAL Study	10%	125%	12.5%
Submit an sNDA based on the SEAL Study	10%	50%	5%
Secure European Medicines Agency approval of selinexor based on the STORM Study	5%	— %	— %
Meet planned year-end revenue targets for U.S. XPOVIO sales	25%	60%	15%
First patient enrolled in the confirmatory study required pursuant to the DLBCL FDA approval	5%	— %	— %
Achieve three key organizational objectives related to employee retention, employee onboarding and compliance training	5%	100%	5%
Achieve target year-end cash	7%	100%	7%
Adherence to latest expense forecast	3%	100%	3%
Additional points were awarded by the Compensation Committee to recognize the Company's accomplishments and numerous achievements over and above the previously approved goals in light of the challenges to all aspects of its operations due to the unprecedented COVID-19 pandemic.			8%
Approved 2020 Corporate Performance Level	100%		93%

For each of the 2020 corporate goals, our Compensation Committee set both "target" performance levels, reflecting achievement of the goal for the period, and "aggressive" performance levels, reflecting exceptional performance. When establishing the 2020 goals, the Board determined, in its discretion, that achievement of the target goal set would be worth 100% and achievement of the aggressive goal set would be worth 125% of the target metric, such as an aggressive goal set for receiving FDA approval by the end of 2020 of XPOVIO in combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy (the "BOSTON Study"). The Compensation Committee determined that for all of the 2020 corporate goals, target or aggressive performance was fully or partially achieved other than for the goals related to (a) approval in the European Union of selinexor in combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, at least two immunomodulatory agents, and an anti- CD38 monoclonal antibody (the "STORM Study"); and (b) the first patient enrolled in the confirmatory study required pursuant to the FDA approval of XPOVIO to treat adult patients with relapsed or refractory diffuse large B-cell lymphoma ("DLBCL"), not otherwise specified, including DLBCL arising from follicular lymphoma, after at least two lines of systemic therapy (the "SADAL Study"), which were not achieved and therefore awarded zero points. In addition to scoring the achievements

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of the pre-established corporate goals for a total of 85%, the Compensation Committee recognized that at the time the goals were determined, neither the Company nor the Compensation Committee was aware of the impending COVID-19 pandemic or the extent of its impact. The Compensation Committee, therefore, determined it would be appropriate to award an extra 8% to the corporate performance score in recognition of management's strong leadership in guiding the Company through the extraordinary challenges it faced during 2020 and for the additional accomplishments that could not be contemplated at the time the corporate goals were set.

The Compensation Committee based its determinations above, among other factors, on the significant progress on our commercial, clinical development and business goals, including:

- Achievement of the aggressive goal of FDA approval by the end of 2020 of XPOVIO based on the results of the BOSTON Study, which was received in December 2020, three months prior to its Prescription Drug User Fee Act target date;
- Achievement of the aggressive goal of FDA approval by the end of June 2020 of XPOVIO based on the results of the SADAL Study, which was received in June 2020;
- Partial performance related to a Phase 3 portion of a randomized, double blind, placebo-controlled, cross-over study evaluating treatment with XPOVIO in patients with unresectable dedifferentiated liposarcoma study (the "SEAL Study");
- Partial performance related to year-end revenue target for net U.S. product sales of XPOVIO by recording \$76.2 million of net product revenue in 2020, in part due to the negative impact of the COVID-19 pandemic;
- Achievement of our three employee engagement and compliance objectives, as described in the table above; and
- Achievement of our target year-end cash goal and adherence to our latest Board-approved expense forecast.

Based on our overall performance during 2020, our Compensation Committee determined that we achieved 85% of our corporate goals for 2020, plus an additional 8% awarded in light of the numerous achievements during the COVID-19 pandemic over and above the pre-established corporate goals, for a total score of 93%. The 2020 bonus amounts for Drs. Kauffman and Shacham were determined solely on the scoring of the Company's corporate goals and the bonus amount for Mr. Mason was determined based on a weighting of 85% to Company performance and 15% to individual performance. The Compensation Committee determined that Mr. Mason achieved an individual performance score of 100% based on his 2020 accomplishments, including his significant contributions toward ensuring that the Company's operating expenses and cash balances were in line with the 2020 budget, managing the Company's overall finance, accounting, reporting and IT functions, ensuring a strong internal control environment, managing the relationship with the Company's audit and tax advisors and successfully managing an equity offering in February 2020. The Compensation Committee approved the 2020 performance bonus for Mr. Mason and recommended to the Board, and the Board approved, the 2020 performance bonus for Drs. Kauffman and Shacham, all of which were paid in February 2021, to each of the NEOs as follows:

Name	2020 Target Bonus (as a % of Base Salary)	Target Bonus Award (\$)	2020 Bonus Received (\$)	Actual Bonus (as a % of Target)
Michael G. Kauffman, M.D., Ph.D.	60%	375,000	348,750	93%
Sharon Shacham, Ph.D., M.B.A.	50%	241,500	224,595	93%
Michael Mason, M.B.A., C.P.A.	40%	166,000	156,123	94%

Equity Incentive Awards

We use our equity awards program to encourage executives to deliver long-term Company performance, align executive and stockholder interests and promote retention. The market for qualified and talented executives in the biopharmaceutical industry is highly competitive and we compete for talent with many companies that have greater

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resources than we do. Accordingly, we believe equity compensation is a crucial component of any competitive executive compensation package we offer.

Historically, our equity awards have generally taken the form of stock options and RSUs. We typically grant stock options and/or RSUs to each of our executive officers upon commencement of employment, annually in conjunction with our review of individual performance, in connection with a promotion or as a special incentive.

Equity awarded to our executive officers is approved by our Compensation Committee or Board, with any equity awards for Drs. Kauffman and Shacham approved by the Board only. Annual equity awards are generally granted at the beginning of each year. Equity awards may vary among our executive officers based on their positions and annual performance assessments. In addition, our Compensation Committee reviews all components of the executive's compensation to ensure that his or her total compensation is aligned with our overall philosophy and objectives. All stock options granted to our executives have exercise prices equal to the fair market value of our common stock on the date of grant, so that the recipient will not earn any compensation from his or her options unless our share price increases above the exercise price on the date of grant. Accordingly, this portion of our executive officers' compensation is at risk and is directly aligned with stockholder value creation.

The equity awards granted to our executive officers generally vest over four years. Typically, the stock options we grant to our executives have a ten-year term and vest as to 25% of the shares on the first anniversary of the grant date and then monthly thereafter until the fourth anniversary of such date and the RSUs vest as to 25% of the shares on each of the four anniversaries of the grant date. Vesting of equity awards to employees ceases upon termination of engagement with the Company and exercise rights for stock options typically cease three months following termination of engagement with the Company, except in the case of death or disability.

In February 2020, our Compensation Committee approved Mr. Mason's annual equity incentive awards and recommended to the Board, and the Board approved, the annual equity incentive awards for Drs. Kauffman and Shacham. The exercise price of the stock options was \$18.00, equal to the closing price per share of the Company's common stock on the Nasdaq Global Select Market on February 5, 2020, the grant date.

<u>Name</u>	<u>Option Awards (#)</u>	<u>RSU Awards (#)</u>
Michael G. Kauffman, M.D., Ph.D.	153,500	57,200
Sharon Shacham, Ph.D., M.B.A.	153,500	57,200
Michael Mason, M.B.A., C.P.A.	87,600	32,600

Given the shared responsibility for oversight of our operations and business activities, in determining the annual equity incentive awards for each of Drs. Kauffman and Shacham in 2020, the target amounts for Drs. Kauffman and Shacham were aggregated and the Board (based on the recommendation of the Compensation Committee) allocated 50% of such aggregate amount to each of Drs. Kauffman and Shacham in order to align long-term value creation incentives across our two most senior executives.

Benefits and Other Compensation

Health and Welfare Benefits

Our NEOs are eligible to participate in all of our employee benefit plans, including our medical, dental, vision, group life and disability insurance plans, in each case on the same basis as other employees. We believe that these health and welfare benefits help ensure that we have a productive and focused workforce through reliable and competitive health and other benefits.

401(k) Retirement Plan

We maintain a 401(k) retirement plan that is intended to be a tax-qualified defined contribution plan under Section 401(k) of the Internal Revenue Code of 1986, as amended (the "Code"). In general, all of our U.S.-based employees aged 18 or older are eligible to participate in the 401(k) plan upon commencement of their employment.

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The 401(k) plan includes a salary deferral arrangement pursuant to which participants may elect to reduce their current compensation by up to the statutorily prescribed limit, equal to \$19,500 in 2020 (an additional \$6,500 in contributions is allowed for participants age 50 and over). We also match employee contributions to our 401(k) plan, up to a maximum of 4% of an employee's cash compensation during each pay period.

Severance and Change in Control Benefits

Under our employment arrangements with our NEOs, we have agreed to provide severance and other benefits in the event of the termination of their employment under specified circumstances. We have provided more detailed information about these benefits, under the caption "*Executive Compensation—Employment, Severance and Change in Control Arrangements*" below.

We believe providing severance and/or change in control benefits as a component of our compensation structure can help us compete for executive talent and attract and retain highly talented executive officers whose contributions are critical to our long-term success. After consultation with Compensia, we believe that our severance and change in control benefits are appropriate.

Tax and Accounting Considerations

Section 162(m) of the Code generally disallows a tax deduction to public companies for compensation in excess of \$1 million paid in any taxable year to each of the Company's chief executive officer, chief financial officer and three most highly compensated officers (other than the chief executive officer and chief financial officer). Historically, compensation paid to our chief financial officer and compensation that qualified under Section 162(m) as performance-based compensation was exempt from the deduction limitation. However, subject to certain transition rules, tax reform legislation signed into law in December 2017, expanded the deduction limitation to apply to compensation in excess of \$1 million paid in any taxable year to our chief financial officer and eliminated the qualified performance-based compensation exception. As a result, for taxable years beginning after December 31, 2017, all compensation in excess of \$1 million paid to each of the executives described above (other than certain grandfathered compensation) will not be deductible by us. Our Board and Compensation Committee reserve the right to use their business judgment to authorize compensation payments that may be subject to the limitations under Section 162(m) when the Board or Compensation Committee, as applicable, believe that compensation is appropriate and in the best interests of the company and our stockholders, after taking into consideration changing business conditions and performance of our employees.

Hedging and Pledging Policy

We have an insider trading policy that is applicable to all of our employees and members of our Board. The policy prohibits those individuals and their related persons from engaging in any speculative transactions involving our stock, including the following activities: short sales of our securities, including short sales "against the box"; purchases or sales of puts, calls or other derivative securities based on our securities; standing orders with brokers other than under an approved trading plan, purchases of financial instruments (including prepaid variable forward contracts, equity swaps, collars and exchange funds) that are designed to hedge or offset any decrease in the market value of our securities; the purchase of our securities on margin; borrowing against our securities held in a margin account; or pledging our securities as collateral for a loan. However, an exception may be granted where a person wishes to pledge our securities as collateral for a loan (other than a margin loan) and clearly demonstrates the financial capacity to repay the loan without resort to the pledged securities. Any person who wishes to pledge our securities as collateral for a loan must submit a request for approval to our principal financial officer. In addition, any such request by a director or executive officer must also be reviewed and approved by the Audit Committee.

Clawback Policy

In February 2021, we adopted a Clawback Policy, which provides that if we are required to prepare an accounting restatement due to our material non-compliance with any financial reporting requirements under federal

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securities laws, then the Board or a duly established committee thereof may require certain officers, including our named executive officers, to repay or forfeit any “excess compensation” in the event it finds, in its sole discretion, that the executive officer contributed to the circumstances requiring the restatement and that it involved either (a) intentional misconduct or an intentional violation of any of the Company’s rules or applicable legal or regulatory requirements or (b) fraud. “Excess compensation” refers to the pre-tax amount in excess of what would have been paid to the executive officer under the accounting restatement of any incentive-based compensation that is granted, earned or vested based on the attainment of a performance measure during the three-year period preceding the date on which we are required to prepare such accounting restatement. The policy applies to incentive-based compensation granted after the adoption of this policy.

Outstanding Equity Awards at December 31, 2020

The following table sets forth information regarding outstanding equity awards held by each of our NEOs at December 31, 2020.

Name	Grant Date	Option Awards(1)				Stock Awards(1)(2)	
		Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable(1)	Option Exercise Price (\$)(1)	Option Expiration Date(1)	Number of Shares or Units of Stock That Have Not Vested (#) (1)	Market Value of Shares or Units of Stock That Have Not Vested (\$)(2)
Michael G. Kauffman, M.D., Ph.D.	09/03/2013	333,561(3)	—	4.75	09/02/2023	—	—
	12/18/2013	140,000	—	23.66	12/17/2023	—	—
	01/19/2015	200,000	—	26.65	01/18/2025	—	—
	01/15/2016	170,000	—	6.54	01/14/2026	—	—
	01/20/2017	244,791	5,209	10.39	01/19/2027	—	—
	01/24/2018	145,833	54,167	10.45	01/23/2028	—	—
	02/15/2019	105,966	125,234	9.21	02/14/2029	—	—
	02/15/2019	—	—	—	—	65,400	1,012,392
	02/05/2020	—	153,500	18.00	02/04/2030	—	—
	02/05/2020	—	—	—	—	57,200	885,456
Sharon Shacham, Ph.D., M.B.A.	09/03/2013	377,803(3)	—	4.75	09/02/2023	—	—
	12/18/2013	140,000	—	23.66	12/17/2023	—	—
	01/19/2015	200,000	—	26.65	01/18/2025	—	—
	01/15/2016	170,000	—	6.54	01/14/2026	—	—
	01/20/2017	244,791	5,209	10.39	01/19/2027	—	—
	01/24/2018	145,833	54,167	10.45	01/23/2028	—	—
	02/15/2019	105,966	125,234	9.21	02/14/2029	—	—
	02/15/2019	—	—	—	—	65,400	1,012,392
	02/05/2020	—	153,500	18.00	02/04/2030	—	—
	02/05/2020	—	—	—	—	57,200	885,456
Michael Mason, M.B.A., C.P.A.	02/25/2019	68,750	81,250	5.06	02/24/2029	—	—
	02/05/2020	—	87,600	18.00	02/04/2030	—	—
	02/05/2020	—	—	—	—	32,600	504,648

- (1) Unless otherwise specified: (a) all option and RSU awards were granted under our 2013 Plan; (b) all option awards have a ten-year term; (c) all option awards vest over four years from the grant date, with 25% vesting on the first anniversary of the grant date and the remainder vesting in equal monthly installments over the next three years thereafter; and (d) all RSU awards vest in equal annual installments over a four-year period beginning on the first anniversary of the grant date. In addition, the exercise price for all stock option awards set forth in this table is the fair market value of a share of our common stock on the date of grant.

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- (2) Each RSU entitles the holder thereof to receive one share of our common stock for each RSU granted upon vesting or settlement. The market value is calculated by multiplying \$15.48, the closing price of a share of our common stock on December 31, 2020, the last trading day of the year, as reported on Nasdaq, by the number of unvested units.
- (3) This award was granted under the Amended and Restated 2010 Stock Incentive Plan (the “2010 Plan”).

Employment, Severance and Change in Control Arrangements

We have entered into employment arrangements with each of our NEOs pursuant to which such NEOs are employed “at will,” meaning the executive or we may terminate the employment arrangement at any time. These agreements establish the NEO’s title, initial compensation arrangements, eligibility for benefits made available to employees generally and also provide for certain benefits upon termination of employment under specified conditions. On August 25, 2020, the Compensation Committee approved certain modifications to the benefits to be provided upon termination of employment for each of our NEOs. The following summarizes the termination benefits under our NEOs’ existing employment arrangements, as amended to date. Receipt of these termination benefits is subject to the NEO’s execution of a general release of claims.

If we terminate Dr. Kauffman’s employment without cause or if Dr. Kauffman resigns for good reason, in either case, prior to a change in control, we will be required to pay as severance to Dr. Kauffman his base salary for 18 months. If we terminate Dr. Kauffman’s employment without cause or if Dr. Kauffman resigns for good reason, in either case, after a change in control, we will be required to pay as severance to Dr. Kauffman his base salary for 18 months and 150% of his target annual bonus for the year in which the termination occurs. If Dr. Kauffman elects to continue his and his eligible dependents’ participation in our medical and dental benefit plans pursuant to the Consolidated Omnibus Budget Reconciliation Act of 1986 (“COBRA”), we will pay the monthly premium to continue such coverage until the earlier of (a) 18 months from termination and (b) the time at which group healthcare coverage is provided to Dr. Kauffman under another employer’s employee benefit plan.

If we terminate Dr. Shacham’s employment without cause or if Dr. Shacham resigns for good reason, in either case, prior to a change in control, we will be required to pay as severance to Dr. Shacham her base salary for 18 months. If we terminate Dr. Shacham’s employment without cause or if Dr. Shacham resigns for good reason, in either case, after a change in control, we will be required to pay as severance to Dr. Shacham her base salary for 18 months and 150% of her target annual bonus for the year in which the termination occurs. If Dr. Shacham elects to continue her and her eligible dependents’ participation in our medical and dental benefit plans pursuant to COBRA, we will pay the monthly premium to continue such coverage until the earlier of (a) 18 months from termination and (b) the time at which group healthcare coverage is provided to Dr. Shacham under another employer’s employee benefit plan.

If we terminate Mr. Mason’s employment without cause or if Mr. Mason resigns for good reason, in either case, prior to a change of control, we will be required to pay as severance to Mr. Mason his base salary for 12 months. If we terminate Mr. Mason’s employment without cause or if Mr. Mason resigns for good reason, in either case, within one year following the consummation of a change of control, we will be required to pay as severance to Mr. Mason his base salary for 12 months and 100% of his target bonus for the year in which the termination occurs. If Mr. Mason elects to continue his and his eligible dependents’ participation in the Company’s medical and dental benefit plans pursuant to COBRA, the Company will pay the monthly premium to continue such coverage until the earlier of (a) 12 months from termination and (b) the time at which group healthcare coverage is provided to Mr. Mason under another employer’s employee benefit plan.

Equity Compensation Plans and Other Benefits

2013 Stock Incentive Plan

Our Board adopted, and our stockholders approved, the 2013 Plan, which became effective immediately prior to the closing of our initial public offering. The 2013 Plan provides for the grant of incentive stock options, non-qualified

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stock options, stock appreciation rights, restricted stock awards, RSU awards, and other stock-based awards. As of March 26, 2021, 1,046,092 shares of our common stock were reserved for issuance under the 2013 Plan. Additional shares of our common stock may also become available for issuance under the 2013 Plan. The number of such additional shares is equal to the sum of (a) the number of shares of our common stock subject to outstanding awards under the 2010 Plan that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by us at their original issuance price pursuant to a contractual repurchase right and (b) an annual increase to be added on the first day of each fiscal year, until, and including, the year ending December 31, 2023, equal to the least of (a) 1,939,393 shares of our common stock, (b) 4% of the number of shares of our common stock outstanding on the first day of each fiscal year, and (c) an amount determined by our Board.

Our employees, officers, directors, consultants, and advisors as well as employees, officers, directors, consultants, and advisors of any of our present or future parent or subsidiary corporations and any other business venture (including, without limitation, joint venture or limited liability company) in which we have a controlling interest, as determined by our Board, are eligible to be granted awards under the 2013 Plan. However, incentive stock options may only be granted to employees who are eligible to receive incentive stock options under the Code.

The 2013 Plan is administered by our Board, a committee appointed by our Board or one or more officers appointed by such committee or the Board. Pursuant to the terms of the 2013 Plan, our Board or such committee or officers (subject to the below) selects the recipients of awards and determines:

- the number of shares of our common stock covered by options and the conditions and limitations applicable to the exercise of options;
- the type of options to be granted;
- the duration of options, which may not be in excess of ten years;
- the exercise price of options, which must be at least equal to the fair market value of our common stock on the date of grant; and
- the number of shares of our common stock subject to any stock appreciation rights, restricted stock awards, RSU awards, or other stock-based awards and the terms and conditions of such awards, including conditions for vesting and repurchase (or forfeiture), issue price and repurchase price (provided that the measurement price of stock appreciation rights must be at least equal to the fair market value of our common stock on the date of grant and the duration of stock appreciation rights may not be in excess of ten years).

Our Board has delegated its powers under the 2013 Plan to our Compensation Committee. Further, our Compensation Committee has delegated the authority to certain members of our senior management to grant stock option and RSU awards to new employees below the level of vice president, subject to specified limitations.

In the event of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spin-off or other similar change in capitalization or event, or any dividend or distribution to holders of our common stock other than an ordinary cash dividend, our Board is required by the 2013 Plan to make equitable adjustments, in a manner determined by our Board, to:

- the number and class of securities available under, and the share counting rules set forth in, the 2013 Plan;
- the number and class of securities and exercise price per share of each outstanding option;
- the share and per-share provisions and measurement price of each outstanding stock appreciation right;
- the number of shares and the repurchase price per share subject to each outstanding restricted stock award or RSU award; and
- the share and per-share-related provisions and purchase price, if any, of any other outstanding stock-based award.

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In connection with a merger or other reorganization event (as defined in the 2013 Plan), our Board may take any one or more of the following actions as to all or any portion of any outstanding awards other than restricted stock, on such terms as it determines:

- provide that all outstanding awards shall be assumed, or substantially equivalent awards shall be substituted, by the acquiring or succeeding corporation (or an affiliate thereof);
- upon written notice to a participant, provide that all of the participant's unvested and/or unexercised awards will terminate immediately prior to the consummation of such reorganization event unless exercised by the participant (to the extent then exercisable) within a specified period following the date of such notice;
- in the event of a reorganization event pursuant to which holders of shares of our common stock will receive a cash payment for each share surrendered in the reorganization event, make or provide for a cash payment to participants with respect to each award held by a participant equal to (a) the number of shares of our common stock subject to the vested portion of the award (after giving effect to any acceleration of vesting that occurs upon or immediately prior to such reorganization event) multiplied by (b) the excess, if any, of the cash payment for each share surrendered in the reorganization event over the exercise, measurement or purchase price of such award and any applicable tax withholdings, in exchange for termination of such award; and/or
- provide that in connection with our liquidation or dissolution, awards shall convert into the right to receive liquidation proceeds (if applicable, net of the exercise, measurement or purchase price thereof and any applicable tax withholdings).

Our Board is not obligated under the 2013 Plan to treat all awards, all awards held by a participant, or all awards of the same type, identically in connection with a reorganization event.

In the case of RSU awards that are subject to Section 409(a) of the Code, no assumption or substitution will be permitted and the RSU awards will instead be settled in accordance with the terms of the applicable RSU agreement, and in certain circumstances, any unvested RSU awards will be terminated immediately prior to the consummation of the reorganization event without any payment in exchange therefor.

Upon the occurrence of a reorganization event other than our liquidation or dissolution, the repurchase and other rights with respect to outstanding awards of restricted stock will continue for the benefit of the successor company and will, unless our Board otherwise determines, apply to the cash, securities or other property into which our common stock was converted into or exchanged for pursuant to the reorganization event in the same manner and to the same extent as they applied to such restricted stock. Upon the occurrence of a reorganization event involving our liquidation or dissolution, all restrictions and conditions on all restricted stock then outstanding will automatically be deemed terminated or satisfied, unless otherwise provided in the instrument evidencing the award of restricted stock or any other agreement between a participant and us.

At any time, our Board may provide that any award under the 2013 Plan shall become immediately exercisable in whole or in part, free of some or all restrictions or conditions, or otherwise realizable in whole or in part, as the case may be.

In addition, the 2013 Plan provides that, notwithstanding the provisions of the plan that may apply upon a reorganization event and except as otherwise provided for in the instrument evidencing an option or award of restricted stock or any other agreement between us and the participant, upon the occurrence of a change in control event (as defined in the 2013 Plan) each option shall become immediately exercisable and each award of restricted stock shall become immediately free from all conditions and restrictions, if, in either case, the employment of the participant holding such award is terminated by us (or our acquiring or succeeding corporation) without cause (as defined in the 2013 Plan) or by the participant for good reason (as defined in the 2013 Plan), on or prior to the first anniversary of the date of the change in control event. Our Board may specify in an award at the time of grant the effect of a change in control event on any stock appreciation right, RSU or other stock-based award.

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Except with respect to certain actions requiring stockholder approval under the Code or the rules of the Nasdaq Stock Market, our Board may amend, modify or terminate any outstanding award under the 2013 Plan, including but not limited to, substituting therefor another award of the same or a different type, changing the date of exercise or realization, and converting an incentive stock option into a non-qualified stock option, subject to certain participant consent requirements. Unless our stockholders approve such action, the 2013 Plan provides that we may not (except as otherwise permitted in connection with a change in capitalization or reorganization event):

- amend any outstanding stock option or stock appreciation right granted under the 2013 Plan to provide an exercise or measurement price per share that is lower than the then-current exercise or measurement price per share of such outstanding award;
- cancel any outstanding option or stock appreciation right (whether or not granted under the 2013 Plan) and grant in substitution therefor new awards under the 2013 Plan (other than substitute awards permitted in connection with a merger or consolidation of an entity with us or our acquisition of property or stock of another entity) covering the same or a different number of shares of our common stock and having an exercise or measurement price per share lower than the then-current exercise or measurement price per share of the cancelled award;
- cancel in exchange for a cash payment any outstanding option or stock appreciation right with an exercise or measurement price per share above the then-current fair market value of our common stock; or
- take any other action that constitutes a “repricing” within the meaning of the rules of the Nasdaq Stock Market.

No award may be granted under the 2013 Plan after October 21, 2023, however, awards previously granted may extend beyond that date. Our Board may amend, suspend or terminate the 2013 Plan or any portion thereof at any time, subject to certain stockholder approval requirements and limitations under the Code.

2013 Employee Stock Purchase Plan

Our Board adopted, and our stockholders approved, the 2013 ESPP in 2013. The 2013 ESPP is administered by our Board or by a committee appointed by our Board. The Board has delegated authority for administering the 2013 ESPP to our Compensation Committee. The 2013 ESPP provides participating employees with the opportunity to purchase shares of our common stock. As of March 26, 2021, 855,104 shares of our common stock were reserved for issuance under the 2013 ESPP. Additional shares of our common stock may also become available for issuance under the 2013 ESPP. The number of shares of our common stock reserved for issuance under the 2013 ESPP will automatically increase on the first day of each fiscal year through December 31, 2023, in an amount equal to the least of (a) 484,848 shares of our common stock, (b) 1% of the total number of shares of our common stock outstanding on the first day of the applicable year, and (c) an amount determined by our Board.

All of our employees and employees of any of our designated subsidiaries, as defined in the 2013 ESPP, are eligible to participate in the 2013 ESPP, provided that:

- such person is customarily employed by us or a designated subsidiary for more than 20 hours a week and for more than five months in a calendar year;
- such person has been employed by us or by a designated subsidiary for at least 30 days prior to enrolling in the 2013 ESPP; and
- such person was our employee or an employee of a designated subsidiary on the first day of the applicable offering period.

No employee may purchase shares of our common stock under the 2013 ESPP in excess of \$25,000 of the fair market value of our common stock (as of the date of the option grant) in any calendar year. In addition, no employee may purchase shares of our common stock under the 2013 ESPP that would result in the employee owning 5% or more of the total combined voting power or value of our stock.

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Each offering to our eligible employees to purchase stock under the 2013 ESPP will consist of a six-month offering period during which payroll deductions will be made and held for the purchase of our common stock at the end of the offering period. Our Board may, at its discretion, choose a different period of not more than 12 months for offerings. The first six-month offering period under the 2013 ESPP began on May 1, 2014 and subsequent offering periods occur over each successive six-month period thereafter until the Board determines otherwise.

Prior to the commencement date of each offering period, each eligible employee may authorize up to a maximum of 15% of his or her compensation to be deducted by us during the offering period. Each employee who continues to be a participant in the 2013 ESPP on the last business day of the offering period will be deemed to have exercised an option to purchase from us the number of whole shares of our common stock that his or her accumulated payroll deductions on such date will pay for, not in excess of the maximum numbers set forth above. Under the terms of the 2013 ESPP, the purchase price shall be determined by our Board for each offering period and will be at least 85% of the applicable closing price of our common stock. If our Board does not make a determination of the purchase price, the purchase price will be 85% of the lesser of the closing price of our common stock on the first business day of the offering period or on the last business day of the offering period.

An employee may for any reason withdraw from participation in an offering prior to the end of an offering period and permanently draw out the balance accumulated in the employee's account. If an employee elects to discontinue his or her payroll deductions during an offering period but does not elect to withdraw his or her funds, funds previously deducted will be applied to the purchase of common stock at the end of the offering period. If a participating employee's employment ends before the last business day of an offering period, no additional payroll deductions will be made and the balance in the employee's account will be repaid to the employee.

We will be required to make equitable adjustments to the number and class of securities available under the 2013 ESPP, the share limitations under the 2013 ESPP, and the purchase price for an offering period under the 2013 ESPP to reflect stock splits, reverse stock splits, stock dividends, recapitalizations, combinations of shares, reclassifications of shares, spin-offs and other similar changes in capitalization or events or any dividends or distributions to holders of our common stock other than ordinary cash dividends.

In connection with a merger or other reorganization event (as defined in the 2013 ESPP), our Board or a committee of our Board may take any one or more of the following actions as to outstanding options to purchase shares of our common stock under the 2013 ESPP on such terms as our Board or committee determines:

- provide that options shall be assumed, or substantially equivalent options shall be substituted, by the acquiring or succeeding corporation (or an affiliate thereof);
- upon written notice to employees, provide that all outstanding options will be terminated immediately prior to the consummation of such reorganization event and that all such outstanding options will become exercisable to the extent of accumulated payroll deductions as of a date specified by our Board or committee in such notice, which date shall not be less than ten days preceding the effective date of the reorganization event;
- upon written notice to employees, provide that all outstanding options will be cancelled as of a date prior to the effective date of the reorganization event and that all accumulated payroll deductions will be returned to participating employees on such date;
- in the event of a reorganization event under the terms of which holders of our common stock will receive upon consummation thereof a cash payment for each share surrendered in the reorganization event, change the last day of the offering period to be the date of the consummation of the reorganization event and make or provide for a cash payment to each employee equal to (a) the cash payment for each share surrendered in the reorganization event times the number of shares of our common stock that the employee's accumulated payroll deductions as of immediately prior to the reorganization event could purchase at the applicable purchase price, where the acquisition price is treated as the fair market value of our common stock on the last day of the applicable offering period for purposes of determining the purchase price and where the

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number of shares that could be purchased is subject to the applicable limitations under the 2013 ESPP minus (b) the result of multiplying such number of shares by the purchase price; and/or

- provide that, in connection with our liquidation or dissolution, options shall convert into the right to receive liquidation proceeds (net of the purchase price thereof).

Our Board may at any time, and from time to time, amend or suspend the 2013 ESPP or any portion thereof. We will obtain stockholder approval for any amendment if such approval is required by Section 423 of the Code. Further, our Board may not make any amendment that would cause the 2013 ESPP to fail to comply with Section 423 of the Code. The 2013 ESPP may be terminated at any time by our Board. Upon termination, we will refund all amounts in the accounts of participating employees.

2010 Stock Incentive Plan

In July 2013, our Board adopted, and our stockholders approved, the 2010 Plan, which provided for the grant of incentive stock options, non-qualified stock options, restricted stock awards, RSU awards, and other stock-based awards. We no longer grant awards under the 2010 Plan, but awards remain outstanding under the 2010 Plan in accordance with their terms.

Upon the consummation of a merger or other event constituting an acquisition (as defined in the 2010 Plan), our Board or the board of directors of the surviving or acquiring entity shall, as to outstanding awards under the 2010 Plan (on the same basis or on different bases), either:

- make appropriate provision for the continuation or assumption of such awards or substitute on an equitable basis for the shares then subject to such awards either (a) the consideration payable with respect to the outstanding shares of our common stock in connection with the acquisition, (b) shares of stock of the surviving or acquiring corporation, or (c) such other securities or other consideration as the applicable board deems appropriate, the fair market value of which shall not materially differ from the fair market value of the shares of our common stock subject to such awards immediately preceding the acquisition;
- upon written notice, provide that one or more awards then outstanding must be exercised (to the extent then vested), in whole or in part, within a specified number of days of the date of such notice, at the end of which period such awards shall terminate; or
- provide that one or more awards then outstanding, in whole or in part, shall be terminated in exchange for a cash payment equal to the excess of the fair market value (as determined by the applicable board in its sole discretion) for the vested shares subject to such awards over the exercise price, if any, thereof.

Unless otherwise determined by the applicable board of directors, any repurchase rights or other rights that relate to an award shall continue to apply to consideration, including cash that has been substituted, assumed or amended for an award in connection with an acquisition. We may require that all or any portion of such consideration payable in respect of an award in connection with an acquisition shall be held in escrow (including in an escrow pursuant to the agreement effecting such acquisition) in order to effectuate any continuing restrictions.

At any time, our Board may provide that any award under the 2010 Plan shall become immediately exercisable in full or in part or free of some or all restrictions or conditions, or otherwise realizable in full or in part, as the case may be.

Our Board may amend, modify or terminate any outstanding award under the 2010 Plan, including, but not limited to, substituting therefor another award of the same or a different type, changing the date of exercise or realization, and converting an incentive stock option to a non-qualified stock option, subject to certain participant consent requirements. In addition, our Board may, without stockholder approval, amend any outstanding option to reduce the exercise price of such option or cancel any outstanding option and grant in substitution therefor new options covering the same or a different number of shares of our common stock and having a lower exercise price than the cancelled options. Our Board may amend, suspend or terminate the 2010 Plan or any portion thereof at any time.

SECURITIES AUTHORIZED FOR ISSUANCE UNDER EQUITY COMPENSATION PLANS

The following table contains information as of December 31, 2020 regarding shares of common stock that may be issued under our equity compensation plans.

Equity Compensation Plan Information

Plan Category	Number of Securities to be Issued upon Exercise of Outstanding Options, Warrants and Rights (a)	Weighted-Average Exercise Price of Outstanding Options, Warrants and Rights (b)	Number of Securities Remaining Available for Future Issuance under Equity Compensation Plans (Excluding Securities Reflected in Column (a)) (c)
Equity compensation plans approved by security holders(1)	9,938,027	\$ 14.58	2,572,001
Equity compensation plans not approved by security holders(2)	3,012,012	\$ 13.17	2,672,620
Total	12,950,039(3)	\$ 14.08	5,244,621

- (1) Includes 9,938,027 shares to be issued pursuant to outstanding awards under the 2013 and 2010 Plans. As of December 31, 2020, there were 1,716,897 shares available for issuance under the 2013 Plan and 855,104 shares available for issuance under the 2013 ESPP.
- (2) Includes shares of common stock issuable upon exercise of outstanding stock options granted pursuant to the Nasdaq inducement grant exception as a component of employment compensation for employees. The inducement grants were approved by our Compensation Committee and were made as an inducement material to employees entering into employment with us in accordance with Nasdaq Listing Rule 5635(c)(4).
- (3) Includes 11,276,316 shares of common stock issuable upon the exercise of outstanding options and 1,673,723 shares of common stock issuable upon the vesting of RSUs. The weighted average exercise price for the outstanding options was \$14.08 and the weighted average remaining contractual term was 6.8 years.

CERTAIN RELATIONSHIPS AND RELATED PERSON TRANSACTIONS

Since January 1, 2019, we have engaged in the following transactions with our directors and executive officers and holders of more than 5% of our voting securities and affiliates of our directors, executive officers and such 5% stockholders. We believe that all of the transactions described below were made on terms no less favorable to us than could have been obtained from unaffiliated third parties.

Severance and Change in Control Agreements

See the “*Executive Compensation—Employment, Severance and Change in Control Arrangements*” section of this proxy statement for a further discussion of these arrangements.

Indemnification of Directors

Our certificate of incorporation limits the personal liability of directors for breach of fiduciary duty to the maximum extent permitted by the Delaware General Corporation Law and provides that no director will have personal liability to us or to our stockholders for monetary damages for any breach of fiduciary duty as a director. In addition,

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we have entered into indemnification agreements with each of our directors that require us, among other things, to indemnify each director for certain expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by him or her in any action or proceeding arising out of his or her service as one of our directors. See the "Corporate Governance—Limitation of Liability and Indemnification" section of this proxy statement for a further discussion of these arrangements.

Consulting Arrangements

We are party to a consulting agreement with Tami Rashal, who is the sister of Dr. Sharon Shacham, our President and Chief Scientific Officer and sister-in-law of Dr. Michael Kauffman, our Chief Executive Officer. Ms. Rashal provides us with services related to medical reviews as part of our clinical development program. Pursuant to the terms of this agreement, we paid to Ms. Rashal an aggregate of \$230,650 and \$116,550 during 2020 and 2019, respectively.

PROPOSAL 3: RATIFICATION OF THE APPOINTMENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Audit Committee has selected Ernst & Young LLP as the Company's independent registered public accounting firm for the year ending December 31, 2021, and the Board has directed that management submit the appointment of the Company's independent registered public accounting firm for ratification by the stockholders at the Annual Meeting. Representatives of Ernst & Young LLP are expected to attend the Annual Meeting online, will have an opportunity to make a statement if they so desire, and be available to respond to appropriate questions.

Stockholder ratification of the appointment of Ernst & Young LLP as the Company's independent registered public accounting firm is not required by Delaware law or the Company's certificate of incorporation or bylaws. However, the Board is submitting this appointment to the stockholders for ratification as a matter of good corporate practice. If the stockholders fail to ratify the appointment of Ernst & Young LLP, the Audit Committee will reconsider whether to continue to retain that firm for future service. Even if the appointment is ratified, the Audit Committee in its discretion may direct the appointment of a different independent 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 the Company and its stockholders.

Independent Registered Public Accountant Fees

The following table summarizes the fees billed for professional services by Ernst & Young LLP for the years ended December 31, 2020 and 2019:

	<u>Year Ended December 31,</u>	
	<u>2020</u>	<u>2019</u>
Audit Fees(1)	\$ 1,091,761	\$ 1,370,000
Audit Related Fees	—	—
Tax Fees(2)	135,100	144,292
All Other Fees	—	—
Total	<u>\$ 1,226,861</u>	<u>\$ 1,514,292</u>

- (1) Audit Fees consist of fees billed for professional services performed by Ernst & Young LLP for the audit of our annual consolidated financial statements, the review of interim consolidated financial statements, and related services that are normally provided in connection with registration statements. Included in the 2020 and 2019 Audit Fees are fees billed in connection with our debt offerings, follow-on offerings and at-the-market offerings.

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- (2) Tax Fees consist of fees for professional services, including tax compliance, tax consulting, Internal Revenue Service Section 382 analysis, research and development tax credit analysis and tax advisory services performed by Ernst & Young LLP.

The Audit Committee has considered the services listed above to be compatible with maintaining Ernst & Young LLP's independence.

Pre-Approval Policies and Procedures

Our Audit Committee has established a policy that all audit and permissible non-audit services provided by our independent registered public accounting firm will be pre-approved by the Audit Committee, and all such services were pre-approved in accordance with this policy during the years ended December 31, 2020 and December 31, 2019. These services may include audit services, audit-related services, tax services and other services. The Audit Committee considers whether the provision of each non-audit service is compatible with maintaining the independence of our auditors. Pre-approval is detailed as to the particular service or category of services and is generally subject to a specific budget. Our independent registered public accounting firm and management are required to periodically report to the Audit Committee regarding the extent of services provided by the independent registered public accounting firm in accordance with this pre-approval, and the fees for the services performed to date.

THE BOARD UNANIMOUSLY RECOMMENDS THAT THE STOCKHOLDERS VOTE TO RATIFY THE APPOINTMENT OF ERNST & YOUNG LLP AS OUR INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM FOR THE YEAR ENDING DECEMBER 31, 2021.

SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The following table sets forth information relating to the beneficial ownership of our common stock as of March 26, 2021, by:

- each person known by us to beneficially own more than 5% of our outstanding shares of common stock;
- each of our directors;
- each of our named executive officers; and
- all directors and executive officers as a group.

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The percentage of shares beneficially owned is computed on the basis of 75,061,474 shares of our common stock outstanding as of March 26, 2021. The number of shares beneficially owned by each stockholder is determined under rules issued by the SEC and includes voting or investment power with respect to securities. Under these rules, beneficial ownership includes any shares as to which the individual or entity has sole or shared voting power or investment power. In computing the number of shares beneficially owned by an individual or entity and the percentage ownership of that person, shares of common stock subject to options or other rights held by such person that are currently exercisable or will become exercisable within 60 days of March 26, 2021 are considered outstanding, although these shares are not considered outstanding for purposes of computing the percentage ownership of any other person. Unless otherwise indicated, the address of all listed stockholders is c/o Karyopharm Therapeutics Inc., 85 Wells Avenue, Newton, Massachusetts 02459. Each of the stockholders listed has sole voting and investment power with respect to the shares beneficially owned by the stockholder unless noted otherwise, subject to community property laws where applicable.

Name of Beneficial Owner	Shares Beneficially Owned	
	Number	Percentage
5% Stockholders		
Blackrock, Inc.(1)	7,475,099	9.96%
Chione Ltd.(2)	5,500,000	7.33%
State Street Corporation(3)	5,339,859	7.11%
Palo Alto Investors, LLC(4)	5,267,652	7.02%
Named Executive Officers and Directors		
Michael G. Kauffman, M.D., Ph.D.(5)	4,268,310	5.47%
Sharon Shacham, Ph.D., M.B.A.(6)	4,268,310	5.47%
Deepika R. Pakianathan, Ph.D.(7)	2,388,406	3.18%
Barry E. Greene(8)	122,036	*
Michael Mason(9)	117,042	*
Garen Bohlin(10)	116,006	*
Mikael Dolsten, M.D.(11)	115,400	*
Mansoor Raza Mirza, M.D.(12)	85,400	*
Richard Paulson(13)	35,842	*
Christy Oliger	—	*
Chen Schor	—	*
All executive officers and directors as a group (17 persons)(14)	8,136,865	10.24%

* Less than 1%.

- (1) Consists of shares of common stock owned directly by BlackRock, Inc. (“Blackrock”). Blackrock has sole voting power with respect to 7,192,384 shares and sole dispositive power with respect to 7,475,099 shares. The address for Blackrock is 55 East 52nd Street, New York NY 10055. For information regarding Blackrock, we have relied on Amendment No. 1 to Schedule 13G filed by Blackrock on January 27, 2021.
- (2) Consists of shares of common stock owned directly by Chione Ltd. (“Chione”). The board of directors of Chione, comprised of Marcin Czernik, Andreas Hadjimichael, George Hadjimichael and Anastasios Nikolaou, and its sole stockholder, Wlaczslaw Smolokowski, may be deemed to share voting and investment power and beneficial ownership of such shares of common stock. Each of such directors and stockholder disclaims such voting and investment power and beneficial ownership. The shares held by Chione do not include shares held by Plio Ltd., which has the same directors as Chione and as to which each of such directors may be deemed to share

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voting and investment power and beneficial ownership. Each of such directors disclaims such voting and investment power and beneficial ownership with respect to shares held by Plio Ltd. The address for Chione is Simou Menardou 5, Kifisia Court, 2nd Floor, Flat/Office 225, 6015 Larnaca, Cyprus. The address for Mr. Smolokowski is Chalet Lenotchka, Chemin des Marais 1, Chesieres, Switzerland. For information regarding Chione and its affiliates, we have relied on Amendment No. 6 to Schedule 13G filed by Chione Ltd. with the SEC on February 16, 2021.

- (3) State Street Corporation (“State Street”) reports shared voting power of 5,072,936 and shared dispositive power with respect to 5,339,859 shares. SSGA Funds Management, Inc. (“SSGA”), a subsidiary of State Street, reports shared voting power with respect to 4,042,882 shares and shared dispositive power with respect to 4,059,082 shares. The address for State Street and SSGA is State Street Financial Center, One Lincoln Street, Boston, MA 02111. For information regarding State Street and SSGA, we have relied on Schedule 13G filed by State Street and SSGA on February 11, 2021.
- (4) Palo Alto Investors LP (“PAI”) is a registered investment adviser and investment adviser of investment limited partnerships and is the investment adviser to other investment funds. PAI LLC is the general partner of investment limited partnerships. PAI’s clients have the right to receive or the power to direct the receipt of dividends from, or the proceeds from the sale of, the shares held by PAI. Dr. Patrick Lee and Dr. Anthony Joonkyoo Yun co-manage PAI. Dr. Lee, Dr. Yun, PAI and PAI LLC each report shared voting power and shared dispositive power with respect to 5,267,652 shares and disclaim beneficial ownership of the shares held by PAI except to the extent of each party’s pecuniary interest therein. The address for PAI is 470 University Avenue, Palo Alto, CA 94301. For information regarding PAI and its affiliates, we have relied on Amendment No. 5 to Schedule 13G filed by PAI with the SEC on February 16, 2021.
- (5) Consists of (a) 1,438,245 shares of common stock underlying options held by Dr. Kauffman that are exercisable as of March 26, 2021 or will become exercisable within 60 days after such date, (b) 571,126 shares of common stock held by Dr. Kauffman, (c) 1,482,487 shares of common stock underlying options held by Dr. Shacham, who is the spouse of Dr. Kauffman, that are exercisable as of March 26, 2021 or will become exercisable within 60 days after such date, and (d) 776,452 shares of common stock held by Dr. Shacham.
- (6) Consists of (a) 1,482,487 shares of common stock underlying options held by Dr. Shacham that are exercisable as of March 26, 2021 or will become exercisable within 60 days after such date, (b) 776,452 shares of common stock held by Dr. Shacham, (c) 1,438,245 shares of common stock underlying options held by Dr. Kauffman, who is the spouse of Dr. Shacham, that are exercisable as of March 26, 2021 or will become exercisable within 60 days after such date, and (d) 571,126 shares of common stock held by Dr. Kauffman.
- (7) Consists of (a) 125,400 shares of common stock underlying options held by Deepika R. Pakianathan that are exercisable as of March 26, 2021 or will become exercisable within 60 days after such date, (b) 2,241,123 shares of common stock held by Delphi Ventures VIII, L.P. and (c) 21,883 shares of common stock held by Delphi BioInvestments VIII, L.P. Delphi Management Partners VIII, L.L.C is the general partner of Delphi VIII and DBI VIII, together, the Delphi VIII Funds, and may be deemed to have sole voting and dispositive power over the shares held by the Delphi VIII Funds. DMP VIII and each of James J. Bochnowski, David L. Douglass, Douglas A. Roeder and Deepika R. Pakianathan, Ph.D., the Managing Members of DMP VIII who may be deemed to share voting and dispositive power over the reported securities, disclaim beneficial ownership of the reported securities held by Delphi VIII Funds except to the extent of any pecuniary interest therein.
- (8) Consists of (a) 6,030 shares of common stock and (b) 116,006 shares of common stock underlying options that are exercisable as of March 26, 2021 or will become exercisable within 60 days after such date.
- (9) Consists of (a) 5,292 shares of common stock and (b) 111,750 shares of common stock underlying options that are exercisable as of March 26, 2021 or will become exercisable within 60 days after such date.

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- (10) Consists of 116,006 shares of common stock underlying options that are exercisable as of March 26, 2021 or will become exercisable within 60 days after such date.
- (11) Consists of 115,400 shares of common stock underlying options that are exercisable as of March 26, 2021 or will become exercisable within 60 days after such date.
- (12) Consists of 85,400 shares of common stock underlying options that are exercisable as of March 26, 2021 or will become exercisable within 60 days after such date.
- (13) Consists of 35,842 shares of common stock underlying options that are exercisable as of March 26, 2021 or will become exercisable within 60 days after such date.
- (14) Includes 4,382,740 shares of common stock underlying options that are exercisable as of March 26, 2021 or will become exercisable within 60 days after such date.

DELINQUENT SECTION 16(a) REPORTS

Under Section 16(a) of the Exchange Act, directors, executive officers and beneficial owners of 10% or more of our common stock, or reporting persons, are required to report to the SEC on a timely basis the initiation of their status as a reporting person and any changes with respect to their beneficial ownership of our common stock. Based solely on our review of copies of reports filed pursuant to Section 16(a), or written representations from reporting persons, we believe that during the fiscal year ended December 31, 2020, all executive officers, directors and greater than 10% stockholders timely complied with all applicable filing requirements of Section 16(a), with the exception of (a) one late Form 4 filing by Jatin Shah to report the vesting of RSUs and the sale of shares to satisfy the payment of withholding tax liability incurred upon such vesting and (b) one late Form 4 filing by Tanya Lewis to report the vesting of RSUs and the sale of shares to satisfy the payment of withholding tax liability incurred upon such vesting.

STOCKHOLDER PROPOSALS

Proposals of stockholders intended to be presented at our annual meeting of stockholders to be held in 2022 must be received by us no later than December 8, 2021, which is 120 calendar days prior to the one-year anniversary of the date on which our proxy statement was released to stockholders in connection with this year's Annual Meeting, in order to be included in our proxy statement and form of proxy relating to the 2022 annual meeting of stockholders, unless the date of the 2022 annual meeting of stockholders is changed by more than 30 days from the anniversary of our 2021 Annual Meeting, in which case the deadline for such proposals will be a reasonable time before we begin to print and send our proxy materials. These proposals must comply with the requirements as to form and substance established by the SEC for such proposals in order to be included in the proxy statement.

In addition, our bylaws establish an advance notice procedure for nominations for election to our Board and other matters that stockholders wish to present for action at an annual meeting of stockholders other than those to be included in our proxy statement. In general, notice must be received at our principal executive offices not less than 90 calendar days before nor more than 120 calendar days before the one-year anniversary of the previous year's annual meeting of stockholders. Therefore, to be presented at our 2022 annual meeting of stockholders, such a proposal must be received by us no earlier than January 21, 2022 and no later than February 20, 2022. However, if the date of the 2022 annual meeting of stockholders is more than 20 days earlier or more than 60 days later than such anniversary date, notice must be received no earlier than the close of business 120 calendar days prior to such annual meeting of stockholders and no later than the close of business on the later of (a) 90 days prior to such annual meeting of stockholders and (b) 10 days following the day on which notice of the date of such annual meeting of stockholders was mailed or public announcement of the date of such annual meeting of stockholders was first made, whichever first

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occurs. Any proposals we do not receive in accordance with the above standards will not be voted on at the 2022 annual meeting of stockholders. Stockholders are advised to review our bylaws which also specify requirements as to the form and content of a stockholder's notice.

Any proposals, notices or information about proposed director candidates should be sent to:

Karyopharm Therapeutics Inc.
85 Wells Avenue
Newton, Massachusetts 02459
Attention: Corporate Secretary

STOCKHOLDERS SHARING THE SAME ADDRESS

The rules promulgated by the SEC permit companies, banks, brokerage firms or other intermediaries to deliver a single copy of a proxy statement and annual report to households at which two or more stockholders reside. This practice, known as "householding," is designed to reduce duplicate mailings and save significant printing and postage costs as well as natural resources. Stockholders sharing an address who have been previously notified by their bank, brokerage firm or other intermediary and have consented to householding will receive only one copy of our proxy statement and annual report. If you would like to opt out of this practice for future mailings and receive separate proxy statements and annual reports for each stockholder sharing the same address, please contact your bank, brokerage firm or other intermediary from whom you received such mailing. We will promptly deliver a separate copy of the proxy statement and/or annual report to you if you contact us at the following address or telephone number: Karyopharm Therapeutics Inc., 85 Wells Avenue, Newton, Massachusetts 02459, Attention: Corporate Secretary, (617) 658-0600. We will promptly send additional copies of the proxy statement or annual report upon receipt of such request. Stockholders sharing an address that are receiving multiple copies of the proxy statement or annual report can request delivery of a single copy of the proxy statement or annual report by contacting their bank, brokerage firm or other intermediary or by contacting us at the address or telephone number above.

OTHER MATTERS

We do not know of any business that will be presented for consideration or action by the stockholders at the Annual Meeting other than that described in this proxy statement. If, however, any other business is properly brought before the meeting, shares represented by proxies will be voted in accordance with the best judgment of the persons named in the proxies or their substitutes.



KARYOPHARM THERAPEUTICS INC.
 C/O PROXY SERVICES
 P.O. BOX 9142
 FARMINGDALE, NY 11735

VOTE BY INTERNET

Before the Meeting - Go to www.proxyvote.com

Use the Internet to transmit your voting instructions and for electronic delivery of information up until 11:59 p.m. Eastern Time on May 20, 2021. Have your proxy card in hand when you access the website and follow the instructions to obtain your records and to create an electronic voting instruction form.

During the Meeting - Go to

www.virtualshareholdermeeting.com/KPTI2021

You may attend the meeting via the Internet and vote during the meeting. Have the information that is printed in the box marked by the arrow available and follow the instructions. There will be no physical location at which stockholders may attend the meeting.

VOTE BY PHONE - 1-800-690-6903

Use any touch-tone telephone to transmit your voting instructions up until 11:59 p.m. Eastern Time on May 20, 2021. Have your proxy card in hand when you call and then follow the instructions.

VOTE BY MAIL

If you have received printed proxy materials, mark, sign and date your proxy card and return it in the postage-paid envelope we have provided or return it to Vote Processing, c/o Broadridge, 51 Mercedes Way, Edgewood, NY 11717.

TO VOTE, MARK BLOCKS BELOW IN BLUE OR BLACK INK AS FOLLOWS:

D42407-P51424

KEEP THIS PORTION FOR YOUR RECORDS

DETACH AND RETURN THIS PORTION ONLY

THIS PROXY CARD IS VALID ONLY WHEN SIGNED AND DATED.

<p>KARYOPHARM THERAPEUTICS INC.</p> <p>The Board of Directors recommends you vote FOR the election of each of the director nominees.</p> <p>1. To elect the following three Class II director nominees:</p> <ul style="list-style-type: none"> 1) Deepika R. Pakianathan, Ph.D. 2) Richard Paulson, M.B.A. 3) Chen Schor, M.B.A., C.P.A. <p>The Board of Directors recommends you vote FOR the following proposal.</p> <p>2. To approve, on an advisory basis, the compensation of Karyopharm's named executive officers.</p> <p>The Board of Directors recommends you vote FOR the following proposal.</p> <p>3. To ratify the appointment of Ernst & Young LLP as Karyopharm's independent registered public accounting firm for the year ending December 31, 2021.</p> <p>In their discretion, the proxies are authorized to vote upon such other matters as may be properly brought before the meeting or any adjournments or postponements thereof.</p> <p>Please sign your name exactly as it appears hereon. When signing as attorney, executor, administrator, trustee or guardian, please add your title as such. When signing as joint tenants, all parties in the joint tenancy must sign. If a signer is a corporation, please sign in full corporate or partnership name by authorized officer.</p>	<p>For All</p> <p><input type="checkbox"/></p>	<p>Withhold All</p> <p><input type="checkbox"/></p>	<p>For All Except</p> <p><input type="checkbox"/></p>	<p>To withhold authority to vote for any individual nominee(s), mark "For All Except" and write the number(s) of the nominee(s) on the line below.</p> <p>_____</p>
<p>The Board of Directors recommends you vote FOR the following proposal.</p> <p>2. To approve, on an advisory basis, the compensation of Karyopharm's named executive officers.</p>	<p>For</p> <p><input type="checkbox"/></p>	<p>Against</p> <p><input type="checkbox"/></p>	<p>Abstain</p> <p><input type="checkbox"/></p>	
<p>The Board of Directors recommends you vote FOR the following proposal.</p> <p>3. To ratify the appointment of Ernst & Young LLP as Karyopharm's independent registered public accounting firm for the year ending December 31, 2021.</p>	<p>For</p> <p><input type="checkbox"/></p>	<p>Against</p> <p><input type="checkbox"/></p>	<p>Abstain</p> <p><input type="checkbox"/></p>	
<p>Signature [PLEASE SIGN WITHIN BOX]</p>	<p>Date</p>	<p>Signature (Joint Owners)</p>	<p>Date</p>	

Important Notice Regarding the Availability of Proxy Materials for the Annual Meeting to be Held May 21, 2021:
The Notice and Proxy Statement and Annual Report on Form 10-K are available at www.proxyvote.com.

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THIS PROXY IS SOLICITED ON BEHALF OF THE BOARD OF DIRECTORS

**ANNUAL MEETING OF STOCKHOLDERS
May 21, 2021**

The stockholder(s) hereby appoint(s) Michael Mano and Michael Mason, 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 ballot, all of the shares of Common Stock of KARYOPHARM THERAPEUTICS INC. that the stockholder(s) is/are entitled to vote at the Annual Meeting of Stockholders to be held at 9:00 a.m. Eastern Time, on May 21, 2021, via the Internet at a virtual web conference at www.virtualshareholdermeeting.com/KPTI2021, and any adjournments or postponements thereof.

THE UNDERSIGNED HEREBY REVOKES ANY PROXY PREVIOUSLY GIVEN WITH RESPECT TO THE ANNUAL MEETING AND ACKNOWLEDGES RECEIPT OF THE NOTICE AND PROXY STATEMENT FOR THE ANNUAL MEETING.

THIS PROXY WHEN PROPERLY EXECUTED WILL BE VOTED AS DIRECTED BY THE STOCKHOLDER(S). IF NO SUCH DIRECTIONS ARE MADE, THIS PROXY WILL BE VOTED "FOR" THE ELECTION OF THE DIRECTOR NOMINEES LISTED ON THE REVERSE SIDE FOR THE BOARD OF DIRECTORS, "FOR" PROPOSALS 2 AND 3 AND, IN THE DISCRETION OF THE PROXIES, ON SUCH OTHER BUSINESS AS MAY PROPERLY COME BEFORE THE MEETING OR ANY ADJOURNMENTS OR POSTPONEMENTS THEREOF.

PLEASE MARK, SIGN, DATE AND RETURN THIS PROXY CARD PROMPTLY USING THE ENCLOSED REPLY ENVELOPE.

CONTINUED AND TO BE SIGNED ON REVERSE SIDE