

**KARYOPHARM THERAPEUTICS INC.**  
**SUPPLEMENT TO PROXY STATEMENT**  
**FOR THE 2021 ANNUAL MEETING OF STOCKHOLDERS**  
**TO BE HELD ON MAY 21, 2021**

This Supplement relates to the proxy statement (the “Proxy Statement”) of Karyopharm Therapeutics Inc., a Delaware corporation (the “Company”), as filed by the Company with the Securities and Exchange Commission (the “SEC”) on April 7, 2021 and furnished to stockholders of the Company in connection with the solicitation of proxies by the Company’s board of directors (the “Board”) for the Company’s 2021 Annual Meeting of Stockholders (the “Annual Meeting”). All capitalized terms used in this Supplement and not otherwise defined herein have the respective meanings ascribed to such terms in the Proxy Statement.

This Supplement, which supplements and amends the Proxy Statement, is being filed with the SEC and being made available to stockholders of the Company on or about May 3, 2021. Except as specifically supplemented or amended by the information contained in this Supplement, all information set forth in the Proxy Statement continues to apply and should be considered when voting your shares using one of the methods described in the Proxy Statement.

**The Proxy Statement contains important additional information, and this Supplement should be read in conjunction with the Proxy Statement.**

**Appointment of Richard Paulson as President and Chief Executive Officer**

On April 27, 2021, the Board appointed Richard Paulson as President and Chief Executive Officer of the Company, effective as of May 3, 2021. Mr. Paulson has served as a member of the Board since February 2020 and will remain on the Board as a non-independent director. Mr. Paulson succeeds Michael G. Kauffman, who resigned on April 28, 2021 as the Company’s Chief Executive Officer effective as of May 3, 2021, and Sharon Shacham, who resigned on April 28, 2021 as the Company’s President effective as of May 3, 2021. Dr. Kauffman will continue in his role as a member of the Board and assume a new role with the Company as Senior Clinical Advisor. Dr. Shacham will continue in her roles as the Company’s Chief Scientific Officer and Chair of the Company’s Scientific Advisory Board.

Mr. Paulson is a Class II director whose term expires at the Annual Meeting. As disclosed in the Proxy Statement, the Board has nominated Mr. Paulson, M.B.A., Deepika R. Pakianathan, Ph.D. and Chen Schor, M.B.A., C.P.A. for election at the Annual Meeting, each to hold office for a three-year term to expire at the Company’s 2024 annual meeting of stockholders and until their resignation or removal or until their successors are duly elected and qualified. Effective as of May 3, 2021, Mr. Paulson will no longer be considered an independent director, he will no longer serve as a member of the Audit Committee of the Board (the “Audit Committee”), and he will not receive any compensation for his service on the Board. The Board has appointed Mr. Schor to serve on the Audit Committee in place of Mr. Paulson.

Mr. Paulson, age 53, most recently served as the Executive Vice President of Ipsen Pharmaceuticals, Inc. and Chief Executive Officer of Ipsen North America, a global biopharmaceutical company focused on innovation and specialty care in areas of oncology, neuroscience and rare diseases, from February 2018 to April 2021. Mr. Paulson was Vice President and General Manager, U.S. Oncology Business Unit at Amgen Inc. (“Amgen”), 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., 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.

There are no family relationships between Mr. Paulson and any director, executive officer or person nominated or chosen by the Company to become a director or executive officer of the Company. There are no transactions in which Mr. Paulson has an interest requiring disclosure under Item 404(a) of Regulation S-K.

#### *Mr. Paulson's Compensation Arrangements*

In connection with his employment with the Company, pursuant to the terms of an offer letter dated April 28, 2021, (the "Offer Letter"), Mr. Paulson will receive an annual base salary of \$670,000 and a \$700,000 sign-on bonus payable in three separate payments of \$300,000 ("Milestone Payment 1"), \$200,000 ("Milestone Payment 2") and \$200,000 ("Milestone Payment 3") to be paid in the payroll period following May 3, 2021, May 3, 2022 and May 3, 2023 (each, a "Milestone Date"), respectively, contingent on Mr. Paulson's commencement of employment with the Company (with respect to Milestone Payment 1) and his continued employment through the applicable Milestone Date (with respect to Milestone Payment 2 and Milestone Payment 3). The Offer Letter provides that if Mr. Paulson's employment is terminated for Cause (as defined in the Offer Letter) or he resigns other than for Good Reason (as defined in the Offer Letter) prior to the one-year anniversary of each applicable Milestone Date or after the one-year anniversary but prior to the two-year anniversary of the applicable Milestone Date, he must repay 100% or 50%, respectively, of the net amount of the applicable Milestone Payment received in connection with such Milestone Date. Mr. Paulson is also eligible for an annual bonus at a target of 65% of his annualized base salary based solely on the Company's performance during the applicable calendar year. In addition, under the terms of the Offer Letter, Mr. Paulson will also be eligible to participate in all Company benefits available to other employees of the Company.

Pursuant to the terms of the Offer Letter, the Board granted to Mr. Paulson, effective as of May 3, 2021, (i) a stock option to purchase 559,800 shares of the Company's common stock, \$0.0001 par value per share (the "Common Stock"), with an exercise price equal to the closing price of the Common Stock, as reported by the Nasdaq Global Select Market, on May 3, 2021, and (ii) 373,200 restricted stock units ("RSUs"). The stock option will vest as to 25% of the shares underlying the stock option on the first anniversary of the grant date and then monthly thereafter until the fourth anniversary of the grant date. 25% of the total number of RSUs will vest on the one-year anniversary of the grant date and 1/48<sup>th</sup> of the total number of RSUs will vest monthly thereafter.

The Offer Letter also provides that, if Mr. Paulson's employment is terminated without Cause or he resigns for Good Reason (other than within one year following the consummation of a Change in Control (as defined in the Offer Letter)), he will be entitled to receive the following severance benefits: (i) salary continuation for 18 months (the "Severance Period"); (ii) a lump sum payment of any unpaid Milestone Payments; (iii) a lump sum, pro-rated target bonus for the year in which the termination occurs; and (iv) an opportunity to enter into a consulting arrangement with the Company during which he will be compensated for services performed and any unvested equity awards granted by the Company will continue to vest. If Mr. Paulson's employment is terminated without Cause or he resigns for Good Reason within one year following the consummation of a Change in Control, he will, in lieu of the severance benefits described above, be entitled to receive the following severance benefits: (i) salary continuation for the Severance Period; (ii) a lump sum payment of any unpaid Milestone Payments; and (iii) an amount equal to 150% of his target annual bonus for the year in which the termination occurs. In addition, if in connection with the termination of Mr. Paulson's employment, he elects to continue his and his eligible dependents' participation in the Company's medical and dental benefit plans pursuant to the Consolidated Omnibus Budget Reconciliation Act of 1986 ("COBRA"), the Company will, as a severance benefit, pay the premiums to continue such coverage for the lesser of (i) the Severance Period and (ii) the end of the calendar month in which he becomes eligible to receive group health plan coverage under another employee benefit plan. Mr. Paulson's receipt of the severance benefits discussed in this paragraph is subject to Mr. Paulson's timely execution and non-revocation of a separation and release of claims agreement as described in the Offer Letter.

A complete copy of the Offer Letter has been filed as Exhibit 10.1 to the Form 8-K filed by the Company with the SEC on May 3, 2021.

#### *Dr. Kauffman's Amended and Restated Letter Agreement*

On April 28, 2021, the Company entered into an amended and restated letter agreement, effective as of May 3, 2021, with Dr. Kauffman (the "Kauffman Agreement"). The Kauffman Agreement amends and restates the amended and restated letter agreement between Dr. Kauffman and the Company, dated as of August 28, 2020 and provides for Dr. Kauffman's employment as Senior Clinical Advisor. Pursuant to the Kauffman Agreement, Dr. Kauffman will be provided with an annual base salary of \$388,125 and an annual bonus target opportunity equal to 50% of his annual base salary based upon the achievement of certain performance goals and corporate milestones. He will also be eligible to receive annual equity grants in the Company's sole discretion and to participate in medical, retirement and other benefits that are made available to other executive level employees of the Company.

The Kauffman Agreement also provides that, if Dr. Kauffman's employment is terminated without Cause (as defined in the Kauffman Agreement) or he resigns for Good Reason (as defined in the Kauffman Agreement) on or before May 3, 2023 (other than within the twelve month period following a Change of Control (as defined in the Kauffman Agreement)), he will be entitled to receive severance pay in the form of salary continuation at the rate of \$646,875 per annum for the Severance Period. If Dr. Kauffman's employment is terminated without Cause or he resigns for Good Reason on or before May 3, 2023 and within the twelve month period following a Change of Control, he will, in lieu of the severance benefits described above, be entitled to receive the following severance benefits: (i) salary continuation at the rate of \$646,875 per annum for the Severance Period; and (ii) an amount equal to 150% of his target annual bonus for the year in which the termination occurs. In addition, if in connection with the termination of Dr. Kauffman's employment on or before May 3, 2023, he elects to continue his and his eligible dependents' participation in the Company's medical and dental benefit plans pursuant to COBRA, the Company will, as a severance benefit, pay the premiums to continue such coverage for the lesser of (i) the Severance Period and (ii) the end of the calendar month in which he becomes eligible to receive group health plan coverage under another employee benefit plan. If Dr. Kauffman's employment is terminated without Cause or he resigns for Good Reason after May 3, 2023, he will be entitled to severance pay in a lump sum in the amount of \$323,500. Dr. Kauffman's receipt of the severance benefits discussed in this paragraph is subject to Dr. Kauffman's timely execution and non-revocation of a separation and release of claims agreement as described in the Kauffman Agreement.

Pursuant to the Kauffman Agreement, Dr. Kauffman also surrendered all right, title and interest to portions of certain outstanding stock options for the purchase of 290,000 shares of Common Stock. Dr. Kauffman's remaining outstanding equity awards will continue to vest, provided that if the Company terminates his employment without Cause or he resigns for Good Reason on or prior to March 1, 2025, then any of the remaining unvested portions of such equity awards will become vested and exercisable and, if such awards are stock options, will remain exercisable until the earlier of March 1, 2026 and the expiration date of such stock option.

A complete copy of the Kauffman Agreement has been filed as Exhibit 10.2 to the Form 8-K filed by the Company with the SEC on May 3, 2021.

#### *Dr. Shacham's Amended and Restated Letter Agreement*

On April 28, 2021, the Company entered into an amended and restated letter agreement, effective as of May 3, 2021, with Dr. Shacham (the "Shacham Agreement"). The Shacham Agreement amends and restates the amended and restated letter agreement between Dr. Shacham and the Company, dated as of August 28, 2020 and provides for Dr. Shacham's continued employment as Chief Scientific Officer, the cessation of Dr. Shacham's direct management responsibilities beginning on January 1, 2022 (the "Transition Date") and her continuing service as Chair of the Company's Scientific Advisory Board through no earlier than January 1, 2024. Pursuant to the Shacham Agreement, Dr. Shacham will be provided with an annual base salary of \$499,905 for the remainder of 2021 and \$300,000 as of the Transition Date, and an annual bonus target opportunity equal to 50%

of her annual base salary based upon the achievement of certain performance goals and corporate milestones. For so long as Dr. Shacham continues to serve as Chief Scientific Officer, she will also be eligible to receive annual equity grants on the same basis as the Company's other executive officers in good standing as determined by the Board in its sole discretion and to participate in medical, retirement and other benefits that are made available to other executive level employees of the Company.

The Shacham Agreement also provides that, if Dr. Shacham's employment is terminated without Cause (as defined in the Shacham Agreement) or she resigns for Good Reason (as defined in the Shacham Agreement) on or before January 1, 2024 (other than within the twelve month period following a Change of Control (as defined in the Shacham Agreement)), she will be entitled to receive severance pay in the form of salary continuation at the rate of \$499,905 per annum for the Severance Period. If Dr. Shacham's employment is terminated without Cause or she resigns for Good Reason on or before January 1, 2024 and within the twelve month period following a Change of Control, she will, in lieu of the severance benefits described above, be entitled to the following severance benefits: (i) salary continuation at the rate of \$499,905 per annum for the Severance Period; and (ii) an amount equal to 150% of her target annual bonus for the year in which the termination occurs. In addition, if in connection with the termination of Dr. Shacham's employment on or before January 1, 2024, she elects to continue her and her eligible dependents' participation in the Company's medical and dental benefit plans pursuant to COBRA, the Company will, as a severance benefit, pay the premiums to continue such coverage for the lesser of (i) the Severance Period and (ii) the end of the calendar month in which she becomes eligible to receive group health plan coverage under another employee benefit plan. If Dr. Shacham's employment is terminated without Cause or she resigns for Good Reason after January 1, 2024, she will be entitled to severance pay in a lump sum in the amount of \$150,000. Dr. Shacham's receipt of the severance benefits discussed in this paragraph is subject to Dr. Shacham's timely execution and non-revocation of a separation and release of claims agreement as described in the Shacham Agreement.

Pursuant to the Shacham Agreement, Dr. Shacham also surrendered all right, title and interest to portions of certain outstanding stock options for the purchase of 290,000 shares of Common Stock. Dr. Shacham's remaining outstanding equity awards will continue to vest, provided that if the Company terminates her employment without Cause or she resigns for Good Reason on or prior to March 1, 2025, then any of the remaining unvested portions of such equity awards will become vested and exercisable and, if such awards are stock options, will remain exercisable until the earlier of March 1, 2026 and the expiration date of such stock option.

A complete copy of the Shacham Agreement has been filed as Exhibit 10.3 to the Form 8-K filed by the Company with the SEC on May 3, 2021.

### **Voting Matters**

This Supplement does not change the proposals to be acted upon at the Annual Meeting, which are described in the Proxy Statement. **If you have already submitted your proxy, you do not need to take any action unless you wish to change your vote. If you have already submitted your proxy and wish to change your vote based on any of the information contained in this Supplement, you may revoke your proxy or change your vote at any time before it is voted at the Annual Meeting.** Information regarding how to vote your shares and how to revoke your proxy or change your vote is available in the Proxy Statement.

May 3, 2021