

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549**

**SCHEDULE 13G**

**INFORMATION TO BE INCLUDED IN STATEMENTS FILED PURSUANT  
TO RULE 13d-1(b), (c), AND (d) AND AMENDMENTS THERETO FILED  
PURSUANT TO RULE 13d-2(b)**

**(AMENDMENT NO. 5)\***

Karyopharm Therapeutics Inc.

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(Name of Issuer)

Common Stock

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(Title of Class of Securities)

48576U106

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(CUSIP Number)

December 31, 2020

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(Date of Event which Requires Filing of this Statement)

Check the appropriate box to designate the rule pursuant to which this Schedule is filed:

☒ Rule 13d-1(b)

☐ Rule 13d-1(c)

☐ Rule 13d-1(d)

\* The remainder of this cover page shall be filled out for a reporting person's initial filing on this form with respect to the subject class of securities, and for any subsequent amendment containing information which would alter disclosures provided in a prior cover page.

The information required on the remainder of this cover page shall not be deemed to be "filed" for the purpose of Section 18 of the Securities Exchange Act of 1934 ("Act") or otherwise subject to the liabilities of that section of the Act but shall be subject to all other provisions of the Act (however, see the Notes).

1. NAMES OF REPORTING PERSONS OR  
I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)

**Patrick Lee, MD**

2. CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP  
(see instructions)

(a) ☐

(b) ☒

3. SEC USE ONLY

4. CITIZENSHIP OR PLACE OF ORGANIZATION  
USA

5. SOLE VOTING POWER

0

NUMBER OF  
SHARES  
BENEFICIALLY  
OWNED BY  
EACH  
REPORTING  
PERSON WITH

6. SHARED VOTING POWER

5,267,652

7. SOLE DISPOSITIVE POWER

0

8. SHARED DISPOSITIVE POWER

5,267,652

9. AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING  
PERSON

5,267,652

10. CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN  
SHARES  
(see instructions) ☐

11. PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)

7.16%

12. TYPE OF REPORTING PERSON (see instructions)

IN, HC

1. NAMES OF REPORTING PERSONS OR  
I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)

**Anthony Joonkyoo Yun, MD**

2. CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) ☐  
(see instructions) (b) ☒

3. SEC USE ONLY

4. CITIZENSHIP OR PLACE OF ORGANIZATION  
USA

NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	5. SOLE VOTING POWER
	0
	6. SHARED VOTING POWER
	5,267,652
	7. SOLE DISPOSITIVE POWER
	0
	8. SHARED DISPOSITIVE POWER
	5,267,652

9. AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING  
PERSON

5,267,652

10. CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN  
SHARES  
(see instructions) ☐

11. PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)

7.16%

12. TYPE OF REPORTING PERSON (see instructions)

IN, HC

1. NAMES OF REPORTING PERSONS OR  
I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)

**Palo Alto Investors LP**

2. CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) ☐  
(see instructions) (b) ☒

3. SEC USE ONLY

4. CITIZENSHIP OR PLACE OF ORGANIZATION  
California

NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	5. SOLE VOTING POWER
	0
	6. SHARED VOTING POWER
	5,267,652
	7. SOLE DISPOSITIVE POWER
	0
	8. SHARED DISPOSITIVE POWER
	5,267,652

9. AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON  
  
5,267,652

10. CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES  
(see instructions) ☐

11. PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)  
  
7.16%

12. TYPE OF REPORTING PERSON (see instructions)  
  
OO, IA

1. NAMES OF REPORTING PERSONS OR  
I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)

**PAI LLC**

2. CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) ☐  
(see instructions) (b) ☒

3. SEC USE ONLY

4. CITIZENSHIP OR PLACE OF ORGANIZATION  
California

NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	5. SOLE VOTING POWER
	0
	6. SHARED VOTING POWER
	5,267,652
	7. SOLE DISPOSITIVE POWER
	0
	8. SHARED DISPOSITIVE POWER
	5,267,652

9. AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

5,267,652

10. CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN  
SHARES  
(see instructions) ☐

11. PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)

7.16%

12. TYPE OF REPORTING PERSON (see instructions)

OO, IA

**Item 1. (a) Name of Issuer****Karyopharm Therapeutics Inc.****(b) Address of Issuer's Principal Executive Offices****85 Wells Avenue, 2nd Floor, Newton, MA 02459****Item 2. (a) Name of Person Filing**

**Palo Alto Investors LP ("PAI")**  
**PAI LLC ("PAI GP")**  
**Patrick Lee, MD ("Dr. Lee")**  
**Anthony Joonkyoo Yun, MD ("Dr. Yun")**  
(collectively, the "Filers").

**(b) The address of the principal place of the Filers:****470 University Avenue, Palo Alto, CA 94301****(c) For citizenship of Filers, see Item 4 of the cover sheet for each Filer.****(d) Title of Class of Securities**

Common Stock

**(e) CUSIP Number**

48576U106

**Item 3. If this statement is filed pursuant to §§240.13d-1(b) or 240.13d-2(b) or (c), check whether the person filing is a:**(a) ☐ Broker or dealer registered under section 15 of the Act (15 U.S.C. 78o).(b) ☐ Bank as defined in section 3(a)(6) of the Act (15 U.S.C. 78c).(c) ☐ Insurance company as defined in section 3(a)(19) of the Act (15 U.S.C. 78c).(d) ☐ Investment company registered under section 8 of the Investment Company Act of 1940 (15 U.S.C. 80a-8).(e) ☒ An investment adviser in accordance with §240.13d-1(b)(1)(ii)(E); (as to PAI)(f) ☐ An employee benefit plan or endowment fund in accordance with §240.13d-1(b)(1)(ii)(F);(g) ☒ A parent holding company or control person in accordance with §240.13d-1(b)(1)(ii)(G); (as to Dr. Lee and Dr. Yun)

- (h) [ ] A savings associations as defined in Section 3(b) of the Federal Deposit Insurance Act (12 U.S.C. 1813);
- (i) [ ] A church plan that is excluded from the definition of an investment company under section 3(c)(14) of the Investment Company Act of 1940 (15 U.S.C. 80a-3);
- (j) [ ] Group, in accordance with §240.13d-1(b)(1)(ii)(J).

**Item 4. Ownership.**

See Items 5-9 and 11 of the cover page for each Filer.

**Item 5. Ownership of Five Percent or Less of a Class.**

N/A

**Item 6. Ownership of More than Five Percent on Behalf of Another Person.**

PAI is a registered investment adviser and investment adviser of investment limited partnerships, and is the investment adviser to other investment funds. PAI GP 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 Stock.

**Item 7. Identification and Classification of the Subsidiary Which Acquired the Security Being Reported on By the Parent Holding Company.**

N/A

**Item 8. Identification and Classification of Members of the Group.**

Dr. Lee and Dr. Yun co-manage PAI. The Filers are filing this Schedule 13G jointly, but not as members of a group, and each of them expressly disclaims membership in a group. Each Filer disclaims beneficial ownership of the Stock except to the extent of that Filer's pecuniary interest therein.

**Item 9. Notice of Dissolution of Group.**

N/A



**Item 10. Certification.**

By signing below I certify that, to the best of my knowledge and belief, the securities referred to above were not acquired and are not held for the purpose of or with the effect of changing or influencing the control of the issuer of the securities and were not acquired and are not held in connection with or as a participant in any transaction having that purpose or effect.

**Exhibits.**

Exhibit A Joint Filing Agreement.

**SIGNATURE**

After reasonable inquiry and to the best of my knowledge and belief, I certify that the information set forth in this statement is true, complete and correct.

Dated: February 16, 2021

**PALO ALTO INVESTORS LP**

By: /s/ Angela Nguyen-Dinh, Chief Compliance Officer

**PAI LLC**

By: /s/ Patrick Lee, MD

/s/ Patrick Lee, MD

/s/ Anthony Joonkyoo Yun, MD

EXHIBIT A  
AGREEMENT REGARDING JOINT FILING  
OF STATEMENT ON SCHEDULE 13D OR 13G

The undersigned agree to file jointly with the Securities and Exchange Commission (the "SEC") any and all statements on Schedule 13D or Schedule 13G (and any amendments or supplements thereto) required under section 13(d) of the Securities Exchange Act of 1934, as amended, in connection with purchases and sales by the undersigned of the securities of any issuer until such time as the undersigned file with the SEC a statement terminating this Agreement Regarding Joint Filing of Statement on Schedule 13D or 13G. For that purpose, the undersigned hereby constitute and appoint Palo Alto Investors, LP, a California limited partnership, as their true and lawful agent and attorney-in-fact, with full power and authority for and on behalf of the undersigned to prepare or cause to be prepared, sign, file with the SEC and furnish to any other person all certificates, instruments, agreements and documents necessary to comply with section 13(d) and section 16(a) of the Securities Exchange Act of 1934, as amended, in connection with said purchases and sales, and to do and perform every act necessary and proper to be done incident to the exercise of the foregoing power, as fully as the undersigned might or could do if personally present, until such time as the undersigned file with the SEC a statement terminating this Agreement Regarding Joint Filing of Statement on Schedule 13D or 13G.

Dated: February 16, 2021

**PALO ALTO INVESTORS LP**

By: /s/ Angela Nguyen-Dinh, Chief Compliance Officer

**PAI LLC**

By: /s/ Patrick Lee, MD

/s/ Patrick Lee, MD

/s/ Anthony Joonkyoo Yun, MD