

**SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

**SCHEDULE 13G**

**(Rule 13d-102)**

**INFORMATION TO BE INCLUDED IN STATEMENTS FILED PURSUANT  
TO § 240.13d-1(b), (c) AND (d) AND AMENDMENTS THERETO FILED PURSUANT TO  
§ 240.13d-2**

**(Amendment No. 5)\***

**KARYOPHARM THERAPEUTICS INC.**

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(Name of Issuer)

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**Common Stock par value \$0.0001 per share**

(Title of Class of Securities)

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**48576U106**

(CUSIP Number)

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**December 31, 2018**

(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 the disclosures provided in a prior cover page.

The information required in 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 Michael G. Kauffman	
<hr/>		
2.	Check the Appropriate Box if a Member of a Group (See Instructions)	
	(a) <input type="checkbox"/>	
	(b) <input type="checkbox"/>	
<hr/>		
3.	SEC Use Only	
<hr/>		
4.	Citizenship or Place of Organization United States of America	
<hr/>		
Number of Shares Beneficially Owned by Each Reporting Person With	5. Sole Voting Power 1,650,927	
	6. Shared Voting Power 1,955,513	
	7. Sole Dispositive Power 1,650,927	
	8. Shared Dispositive Power 1,955,513	
<hr/>		
9.	Aggregate Amount Beneficially Owned by Each Reporting Person 3,606,440	
<hr/>		
10.	Check if the Aggregate Amount in Row (9) Excludes Certain Shares (See Instructions) <input type="checkbox"/>	
<hr/>		
11.	Percent of Class Represented by Amount in Row (9) 5.71%(1)	
<hr/>		
12.	Type of Reporting Person (See Instructions) IN	
<hr/>		

(1) Based upon 60,829,308 shares of Karyopham Therapeutics Inc. Common Stock outstanding on December 31, 2018.

1.	Names of Reporting Persons Sharon Shacham	
<hr/>		
2.	Check the Appropriate Box if a Member of a Group (See Instructions)	
(a)	<input type="checkbox"/>	
(b)	<input type="checkbox"/>	
<hr/>		
3.	SEC Use Only	
<hr/>		
4.	Citizenship or Place of Organization United States of America	
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Number of Shares Beneficially Owned by Each Reporting Person With	5. Sole Voting Power 1,955,513	
	6. Shared Voting Power 1,650,927	
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11.	Percent of Class Represented by Amount in Row (9) 5.71%(1)	
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12.	Type of Reporting Person (See Instructions) IN	
<hr/>		

(1) Based upon 60,829,308 shares of Karyopham Therapeutics Inc. Common Stock outstanding on December 31, 2018.

## Item 1.

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

- (a) Name of Person Filing:  
This Schedule is filed by Michael G. Kauffman and Sharon Shacham (each a "Reporting Person" and collectively, "Reporting Persons").
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- (b) Address of Principal Business Office or, if none, Residence:  
c/o Karyopharm Therapeutics Inc., 85 Wells Avenue, 2nd Floor, Newton, MA 02459.
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- (c) Citizenship:  
See Row 4 of cover page for each Reporting Person.
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- (d) Title of Class of Securities:  
Common stock par value \$0.0001 per share.
- 
- (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);
- (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);
- (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)  A non-U.S. institution in accordance with §240.13d-1(b)(1)(ii)(J).
- (k)  Group, in accordance with §240.13d-1(b)(1)(ii)(K).

If filing as a non-U.S. institution in accordance with §240.13d-1(b)(1)(ii)(J), please specify the type of institution: \_\_\_\_\_

## Item 4. Ownership

Provide the following information regarding the aggregate number and percentage of the class of securities of the issuer identified in Item 1.

## (a) Amount beneficially owned:

For each Reporting Person, 3,606,440 shares of Common Stock, consisting of (a) 529,767 shares of Common Stock held by Dr. Kauffman, (b) 29,685 shares of Common Stock held by Dr. Kauffman as Trustee of the Michael G. Kauffman 2016 Qualified Annuity Interest Trust, (c) 1,091,475 shares of Common Stock underlying options held by Dr. Kauffman that are exercisable as of December 31, 2018 or will become exercisable within 60 days after such date, (d) 731,134 shares of Common Stock held by Dr. Shacham, (e) 29,685 shares of Common Stock held by Dr. Shacham as Trustee of the Sharon Shacham 2016 Qualified Annuity Interest Trust and (f) 1,194,694 shares of Common Stock underlying options held by Dr. Shacham that are exercisable as of December 31, 2018 or will become exercisable within 60 days after such date.

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## (b) Percent of class:

See Row 11 of cover page for each Reporting Person.

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## (c) Number of shares as to which the person has:

## (i) Sole power to vote or to direct the vote

See Row 5 of cover page for each Reporting Person.

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## (ii) Shared power to vote or to direct the vote

See Row 6 of cover page for each Reporting Person.

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## (iii) Sole power to dispose or to direct the disposition of

See Row 7 of cover page for each Reporting Person.

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## (iv) Shared power to dispose or to direct the disposition of

See Row 8 of cover page for each Reporting Person.

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

If this statement is being filed to report the fact that as of the date hereof the reporting person has ceased to be the beneficial owner of more than five percent of the class of securities, check the following .

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

Not applicable.

## Item 7. Identification and Classification of the Subsidiary Which Acquired the Security Being Reported on By the Parent Holding Company or Control Person

Not applicable.

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

Not applicable.

## Item 9. Notice of Dissolution of Group

Not applicable.

Item 10. Certification

Not applicable.

**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.

February 11, 2019

\_\_\_\_\_  
Date

/s/ Michael G. Kauffman

\_\_\_\_\_  
Signature

Michael G. Kauffman, M.D., Ph.D.

\_\_\_\_\_  
Name

February 11, 2019

\_\_\_\_\_  
Date

/s/ Sharon Shacham

\_\_\_\_\_  
Signature

Sharon Shacham, Ph.D., M.B.A.

\_\_\_\_\_  
Name

Exhibit Index

Exhibit 1. Joint Filing Agreement, dated as of February 14, 2014, by and between the Reporting Persons (incorporated by reference to Exhibit 1 to the Schedule 13G filed by the Reporting Persons with the Securities and Exchange Commission on February 14, 2014).