

**SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

**FORM S-1****REGISTRATION STATEMENT  
UNDER  
THE SECURITIES ACT OF 1933****KARYOPHARM THERAPEUTICS INC.**

(Exact Name of Registrant as Specified in its Charter)

**Delaware**  
(State or Other Jurisdiction of  
Incorporation or Organization)**2834**  
(Primary Standard Industrial  
Classification Code Number)**26-3931704**  
(I.R.S. Employer  
Identification Number)**2 Mercer Road  
Natick, MA 01760  
(508) 975-4820**

(Address, Including Zip Code, and Telephone Number, Including Area Code, of Registrant's Principal Executive Offices)

**Michael G. Kauffman, M.D., Ph.D.**  
**Chief Executive Officer**  
**Karyopharm Therapeutics Inc.**  
**2 Mercer Road**  
**Natick, MA 01760**  
**(508) 975-4820**

(Name, Address, Including Zip Code, and Telephone Number, Including Area Code, of Agent for Service)

**Copies to:****Steven D. Singer, Esq.**  
**Joshua D. Fox, Esq.**  
Wilmer Cutler Pickering Hale  
and Dorr LLP  
60 State Street  
Boston, MA 02109  
Telephone: (617) 526-6000**Christopher B. Primiano, Esq.**  
Vice President, General Counsel  
Karyopharm Therapeutics Inc.  
2 Mercer Road  
Natick, MA 01760  
Telephone: (508) 975-4820**Patrick O'Brien, Esq.**  
Ropes & Gray LLP  
Prudential Tower  
800 Boylston Street  
Boston, MA 02199  
Telephone: (617) 951-7000**Approximate date of commencement of proposed sale to the public: As soon as practicable after this Registration Statement becomes effective.**If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box. If this Form is filed to register additional securities for an offering pursuant Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.  333-196892If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. 

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer Accelerated filer Non-accelerated filer  (Do not check if a smaller reporting company)Smaller reporting company **CALCULATION OF REGISTRATION FEE**

Title of each class of securities to be registered	Amount to be registered (1)	Proposed maximum offering price per share (2)	Proposed maximum aggregate offering price (2)	Amount of registration fee
Common Stock, \$0.0001 par value per share	514,334 shares	\$ 42.50	\$ 21,859,195	\$ 2,815.47

(1) Includes shares that the Underwriters have the option to purchase to cover over-allotments, if any.

(2) Estimated in accordance with Rule 457(a) of the Securities Act of 1933 solely on the basis of \$42.50, the Public Offering Price set forth on the cover page of the Registrant's Prospectus dated June 26, 2014 relating to its initial public offering pursuant to the Company's Registration Statement on Form S-1



**EXPLANATORY NOTE AND INCORPORATION BY REFERENCE**

This registration statement is being filed with respect to the registration of additional shares of common stock, par value \$0.0001 per share, of Karyopharm Therapeutics Inc., a Delaware corporation, pursuant to Rule 462(b) under the Securities Act of 1933, as amended. The contents of the earlier registration statement on Form S-1 (File No. 333-196892), which was declared effective by the Commission on June 26, 2014, are incorporated in this registration statement by reference.

The required opinions and consents are listed on an Exhibit Index attached hereto and filed herewith.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the Registrant has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Natick, Commonwealth of Massachusetts, on this 26<sup>th</sup> day of June, 2014.

KARYOPHARM THERAPEUTICS INC.

By: /s/ MICHAEL G. KAUFFMAN  
Michael G. Kauffman, M.D., Ph.D.  
*Chief Executive Officer*

Pursuant to the requirements of the Securities Act of 1933, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ MICHAEL G. KAUFFMAN</u> Michael G. Kauffman, M.D., Ph.D.	Chief Executive Officer and Director (principal executive officer)	June 26, 2014
<u>/s/ PAUL BRANNELLY</u> Paul Brannelly	Senior Vice President, Finance and Administration and Treasurer (principal financial and accounting officer)	June 26, 2014
<u>*</u> Garen G. Bohlin	Director	June 26, 2014
<u>*</u> Barry E. Greene	Director	June 26, 2014
<u>*</u> Deepa R. Pakianathan, Ph.D.	Director	June 26, 2014
<u>*</u> Mansoor Raza Mirza, M.D.	Director	June 26, 2014
<u>*</u> Kenneth E. Weg	Director	June 26, 2014

\*By: /s/ PAUL BRANNELLY  
Name: Paul Brannelly  
Title: *Attorney-in-Fact*

## EXHIBIT INDEX

<u>Exhibit No.</u>	<u>Description</u>
5.1	Opinion of Wilmer Cutler Pickering Hale and Dorr LLP
23.1	Consent of Wilmer Cutler Pickering Hale and Dorr LLP (included in Exhibit 5.1)
23.2	Consent of McGladrey LLP
24.1*	Powers of Attorney

\* Filed as Exhibit 24.1 to the Registrant's Registration Statement on Form S-1 (File No. 333-196892) filed with the Commission on June 19, 2014.

WILMERHALE

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Wilmerhale.com

June 26, 2014

Karyopharm Therapeutics Inc.  
2 Mercer Road  
Natick, MA 01760

Re: Registration Statement on Form S-1

Ladies and Gentlemen:

This opinion is furnished to you in connection with a Registration Statement on Form S-1 (File No. 333-196892) (the "Registration Statement") filed with the Securities and Exchange Commission (the "Commission") under the Securities Act of 1933, as amended (the "Securities Act"), pursuant to Rule 462(b) of the Securities Act, for the registration of an aggregate of 514,334 shares of Common Stock, \$0.0001 par value per share (the "Shares"), of Karyopharm Therapeutics Inc., a Delaware corporation (the "Company"), of which up to 67,087 Shares may be issued and sold by the Company upon exercise of an option granted by the Company.

The Shares are to be sold by the Company pursuant to an underwriting agreement (the "Underwriting Agreement") entered into by and among the Company, certain selling stockholders and the several underwriters named in Schedule A thereto, for whom Merrill Lynch, Pierce, Fenner & Smith Incorporated and Leerink Partners LLC are acting as representatives, the form of which has been filed as Exhibit 1.1 to the Registration Statement.

We are acting as counsel for the Company in connection with the sale by the Company of the Shares. We have examined signed copies of the Registration Statement as filed with the Commission. We have also examined and relied upon the Underwriting Agreement, minutes of meetings and actions of the stockholders and the Board of Directors of the Company as provided to us by the Company, stock record books of the Company as provided to us by the Company, the Certificate of Incorporation and By-Laws of the Company, each as restated and/or amended to date, and such other documents as we have deemed necessary for purposes of rendering the opinions hereinafter set forth.

In our examination of the foregoing documents, we have assumed the genuineness of all signatures, the authenticity of all documents submitted to us as originals, the conformity to original documents of all documents submitted to us as copies, the authenticity of the originals of such latter documents and the legal competence of all signatories to such documents.

We express no opinion herein as to the laws of any state or jurisdiction other than the state laws of the Commonwealth of Massachusetts, the General Corporation Law of the State of Delaware and the federal laws of the United States of America.

Wilmer Cutler Pickering Hale and Dorr LLP, 850 Winter Street, Waltham, MA 02451

Beijing Berlin Boston Brussels Frankfurt London Los Angeles New York Oxford Palo Alto Waltham Washington

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Based upon and subject to the foregoing, we are of the opinion that the Shares to be issued and sold by the Company have been duly authorized for issuance and, when such Shares are issued and paid for in accordance with the terms and conditions of the Underwriting Agreement, such Shares will be validly issued, fully paid and nonassessable.

Please note that we are opining only as to the matters expressly set forth herein, and no opinion should be inferred as to any other matters. This opinion is based upon currently existing statutes, rules, regulations and judicial decisions, and we disclaim any obligation to advise you of any change in any of these sources of law or subsequent legal or factual developments which might affect any matters or opinions set forth herein.

We hereby consent to the filing of this opinion with the Commission as an exhibit to the Registration Statement in accordance with the requirements of Item 601(b)(5) of Regulation S-K under the Securities Act and to the use of our name therein and in the related Prospectus under the caption "Legal Matters." In giving such consent, we do not hereby admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations of the Commission.

Very truly yours,

WILMER CUTLER PICKERING  
HALE AND DORR LLP

By: /s/ Joshua D. Fox  
Joshua D. Fox, a Partner

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in this Registration Statement on Form S-1 of Karyopharm Therapeutics Inc. filed pursuant to Rule 462(b) of the Securities Act of 1933, as amended, of our report dated March 21, 2014, relating to our audits of the consolidated financial statements, appearing in the Prospectus, which is part of the Registration Statement (Form S-1 No 333-196892).

We also consent to the reference to our Firm under the caption "Experts" in such Prospectus.

*McGladrey LLP*

Boston, Massachusetts  
June 25, 2014

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