



DIVISION OF  
CORPORATION FINANCE

UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, D.C. 20549

November 4, 2013

Via E-mail

Michael G. Kauffman, M.D., Ph.D.  
Chief Executive Officer  
Karyopharm Therapeutics Inc.  
2 Mercer Road  
Natick, MA 01760

**Re: Karyopharm Therapeutics Inc.  
Amendment No. 1 to Registration Statement on Form S-1  
Filed October 28, 2013  
File No. 333-191584**

Dear Dr. Kaufman:

We have reviewed your amendment and related correspondence filed October 28, 2013 and we have the following comments.

Please respond to this letter by amending your registration statement and providing the requested information. If you do not believe our comments apply to your facts and circumstances or do not believe an amendment is appropriate, please tell us why in your response.

After reviewing any amendment to your registration statement and the information you provide in response to these comments, we may have additional comments.

Capitalization, page 51

1. Please explain how the share amounts shown in the section (ii) (a) through (d) aggregate to 19,114,241 shares and are consistent with the amounts shown in the relevant caption disclosure on page 52.

Dilution, page 54

2. Please explain how you computed the historical net tangible book value per share of (\$14.50 per share), pro forma net tangible book value per share of \$2.74 per share and pro forma net tangible book value per share adjusted for the planned offering of \$4.95 per share. In particular, explain how you determined the shares amounts used in each of these calculations and how these share amounts are consistent with corresponding disclosure in the section, Capitalization, and the consolidated statement of convertible preferred stock and stockholders' equity.

3. Please explain how the amount of shares purchased by existing shareholders of 21,864,198 shares, disclosed on page 55, is consistent with the corresponding amount at June 30, 2013 on page F-5.

We urge all persons who are responsible for the accuracy and adequacy of the disclosure in the filing to be certain that the filing includes the information the Securities Act of 1933 and all applicable Securities Act rules require. Since the company and its management are in possession of all facts relating to a company's disclosure, they are responsible for the accuracy and adequacy of the disclosures they have made.

Notwithstanding our comments, in the event you request acceleration of the effective date of the pending registration statement please provide a written statement from the company acknowledging that:

- should the Commission or the staff, acting pursuant to delegated authority, declare the filing effective, it does not foreclose the Commission from taking any action with respect to the filing;
- the action of the Commission or the staff, acting pursuant to delegated authority, in declaring the filing effective, does not relieve the company from its full responsibility for the adequacy and accuracy of the disclosure in the filing; and
- the company may not assert staff comments and the declaration of effectiveness as a defense in any proceeding initiated by the Commission or any person under the federal securities laws of the United States.

Please refer to Rules 460 and 461 regarding requests for acceleration. We will consider a written request for acceleration of the effective date of the registration statement as confirmation of the fact that those requesting acceleration are aware of their respective responsibilities under the Securities Act of 1933 and the Securities Exchange Act of 1934 as they relate to the proposed public offering of the securities specified in the above registration statement. Please allow adequate time for us to review any amendment prior to the requested effective date of the registration statement.

Michael G. Kaufman, M.D., Ph.D.  
Karyopharm Therapeutics Inc.  
November 4, 2013  
Page 3

You may contact Frank Wyman at (202) 551-3660 or Joel Parker at (202) 551-3651 if you have questions regarding comments on the financial statements and related matters. Please contact Scot Foley at (202) 551-3383, Bryan Pitko at (202) 551-3203 or me at (202) 551-3715 with any other questions.

Sincerely,

/s/ Bryan J. Pitko for

Jeffrey P. Riedler  
Assistant Director

cc: Steven D. Singer, Esq.  
Joshua D. Fox, Esq.  
Wilmer Cutler Pickering Hale and Dorr LLP  
60 State Street  
Boston, MA 02109