



DIVISION OF  
CORPORATION FINANCE

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

October 24, 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.  
Registration Statement on Form S-1  
Response dated October 18, 2013  
File No. 333-191584**

Dear Dr. Kaufman:

We have reviewed your correspondence filed on October 18, 2013 and have the following comments. Please respond to this letter by providing the requested information. If you do not believe our comments apply to your facts and circumstances, please tell us why in your response.

After reviewing the information you provide in response to these comments, we may have additional comments.

Management's Discussion and Analysis of Financial Condition and Results of Operations  
Critical Accounting Policies and Estimates  
Share-Based Compensation, page 62

1. It is unclear how you have sufficiently addressed the quantitative or qualitative components in our initial comment in your discussion of each significant factor contributing to the difference between the latest common stock valuation and the estimated IPO price, considering the significant increase in fair value from the September 24, 2013 price to the midpoint of your IPO price range. Please revise your disclosure to further support this increase and quantify the impact that the following items had on your increased valuation:
  - The enrollment of 22 additional patients in clinical trials of Selinexor;
  - The receipt of updated clinical data;
  - The agreement with Fast Forward LLC; and

- The 65% weighting of your IPO scenario.
2. You cite improved capital market conditions for companies in your industry as a reason for the increase in fair value, reflected in the estimated IPO price. Please explain to us why you were unaware of this information and presumably did not include it in your September 24, 2013 common stock valuation.
  3. During the three months ended September 30, 2013, you granted an additional 3,959,000 options to employees and 140,500 options to non-employees per page F-22. Please include these options in your tabular disclosure on page 63.
  4. We will further evaluate your accounting for stock compensation and related disclosures, once you have finalized an estimated offering price range and disclosed this information in a subsequent amendment to your Registration Statement.

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.  
October 24, 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  
Telephone: (617) 526-6000