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

DIVISION OF
CORPORATION FINANCE

October 2, 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.
Draft Registration Statement on Form S-1
Submitted September 5, 2015
CIK No. 0001503802

Dear Dr. Kaufman:

We have reviewed your draft registration statement and have the following comments. In some of our comments, we may ask you to provide us with information so we may better understand your disclosure.

Please respond to this letter by providing the requested information and either submitting an amended draft registration statement or publicly filing your registration statement on EDGAR. 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 the information you provide in response to these comments and your amended draft registration statement or filed registration statement, we may have additional comments.

General

1. We note that you have submitted an application for confidential treatment relating to one of your exhibits. Please be advised that comments to this application, if any, will be sent under separate cover and that any such comments must be resolved prior to our acting on any acceleration request relating to your registration statement.

2. Please confirm that the graphics included in your registration statement are the only graphics you will use in your prospectus. If those are not the only graphics, please provide any additional graphics prior to their use for our review.

3. Please supplementally provide us with copies of all written communications, as defined in Rule 405 under the Securities Act, that you, or anyone authorized to do so on your behalf, present to potential investors in reliance on Section 5(d) of the Securities Act, whether or not they retain copies of the communications. Similarly, please supplementally provide us with any research reports about you that are published or distributed in reliance upon Section 2(a)(3) of the Securities Act of 1933 added by Section 105(a) of the Jumpstart Our Business Startups Act by any broker or dealer that is participating or will participate in your offering.

Prospectus Summary
Overview, page 1

4. Please revise your summary to include the percentage of total patients with relapsed and/or refractory acute myeloid leukemia who experienced complete remission or stable disease.

5. Please indicate here that your first Phase 1 clinical trial relating to advanced hematological malignancies has three arms, and list the indications for each arm

6. Here, and in your Business discussion, please explain how your planned clinical trial for Selinexor will qualify as both a Phase 2 and Phase 3 clinical trial.

Risks Associated with Our Business, page 5

7. In your first bullet point, please include the amount of your accumulated deficit to date.

8. In your sixth bullet point, please note that both adverse events and serious adverse events have been experienced by patients in your clinical trials for Selinexor including several which have been determined to relate to the use of Selinexor.

9. In your eighth bullet point, please clarify that you have applied for but have not yet been granted any patents in relation to your key drug candidates.

Risk Factors

"We will need substantial additional funding…," page 12

10. Please include an estimate of the capital you believe you will require for the remainder of this fiscal year and the next complete fiscal year.

"Product liability lawsuits against us could cause us to incur substantial liabilities…," page 24

11. Please revise your risk factor discussion to identify the amount of clinical trial liability insurance coverage you maintain.

"Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights . . .," page 31

12. Please indicate in this risk factor whether or not any such litigation is currently pending against you and/or whether you have ever been held by a court of competent jurisdiction to have infringed on a third party's intellectual rights.

"We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers," page 31

13. Please include in this risk factor examples of any such claims that has been filed against you or any of your founders, scientific advisors, directors and/or executive officers.

"We will incur increased costs as a result of operating as a public company . . .," page 45

14. In this risk factor, please include, to the extent practicable, an estimate of the annual costs associated with being a public company.

Use of Proceeds, page 48

15. Please bifurcate the approximate amount of net proceeds you intend to allocate to the Phase 2/3 clinical trials of Selinexor and the amount you intend to allocate to Selinexor's Phase 2 trials for the two solid tumor indications.

Industry and Other Data, page 50

16. Please revise your prospectus to remove your statements that you have not independently verified market and industry and competitive position date from third-party sources and that internal company research and estimates and market definitions have not been verified by any independent source. It is not appropriate to directly or indirectly disclaim liability for information in the registration statement.

Dilution, page 54

17. Your historical net tangible book value as of June 30, 2013 appears to be a deficit. Please revise your disclosure or tell why your presentation is appropriate.

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

18. We will further evaluate your accounting for stock compensation and related disclosure once you have disclosed an estimated offering price. Please expand your disclosure to address the following:

- Once you can reasonably estimate the IPO price, qualitatively and quantitatively discuss each significant factor contributing to the difference between each valuation and the estimated IPO price;

- Continue to update your disclosure for all equity related transactions through the effectiveness date of the registration statement; and

- Please revise your disclosure to present the intrinsic value of outstanding vested and unvested options as of the most recent balance sheet date based on the estimated IPO price.

Business
Our Drug Candidates, page 86

19. Please indicate in your disclosure when you filed the Investigational New Drug application(s) for Selinexor and the various indications it is being developed to treat.

20. We note your disclosure that Selinexor has been generally well-tolerated despite the occurrence of a number of adverse and serious adverse events in your Phase 1 clinical trials. In light of the occurrence and frequency of these events, please revise your disclosure to provide your basis for the conclusion that Selinexor has generally been well-tolerated.

Advanced Hematological Malignancies, page 86

21. We note that your disclosure, as currently written, only provides examples of complete response and partial response for chronic lymphocytic leukemia. Please revise your disclosure to identify what results qualify as a CR, PR, MR, and SD under the "commonly accepted evaluation criteria" for each indication tested in arm 1 of your Phase I trial for hematological malignancies. Please also discuss the results constituting progressive disease for each indication.

Intellectual Property, page 100

22. Please identify the three foreign jurisdictions in which you have pending patent applications for Selinexor.

Management, page 119

23. We note that the biographical information provided for Drs. Kauffman and Shacham discusses their employment at Epix Pharmaceuticals, Inc. which underwent liquidation proceedings in 2009. If a petition under the federal bankruptcy laws or any state insolvency law was filed by or against, or a receiver, fiscal agent or similar officer was appointed by a court for Epix, please revise the biographical information for Drs.

Kauffman and Shacham to provide this information. Please refer to requirements of Item 401(f)(1) of Regulation S-K.

Narrative Disclosure to Summary Compensation Table, page 127
Annual Performance-based Cash Incentives, page 127

24. Please revise your disclosure to provide a description of the material terms of your annual performance-based cash incentive program including any formula or criteria applied to determine the amount paid to Drs. Kauffman and Shacham. Please also highlight the specific corporate and individual performance that led the board to award the cash incentive payments paid.

Shares Eligible for Future Sale
Lock-Up Agreements, page 152

25. Please file a copy of the form lock-agreement as an exhibit to your registration statement. If it is to be filed as an exhibit to your underwriting agreement, please confirm this for us.

Note 2. Summary of Significant Accounting Policies
Principles of Consolidation, page F-9

26. Please tell us and disclose where you have recorded the non-controlling interest for NPM.

If you intend to respond to these comments with an amended draft registration statement, please submit it and any associated correspondence in accordance with the guidance we provide in the Division's October 11, 2012 announcement on the SEC website at http://www.sec.gov/divisions/corpfin/cfannouncements/drsfilingprocedures101512.htm.

Please keep in mind that we may publicly post filing review correspondence in accordance with our December 1, 2011 policy (http://www.sec.gov/divisions/corpfin/cfannouncements/edgarcorrespondence.htm). If you intend to use Rule 83 (17 CFR 200.83) to request confidential treatment of information in the correspondence you submit on EDGAR, please properly mark that information in each of your confidential submissions to us so we do not repeat or refer to that information in our comment letters to you.

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