Mail Stop 6010

January 25, 2008

Tod Woolf, Ph.D.
Chief Executive Officer
RXi Pharmaceuticals Corporation
One Innovation Drive
Worcester, Massachusetts 01605

Re: RXi Pharmaceuticals Corporation
Registration Statement on Form S-1/A
Filed January 10, 2008
File No. 333-147009

Dear Dr. Woolf:

We have reviewed your filing and have the following comments. Where indicated, we think you should revise your document in response to these comments. If you disagree, we will consider your explanation as to why our comment is inapplicable or a revision is unnecessary. Please be as detailed as necessary in your explanation. In some of our comments, we may ask you to provide us with information so we may better understand your disclosure. After reviewing this information, we may raise additional comments.

Please understand that the purpose of our review process is to assist you in your compliance with the applicable disclosure requirements and to enhance the overall disclosure in your filing. We look forward to working with you in these respects. We welcome any questions you may have about our comments or any other aspect of our review. Feel free to call us at the telephone numbers listed at the end of this letter.

General

1. Unless otherwise stated, all comments are applicable to the distribution prospectus, award prospectus and resale prospectus.

2. We are reissuing part of prior comment 6. Throughout the registration statement, you should clearly articulate the basis of the various beliefs and assertions you make. In each of the below statements and each similar case throughout the filing, you should disclose the basis for your belief. If any of your assertions or

beliefs are not supported by ample evidence or knowledge, you should delete them. Alternatively, in each case and as applicable, clarify that these are goals or beliefs articulating what you hope to achieve.

a. Page 2: "There are many well-studied genes associated with numerous diseases that have been identified but have been difficult to target with normal medicinal chemistry and which we believe RNAi technology may be able to target and, therefore, potentially treat such diseases."

b. Page 35: "We believe we will be able to discover and develop lead compounds and move them into and through development for potential commercialization more efficiently than traditional drug development approaches."

c. Page 52: "We believe that the RNAi platform will create a successful new class of potent and specific therapeutics with significant advantages over traditional drug development methods. These advantages include: high specificity for targeted genes; high potency (low doses); potential interference with the expression of any gene; and accelerated development of lead compounds." In addition, we note you also make similar statements, without support, on page 53, to the extent you cannot support these statements, please delete them.

d. Page 53: "rxRNA is an alternative to classic siRNA used by other companies developing RNAi therapeutics and is: up to 100x more active than conventional siRNA (depending on the target site), nuclease resistant, readily manufactured, comprised of elements from RXi's IP portfolio, and potentially more specific for the target gene."

e. Page 54: "We believe that nanotransporter delivery has the following potential advantages: inhibition of liver target with 1 mg RNAi compound per kg of body weight; no immune stimulation detected; defined particle size; and readily formulated."

f. Page 55: "We believe RNAi compounds have the potential to target any gene."

g. Page 56: "RNAi reagents targeting multiple genes could be developed to treat cancers originated from malfunctioning of multiple intracellular pathways."

h. Page 56: "RNAi may be used to inhibit cell division in non-cancerous tissues which are damaged by chemotherapy in order to protect these cells from chemotherapy. RNAi screening methods may potentially also be

used to rapidly prioritize molecular targets within large gene families by conducting in vitro experiments to identify which gene family members are the most appropriate targets to pursue."

Prospectus Summary, page 1

3. We note our prior comment 12 and reissue it in part. In the Prospectus Summary, please clarify how much of their professional time your advisory board members will devote to the company, as opposed to other professional endeavors, and explain, if true, that they are not employees of the company, have other professional commitments that require significantly more of their professional time and attention than any obligations they have to the company, and that they have no obligations or duties to perform any advisory services for the company or remain as advisors to the company. Provide similar disclosure in the Business section.

Risk Factors, page 10

"We will be subject to competition and may not be able to compete successfully." Page 13

4. Please expand your discussion to discuss the additional risk that occurs when a competitor's drug, which has been granted orphan drug status, is approved by the FDA.

"We use biological and hazardous materials…" page 21

5. We are reissuing prior comment 29. Please disclose your level of workers' compensation insurance coverage and briefly describe what potential liabilities are and are not covered.

Executive Compensation, page 74

2007 Executive Compensation Components, page 75

Performance-Based Compensation, page 76

6. Please disclose any performance goals set by the compensation committee or board for 2007, including, but not limited to, the performance goals in connection with Mr. DiPalma's and Dr. Samarsky's awards.

7. Please also revise to state any target performance based compensation amounts for the other executive officers which were set in 2007.

Summary Compensation Table, page 78

8. Please revise the table to provide a footnote which discloses all assumptions made in the valuation of the option awards. See Instruction 1 to Item 402(c)(v) and (vi) of Regulation S-K.

9. Please revise footnote 1 to provide disclosure regarding any formula or criteria that will be used and any other pertinent information in determining the bonus amount. See Telephone Interpretation J.8B.

Director Compensation, page 87

10. Please revise the table to provide a footnote which discloses the aggregate number of option awards outstanding at fiscal year end. See the Instruction to Item 402(k)(2)(iii) and (iv) of Regulation S-K.

Certain Relationships and Related Transactions, page 92

Relationships with Employees, page 92

11. Please file a copy of your license agreement with Invitrogen.

Material United States Federal Income Tax Considerations, page 100

12. Please revise to clearly state that the disclosure in this section is the opinion of Troy & Gould, rather than stating that it has delivered an opinion "to the following effects."

Legal Matters, page 103

13. Please disclose in the distribution prospectus the required information regarding the interests of Mr. Hillsberg and Troy & Gould pursuant to Item 509 of Regulation S-K, as we note that Troy & Gould is providing a tax opinion regarding this transaction.

RXI Pharmaceuticals Corporation and Predecessor Carve-Out Financial Statements

RXI Pharmaceuticals Corporation and Predecessor Carve-Out Statements of Expenses and Statements of Cash Flows, pages F-4 and F-6, respectively.

14. With regards to the cumulative data presented for the period from April 3, 2006 (date of incorporation) to September 30, 2007, please include all financial data related to the period from January 1, 2003 through September 30, 2007 which

would include predecessor financial information. In that regard, please remove the parenthetical reference to Successor under that column. Please revise this presentation throughout the filing.

Notes to Financial Statements

5. Development Stage Supplemental Equity Disclosure, page F-15

15. We acknowledge your response to our comment 60. Please revise your disclosure added on pages 28, 35 and 46 to clarify that you include the 462,112 shares of common stock in determining your $5.00 share value because you committed to issue these shares prior to the date of your third-party valuation consistent with your response.

16. In addition, with regards to your common stock issuance of 188,387 on September 28, 2007, please revise throughout the filing, specifically pages 28 and 35, the actual price of $5.19 per share as indicated in this footnote.

17. We acknowledge your response to our comment 61. Please revise your disclosure added in footnote (B) to your table to clarify that the pro rata share of offering costs allocated to RXi relates to the private offering conducted by CytRx to fund your capital contribution consistent with your response.

18. In addition, as previously requested in our comment 61, please revise your liquidity discussion in MD&A to provide an indication of the costs you expect to incur in this offering as indicated on page B-22. We did not note any revision to your disclosure with regards to this comment.

9. Commitments and Contingencies, page F-16

19. Refer to your response to our comment 62 and we reissue our comment. It appears from footnote 3 that the payments included in the table represent minimum annual royalty payment obligations. Please revise your footnote disclosure to quantify the milestone payment amounts that maybe required under your agreements which you state that you have omitted from the table. In addition, please discuss, similar to the discussion provided in your response, how these potential milestone payments were determined.

Resale Prospectus

20. We note your response to prior comment 66. It appears that CytRx's proposed offering of shares in what you have termed the "Resale Prospectus" would be a primary offering and that CytRx would be an underwriter. Since RXi is not eligible to conduct a primary offering on Form S-3 or "at-the-market" under Rule

415(a)(4), you should remove CytRx as a selling shareholder in this offering. If you would like to register the offer and sale of these shares of RXi common stock, you should register that transaction at a fixed price and name CytRx as an underwriter.

21. As to UMMS's resale of its RXi shares, in the "Resale Prospectus" please provide the pricing information required by Item 501(b)(3) of Regulation S-K. Absent a market price, disclosing that the shares would be sold at market does not satisfy this Item requirement. Please revise the cover page of the "Resale Prospectus" to state, "The selling shareholder will sell at a price of $x.xx (or a range) per share until our shares are quoted on the NASDAQ Capital Market and thereafter at prevailing market prices or privately negotiated prices."

Selling Stockholders, page B-85

22. It appears that UMMS is offering 462,112 shares under this "Resale Prospectus;" please revise your table accordingly.

Part II

Item 17. Undertakings

23. Please review Item 512 of Regulation S-K and provide all undertakings required by that Item. For example, we note that the offering described in the "Resale Prospectus" is an offering under Rule 415 and you have not provided the undertaking required by Item 512(a).

* * *

As appropriate, please amend your registration statement in response to these comments. You may wish to provide us with marked copies of the amendment to expedite our review. Please furnish a cover letter with your amendment that keys your responses to our comments and provides any requested information. Detailed cover letters greatly facilitate our review. Please understand that we may have additional comments after reviewing your amendment and responses to our comments.

We direct your attention to Rules 460 and 461 regarding requesting acceleration of a registration statement. Please allow adequate time after the filing of any amendment for further review before submitting a request for acceleration. Please provide this request at least two business days in advance of the requested effective date.

You may contact Sasha Parikh at (202) 551-3627 or Mark Brunhofer at (202) 551-3638 if you have questions regarding comments on the financial statements and related matters. Please contact Jennifer Riegel at (202) 551-3575, Michael Reedich, Special Counsel, at (202) 551-3612 or me at (202) 551-3715 with any other questions.

Sincerely,

Jeffrey Riedler
Assistant Director

cc: Marc Rubenstein, Esq.
Ropes & Gray LLP
One International Place
Boston, MA 02110-2624