Mail Stop 6010

November 26, 2007

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
Filed October 30, 2007
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.

FORM S-1

General

1. We note that you are submitting a number of documents in a confidential treatment request. Please note that you will be receiving comments to the confidential treatment request under separate cover and that all confidential treatment issues must be resolved before we will consider a request for acceleration of the registration statement.

2. Please file as promptly as possible all exhibits required by the Exhibit Table provided in Item 601(a) of Regulation S-K. We note, for example, that you have not filed the opinion or consent of your legal counsel.

3. Please note that where we provide examples to illustrate what we mean by our comments, they are examples and not exhaustive lists. If our comments are applicable to portions of the filing that we have not cited as examples, make the appropriate changes in accordance with our comments.

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

5. Throughout the registration statement, you cite various estimates, statistics and other figures. For example:

    a. The statement that "The potential market for RNAi therapeutics is substantial" which is found on page 50
    b. Information included under the "Neurology – Market Opportunity" subheading on page 52;
    c. The first sentence included under the "Metabolic Disease – Market Opportunity" subheading on page 53; and
    d. Information included under the "Oncology – Market Opportunity" subheading on page 53.

    In the prospectus, please attribute these statements and other similar statements to the source from which you obtained the information. In addition, where you cite your own estimates, please explain how you arrived at those estimates and disclose any third-party sources you relied upon.

6. Throughout the registration statement, you should clearly articulate the basis of the various beliefs and assertions you make. As a non-exclusive example, on page 1, you state, "It is believed that this inhibition may potentially treat diseases by 'turning off' genes that lead to disease." In this and each similar case throughout the filing, you should disclose who has expressed the belief and the basis for the belief. If any of your assertions of beliefs are not supported by ample evidence or knowledge, you should delete them. Also, given that you are a discovery-stage company and none of your therapeutics are in the pre-clinical or clinical stages, you should not make any assertions regarding the effectiveness of any of your therapeutics.

7. Please update your financial information throughout the filing in accordance with Rule 3-12 of Regulation S-X.

Prospectus Cover Pages

8. The cover pages of the respective prospectuses should contain the information required by Item 501(b) of Regulation S-K and not include the other information you provide. While we recognize that the information regarding taxation and the particulars of the distribution are important to investors, you should articulate that information more prominently at the beginning of the Summary, rather than on the cover page.

Prospectus Summary, page 1

9. We note that you state here on page A-1 that all share data in these prospectuses assumes no effect to any possible resale of your shares by CytRx pursuant to the resale prospectus. We further note that on page B-80 of the resale prospectus, you state that CytRx intends to sell all of its remaining 49% ownership interest in the company. Please revise the disclosure throughout the distribution prospectus and award prospectus to reflect that CytRx plans to sell all of its shares. You should also disclose what specific arrangements, if any, that CytRx has initiated to facilitate the sale of its remaining shares.

RXi Pharmaceuticals Corporation, page 1

10. Since you are still a discovery-stage company, please remove all references to commercialization from your business description here, pages 5 and 48 and elsewhere as appropriate.

11. We note that the information provided in “Our Business” and “Our Competitive Strengths” is identical to the information provided on pages 48-29 and the information provided in “Business Strategy” is identical to the information provided on pages 54-55. Please revise this discussion to highlight the key points of these topics rather than repeating the same disclosure.

12. Throughout the Summary and rest of the prospectus you mention the contributions of your scientific advisory board members. Please clarify briefly in the Summary and in more detail in the rest of the prospectus exactly what role each of these advisors will have in the development of your therapeutics. Also, clarify how much time they will devote to the company, as opposed to other professional endeavors.

13. You state throughout the filing that some of your advisory board members are “leading” researchers. In each case, please explain the basis for these assertions or delete them.

The Distribution, page 5

14. Please provide more information on why you believe the partial distribution of the company's common stock will establish your company as one of the leading companies dedicated to developing RXi therapeutics as stated here and on page 27.

15. Please revise the section entitled "Relationship with CytRx after the Distribution," pages 23 and 30 and elsewhere as appropriate to state that following the distribution, CytRx intends to sell all of its remaining 49% ownership interest in the company under the Resale Prospectus as stated on page B-80.

16. In the Summary, and in more detail later in the prospectus, explain why CytRx is not distributing all of the RXi shares it owns, and why it has decided to offer for resale the 49% stake it will own immediately after the distribution.

Risk Factors, page 11

"We may be unable to achieve some or all of the benefits that we expect to achieve…" page 11

17. It appears from the last sentence of this risk factor that the company faces additional risks other than "not achieving some or all of the benefits" that it expects to achieve. For example, please expand the risk factor or add separate risk factors to discuss why the company may not be able to raise funds as a separate company that might have been available to a combined company. Also, we note from your disclosure on page 44 that the company has and will continue to have significant increased expenses as a separate company. Please describe and quantify these increased expenses. In addition, please revise the heading of this risk factor to accurately describe this risk, highlighting that, as a separate company, it not be able to receive the same amount of benefits it currently has as a combined company.

"You may have difficulty evaluating our business…" page 11

18. Please separate into a separate risk factor the last paragraph of this section which discusses the risk that the company may not be able to effectively operate as a separate company. Please use the last sentence of the current risk factor heading as the heading of this new risk factor.

"We may not be able to obtain financing…" page 12

19. Please separate into a separately headed risk factor the last paragraph of this section which discusses the risks associated with the company's issuance of debt

or equity in the future. Please expand your discussion to thoroughly discuss the risks associated with these possible issuances.

"We expect to continue to incur significant research and development expenses…" page 12

20. Please delete the statement, "If the actual funds required exceed our estimates" as this appears to be inconsistent with your statement in the prior sentence that you are unable to estimate the actual funds required to develop and commercialize the products.

21. Please delete the reference to "lower than anticipated revenues" as it appears from your disclosure on page 10 that you do not currently have any anticipated revenues.

"We will no longer be able to rely on CytRx…" page 13

22. We note your reference to "commercializing" your products in the last paragraph of this risk factor. Since you are still in the developing stage, please revise this to be "developing" your products.

23. You state that following the distribution, you will be more susceptible to specific risks relating to RNAi technologies. Please add separate risk factors to explain these specific risks to the extent there are any additional risks that you have not disclosed in the other risk factors.

"We will rely upon third parties for the manufacture of our clinical product candidates." page 14

24. Please name the specialty organic chemistry synthesis company with which you intend to manufacture nanotransporters.

25. In addition, please describe how the company intends to use these nanotransporters once they are manufactured. For example, does the company intend to use these to identify lead compounds?

26. To the extent the company is aware of any litigation, threatened litigation or challenge to the company's intellectual property, please revise to describe here and in the first complete risk factor on page 19.

"Any drug candidates we develop may fail in development…" page 14

27. Please separate into a separately headed risk factor the fact that the company has not yet any nominated lead compounds for therapeutic development nor has the

company begun any pre-clinical trials. Please expand your discussion to thoroughly discuss the risks associated with the fact that no lead compounds have been identified.

"We are dependent on technologies we license…" page 19

28. Please file a copy of your license agreement with Caregie Institution of Washington as discussed here and on page 37.

"We use biological and hazardous materials…" page 21

29. Please disclose your level of workers' compensation insurance coverage and briefly describe what potential liabilities are and are not covered. Please also disclose the cost to you of such coverage, if material.

"The market price of our common stock…" page 22

30. If any of the factors you have listed in the bullets in this risk factor represent material risks to investors in your common stock, you should discuss them in more detail in separate properly captioned risk factors.

The Founding and Initial Fundiong of RXi, page 28

31. Please clarify here who will own the remaining 14% of the company.

Results of the Distribution, page 29

32. Please clarify whether the approximate number of holders that you will disclose represents record or beneficial ownership.

Management's Discussion and Analysis of Financial Condition and Results of Operations, page 35

Strategic Licenses and Alliances, page 36

33. Please revise to discuss the company's planned product research and development over the next 12 months, including, but not limited to, any development within the scope of the described strategic relationships.

34. It appears that your license agreement with TriLink is a material agreement pursuant to Item 601(b)(10) of Regulation S-K. Please file a copy of this agreement with your next amendment. Alternatively, if you do not believe this is a material agreement, please provide an analysis of why you believe this is not a material agreement.

Basis of Presentation, page 37

35. It appears that your sponsored research agreement with Massachusetts General Hospital is a material agreement pursuant to Item 601(b)(10) of Regulation S-K. Please file a copy of this agreement with your next amendment. Alternatively, if you do not believe this is a material agreement, please provide an analysis of why you believe this is not a material agreement.

Liquidity and Capital Resources, page 45

36. We note that you state that you have adequate working capital to support your currently planned level of operations through the first quarter of 2009. Please expand your discussion to disclose your sources of working capital and your material commitments.

Quantitative and Qualitative Disclosures About Market Risk, page 47

37. To the extent material, please include the information required by Item 305(a) of Regulation S-K. Note that this item lists three possible disclosure alternatives from which you may present this information. Alternatively, if you believe the risk is not material, please revise to so indicate.

Business, page 48

License Agreements, page 59

38. Please revise the first sentence of this paragraph to indicate that the UMMS license agreements which were assigned by CytRx included four exclusive licenses, one co-exclusive license and one non-exclusive license. In addition, please revise the name of Exhibit 10.13 in your exhibit index accordingly.

39. Please revise your discussion of your agreement with Cold Spring Harbor Laboratory to discuss the material terms of this agreement, including, but not limited to any payment provisions, the existence of royalty provisions, aggregate milestones, usage restrictions, exclusivity provisions, obligations/rights to defend, other rights obtained and material obligations that must be met to keep the agreement in place, duration and termination provisions.

Government Regulation, page 62

40. Please define cGMP the first time you use the acronym.

Executive Compensation, page 72

41. We note your disclosure that the company did not pay any compensation or grant any equity awards to any employee prior to 2007, however, pursuant to Item 402(a)(2) of Regulation S-K, the Item requires "disclosure of all plan and non-plan compensation awarded to, earned by, or paid to the named executive officers designated under paragraph (a)(3) of this Item, and directors covered by paragraph (k) of this Item, *by any person for all services rendered in all capacities to the registrant* and its subsidiaries, unless otherwise specifically excluded from disclosure in this Item." (emphasis added). Please provide the required information for any of the persons covered in Item 402(a)(3) in the last fiscal year. Alternately, if the direct or indirect expenses for such persons rendering services to RXi do not exceed $100,000 pursuant to Instruction 1 to Item 403(a)(3), please so indicate.

2007 Executive Compensation Components, page 73

42. Please add analysis addressing how you determined the amount for each element to pay and the specific awards. Ensure that your disclosure explains and places in context how and why determinations with respect to one element may or may not have influenced the Committee's decisions with respect to other allocated or contemplated awards. See Item 402(b)(1)(v) and (vi) of Regulation S-K.

Potential Payments Upon a Termination or Change in Control, page 76

43. Please include Jim Warren in the table and provide the amount which was actually paid pursuant to the triggering event. See Instruction 4 to Item 402(j) of Regulation S-K.

44. Please describe your basis and rationale for selecting the triggering event for acceleration of vesting which you describe for Messrs. Woolf, DiPalma and Samarsky and Ms. Pavco. See Item 402(b)(2)(xi) of Regulation S-K.

Employment Agreements, page 80

45. We note the different payment levels for each of the compensation elements you pay to the named executive officers under the employment agreements. Please provide an analysis explaining why you structured these terms, payout levels and vesting schedules as you have. See Item 402(b)(1)(v) of Regulation S-K.

James Warren, page 81

46. Please file a copy of this employment agreement. See Item 601(b)(10) of Regulation S-K.

47. Please confirm that the company did not enter into a separation agreement with Mr. Warren. If the company has entered into such an agreement, please file a copy as an exhibit and describe the material terms of the agreement.

Compensation Committee Interlocks and Insider Participation in Compensation Decisions, page 82

48. Please either identify each person who served as a member of the compensation committee in the last completed fiscal year or identify each officer and employee of the registrant, and any former officer of the registrant, who, during the last completed fiscal year, participated in deliberations of the registrant's board of directors concerning executive officer compensation. In that regard, from your disclosure on page 67, it appears that Mr. Kriegsman is the only current director who served in 2006. If you need to identify Mr. Kriegsman, please also disclose whether Mr. Kriegsman was also ever an officer of the company, or ever acted in such a capacity.

Arrangements with CytRx Corporation, page 83

49. Please delete the reference to "arm's-length negotiations" in connection with the Contribution Agreement dated January 8, 2007 and the Contribution Agreement dated April 30, 3007 as these are related party transactions and such term is inappropriate under the circumstances.

50. In addition, please state what members of the company's management took part in the negotiations for the contribution agreements as none of the officers identified on page 65 were employed by the company at the time the company entered into the January 2007 agreement and it appears that only Mr. Woolf and Ms. Pavco were employed by the company in April 2007.

Reimbursement Agreement, page 83

51. Please clarify whether or not there are any additional payments or obligations under this agreement. If there are, please quantify and describe them.

Certain Relationships and Related Transactions, page 85

52. Note that all agreements which are discussed in this section appear to be material agreements and should be filed as exhibits to the registration statement. For example, we note that you have not filed a copy of Dr. Woolf's or Mr. Warren's consulting contract, the subscription agreement with Dr. Ahn, and Messrs. Galliker and Hillsburg, the Scientific Advisory Board Agreements and the related letter agreements dated April 30, 2007. Please file copies of these agreements with your

next amendment. We may have further comments once we obtain copies of these agreements.

53. Please state the amount of fees which have been billed to each of CytRx and RXi by Troy & Gould.

54. Please disclose here that Mr. Kriegsman will receive approximately 240,768 shares of the company's common stock as a result of the distribution under this prospectus and the award under the award prospectus.

55. Please revise your discussion of the subscription agreement with Dr. Ahn, and Messrs. Galliker and Hillsburg to discuss the material terms of the registration rights agreement which you have filed as Exhibit 4.4.

56. We note that pursuant to your disclosure on page II-2, on April 3, 2006, the company sold shares of the company's common stock to CytRx and Drs. Rana, Hannon, Czech and Mello. Please revise your disclosure to contain a discussion of such transaction. In addition, please file a copy this agreement and any related agreements.

Material United States Federal Income Tax Considerations, page 93

57. Please provide us with a supplemental analysis explaining your apparent conclusion that a tax opinion is not required pursuant to Item 601(b)(8) of Regulation S-K.

RXi Pharmaceuticals Corporation and Predecessor Carve-Out
Notes to Financial Statements

1. Nature of Business, page F-7

58. We believe the objective of the historical carve-out financial statements is to demonstrate the track record of management and the normal evolution of the business over time with respect to the business being sold to the public. In this regard, we believe the pro forma financial statements may be the best place to reflect the assets and results of operations to be included in RXi's financial statements. As SAB Topic 1.B.2 indicates, the effects of changes in cost sharing and other contractual arrangements should be reflected in the pro forma financial statements as well as adjustments to exclude the assets and operations not transferred to RXi. Refer to SAB 93 (Topic 5.Z.7 Question 8) by analogy. The conditions listed that are relevant, among other factors, in evaluating whether carve-out financial statements make sense and fairly present the history of the business are:

a. The Company and the subsidiary are in dissimilar businesses
b. They were and will be operated autonomously both before and after the spin-off, and
c. They have no more than incidental common facilities and costs.

Please explain to us why the presentation of the carve-out financial statements from the historical operations of CytRx are appropriate and ensure you address each of the three factors noted above in your response. Please reference for us the authoritative literature you rely upon to support your position. Otherwise, please revise your filing to include the historical financial statements of CytRx, the historical financial statements of RXi and pro forma financial statements for the latest year and interim period under Article 11 of Regulation S-X.

2. Summary of Significant Accounting Policies, page F-8
Valuations, page F-10

59. We note here as well as in other portions of the filing your reference to an independent third party valuation firm for the purpose of valuing the transactions at both January 8, 2007 and at April 30, 2007. Please name the independent third party valuation firm and provide their consent in the registration statement.

4. Development Stage Supplemental Equity Disclosure, page F-14

60. With regards to your common stock issuance of 3,273,292 on April 30, 2007, it appears that the price per share should reflect the actual price of $5.19 per share without regards to the reimbursement to CytRx. Please revise accordingly. In addition, please revise your disclosure throughout your filing to reflect the $5.19 per share price. In this regard, at a minimum it appears that you reflect the issuance price as $5.00 on pages 28, 35 and 45.

61. Please revise your disclosure to explain why the $1.3 million in offering costs and the $363,000 in expenses incurred on your behalf are properly charged as reductions to paid-in capital. In this regard, it is unclear why the expenses incurred on your behalf should not be charged to expense in accordance with SAB 1:B1. Also, it is unclear why the costs associated with the issuance of stock of a subsidiary are so significant. Please explain whether your offering costs include formation expenses that should be expensed under SOP 98-5 or whether they include costs associated with this registration statement. Also, 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-23.

8. Commitments and Contingencies, page F-15

62. Please quantify here and on page 45 under "Contractual Obligations" the potential milestone payments related to your research and development arrangements.

9. Stock Based Compensation, page F-16

63. Please note that, because the initial filing did not include an estimated offering price, we are deferring evaluation of common stock related compensation until you specify the estimated offering price. Once determined, please disclose the significant factors contributing to the difference between the fair value as of the date of each grant and your estimated IPO price.

11. License Agreements, page F-19

64. Please quantify the potential milestone payments related to the license agreement with Cold Spring Laboratory.

Award Prospectus

Risks Related to Ownership of Our Common Stock, page A-21

"The award of our common stock to you is taxable…" page A-21

65. Please revise this risk factor to discuss the tax implications of the award to management of CytRx, rather than the distribution to the shareholders of CytRx.

Resale Prospectus

66. Given the relative size and nature of the offering, it appears that CytRx may be an underwriter and that the transaction may be a primary offering. We note that you are not eligible to conduct an offering on Form S-3 or an at-the-market primary offering under Rule 415(a)(4). Please provide us with a supplemental analysis explaining your apparent conclusions that CytRx is not an underwriter, the offering is not a primary offering and can be conducted at the market, and Rule 415 permits the offering to be conducted as you have structured it.

67. Supplementally, please provide us in tabular format information regarding all prior securities transactions between RXi (or any of its predecessors) and CytRx, any affiliates of CytRx, or any person with whom CytRx has a contractual relationship regarding transactions involving RXi securities (or any predecessors of those persons), with the following information for each transaction:
    a. the date of the transaction,

b. the number of shares of the class of securities subject to the transaction that were outstanding prior to the transaction,
c. the number of shares of the class of securities subject to the transaction that were issued or issuable in connection with the transaction and the price paid for any securities issued or issuable in the transaction, and
d. the percentage of total issued and outstanding securities that were issued or issuable in the transaction (assuming full issuance).

Exhibits

68. We note that you have not filed various schedules and exhibits to Exhibits 2.1 and 2.2. Please revise to provide a list briefly identifying the contents of the omitted schedules or if separately filed please reference such exhibit number, together with an agreement to furnish supplementally a copy of any omitted schedule to the Commission upon request. See Item 601(b)(2) of Regulation S-K.

69. We note that the exhibits in the below table each refer to one or more exhibits, annexes or schedules which are attached to these agreements and which do not appear to have been provided.

Exhibit Number	Missing exhibit, annex or schedule
10.16	Schedule A
10.17	Exhibit I and Schedule A
10.18	Exhibit I

Please be aware that when you file an agreement pursuant to Item 601(b)(10) of Regulation S-K, you are required to file the entire agreement, including all exhibits, schedules, appendices and any document which is incorporated in the agreement. Please provide a copy of the above exhibits with the full and complete agreement, including any exhibits, schedules and appendices which are included in such agreement. Please note that if these agreements are otherwise filed as an exhibit to this registration statement you may insert a note in brackets on the page which the annex or schedule is to be located as to the exhibit number of the filed document. Also, confirm in your response letter that all agreements provided pursuant to Item 601(b)(10) are provided in their entirety.

* * *

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 urge all persons who are responsible for the accuracy and adequacy of the disclosure in the filing to be certain that the filing includes all information required under the Securities Act of 1933 and that they have provided all information investors require for an informed investment decision. 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 the company requests acceleration of the effective date of the pending registration statement, it should furnish a letter, at the time of such request, 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.

In addition, please be advised that the Division of Enforcement has access to all information you provide to the staff of the Division of Corporation Finance in connection with our review of your filing or in response to our comments on your filing.

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. We will act on the request and, pursuant to delegated authority, grant acceleration of the effective date.

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