



DIVISION OF
CORPORATION FINANCE

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

December 22, 2011

Via E-mail
Dr. Mark J. Ahn, Ph.D.
President
RXi Pharmaceuticals Corporation
60 Prescott Street
Worcester, MA 01605

**Re: RXi Pharmaceuticals Corporation
Form S-1/A
Filed December 8, 2011
File No. 333-177498**

Dear Dr. Ahn:

We have reviewed your amended registration statement and response letter each filed on December 8, 2011 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 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 further amendments to your registration statement and the information you provide in response to these comments, we may have additional comments.

FORM S-1/A

Cover Page

1. In response to prior comment 8, you disclose that you are in the process of applying for trading of your common stock in the OTC Markets Group. We are re-issuing our prior comment. Please disclose here and on pages 31 and 73 whether you have filed an application for listing. If an application has not been filed, please disclose when you intend to do so.

Plan of Distribution

Reasons for the Distribution, page 28

2. We note your response to prior comment 20, in which you bullet-point and clearly discuss each of the potential benefits of the separation from Galena. Please expand your disclosure of the negative factors of the separation from Galena to similarly present each factor considered.

Business, page 46

Introduction to the Field of RNAi Therapeutics, page 48

3. We note your response to our prior comment 28 and your citation of the National Review of Drug Discovery in support for the statement referenced in our comment. Please provide additional factual support. For example, was there a particular study cited in the National Review of Drug Discovery that supports your assertion? If so, please revise your disclosure to describe the study and its material findings.

License Agreements, page 54

4. We note your response to our prior comment 31. While we are reviewing your request for confidential treatment and may grant confidential treatment for the specific royalty percentages, please revise your disclosure in the registration statement to include a range of royalty payments not to exceed ten percent as we believe these are material terms of the agreement.
5. We note your response to our prior comment 32. While we are reviewing your request for confidential treatment and may grant confidential treatment for the specific milestone payments and specific royalty percentages set forth in the license agreement with Dharmacon, Inc., please revise your disclosure in the registration statement to include the potential aggregate milestone payments and a range of royalty payments not to exceed ten percent as we believe these are material terms of the agreement.

Management, page 59

6. In response to prior comment 34, you disclose that Dr. Ahn serves on a part-time basis as your President and Chief Financial Officer. We are re-issuing our comment to request that you disclose here and on pages 11, 59 and 66 the number of hours, on a monthly or weekly basis, that Dr. Ahn expects to work in this capacity.

Executive Compensation, page 61

7. Please confirm that you will update your executive compensation disclosure for 2011 in any amendment filed on or after January 1, 2012.

Certain Relationships and Related Party Transactions, page 65

8. Please provide us with an analysis that supports your conclusion that you are not substantially dependent on your agreements with Northwestern University and Carnegie Institute of Washington. Alternatively, please file the license agreements as exhibits to your filing and describe the material terms of any such agreements in your Business section, including, but not limited to any payment provisions, aggregate milestone payments, a range of royalty payments, exclusivity provisions, material obligations that must be met to keep the agreement in place, duration and termination provisions.

Beneficial Ownership of Certain Beneficial Owners and Management, page 68

9. We note your response to prior comment 37. It appears that footnotes (2) and (4) also apply to the After the Spin-Off Transaction Percentage columns for Mr. Tang, Mr. Wong, Tang Capital Partners and RTW Investments. Please revise your table accordingly.

Financial Statements

Notes to Financial Statements

1. Nature of Business, page F-8

10. You state that “management believes the assumptions underlying the allocations of indirect expenses in the carve-out financial information are reasonable; however, RXi’s financial position, results of operations, and cash flows may have been materially different if it had operated as a stand-alone entity as of and for nine months ended September 30, 2011”. Please tell us what is meant by the last statement and why the statement only relates to the nine months ended September 30, 2011 and not to the two years ended December 31, 2010.

12. Subsequent Events, page F-30

11. You state that on December 6, 2011 Galena entered into a transaction with warrant holders in which Galena stock will be issued in exchange for cancellation of warrants. The warrants were issued in the April 2011 offering. As a result of this transaction, the derivatives recorded in RXI’s financial statements will be reduced. Please clarify to us what the proceeds of the 2011 offerings were used for and where they are reflected in RXI’s financial

statements. If the proceeds were not used for the historical operations of RXI, please tell us why the warrants relating to the offerings are included as derivatives in the financial statements of RXI.

Exhibits

12. We have reviewed your response to prior comment 38. Please confirm that prior to requesting acceleration of this registration statement, if you are required to obtain prior written consent of a counterparty prior to the assignment and transfer, you will disclose the name of all counterparties which consent is required and has not been obtained and the effect of not obtaining such consent.

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.

Dr. Mark J. Ahn
RXi Pharmaceuticals Corporation
December 22, 2011
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You may contact James Peklenk at (202) 551-3661 or Mary Mast at (202) 551-3613 if you have questions regarding comments on the financial statements and related matters. Please contact Nandini Acharya at (202) 551-3495, Jennifer Riegel, Special Counsel, at (202) 551- 3575 or me at (202) 551-3715 with any other questions.

Sincerely,

/s/ Jennifer Riegel for

Jeffrey Riedler
Assistant Director

Via E-mail
cc: Dale E. Short, Esq.
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