



DIVISION OF
CORPORATION FINANCE

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

November 21, 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
Filed October 25, 2011
File No. 333-177498**

Dear Dr. Ahn:

We have reviewed your 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 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 amendment to your registration statement and the information you provide in response to these comments, we may have additional comments.

FORM S-1

General

1. We note that you have submitted 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 provide updated interim financial statements and related financial information for the period ending September 30, 2011, pursuant to Rule 3-01 and 3-12 of Regulation S-X. Please also file an updated, signed consent report from your independent auditors prior to going effective.
3. Please note that before we will declare the registration statement effective, you must revise your filing throughout to include any omitted information that is currently denoted by blanks.
4. Please note that where we provide examples to illustrate what we mean by our comments, they are examples and not complete lists. If our comments are applicable to portions of the filings that we have not cited as examples, please make the appropriate changes in accordance with our comments.
5. We note that the tax opinion, legal opinion and related consents have not been filed. Please file them as soon as practicable, as we will need time to review this exhibits once they have been filed.
6. In several places in the registration statement, you cite various estimates, statistics and other figures. For example:
 - a. The statement that “Approximately 42 million surgical procedures are performed annually...” which is found on pages 1 and 46; and
 - b. The statement that “Numerous studies implicate CTGF overexpression in scarring...” which is found on pages 1 and 46.

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.

7. Throughout the registration statement, you should clearly articulate the basis of the various beliefs and assertions you make. As a non-exclusive example, on pages 1 and 35, you state, “We believe that RXI-109 or other CTGF-targeting compounds may be able to treat other indications, including pulmonary fibrosis, liver fibrosis, acute spinal injury, ocular scarring and restenosis.” As another example, on page 49, you state, “The specificity of RNAi may be sufficient to permit therapeutic targeting...and...may even selectively reduce or eliminate expression...” If you haven’t done so, please clarify whether the relevant statement is your belief or opinion. In addition, please disclose the basis for your belief. If any of your assertions of beliefs are not supported by ample evidence or knowledge, you should delete them.

Cover Page

8. You disclose that following the completion of the distribution, you anticipate that your common stock will trade in the OTC Markets Group under the symbol ["RXII."] Please revise your disclosure here and on pages 31 and 73 to clarify whether you have filed an application for listing. If an application has not been filed, please disclose when you intend to do so.

Table of Contents, page i

9. You state that "We have not independently verified any of this [data derived from third-party sources] and cannot assure you of its accuracy or completeness." Please delete this statement as it is not appropriate to disclaim or imply that you are not taking liability for the statements in your registration statement. Alternatively, please expand your disclosure to include a statement specifically accepting liability for these statements.

Prospectus Summary, page 1

10. You disclose on page 42 that you have not generated revenue to date and may not generate product revenue in the foreseeable future, if ever. Furthermore, you expect to incur significant operating losses as you advance your product candidates through the drug development and regulatory process. Please expand your disclosure under "Our Business" to clarify to disclose this information.

Risk Factors, page 11

11. On page 57, you note that your research and development activities involve the controlled use of potentially harmful biological materials as well as hazardous materials, chemicals and various radioactive compounds. Please consider whether you should include a risk factor that addresses the resulting risks to you and your business as a result of your use of these materials.

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

12. You disclose that you may not be able to obtain approval from one or more granting institutions to Galena's assignment to you of approximately \$800,000 of research grants. Please disclose whether you are aware of any granting institution that has indicated that it will not consent to the assignment of the respective grant.

“We may be unsuccessful in recruiting a Chief Executive Officer...” page 11

13. You disclosed that you will need to recruit and hire a Chief Executive Officer to replace Mark J. Ahn, Ph.D., who currently serves as our President and Chief Financial Officer, and other executive officers and key employees. Please expand your disclosure to list all the executive officers you are seeking to recruit and hire. For example, are you also seeking to recruit and hire a Chief Financial Officer?

“We will be subject to competition and may not be able to compete...” page 15

14. Please clarify the diseases you are targeting which are also being targeted by your competitors.

“We may be unable to protect our intellectual property rights licensed from other parties...” page 16

15. Please expand your disclosure to disclose the name of the third party that sent you a letter claiming that you require access to such third party’s patent and patent applications and demanding that you stop engaging in unspecified alleged infringing activities unless you obtain a license from such third party as this appears to be information that may be material to your business.

“Our success depends upon our ability to obtain and maintain intellectual property protection...” page 17

16. Please disclose whether there are any other entities which currently have legally blocking proprietary rights of which you are aware.

“We will rely upon third parties for the manufacture of our clinical product.” page 17

17. Please disclose whether there are any third-party manufacturers upon which you are substantially dependent. Please file the related 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, exclusivity provisions, material obligations that must be met to keep the agreement in place, duration and termination provisions.

“If we fail to attract, hire and retain qualified personnel...” page 20

18. To the extent that you have experienced difficulties attracting and retaining key personnel, please revise to discuss these difficulties. Also, disclose whether any key personnel have plans to retire or leave your company in the near future.

“You may have difficulty selling our shares of common stock if they are deemed “penny stocks.” page 22

19. Please clarify whether you believe that your common stock will be deemed a “penny stock.”

Plan of Distribution, page 28

Reasons for the Distribution, page 28

20. Please expand this section to describe in more detail the negative factors and potential benefits the Galena board considered in evaluating the separation of RXi from Galena.
21. Please clarify whether you are responsible for the entire cost of the fees and expenses disclosed on the top of page 29, as we note that you have agreements related to the reimbursement of transaction costs as described on page 30.

Trading Market, page 31

22. You state on page 32, “These are just some of the factors that may adversely affect the market price of our common stock.” Please confirm that you have described all material factors likely to adversely impact the market price of your common stock or revise the disclosure to include additional material factors.

Trading Between the Record Date and Distribution Date, page 32

23. Please confirm that your record date will be after the effectiveness of this registration statement. Alternatively, please provide us with a detailed analysis which supports your conclusion that the “when-issued” trading is consistent with Section 5 of the Securities Act of 1933.

Management’s Discussion and Analysis of Financial Condition and Results of Operations

Liquidity and Capital Resources, page 42

24. You disclose that you had cash and cash equivalents of approximately \$1.9 million as of October 15, 2011. Please clarify whether this includes the \$1.5 million contribution by Galena which you disclosed on page 30.

Business, page 46

25. Please clarify which human diseases or types of human diseases you believe can be potentially treated by silencing targeted genes that lead to disease together with your basis for such belief.

Recent Business Developments, page 47

26. In each discussion of the initial results of your preclinical research and data please clarify if there was a specific duration in which the silencing was experienced. In this regard, we notice your reference to one week on page 1.
27. In the third bullet point you note that the collaboration demonstrated efficacy. Please revise your disclosure to clarify what you mean by “demonstrated efficacy” as it does not appear to be appropriate to use this term in reference to a pre-clinical collaboration.

Introduction to the Field of RNAi Therapeutics, page 48

28. Please characterize as your belief or opinion the statement that “The specificity of RNAi may be sufficient to permit therapeutic targeting...and...may even selectively reduce or eliminate expression...” Alternatively, provide additional factual support for this assertion.

Patents and Patent Applications, page 54

29. In this section, you reference both patents and patent applications, but you appear to only discuss your material patent applications. Please expand your disclosure in this section to also discuss any material patents, including for each patent or group of patents the technology to which the patent relates and the expiration date of the patent.
30. Please clarify if you have any patents or patent applications in jurisdictions outside the United States.

License Agreements, page 54

31. Please disclose the aggregate milestone payments you are required to pay under the license agreement with the University of Massachusetts Medical School.

32. Please disclose the aggregate clinical milestone payments and a range of royalty payments (not to exceed ten percent) under the license agreement with Dharmacon, Inc.
33. For each of the license agreements below, please provide us with an analysis that supports your conclusion that you are not substantially dependent on the following agreements disclosed on page F-28:
- License agreement with Cold Spring Harbor Laboratory;
 - License agreement with TriLink Biotechnologies;
 - License agreement with Life Technologies; and
 - License agreements with University of Massachusetts Medical School, other than the license agreement already disclosed on page 54.

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.

Management, page 59

34. We note that Mark Ahn also serves as the President, Chief Executive Officer and a director of Galena. Please expand your disclosure here and on page 66 to disclose the number of hours Mr. Ahn has agreed to dedicate to you. Please also consider adding a risk factor to discuss the risks that your President and Chief Financial Officer is not working full time for you, is not being compensated by you and may have conflicts of interests with you.

Certain Relationships and Related Party Transactions, page 65

Agreements with Galena Biopharma, Inc., page 65

35. Here, and in the Business section as appropriate, please disclose the names of the institutions which granted the research grants and the license agreements that Galena has assigned to you in connection with the contribution agreement.

Advirna Agreement, page 66

36. Please disclose the exact nature of the affiliation between Advirna and Anastasia Khvorova.

Beneficial Ownership of Certain Beneficial Owners and Management, page 68

37. Although we note that there is a “conversion cap” limitation for certain of your investors, the security holders’ ability to acquire and sell a large amount of your common stock is material information which is required to be disclosed in your registration statement. See Securities Act Rule 408. Accordingly, please revise your table to include the ownership of Tang Capital Partners, RTW Investments, Mr. Tang and Mr. Wong without consideration of the “conversion limitation.” In addition, please include a footnote to your beneficial ownership table that discloses the “conversion limitation” and the impact on the respective security holders.

Exhibits

38. We note that Exhibits 2.1 and 2.2 each omit various schedules and exhibits thereto. Please either file complete copies of these agreements or provide us with a detailed analysis of each omitted schedule, exhibit or other attachment thereto that supports your belief that such schedule does not contain information which is material to an investment decision or which is otherwise disclosed in the agreement or the filing and provide us copies of each omitted schedule, exhibit or other attachment thereto. In addition, please re-file each agreement with a list briefly identifying the contents of all omitted schedules, 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.

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

Dr. Mark J. Ahn
RXi Pharmaceuticals Corporation
November 21, 2011
Page 9

- 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.

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.
TroyGould PC
1801 Century Park East, Suite 1600
Los Angeles, CA 90067-2367