

Mail Stop 4720

May 18, 2009

Tod Woolf
Chief Executive Officer
RXi Pharmaceuticals Corporation
60 Prescott Street
Worcester, MA 01605

**Re: RXi Pharmaceuticals Corporation
Registration Statement on Form S-3
Filed May 4, 2009
File No. 333-158968**

Dear Mr. Woolf:

We have limited our review of your filing to those issues we have addressed in the comments below. 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.

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. We note that you have filed this registration statement in reliance on the eligibility requirements of General Instruction I.B.6 of Form S-3. General Instruction I.B.6 of Form S-3 requires in part that the aggregate market value of securities sold by or on behalf of the registrant pursuant to Instruction I.B.6 during the period of 12 calendar months immediately prior to, and including, the sale is no more than one-third of the aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant. We further note your disclosure that, prior to the filing of this registration statement, you explored the possibility of conducting a private placement of common stock with certain prospective investors but then terminated all offering activity related to the proposed private placement on April 29, 2009. Accordingly, we must consider whether the shares

offered pursuant to the abandoned private placement must be integrated with the shares offered pursuant to this registration statement when determining whether the size of the offering meets the eligibility requirements of General Instruction I.B.6 of Form S-3. Rule 155 of the Securities Act of 1933 provides a non-exclusive safe harbor with respect to integration of abandoned offerings. Rule 155 states in relevant part that a private offering of securities will not be considered part of an offering for which the issuer later files a registration statement if, among other things, the issuer does not file the registration statement until at least 30 calendar days after the termination of all offering activity in the private offering, unless securities offered in the private offering were only offered to accredited investors (as that term is defined in Rule 501(a)) or persons who satisfy the knowledge and experience standard of Rule 506(b)(2). We note that you have filed this registration statement less than 30 calendar days after the abandonment of your proposed private placement. Accordingly, please reduce the size of the offering, withdraw the registration statement or provide us with an analysis supporting your determination that the private placement should not be integrated with this registration statement for purposes of determining that the number of shares offered meets the eligibility requirements of General Instruction I.B.6 of Form S-3.

* * *

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;

Tod Woolf
RXi Pharmaceuticals Corporation
May 18, 2009
Page 3

- 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.

Please contact Nandini Acharya at (202) 551-3495 or me at (202) 551-3715 with any questions.

Sincerely,

Jeffrey P. Riedler
Assistant Director

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