

Filed Pursuant to Rule 424(b)(3)  
Registration No. 333-181534

PROSPECTUS SUPPLEMENT NO. 2  
(To Prospectus dated July 6, 2012)

138,941,780 Shares



## **RXi Pharmaceuticals Corporation**

This Prospectus Supplement No. 2 supplements the prospectus dated July 6, 2012 (as supplemented to date, the “Prospectus”), which forms a part of our Registration Statement on Form S-1 (Registration Statement No. 333-181534). The Prospectus and this prospectus supplement relate to the disposition from time to time of up to 138,941,780 shares of our common stock, which are held or may be held by the selling stockholders named in the Prospectus. We are not selling any common stock under this prospectus and will not receive any of the proceeds from the sale of shares by the selling stockholders.

This prospectus supplement should be read in conjunction with the Prospectus, which is to be delivered with this prospectus supplement. This prospectus supplement updates, amends and supplements the information included or incorporated by reference in the Prospectus. If there is any inconsistency between the information in the Prospectus and this prospectus supplement, you should rely on the information in this prospectus supplement.

This prospectus supplement is not complete without, and may not be delivered or utilized except in connection with, the Prospectus, including any amendments or supplements to it.

### **Current Report on Form 8-K**

On June 22, 2012, we filed a Current Report on Form 8-K with the Securities and Exchange Commission. The text of such Form 8-K is attached hereto.

**Investing in our common stock involves a high degree of risk. In reviewing the Prospectus and this prospectus supplement, you should carefully consider the matters described under the heading “Risk Factors” beginning on page 5 of the Prospectus.**

**Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities, or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.**

The date of this prospectus supplement is July 6, 2012.

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

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**FORM 8-K**

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**CURRENT REPORT**

**PURSUANT TO SECTION 13 OR 15(d) OF THE  
SECURITIES EXCHANGE ACT OF 1934**

**Date of report (Date of earliest event reported): June 18, 2012**

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**RXi PHARMACEUTICALS CORPORATION**

**(Exact name of registrant as specified in its charter)**

**Delaware**  
(State or other jurisdiction of  
incorporation or organization)

**333-177498**  
(Commission  
File Number)

**45-3215903**  
(I.R.S. Employer  
Identification No.)

**60 Prescott Street**  
**Worcester, Massachusetts 01605**  
(Address of Principal Executive  
Offices) (Zip Code)

**Registrant's telephone number, including area code: (508) 767-3861**

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

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**Item 5.02 Departure of Directors or Certain Officers; Election of Directors; Appointment of Certain Officers; Compensatory Arrangements of Certain Officers.**

Effective as of June 18, 2012 and June 19, 2012, RXi Pharmaceuticals Corporation (the “Company”) appointed Keith L. Brownlie and Robert J. Bitterman, respectively, to serve on the Company’s Board of Directors (the “Board”) until the 2013 annual meeting of stockholders. The Board has not yet determined the committees on which Messrs. Brownlie or Bitterman will serve.

The Company has entered into an agreement with each of Messrs. Brownlie and Bitterman pursuant to which each will receive the following compensation for their service on the Board: (i) an annual retainer of \$20,000, payable in quarterly installments of \$5,000, (ii) a one-time option grant representing the right to purchase up to 1,000,000 shares of common stock, which options will vest quarterly over a one-year period and will be granted pursuant to the Company’s 2012 Incentive Plan (the “Plan”), and (iii) commencing in 2013, an annual option grant representing the right to purchase up to 500,000 shares of common stock, which options will vest quarterly over a one-year period and will also be granted pursuant to the Plan. Additionally, the Company will reimburse Messrs. Brownlie and Bitterman for their travel and other reasonable out-of-pocket expenses incurred in connection with their Board service.

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**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

RXi PHARMACEUTICALS CORPORATION

Date: June 22, 2012

By: /s/ Geert Cauwenbergh  
Geert Cauwenbergh, Dr. Med. Sc.  
Chief Executive Officer