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

PROSPECTUS SUPPLEMENT NO. 1
(To Prospectus dated July 6, 2012)

138,941,780 Shares

RXi Pharmaceuticals Corporation

This Prospectus Supplement No. 1 supplements the prospectus dated July 6, 2012 (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 May 31, 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.

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

FORM 8-K

CURRENT REPORT

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

Date of report (Date of earliest event reported): May 31, 2012

RXi PHARMACEUTICALS CORPORATION

(Exact name of registrant as specified in its charter)

Delaware	**333-177498**	**45-3215903**
(State or other jurisdiction of incorporation or organization)	**(Commission File Number)**	**(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))

Item 7.01 Regulation FD Disclosure.

On May 31, 2012, RXi Pharmaceuticals Corporation (the "Company") issued the press release attached as Exhibit 99.1 to this Current Report on 8-K, which press release is incorporated herein by reference.

The information in this Item 7.01 and Exhibit 99.1 is being "furnished" pursuant to Item 7.01 and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or incorporated by reference into those filings of the Company that provide for the incorporation of all reports and documents filed by the Company under the Exchange Act.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

99.1 Press release of RXi Pharmaceuticals Corporation dated May 31, 2012.

* * *

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: May 31, 2012

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

Exhibit 99.1

RXi Pharmaceuticals Receives FDA Clearance to Begin Clinical Trial with RXI-109

First study to evaluate tolerance and potential surrogate parameters for scar reduction

WORCESTER, Mass. - (BUSINESS WIRE) - RXi Pharmaceuticals Corporation (OTCBB: RXII.OB) today announced that it has received clearance for its investigational new drug application (IND) from the U.S. Food and Drug Administration (FDA) to initiate clinical trials with RXI-109, a self-delivering RNAi compound that selectively targets Connective Tissue Growth Factor (CTGF). The Phase 1 trial will investigate the compound in subjects to evaluate its safety and tolerability, and to look for surrogate parameters that might predict the potential of the compound to reduce dermal scarring in planned surgeries.

This is the first time that a self-delivering RNAi technology will be tested in humans. This proprietary technology is expected to reduce the issues with tissue delivery that have traditionally plagued RNAi applications since they were introduced to medicinal biotechnology over 5 years ago.

“RXi’s next generation RNAi platform has shown great promise” stated Dr. Cauwenbergh, President and CEO of RXI Pharmaceuticals. “In a short period of time, the company has been able to advance its lead product candidate for dermal scarring, RXI-109, into human clinical trials. As we aggressively pursue the potential of this compound for this condition with major social impact, we will also continue to work to create long-term shareholder value through the advancement of RXi’s robust IP platform, based on self-delivering RNAi technology.”

About Scarring

With cosmetic surgical procedures becoming increasingly more common to improve appearance, or to correct skin imperfections as a result of trauma or disease, scarring has become a much more significant side effect of such interventions. RXI-109 has been shown in cell culture and animal models to suppress or silence the over-expression of CTGF, a growth factor that is essential in the wound healing cascade, and which is also the cause of excessive scarring when it continues to exert its effect on a healing wound for too long.

About RXi Pharmaceuticals

RXi Pharmaceuticals Corporation (OTCBB: RXII.OB) is a biotechnology company focused on discovering, developing and commercializing innovative therapies based on its proprietary, next-generation RNAi platform. Therapeutics that use RNA interference, or “RNAi,” have great promise because of their ability to “silence,” or down-regulate, the expression of a specific gene that may be overexpressed in a disease

condition. Building on the pioneering work of scientific founder and Nobel Laureate Dr. Craig Mello, RXi's first RNAi product candidate, RXI-109, is now entering into a new phase of its development, in which clinical studies in humans will evaluate if the promising results that have been obtained in cell culture and animal studies will prove to be relevant in humans.

About RXI-109

RXI-109 is designed to reduce the expression of CTGF, a critical regulator of several biological pathways involved in fibrosis, including scar formation in the skin.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Such statements include, but are not limited to, statements about future expectations, plan and future development of RXi Pharmaceuticals Corporation's products and technologies. These forward-looking statements about future expectations, plans and prospects of the development of RXi's products and technologies involve significant risks, uncertainties and assumptions, including the risk that RXi may not be able to successfully develop its candidates, the risk that the development of our RNAi-based therapeutics may be delayed or may not proceed as planned and we may not be able to complete development of any RNAi-based product, the risk that the development process for our product candidates may be delayed, risks related to development and commercialization of products by our competitors, risks related to our ability to control the timing and terms of collaborations with third parties and the possibility that other companies or organizations may assert patent rights that prevent us from developing our products. Actual results may differ materially from those contemplated by these forward-looking statements. RXi does not undertake to update any of these forward-looking statements to reflect a change in its views or events or circumstances that occur after the date of this release.

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