**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): September 26, 2018**

# RXi PHARMACEUTICALS CORPORATION

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

| **Delaware** | **001-36304** | **45-3215903** |
|---|---|---|
| **(State or other jurisdiction of incorporation or organization)** | **(Commission File Number)** | **(I.R.S. Employer Identification No.)** |

**257 Simarano Drive, Suite 101**
**Marlborough, Massachusetts 01752**
**(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))

Indicate by check mark whether the registrant is an emerging growth company as defined in as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

**Item 7.01 Regulation FD Disclosure**.

On September 26, 2018, representatives of RXi Pharmaceuticals Corporation participated in the 16th Annual Discovery on Target Conference in Boston, Massachusetts. A copy of the poster to be used during the conference is attached hereto as Exhibit 99.1 and is incorporated herein by reference.

The information in this Item 7.01 and attached as Exhibit 99.1 to this Current Report on Form 8-K will not be treated as "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section. This information will not be incorporated by reference into any filing under the Securities Act of 1933, as amended, or into another filing under the Exchange Act, unless that filing expressly incorporates this information by reference.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits

99.1 Conference Poster, dated September 26, 2018.

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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: September 26, 2018

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

Exhibit 99.1

# The Use of Self-delivering RNAi to Enhance NK Cell Cytotoxicity

Melissa Maxwell, Dingxue Yan, James Cardia, Gerrit Dispersyn
RXi Pharmaceuticals, Marlborough, MA, 01752 USA

## Abstract

NK cells are key players in a body's fight against cancer. They rapidly recognize and kill tumor cells without prior sensitization. NK cells are an attractive candidate for use in adoptive cell therapy (ACT) because they are not required to be matched to a specific patient, making an off-the-shelf NK therapy product possible. Therapeutic use of NK cells shows promise against hematological cancers but the cytotoxic activity of these cells is limited by inhibitory receptors and pathways. Overexpression of such receptors has been shown to reduce NK cell-mediated cytotoxicity. Overcoming this inhibition would allow for a more potent antitumor response following ACT. We have developed a new class of stable, self-delivering RNAi compounds or sd-rxRNAs® that incorporate features of RNAi and antisense technology. The work presented here shows that sd-rxRNAs are rapidly and efficiently taken up by immune effector cells without the use of transfection reagents. Using sd-rxRNA compounds against checkpoint inhibitors, we can suppress their expression levels by up to 95% in immune cells including T cells and NK cells. Furthermore, we demonstrate potent activity and stability in NK cells which is maintained through cryopreservation. By treating NK cells ex vivo, prior to ACT with sd-rxRNA reducing the expression of proteins such as Cbl-b, the anti-tumor response of these cells can be improved. Ongoing work expands these findings to include compounds for more NK specific targets, including NK specific inhibitory receptors, which could be used alone or in combination. Improved NK cytotoxic activity as a result of sd-rxRNA treatment during NK manufacturing is a promising approach towards more potent off-the-shelf therapy for hematological malignancies.

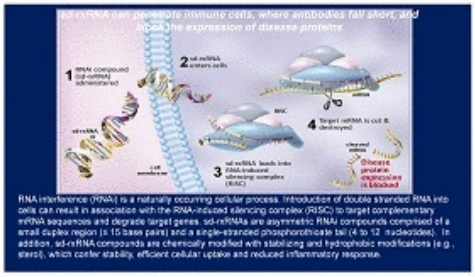


Figure 1: Mechanism of Cellular Gene Silencing using sd-rxRNA

## Results

To test the uptake of sd-rxRNAs by immune effector cells without the use of transfection reagents, various human immune effector cells were transfected with 2uM fluorescently labeled sd-rxRNA in standard culture media for 24 hours. Cells were fixed with paraformaldehyde for 10 minutes and mounted for confocal microscopy. Results show rapid and efficient uptake in all cell types tested (Figure 2).


Figure 2: Fluorescently labeled sd-rxRNA is taken up efficiently within 24 hours

NK cell work included tests with RNAi against an immune checkpoint protein and an NK specific inhibitory receptor. Fresh human NK cells were isolated using negative selection and cultured in standard culture media containing IL-2. Twenty-four hours after isolation, cells were collected for transfection and the cell concentration was adjusted to ~1 x $10^6$ cells/mL in RMPI media containing IL-2. Cells were seeded directly into 24-well plates containing chemically-optimized sd-rxRNA targeting Cbl-b ranging in final concentration from 0.5 µM to 2 µM. Taqman gene expression assays were used to determine expression levels of Cbl-b following the RNA to CI 1-step protocol. Cbl-b targeting sd-rxRNA in human NK cells cause potent and long-lasting reduction of Cbl-b mRNA (Figure 3). Further analysis of the effects of siRNA on NK cells was performed on an NK-specific target. mRNA levels were measured after a 72 hour transfection, and surface expression of the target protein was analyzed by flow cytometry after 5 days (Figure 4).

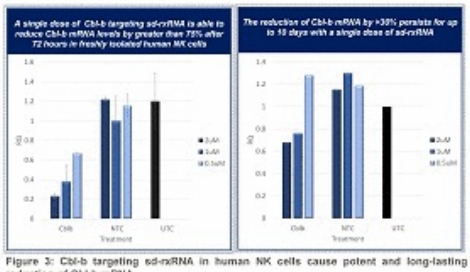


Figure 3: Cbl-b targeting sd-rxRNA in human NK cells cause potent and long-lasting reduction of Cbl-b mRNA

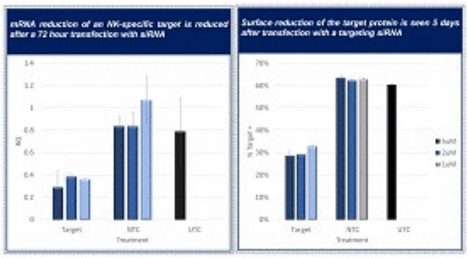


Figure 4: using siRNA in human NK cells cause reduction of target mRNA which leads to a reduction in surface expression of the target protein

To test whether a freeze/thaw cycle would negatively impact sd-rxRNA silencing of Cbl-b, freshly isolated human NK cells were transfected with Cbl-b-targeting sd-rxRNA for 48 hours. After 48 hours, cells were pelleted and resuspended in freeze medium containing 10% DMSO, cooled to -80°C overnight then transferred to cryostorage for 72 hours. After 72 hours, the cells were thawed into standard culture medium and incubated an additional 24 hours. Silencing of Cbl-b expression after a freeze/thaw cycle was similar to that of cells that had been transfected for 72 hours without freeze/thaw cycle (Figure 5).

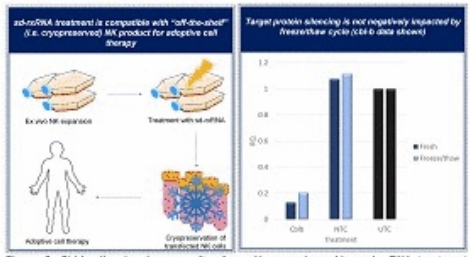


Figure 5: Cbl-b silencing is seen after freeze/thaw cycle making sd-rxRNA treatment compatible with current NK cell therapy protocols

## Conclusions

These data demonstrate the potential of using sd-rxRNA to change NK cell phenotype for use in adoptive cell therapy. The use of these compounds is compatible with existing manufacturing paradigms (no need for transfection reagents, compatible with freeze/thaw cycles). Potent and long lasting reduction of target proteins can be achieved. By treating NK cells with sd-rxRNA targeting immune checkpoints - such as Cbl-b - or other inhibitory receptors, the anti-tumor response of these cells may be enhanced.



Discovery on TARGET

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