Developing the next generation of immuno-oncology therapeutics

RXi Pharmaceuticals Announces Positive Results From Phase 1/2 Trial With RXI-109 For Retinal Scarring

August 1, 2018

- RXI-109 is a self-delivering RNAi (sd-rxRNA®) compound that targets connective tissue growth factor (CTGF), a key regulator of fibrosis and scar formation.
- Study successfully meets primary objective by showing that RXI-109 is safe and well tolerated in this dose escalation study.
- RXI-109 meets secondary objectives with improved or stable disease in the study eyes.

MARLBOROUGH, Mass., Aug. 1, 2018 /PRNewswire/ -- RXi Pharmaceuticals Corporation (NASDAQ: RXII) a biotechnology company developing the next generation of immuno-oncology therapeutics based on its proprietary self-delivering RNAi (sd-rxRNA) therapeutic platform, today announced positive results with RXI-109 in a Phase 1/2 clinical trial. RXI-109-1501 is an open-label, multi-dose, dose escalation study with three dose cohorts, enrolled sequentially, evaluating the safety and tolerability of RXI-109 injections in the eye of subjects with advanced neovascular age-related macular degeneration (NVAMD), and accompanying subretinal fibrosis. During this study, the clinical effect of these injections was evaluated as a secondary endpoint.

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The primary objective was met as shown by the absence of dose-limiting and serious toxicities, and only mild to moderate procedure related adverse events. None of the adverse events were drug related. In addition, comprehensive ocular examinations showed no indications of inflammation nor any other tolerability issues related to the treatment. Therefore, these study results show that RXI-109 was safe and well tolerated for all patients included in the three dosage groups.

Even though the primary objective of this study was to evaluate the safety and tolerability of ocular injections with RXI-109, several assessments were included to measure a potential clinical effect. These assessments included measuring the change from baseline in subretinal fibrosis lesion size, as measured by spectral domain (SD) optical coherence tomography (OCT), fundus photography and fluorescein angiography, as well as a potential effect on visual function by measuring the best corrected visual acuity (BCVA), i.e. the best vision a patient could achieve with correction (such as glasses), as measured on the standard eye charts.

RXi's Chief Development Officer, Gerrit Dispersyn, Dr. Med. Sc., commented: "This study is exciting on several levels. First, the impressive safety and tolerability of intravitreal injections of RXI-109 and the promising clinical data, support further development of this compound in retinal scarring. In addition, these positive findings also open significant avenues for the use of our platform technology in ophthalmology, with sd-rxRNA targeting other proteins for other ocular indications. Also, the results contribute to an already extensive set of data that RXI-109, by preventing the overexpression of connective tissue growth factor, can result in a positive impact in various indications where excessive fibrosis is seen. Even though this is a small study, it is encouraging that some of the summary statistics on ocular assessments performed in the study eye at the last follow-up visit, suggest a more pronounced change over baseline in the highest dose group (Cohort 3), compared to other groups."

About the RXI-109-1501 Study

RXI-109-1501 is a multi-center, multi-dose, dose escalation trial conducted in subjects with advanced neovascular or 'wet' age-related macular degeneration and accompanying subretinal fibrosis. It is the first clinical study (phase 1/2 trial) on the use of RXI-109 by ocular injections. Per the protocol, three dose levels were evaluated in a small number of subjects in order to establish safety information and to help determine the dosing regimen for a future Phase 2 study. Nine subjects were enrolled, three in each of the following dosage groups: Cohort 1 (low dose), Cohort 2 (intermediate dose), Cohort 3 (high dose). Each subject received a total of four doses of RXI-109 at one-month intervals. RXI-109 was administered by intravitreal injection in one eye only. The dosing period (3 months) was followed by a four-month observation period.

Overall Safety and Tolerability Results

- There were no instances of Dose Limiting Toxicities or Serious Toxicities throughout the study. In other words, there were no instances of clinically significant ocular inflammation (such as 3+ aqueous and vitreous cells), retinal toxicities (such as moderate or severe retinal hemorrhages), reduction from baseline BCVA ≥30 letters, drug related adverse events with a CTCAE grade of 3 or higher or sustained intraocular pressure ≥30 mmHg.
- In total twenty-five AEs were reported, thirteen in Cohort 1, seven in Cohort 2 and five in Cohort 3. The severity of all these AEs was either mild or moderate: Eighteen of these AEs were considered mild and the other seven AEs were considered moderate. Of the twenty-five AEs, none were related to the study drug, and eight AEs occurring in five subjects were deemed related to the study procedures (i.e. the intra-ocular injections).
- There were no negative clinically significant changes in physical examination findings, ocular examinations and assessments, and clinical laboratory results that were deemed related to the study drug.

Clinical activity

- Compared to the baseline visit, all but one subject had an improved BCVA of the study eye at the last follow up visit. One subject (Cohort 1) had a lower score compared to baseline. The average increase in BCVA was +2.3 for Cohort 1, +3.7 for Cohort 2 and +10.0 for Cohort 3. The median change from baseline BCVA was 32.0% for the study eye and 4.9% for the contralateral eye.
- The various imaging modalities and image analysis techniques used, suggest a halt or even reversal of the disease progression in the study eye of several subjects. For example, at the last follow-up visit the mean central lesion thickness change compared to baseline (as measured by OCT) was -6.9%, with a range of -14.8% to +3.6%. The largest change was again seen in Cohort 3 (mean reduction of -10.2%) followed by Cohort 2 (mean reduction of -6.7%) and Cohort 1 (mean reduction of -3.8%).
- A criterium for patient "success" was not predefined in this study, but if the same criteria would be applied in this study as in pivotal trials with anti-VEGF treatments[1] (i.e. "maintaining vision" defined as losing fewer than 15 letters in BVCA tests at 52 weeks), treatment success would be declared in all but one patient.

About Advanced Neovascular Age-related Macular Degeneration, and Retinal Scarring

In the United States, there is no FDA-approved targeted therapy for the treatment and prevention of subretinal scarring in advanced wet age-related macular degeneration. This presents a large unmet market opportunity with approximately 11M Americans have some form of AMD, while 1.1M have NVAMD. We believe that RXI-109 is an excellent candidate to help patients with advanced NVAMD to reduce the progression of subretinal fibrosis, or as a potential prophylactic treatment for early stage NVAMD patients prior to the development of subretinal fibrosis.

About RXi's Ophthalmology Franchise

RXI-109 and RXi's sd-rxRNA technology platform are broadly protected in the United States and International regions. The Company's robust patent estate provides for multiple commercial and business development opportunities.

RXi announced in January 2018 that it would exclusively focus on developing the next generation of immuno-oncology therapeutics based on its self-delivering RNAi therapeutic platform. As such, it is actively seeking to partner or out-license both its Dermatology and Ophthalmology Franchises.

Each of these Franchises is comprised of a number of preclinical and clinical-stage assets broadly covered by a robust intellectual property estate. To obtain more information about these assets, contact RXi's Vice President of Business Operations, Dr. James Cardia at jcardia@rxipharma.com.

About RXi Pharmaceuticals

RXi Pharmaceuticals Corporation (NASDAQ: RXII) is a biotechnology company developing the next generation of immuno-oncology therapeutics based on its self-delivering RNAi (sd-rxRNA®) therapeutic platform. The Company's discovery and research efforts are focused on developing sd-rxRNA therapeutic compounds to be used with an Adoptive Cell Transfer (ACT) approach. This process uses immune cells, such as T-lymphocytes that are isolated from the patient or retrieved from allogeneic immune cell banks, and then expanded and in some cases processed to express tumor-binding receptors. Our approach introduces a new and important step in ex-vivo processing of the immune cells where sd-rxRNA is used to eliminate the expression of immunosuppressive receptors or proteins from the therapeutic immune cells, making them less sensitive to tumor resistance mechanisms and thus improving their ability to destroy the tumor cells. Essentially, we aim to maximize the power of our sd-rxRNA therapeutic compounds by weaponizing therapeutic immune effector cells to attack cancer and ultimately provide patients battling terminal cancers with a powerful new treatment option that goes beyond current treatment modalities.

For additional information, visit the Company's website, www.rxipharma.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements are neither historical facts nor assurances of future performance. These statements are based only on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, projections, anticipated events and trends, the economy and other future conditions. Because forward-looking statements relate to the future, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict and many of which are outside of our control. Our actual results may differ materially from those indicated in the forward-looking statements as a result of a number of important factors, including the safety and efficacy of our product candidates, future success of our clinical trials and scientific studies, our ability to enter into strategic partnerships and the future success of these strategic partnerships, the availability of funds and resources to pursue our research and development projects and general economic conditions. Our Annual Report on Form 10-K and subsequent Quarterly Reports on Form 10-Q include detailed risks under the caption "Risk Factors" that may affect our business, results of operations and financial condition. Readers are urged to review these risk factors and to not act in reliance on any forward-looking statements, as actual results may differ from those contemplated by our forward-looking statements. RXi does not undertake to update forward-looking statements to reflect a change in its views, events or circumstances that occur after the date of this release.

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[1] Lucentis – full prescribing information: https://www.gene.com/download/pdf/lucentis_prescribing.pdf

Eylea – full prescribing information: https://www.regeneron.com/sites/default/files/EYLEA_EPI.pdf

View original content:http://www.prnewswire.com/news-releases/rxi-pharmaceuticals-announces-positive-results-from-phase-12-trial-with-rxi-109-for-retinal-scarring-300690078.html

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