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Pharmaceuticals & Biotechnology

Source: Eikon Thomson Reuters

Market data

EPIC/TKR	**REDX**
Price (p)	8.5
12m High (p)	28.6
12m Low (p)	3.5
Shares (m)	126.5
Mkt Cap (£m)	10.7
EV (£m)	3.7
Free Float*	69%
Market	AIM

**As defined by AIM Rule 26*

Description

Redx is focused on the discovery and development of novel therapeutics to address areas of high unmet medical need, in cancer and fibrosis. The aim is to develop putative drugs through early trials and then to partner them for late stage development and commercialisation.

Company information

CEO	Lisa Anson
CFO	Dominic Jackson
Chairman	Iain Ross
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	www.redxpharma.com

Key shareholders

Directors	0.5%
Jon Moulton	18.2%
Seneca Partners	12.6%
AXA	9.7%
Aviva	8.2%
Graham Edwards	3.2%

Diary

Dec'18	Results
1H'19	Resume Ph. I/IIa with RXC004

Analysts

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Redx Pharma

Back to the clinic

Redx Pharma's (REDX) new management team is continuing to focus its financial resources on progressing its lead candidates in oncology and fibrotic disease into the clinic. When the first patient was treated with RXC004, its porcupine inhibitor, in a Phase I/IIa proof-of-concept trial, some on-target adverse events (anticipated at higher doses) were observed, management took the prudent decision to halt patient recruitment. Based on a draft modified protocol using significantly lower doses, Redx has received positive feedback from the MHRA. Redx is currently preparing the final protocol with the aim of re-starting the clinical study in 1H'19.

- **Strategy:** Redx is focused on the discovery and early clinical development of novel therapeutics in oncology and fibrotic diseases. It is also focused on taking assets through proof-of-concept clinical trials and potentially partnering them to the drug major(s) for late-stage development and commercialisation.

- **Positive meeting with MHRA:** Following suspension of the trial in March 2018, the Medicines and Healthcare products Regulatory Agency (MHRA) has agreed in principle with the proposed plan to re-start of the Phase I/IIa study at a significant lower dose of RXC004, with the aim to start the clinic in 1H'19.

- **Development strategy for RXC004:** Redx proposes to focus the development of RXC004 in combination with a checkpoint inhibitor (CPI) in cancer patients with advanced disease. This is to utilise the specificity of the Wnt pathway in converting immune 'cold' tumours to 'hot' and improving the CPI response rate.

- **Risks:** After a difficult period, REDX has emerged in much better shape. While all early-stage pharma/biotech companies carry substantial risks and are capital-intensive, the rewards can be substantial, as evidenced by the successful disposal of its pre-clinical BTK programme for $40m in 2017.

- **Investment summary:** Redx's new management team is moving forward with a revised business plan that focuses cash resources on progressing its drug leads in oncology and fibrotic disease to clinical proof-of-concept. With a positive response from the MHRA, patient recruitment in the Phase I/IIa with RXC004 is set to resume early in 2019. While Novartis is paving the way with Wnt inhibition, Redx is a close follower, with a potentially best-in-class compound.

Financial summary and valuation

Year-end Sep (£000)	2015	2016	2017	2018E	2019E	2020E
Milestones/royalties	0	0	0	0	0	0
Other income	2,648	2,380	1,291	1,000	1,000	1,000
R&D investment	-9,463	-14,315	-13,000	-6,528	-11,078	-11,410
SG&A (corp. cost)	-2,008	-2,212	-5,698	-3,150	-3,276	-3,407
Underlying EBIT	-8,823	-14,147	-17,407	-8,678	-13,354	-13,817
Underlying PBT	-9,112	-14,606	-17,737	-8,648	-13,327	-13,817
Statutory PBT	-8,825	-15,407	1,646	-9,240	-13,547	-14,057
R&D tax credit	650	637	-118	392	665	685
Underlying EPS (p)	-14.6	-17.8	-15.8	-6.5	-8.8	-8.2
Statutory EPS (p)	-14.1	-19.8	1.4	-7.0	-9.0	-8.4
Net (debt)/cash	7,436	3,758	23,806	5,595	2,718	-10,382
Capital increase	13,447	9,296	11,066	0	10,000	0

Source: Hardman & Co Life Sciences Research

RXC004: trial to resume

Positive discussions with the MHRA

Redx has received the agreement, in principle, to resume the Phase I/IIa trial with RXC004 in 1H'19

Redx is returning to the clinic with a revised protocol for its lead programme, the porcupine inhibitor RXC004. The company has been in discussions with the Medicines and Healthcare product Regulatory Agency (MHRA), which has agreed, in principle, to proposed modifications to its trial protocol, allowing the trial to re-start in 1H'19. It is not unusual to pause a clinical study, especially at an early stage and with cancer patients with advanced disease, who have undergone several treatments prior to enrolling in the trial.

The prudent decision to suspend the Phase I/IIa trial was based on the observation of some adverse events in the first subject following a dose of RXC004. Such events should be anticipated with Wnt inhibition, but at a much higher dose than that used in the previous clinical study (10mg per day). On the positive side, analysis of the data suggested that RXC004 was well absorbed and had an on-target effect, but the data also demonstrated that the compound possesses a different pharmacokinetic profile in humans compared with that seen in animal studies. Despite achieving the predicted maximal concentration (C_{max}) in the blood system, an extended half-life in circulation meant that the exposure to RXC004 in the body was longer than predicted, leading to levels of the compound above the therapeutic window. These events could not have been foreseen from translational studies performed in different animal species (allometric scaling) due to the difference in metabolism between species.

Resuming the trial

A final version of the protocol will be submitted to the MHRA, this includes a much lower starting dose of RXC004, and is anticipated to start in 1H'19

On the basis of this clinical information, in conjunction with the study investigators, Redx believes that safety, tolerability and ultimately the therapeutic window and clinical benefit can be achieved with a lower dose of RXC004, which is the basis of the new trial protocol. Following positive discussions with the MHRA, Redx is now finalising the revised protocol of the Phase I/IIa trial, with submission expected before year-end. This would allow the study to re-start in 1H'19 with a reformulated starting dose 20-fold lower (0.5mg per day) compared with the original protocol. Safety will be the driver of the first part of the study with enhanced monitoring.

Proof-of-concept study

The trial aims to evaluate the safety and tolerability of RXC004 as the primary end-point

The clinical study will be led by the Principal Investigator, Natalie Cook, at the NHS Foundation Trust in Manchester and will enrol a total of ca.50 patients at three sites (Manchester, Oxford and Newcastle), with the possibility of adding a fourth site. This first-in-man study represents a major milestone for the company, being the first programme that REDX has advanced into the clinic since its incorporation in 2010, from discovery all the way to the clinic.

Phase I/IIa clinical trial

The Phase I/IIa clinical trial is focusing on cancers that have a poor prognosis. The study will comprise of two parts:

- **Phase I:** a multi-arm dose-escalating study, from 0.5mg to 3mg (and possibly higher), designed to assess the safety and tolerability of RXC004 in advanced cancer patients with solid tumours, as a single agent and to establish the optimal dose for Phase IIa. The trial is expected to complete in 1H'20 with the release of the data read-out. It is also possible that early data could be made available during 2019.

Following positive results, a study in combination with an immuno-oncology agent such as anti-PD-1 inhibitor is also confirmed

- **Phase IIa:** an expansion arm of RXC004 in combination with immuno-oncology agents such as anti-PD-1 checkpoint inhibitor (CPI) in colorectal cancer.

Additionally, targeting tumours with specific Wnt pathway alterations may benefit from treatment with RXC004 as a monotherapy or in combination with standard-of-care treatment, such as pancreatic, colorectal and prostate cancers.

Porcupine inhibitor RXC004

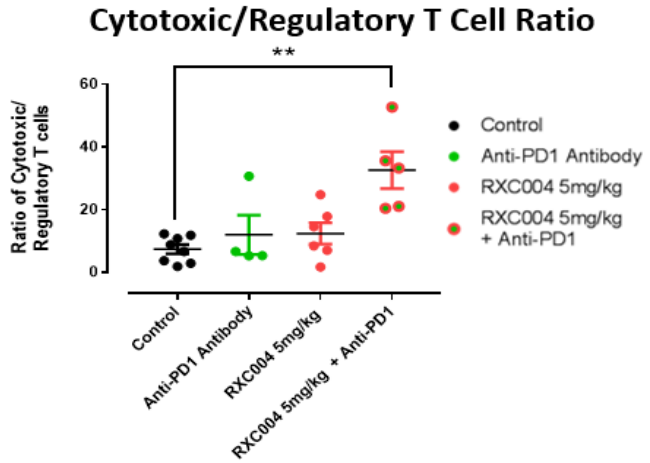
Scientific rationale

RXC004 is an orally bioavailable small molecule porcupine inhibitor. The porcupine enzyme is a key protein that is required for the function of the Wingless-type (Wnt) pathway, an embryonic signalling pathway that is implicated in cell proliferation, survival, migration, cell death and polarity, as well as the maintenance of cancer stem cells (CSC) in many cancer types, which results in the recurrence and emergence of cancer resistance. The protein is also believed to play a key role in the field of immuno-oncology when it is combined with CPI.

- **Immuno-oncology:** Redx has confirmed that RXC004 enhances immune system activation. Concomitant administration with a PD-1 CPI has a beneficial immune system effect through down-regulation of certain immune cells (regulatory T-cells), which prevent the immune system from recognising and killing cancer cells. The mechanism of action of RXC004 and the effect in enhancing the immune response, when combined with a PD-1 inhibitor, may turn the 'cold' immune-suppressive tumour environment to 'hot'. The aim of combination therapy is to potentiate the effect of anti-PD-1 CPI and increase both the response rate (number of patients who respond) and the duration of response (a longer sustained shrinkage in the tumour).

- **Targeted therapy:** Pre-clinical experiments demonstrated that RXC004 could inhibit tumour growth in a variety of cancer models as a single agent. Importantly, RXC004 was shown to inhibit tumour growth in a pancreatic tumour model at lower doses than WNT974, Novartis's lead compound, currently in Phase I/II with a PD-1 CPI.

RXC004 – combination efficacy



Source: Redx Pharma, 14-16 April 2018, AACR Annual Meeting, poster session

Dual immune response and anti-cancer effects provide RXC004 with an attractive profile

The dual immune response and anti-cancer effects provide RXC004 with an attractive profile, targeting specifically the immune-suppressive microenvironment usually seen in tumours. It is important to reiterate that the prime focus in the development of RXC004 is on the second phase of the trial, assessing the benefits of the combination therapy in enhancing the response rate and duration of the CPI. This should be attractive to companies in the immuno-oncology space.

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