hardman&co

Pharmaceuticals & Biotechnology

Source: Eikon Thomson Reuters

Market data	
EPIC/TKR	**REDX**
Price (p)	15.8
12m High (p)	43.0
12m Low (p)	14.5
Shares (m)	126.5
Mkt Cap (£m)	19.9
EV (£m)	6.9
Free Float*	76%
Market	AIM

**As defined by AIM Rule 26*

Description

Redx is focused on the discovery and development of proprietary, small molecule 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

Exec. Chairman	Iain Ross
CEO	-
CFO	Dominic Jackson
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	www.Redxpharma.com

Key shareholders

Directors	0.5%
Seneca Partners	12.5%
Jon Moulton	10.8%
AXA	9.8%
Aviva	8.4%
Lanstead Capital	7.6%

Diary

6 March	AGM
Apr-18	Interims
2H'18	First data with RXC004

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Redx Pharma

Entering the clinical stage

The new Board & Management team of Redx is focusing its financial resources (ca.£12.5m) on progressing its lead candidates in oncology and fibrotic disease into the clinic. The company has announced recently that the first patient has been treated with RXC004, a porcupine inhibitor indicated for a number of tumour types, in a Phase I/IIa proof-of-concept clinical trial. By entering humans, Redx has hit an important development milestone and evolved into a clinical-stage biopharmaceutical company. The group's strategy was validated in 2017 by the successful disposal of its pre-clinical programme BTK for $40m.

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

- **RXC004:** Porcupine inhibitors target the Wnt pathway, an embryonic signalling pathway that is implicated in many survival cellular functions, including the maintenance of cancer stem cells. RXC004 is a specific small molecule inhibitor being used in the clinic in an oral, once-daily formulation.

- **Proof-of-concept trial:** Redx has announced that the first patient has been dosed with RXC004 in a Phase I/IIa trial. Initially, the safety and tolerability of RXC004 will be assessed, with headline data expected in late 2018. This will be followed by an expansion arm focusing on gastric, biliary and pancreatic cancers.

- **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 BTK programme for $40m in 2017.

- **Investment summary:** Redx had already started the process of refining its strategy, but the new management team has simply accelerated this process. The revised business plan is focusing cash resources on progressing its drug leads in oncology and fibrotic disease into early clinical development. The commencement of clinical trials represents an important value inflection point.

Financial summary and valuation

Year-end Sept (£000)	2014	2015	2016	2017	2018E	2019E
Milestones/royalties	0	0	0	0	0	0
Other income	6,157	2,648	2,380	650	1,000	1,000
R&D investment	-8,342	-9,463	-14,315	-13,000	-8,715	-11,079
SG&A (corp. cost)	-1,815	-2,008	-2,212	-5,150	-3,150	-3,276
Underlying EBIT	-4,000	-8,823	-14,147	-17,500	-10,865	-13,355
Underlying PBT	-4,249	-9,112	-14,606	-21,671	-10,837	-13,329
Statutory PBT	-4,263	-8,825	-15,407	1,709	-10,860	-13,372
R&D tax credit	910	650	637	520	523	665
Underlying EPS (p)	-7.5	-14.6	-17.8	-18.7	-8.2	-8.8
Statutory EPS (p)	-7.6	-14.1	-19.8	2.0	-8.2	-8.9
Net (debt)/cash	892	7,436	3,758	23,800	4,241	1,740
Capital increase	4,383	13,447	9,296	11,170	0	10,000

Source: Hardman & Co Life Sciences Research

RXC004: first patient dosed

Proof-of-concept study

Redx is now a clinical-stage pharmaceutical company, with the first patient having been dosed with the porcupine inhibitor, RXC004, at the Christie NHS Foundation Trust in Manchester. 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. The porcupine programme has now progressed all the way from discovery, through lead-optimisation and pre-clinical development stages, and into humans. This is another example of Redx's ability to deliver on its research programmes and a further validation of its strategy.

In readiness for the trial, the company recently appointed Dr Andrew Saunders as its Chief Medical Officer (CMO). Andrew has 25 years' of experience in the field of cancer and was previously the CMO of Lytix Biopharma, a Norwegian immuno-oncology company. His prime responsibility will be to oversee this trial.

Phase I/IIa clinical trial

A first-in-man dose-escalating study with RXC004 has commenced in hard-to-treat cancers, measuring safety and tolerability

RXC004 is an orally bioavailable selective porcupine inhibitor. The Phase I/IIa clinical trial is focusing on hard-to-treat cancers that have a poor prognosis and will be run in three UK sites, with the Christie Hospital being the lead site. The study will comprise two parts:

- **Phase I:** a dose-escalating study designed to establish the optimal dose for Phase IIa, as well as assessing the safety and tolerability of RXC004 in advanced cancer patients with solid tumours, as a single agent. Data available are anticipated in 2H 2018.
- **Phase IIa:** expansion arms into gastric, biliary and pancreatic cancers, with first data available early in 2020.

Following positive results, a study in combination with a PD-1 inhibitor is envisaged

On the expectation of a positive outcome in the safety and tolerability part of the trial, Redx is also contemplating the potential of using RXC004 in combination with a PD-1 checkpoint inhibitor (CPI) for efficacy studies in melanoma patients.

Porcupine inhibitor RXC004

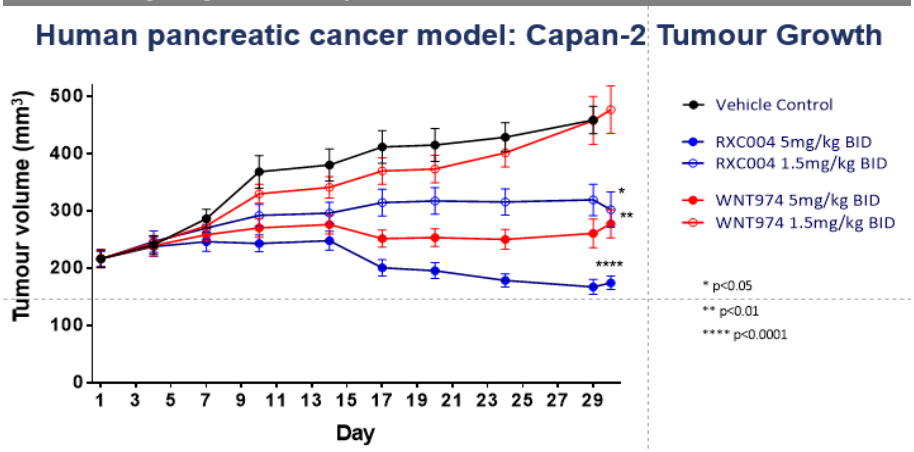
Scientific rationale

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[1]. The protein is also believed to have a potential role in the field of immuno-oncology when it is combined with CPI.

- **Targeted therapy:** Previous pre-clinical experiments demonstrated that RXC004 could inhibit tumour growth in a variety of cancer models, and appeared to have a suitable safety profile. Redx hypothesised that RXC004, as a single agent, had potent activity in hard-to-treat cancers – e.g. gastric, biliary and pancreatic cancers. Importantly, RXC004 was also shown to be efficacious at inhibiting tumour growth at lower doses than WNT974 (LGK974), Novartis's lead compound in this field, in a pancreatic tumour model.

[1] Can we safely target the WNT pathway? Michael Kahn, *Nature Rev. Drug Discovery* **2014**, *13*, 513-532.

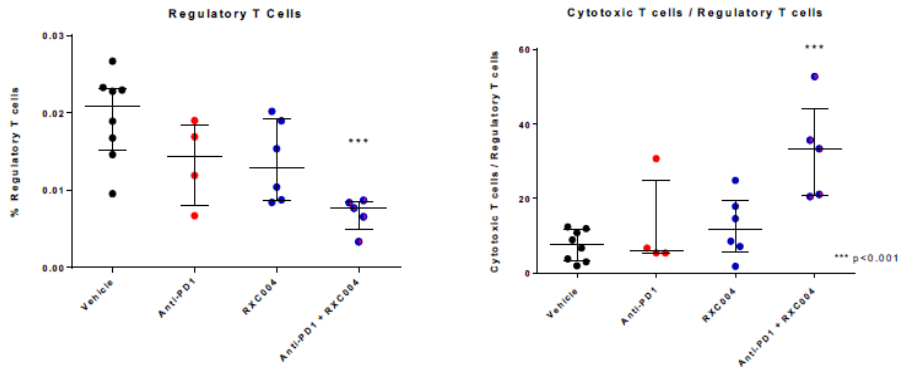
RXC004 single agent efficacy



Source: Redx Pharma

- **Immuno-oncology:** In addition to its anti-tumour effect, RXC004 has provided evidence of an immune system stimulation. Concomitant administration with a PD-1 CPI has a beneficial immune system effect with the down regulation of regulatory T-cells which are responsible for fooling the immune system and hiding tumour cells, and up-regulation of the ratio of cytotoxic T-cells to regulatory T-cells improving the immune response against foreign antigens. By using combination therapy, the aim is to potentiate the effect of a PD-1 CPI and increase its response rate, as demonstrated in the following *in vivo* syngeneic CT26 colorectal cancer model.

RXC004 in combination with a PD-1 CPI



Source: Redx Pharma

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

The dual anti-cancer and immune response effects provide RXC004 with an attractive profile, targeting specifically the immunosuppressive microenvironment usually seen in tumours.

Conclusion

The porcupine protein has generated substantial external interest, given the better understanding of the Wnt pathway. Novartis is considered to be in the lead with WNT974 (LGK974) in on-going Phase I/II trials for a range of solid malignancies in combination with a PD-1 CPI. Initial clinical findings (pharmacokinetic, safety and tolerability) with WNT974 have been published, but no efficacy data have been disclosed to date. Given its improved efficacy and pharmacokinetic (PK) profile in pre-clinical studies, Redx believes that RXC004 could potentially result in a best-in-class drug.

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(Disclaimer Version 4 – Effective from January 2018)

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The fact that we are commissioned to write the research is disclosed in the disclaimer, and the research is widely available.

The full detail is on page 26 of the full directive, which can be accessed here: http://ec.europa.eu/finance/docs/level-2-measures/mifid-delegated-regulation-2016-2031.pdf

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