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Redx Pharma

Clinical and corporate update

The new management team of Redx Pharma is focusing its financial resources (ca.£10m) on progressing its lead candidates in oncology and fibrotic disease into the clinic. Although the first patient was treated recently in a Phase I/II proof-of-concept trial with its porcupine inhibitor RXC004, some on-target adverse events (anticipated at higher doses) were observed, which caused management to take the prudent decision to stop patient recruitment. A revised study with a lower dosing regimen is being prepared. Meanwhile, pre-clinical data on the synergy between RXC004 and a PD-1 checkpoint inhibitor in cancer was presented at AACR.

- **Strategy:** Redx is focused 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.

- **New CEO appointed:** Redx has announced the appointment of Lisa Anson as CEO, having been President of AstraZeneca (AZN) UK since 2012. She brings considerable industry experience, having held a variety of senior management roles at AZN in the UK and the US. Lisa is also currently President of the ABPI.

- **AACR Poster:** Redx presented a poster at the American Association for Cancer Research (AACR) annual meeting in Chicago (14-16 April) highlighting the mechanism of action and observations of the porcupine inhibitor RXC004, and its effect in enhancing the immune response.

- **Clinical update:** A decision was made to temporarily suspend the Phase I/IIa trial with RXC004 in light of adverse events in the first patient dosed. Early data suggest a higher exposure and longer half-life in humans that could not have been predicted. A lower dose protocol is expected to be submitted in 2H'18.

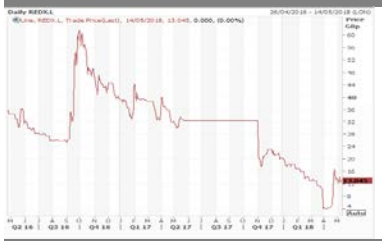
- **Investment summary:** Redx's new management team is moving forward with a revised business plan that focuses cash resources on progressing its drug leads in oncology and fibrotic disease into early clinical development. The temporary 'hold' on the RXC004 clinical trial has extended these cash resources by an estimated four months. 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 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	-6,528	-11,078
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	-8,678	-13,354
Underlying PBT	-4,249	-9,112	-14,606	-21,671	-8,648	-13,327
Statutory PBT	-4,263	-8,825	-15,407	1,709	-8,681	-13,380
R&D tax credit	910	650	637	520	392	665
Underlying EPS (p)	-7.5	-14.6	-17.8	-18.7	-6.5	-8.8
Statutory EPS (p)	-7.6	-14.1	-19.8	2.0	-6.6	-8.9
Net (debt)/cash	892	7,436	3,758	23,800	6,023	3,350
Capital increase	4,383	13,447	9,296	11,170	0	10,000

Source: Hardman & Co Life Sciences Research

Pharmaceuticals & Biotechnology



Source: Eikon Thomson Reuters

Market data

EPIC/TKR	**REDX**
Price (p)	13.0
12m High (p)	35.0
12m Low (p)	3.5
Shares (m)	126.5
Mkt Cap (£m)	16.4
EV (£m)	6.4
Free Float*	69%
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

CEO (from 01 Jun)	Lisa Anson
CFO	Dominic Jackson
Chairman	Iain Ross
	+44 1625 469 900
	www.redxpharma.com

Key shareholders

Directors	0.5%
Jon Moulton	18.2%
Seneca Partners	12.5%
AXA	9.8%
Aviva	8.4%

Diary

Jun'18	Interims
2H'18	Submit revised protocol for Ph. I with RXC004

Analysts

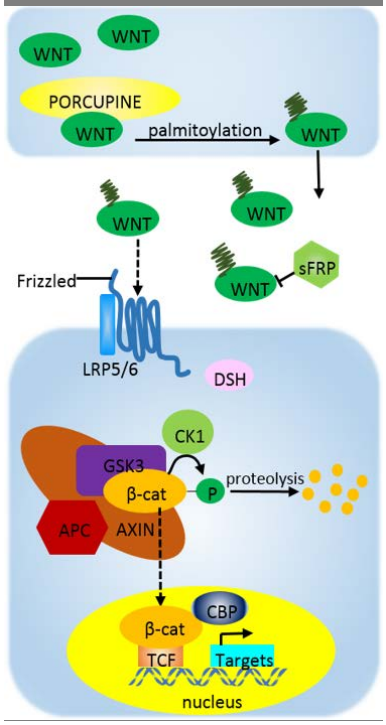
Martin Hall	020 7194 7632
	mh@hardmanandco.com
Dorothea Hill	020 7194 7626
	dmh@hardmanandco.com
Grégoire Pavé	020 7194 7628
	gp@hardmanandco.com

RXC004 update

Conference presentation

Redx presented a poster at the recent (14-16 April 2018) AACR annual meeting in Chicago, highlighting pre-clinical studies of its lead candidate, the porcupine inhibitor RXC004 in an immune-oncology setting. In addition to having efficacy through the direct tumour targeting approach, the poster highlighted the mechanism of action and the synergistic effect in enhancing the immune response of RXC004 when combined with a PD-1 inhibitor, by turning the 'cold' immunosuppressive tumour environment to 'hot'. This data supports the rationale for expanding its trial programme from monotherapy with RXC004 to include combination with a checkpoint inhibitor (CPI).

Wnt pathway



Source: Redx Pharma

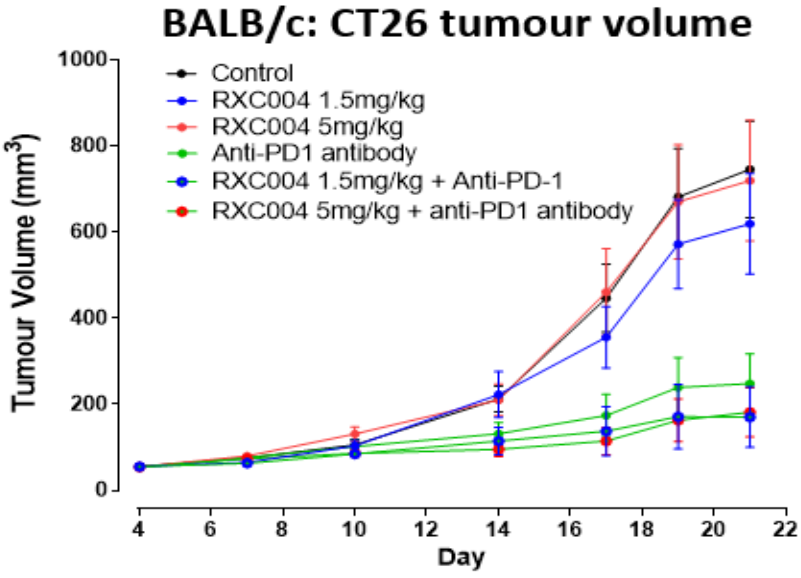
The porcupine enzyme is a key protein required for the function of the Wingless-type (Wnt) pathway, an embryonic signalling pathway that is implicated in cell proliferation, survival, migration, cell death and polarity, as well as the maintenance of cancer stem cells (CSC) in many cancer types, which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

Enhancing the immune response

Key findings

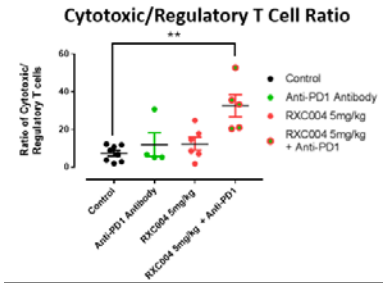
- **RXC004 improves the anti-tumour effects of anti-PD-1 CPI:** In an *in vivo* pre-clinical study using a CT26 (colon carcinoma) mouse model, it is interesting to note that in contrast to the anti-PD-1 CPI, the porcupine inhibitor did not induce a significant reduction in tumour volume on its own. However, when administrated together, RXC004 showed trends to enhance the anti-tumour effect of the checkpoint inhibitor, as shown in the following graph.

Effect of RDX004 in combination with a CPI



Source: Redx Pharma

RXC004 improves the T-cell ratio

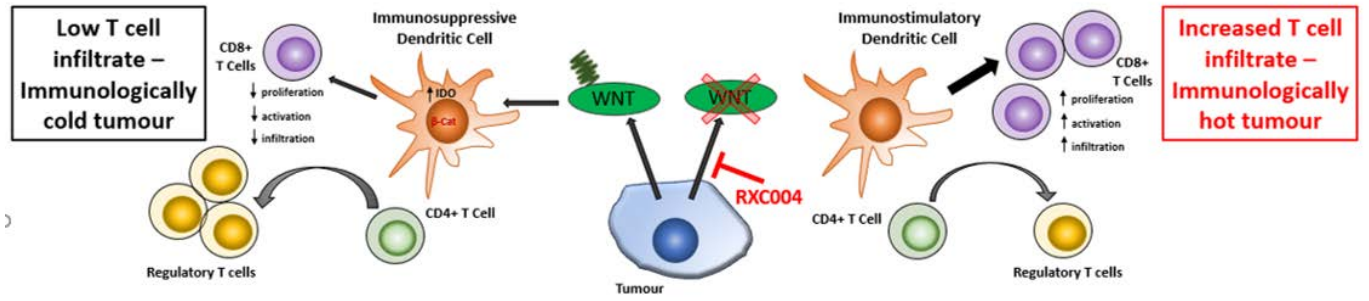


Source: Redx Pharma

- **Modulation of the ratio cytotoxic T-cells/regulatory T-cells:** The synergistic effect of RXC004 with the PD-1 inhibitor induced a significant change in the ratio of cytotoxic/regulatory T-cells. The cytotoxic T-cell are able to kill cancer cells while the regulatory T-cells are responsible for modulating the immune system. Increasing this ratio changes the tumour immunosuppressive environment into a more active setting prone to effective anti-cancer effect.

- **RXC004 efficacy in immunologically "cold" tumours:** The hypothesis is that RXC004 has the ability to turn immunologically 'cold' tumours into immunologically 'hot' tumours, making them more sensitive to the PD-1 CPI. Indeed, by blocking the secretion and function of the Wnt proteins through inhibition of the porcupine protein, RXC004 has the potential to enhance the immune response in the tumour micro-environment. Theoretically, RXC004 would have the possibility of improving the effect of the commercially available PD-1 inhibitors nivolumab (Opdivo, Bristol-Myers Squibb (BMS) and pembrolizumab (Keytruda, Merck & Co) as well as the CTL-4 inhibitor ipilimumab (Yervoy, BMS).

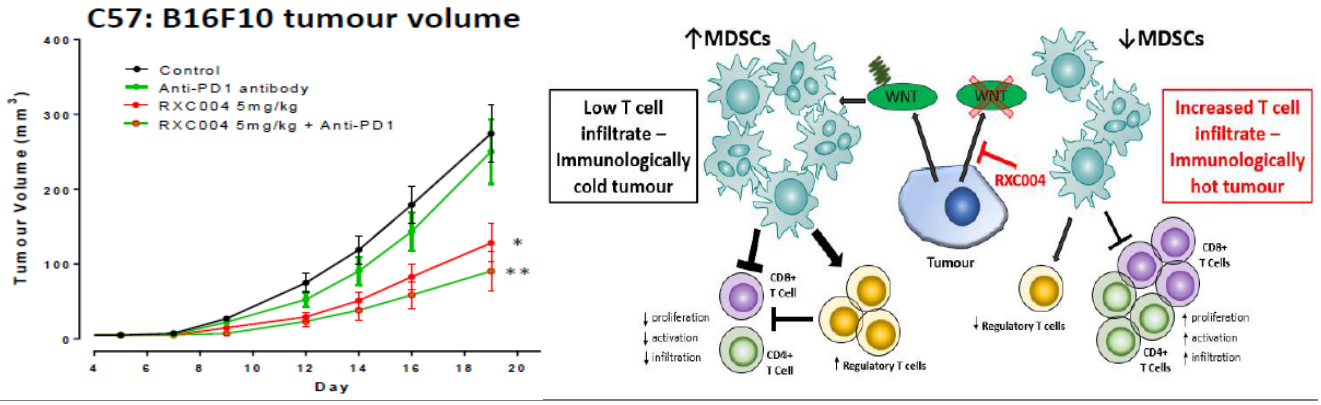
Mechanism of action



Source: Redx Pharma

- **REDX004 triggers immune response by turning cold tumours to hot:** In a B16F10 model (a mouse skin cancer model which is non-responsive to immune checkpoint inhibitors), in addition to be effective as a single agent, the porcupine inhibitor has an additive/synergistic effect with the PD-1 CPI giving an enhanced anti-tumour response. The experiment demonstrated also that, by blocking the Wnt pathway, the inhibitor reduces the myeloid derived suppressor cell population that possess strong immunosuppressive activities, which are usually associated with poor patient prognosis and resistance to therapy.

Mechanism of action



Source: Redx Pharma

Clinical update

RXC004 study update

In February 2018, Redx achieved an important milestone with the initiation of its first clinical study, which is investigating RXC004 in a Phase I/II trial. However, on 29 March, Redx decided to temporarily stop patient recruitment because the first subject had experienced some adverse events that were anticipated with Wnt inhibition (but at a higher dose that the one used in the clinical study). The first patient was withdrawn to allow recovery. Pharmacokinetic analysis clearly demonstrated that RXC004 was well absorbed with a long terminal half-life. Management has taken the prudent view to suspend the trial to allow a protocol revision.

The effect of the drug suggests that it might have a different pharmacokinetic profile in humans compared with that seen in animal studies, extending the half-life in circulation thereby giving longer exposure in the body than anticipated. These events could not have been predicted from translational studies performed in different animal species (allometric scaling). The trial was initiated at a dose level of 10mg per day. While this is a disappointing outcome, it is too early to draw any conclusions.

After reviewing the clinical data with RXC004, management intends to submit a new protocol to the MHRA starting at a much lower dose, with the expectation that the trial could resume in several months time.

The consequence of this is that about £2.0m-£2.5m that would have been spent on the RXC004 clinical trial programme in fiscal 2018 has been pushed back to fiscal 2019, which will extend the company's cash runway accordingly.

Novartis WNT programme

At the same 2018 AACR meeting, Novartis presented data from a Phase I/II trial using its porcupine inhibitor, WNT974/LGK974 in a range of solid tumour types. Novartis demonstrated that there were no concerns with adverse events precipitated through targeting the Wnt pathway at the dose they used. The study suggested also that its porcupine inhibitor affect immune cell signatures in the tumour microenvironment.

Novartis indicated that a second arm of the study is currently running using WNT974 in combination with its anti-PD-1 antibody spartalizumab. The study will include patients with melanoma and squamous cell carcinoma of the lung that were refractory to PD-1 inhibitors. The trial will consist of a dose escalation study that will be followed by a dose expansion at the maximum tolerated dose in pancreatic cancer, triple negative breast cancer, melanoma and head and neck cancer. While Novartis is leading the field, Redx is following with a compound that seems to have greater exposure (longer half-life) compared to WNT974.

Corporate update

CEO appointment – Lisa Anson

On 24 April, the Board announced the appointment of Lisa Anson as Chief Executive Officer of the group. She will take up her appointment on 1 June. The market responded very positively to this news almost tripling over a three-day trading period.

Lisa has held significant leadership positions over a 20-year career with AstraZeneca, notably President of AZN UK since 2012 and Global Vice President Oncology and Vice President of Emerging Brands in the US and the UK, working closely with the Research and Development teams in both cases.

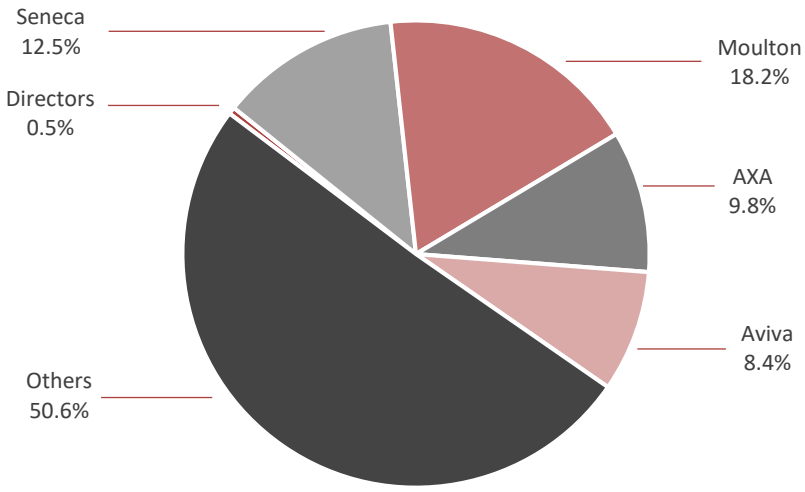
She studied Natural Sciences at Cambridge University and has an MBA from INSEAD, France. Upon graduating Lisa joined KPMG in London as a management consultant and then moved to California where she worked for Salick Health Care (now Aptium), a cancer disease management company, prior to joining Zeneca Pharmaceuticals (USA) in 1998 as a business development manager. She is the current President of the Association of the British Pharmaceutical Industry (ABPI).

When she joins Redx in the summer, Iain Ross will move from Executive Chairman to non-executive Chairman.

Shareholder update

This appointment also came shortly after the news that Lanstead Partners had sold out its entire (7.2% down from 12%) stake in the company thereby removing the stock overhang. This stake has been picked up by existing shareholder, Jon Moulton.

Shareholders



Source: London Stock Exchange announcements

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Hardman & Co Research Limited (trading as Hardman & Co)
35 New Broad Street
London
EC2M 1NH

+44 (0) 20 7194 7622
Follow us on Twitter @HardmanandCo

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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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Hardman & Co team

Management team

+44 (0)20 7194 7622

John Holmes	jh@hardmanandco.com	+44 (0)20 7194 7629	Chairman
Keith Hiscock	kh@hardmanandco.com	+44 (0)20 7194 7630	CEO

Business development and investor engagement

+44 (0)20 7194 7622

Richard Angus	ra@hardmanandco.com	+44 (0)20 7194 7635	Business development
David Banks	db@hardmanandco.com	+44 (0)20 7194.7622	Corporate advisory
Max Davey	md@hardmanandco.com	+44 (0)20 7194 7622	Investor engagement
Antony Gifford	ag@hardmanandco.com	+44 (0)20 7194 7622	Investor engagement
Ann Hall	ah@hardmanandco.com	+44 (0)20 7194 7622	Business development
Gavin Laidlaw	gl@hardmanandco.com	+44 (0)20 7194 7627	Investor engagement
Vilma Pabilionyte	vp@hardmanandco.com	+44 (0)20 7194 7637	Business development

Analysts

+44 (0)20 7194 7622

Agriculture		**Bonds / Financials**	
Doug Hawkins	dh@hardmanandco.com	Brian Moretta	bm@hardmanandco.com
Yingheng Chen	yc@hardmanandco.com	Mark Thomas	mt@hardmanandco.com
Building & Construction		**Consumer & Leisure**	
Tony Williams	tw@hardmanandco.com	Steve Clapham	sc@hardmanandco.com
Mike Foster	mf@hardmanandco.com	Mike Foster	mf@hardmanandco.com
		Jason Streets	js@hardmanandco.com
Life Sciences		**Media**	
Martin Hall	mh@hardmanandco.com	Derek Terrington	dt@hardmanandco.com
Dorothea Hill	dmh@hardmanandco.com		
Grégoire Pavé	gp@hardmanandco.com		
Mining		**Oil & Gas**	
Paul Mylchreest	pm@hardmanandco.com	Angus McPhail	if@hardmanandco.com
Property		**Services**	
Mike Foster	mf@hardmanandco.com	Mike Foster	mf@hardmanandco.com
Special Situations		**Tax Enhanced Services**	
Steve Clapham	sc@hardmanandco.com	Brian Moretta	bm@hardmanandco.com
Paul Singer	ps@hardmanandco.com		
Yingheng Chen	yc@hardmanandco.com		
Technology		**Utilities**	
Milan Radia	mr@hardmanandco.com	Nigel Hawkins	nh@hardmanndco.com

Hardman & Co

35 New Broad Street
London
EC2M 1NH

Tel: +44(0)20 7194 7622

www.hardmanandco.com