Pharmaceuticals & Biotechnology

Source: Eikon Thomson Reuters

Market data

EPIC/TKR	**REDX**
Price (p)	5.5
12m High (p)	23.7
12m Low (p)	3.5
Shares (m)	126.5
Mkt Cap (£m)	6.9
EV (£m)	0.4
Free Float*	69%
Market	AIM

**As defined by AIM Rule 26*

Description

Redx Pharma (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	Lisa Anson
CFO	Dominic Jackson
Chairman	Iain Ross

+44 1625 469 900

www.redxpharma.com

Key shareholders

Directors	0.6%
Jon Moulton	18.2%
Seneca Partners	12.6%
AXA	9.7%
Aviva	8.2%

Diary

29 Nov	RXC006 data
1H'19	Resume Ph. I with RXC004
1H'19	Dev candidate for NASH
1H'19	Dev candidate for Crohn's

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REDX PHARMA

Streamlined, focused and good value

Redx Pharma (REDX) is a clinical-stage R&D company focused on drugs targeting oncology and fibrotic disease. 2018 was a year that reset the benchmarks – new management team, restructured organisation focused on two therapeutic areas, and a clean balance sheet with £6.5m cash. 2019 should be a busy year for the company, with several major milestones expected. RXC004, is due to re-start a Phase I/IIa trial for cancer with a revised formulation and dosing schedule. RXC006 has been nominated as the first development candidate in the anti-fibrotic programmes for progression to proof-of-concept trials.

- **Strategy:** REDX is focused on the discovery and early clinical development of small molecule therapeutics in oncology and fibrotic disease. Its strategy is to develop assets through proof-of-concept clinical trials and then partner them for late-stage development and commercialisation.

- **2019:** Having reset the scene last year, 2019 will be characterised by the new team managing a streamlined organisation that is focused on progressing novel products in two disease areas, supported by a clean balance sheet. Both programmes are due to have value-enhancing milestones during the year.

- **Valuation:** REDX trades on a market capitalisation of £6.9m. The novelty and development stage of its assets suggests that the market does not fully grasp the value proposition of the company, especially given its track record of successfully disposing its pre-clinical BTK programme for $40m cash in 2017.

- **Risks:** REDX has emerged from fiscal 2018 in a clean position with a focused strategy. The company has enough cash until 2Q'19 but will require more capital to advance the proof-of-concept trials for both of its porcupine and ROCK inhibitor development programmes.

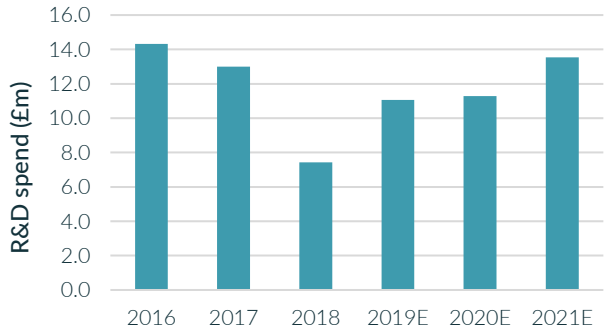
- **Investment summary:** New management is moving forward with a revised business plan that focuses cash resources on progressing its drug leads in oncology and fibrotic disease to proof-of-concept early clinical development. Big pharma has been shown to pay substantial prices for good science and novel and/or de-risked assets with clinical data, reinforcing REDX's strategy, potentially generating good returns and enhancing shareholder value.

Financial summary and valuation

Year-end Sep (£m)	2016	2017	2018	2019E	2020E	2021E
Other income	2.38	1.29	1.32	1.00	1.00	1.00
R&D investment	-14.32	-13.00	-7.42	-11.06	-11.29	-13.54
SG&A (corp. cost)	-2.21	-5.70	-2.81	-2.59	-2.74	-2.88
Underlying EBIT	-14.15	-17.41	-8.92	-12.65	-13.03	-15.42
Underlying PBT	-14.61	-17.74	-8.90	-12.64	-13.02	-15.42
Statutory PBT	-15.41	1.65	-10.15	-12.94	-13.35	-15.76
R&D tax credit	0.64	-0.12	1.30	1.94	1.98	2.37
Underlying EPS (p)	-17.83	-15.80	-6.01	-3.87	-2.59	-3.06
Statutory EPS (p)	-19.81	1.35	-6.99	-3.98	-2.67	-3.22
Disposals	0.00	30.47	-0.02	0.00	0.00	0.00
Net cash/(debt)	3.76	23.81	6.47	8.95	-2.56	-16.73
Capital increase	9.30	11.07	0.00	14.10	0.00	0.00

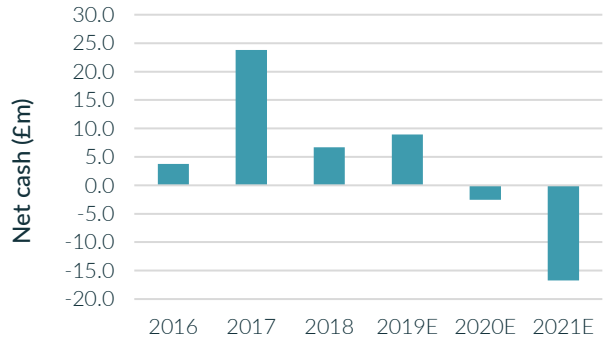
Source: Hardman & Co Life Sciences Research

R&D investment



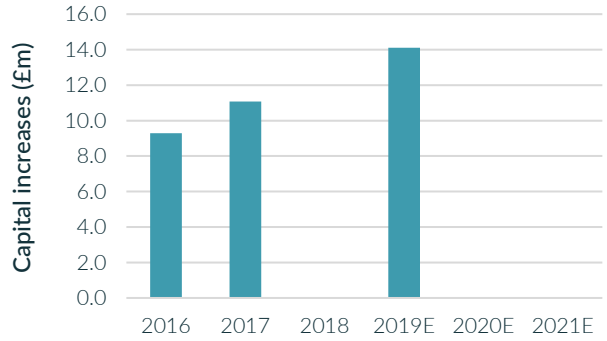
- R&D investment is expected to increase in light of the Phase I/IIa trial due to resume in early 2019 and additional late pre-clinical work for other programmes
- Savings from the strategic restructuring will be reallocated to fund two clinical trials
- Discovery programmes will still support the core areas, but less investment will be made overall in early projects

Net cash/(debt)



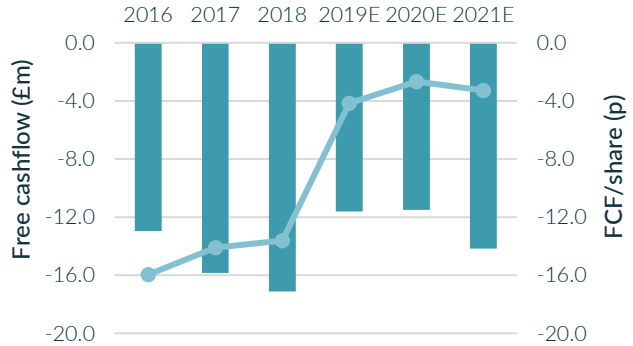
- Net cash at 30 September 2018 was £6.5m
- Strategic restructuring has reduced the operating expenses by one third
- The net cash position mainly reflects investment in R&D and working capital requirements

Capital increases



- Cashflow forecasts indicate that more capital will be needed to fund the planned clinical trial programmes
- Forecasts assume that gross new funds of £15m will be raised in fiscal 2019
- Further funds will also be required in 2020, which could come in the form of a licensing deal or equity funding

Free cashflow



- The average monthly cashburn of the streamlined organisation is estimated at ca.£0.65m
- Investment in clinical trials (ca.£5m per programme) is in addition, but dependent on timing of commencement
- Forecasts take account of a predicted capital increase in fiscal 2019, but do not reflect the need for any further increase in 2020

Source: Company data; Hardman & Co Life Sciences Research

2018 results

Key features

Operational highlights

- REDX exited administration on 2 November 2017, with a new strategy and management team that has concentrated resources on a much more focused R&D programme in two core areas: oncology and fibrotic disease.
- REDX hit an important development milestone in 2018 when its porcupine inhibitor, RXC004, entered Phase I/IIa trials. However, this was suspended temporarily due to the manifestation of some adverse events that could reasonably be expected at much higher doses. REDX has reformulated the drug at lower doses and aims to re-start the trial in 1H'19 having reached an agreement, in principle, with the MHRA.
- Porcupine inhibitor RXC006: First fibrosis development candidate nomination for the treatment of idiopathic pulmonary fibrosis (IPF). First-in-man clinical trial expected in 2020.
- Progress in both ROCK programmes with the nomination of the development candidate for NASH (ROCK2) and selection of a development candidate in Crohn's disease (GI-targeted ROCK) expected in 1H'19.
- Development of the exploratory pipeline, including an SHP2 inhibitor programme in oncology.

Partnering highlights

Following the decision to shut down its anti-infective unit, REDX has made progress in partnering some of its assets:

- Option and licence agreement with Deinove in March 2018 for the novel bacterial topoisomerase inhibitor (NBTI) programme, evaluation due date end December 2018.
- Option and license agreement with Kyrelum, a company focused on the development of novel agents for the treatment of bacterial infections, in September 2018 for the novel tricyclic topoisomerase inhibitor (NTTI).

Financial highlights

Following a number of one-off events during 2017 – administration, the disposal of the BTK programme, restructuring, and implementation of a new strategy – the statutory fiscal 2018 results are not directly comparable. However, 2018 sets a new base, with a clean balance sheet with no debt. REDX has exceeded its target to reduce by £4m its operating cost and delivered a saving of about one-third (£5.2m), with ca.80% derived from overhead reduction.

- **R&D:** R&D spend was reduced by 43% to -£7.42m (-£13.0m), which was slightly higher than our forecast. Headcount has been reduced drastically to reflect the revised approach. The temporary pause in the Phase I trial brought down overall R&D spend for the full year, but this spend will simply move into fiscal 2019 when the trial re-starts.
- **SG&A:** The underlying administration cost was reduced by 51% to an estimated -£2.81m (-£5.70m), even better than the forecast reduction.
- **EBIT:** Underlying operating profits/losses were reduced by 54% to -£8.92m (-£17.41m), which was slightly better than forecast due to an improvement in 'other income'.

- **Net cash:** At 30 September 2018, net cash on the balance sheet was slightly ahead of our forecast, at £6.47m. Underlying cashburn (excluding external R&D spend) is now estimated to be ca.£0.65m per month.
- **Clinical trial:** The cost of the suspended Phase I/IIa trial with RXC004 – estimated at £2.0m-£2.5m in fiscal 2018 – has been pushed back to fiscal 2019.

REDX 2018 results– actual vs expectations

Year to end-Sept (£m)	2017 actual	2018 actual	Growth %	2018 forecast	Delta Δ
R&D spend	-13.00	-7.42	-43%	-6.53	-0.89
Administration	-5.70	-2.81	-51%	-3.15	+0.34
Underlying EBIT loss	-17.41	-8.92	-49%	-8.68	-0.24
Tax credit	-0.12	+1.30	-	+0.39	+0.91
Underlying net loss	**-17.86**	**-7.60**	**-57%**	**-8.26**	**+0.66**
Net cash/(debt)	+23.81	+6.47	-	+5.60	+0.87

Figures may not add up exactly due to rounding
Source: Hardman & Co Life Sciences Research

Corporate highlights

Over the course of 2018, the management team has been strengthened with a number of key appointments to drive the right-sized business going forward.

- Appointment of Lisa Anson (ex-AstraZeneca) as CEO – started 1 June 2018.
- Appointment of Dr James Mead (ex-AstraZeneca) as CFO, effective 1 February 2019.
- Appointment of Dr Andrew Saunders (ex-Eli-Lilly and Roche) as CMO, started January 2018

Milestones

Several major milestones and, hence, many potential value inflection points are expected in 2019. With agreement in principle from the MHRA to resume the Phase I/IIa with RXC004, REDX is scheduled to submit the new protocol before the end of 2018, which will allow it to restart the clinical trial in 1H'19.

In addition, REDX has ambitions to progress three anti-fibrotic assets into development in 2019, with the aim of entering the first into the clinic in 2020.

REDX near-term milestones and value drivers to 2020

		2018	2019	2020
Oncology	RXC004	✓ *1Q First patient treated in Phase 1 study* ✓ *1H Read-out on pre clinical PoC studies in fibrosis* ✓ *MHRA agreement in principle to re-start Phase 1*	1H Phase 1 re-start 1H ASCO Wnt pathway updates 2H Phase 1 initial cohort safety data	1H Phase 1 safety data readout 1H IO partnering company decision on phase 1b
Anti-Fibrotics	PORCN/ RXC006	✓ *Patents filed,* ✓ *Development candidate selected*	1H IND preparation 2H GLP toxicity	1H First time in man ready (IPF)
	ROCK2 selective	✓ *Patents filed, series assessment ongoing* ✓ *Data presented*	1H In vivo data completed 1H Development candidate selected for NASH	2H First time in man ready
	GI targeted ROCK	✓ *Patents filed, series assessment ongoing*	1H Development candidate selected for Crohn's Disease	2H First time in man ready

Source: REDX, 2018 FY results presentation

Pathways to the clinic

Focus on the clinical stage

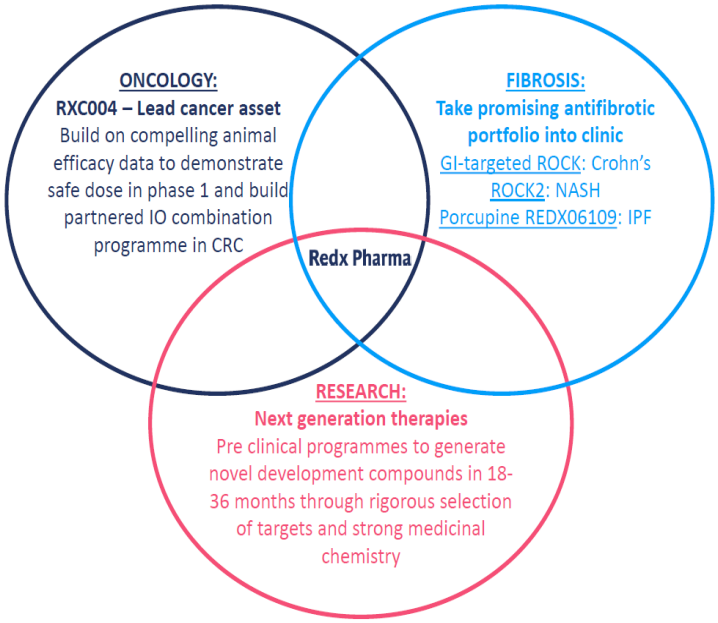
REDX's pipeline focus is on two major disease areas in oncology and fibrosis

Strategy

One of the first tasks of the strengthened management team was to take a fresh look at the assets of the company. Following an extensive internal review, REDX has emerged with a more focused vision and streamlined pipeline, leveraging its proven expertise in the medicinal chemistry group and driving innovative products in two major disease areas with high unmet medical need:

- **Oncology:** With the porcupine inhibitor, RXC004, as the lead programme due to re-start Phase I/IIa clinical trials in 1H'19.
- **Fibrosis:** With three programmes in late research for three different indications – RXC006 is the most advanced having been nominated as the development candidate in IPF.

Three inter-related investment pillars



Source: REDX, 2018 FY results presentation

- **Leverage the medicinal chemistry expertise:** REDX has maintained a strong medicinal chemistry group with expertise in progressing core assets towards the clinic as exemplified by the porcupine inhibitors RXC004 and REDX006 in oncology and fibrosis, respectively. This group was also responsible for the BTK programme that was divested successfully to US-based Loxo Oncology for $40m (£30.5m net) in July 2017. This presents a strong track record for REDX's medicinal chemistry team in rigorously identifying biologically attractive targets and optimising the right molecules, which are then internally developed into commercially attractive assets.
- **Partnering:** To be undertaken at the clinical or pre-clinical stage, when appropriate, to enable additional development and increase shareholder value.

Meanwhile, REDX has managed to reduce and control costs through prioritisation of its pipeline, effective resolution of financial and tax issues, and a reduced footprint at its Alderley Park location.

R&D pipeline

The overall R&D strategy consists of a focused pipeline to develop small molecule therapeutics from discovery to Phase I and up to Phase II proof-of-concept trials in oncology and fibrotic diseases, with the possibility of out-licensing these assets for late-stage development and commercialisation. This will maximise shareholder value per product.

REDX aims to bring research programmes to development candidate nomination in a relatively short time frame (18 to 36 months) by leveraging its strong medicinal chemistry capability and delivering clinical proof-of-concept. Pipeline development is based on two key characteristics:

- Work on biologically and/or clinically validated targets with the aim of being first-in-class or best-in-class, through the development of the in-house programmes and the acquisition/in-licencing of assets from other parties.
- Work on commercially attractive targets with high unmet medical need.

REDX's R&D pipeline

	Target/ Product	Primary Focus	Research	Pre-clinical (CTA/ IND enabling)	Clinical (Phase 1)	Milestone Date
RXC004	**Porcupine**	Combination with PD1 / PDL1 in solid tumor (colorectal cancer)				Phase 1 completion – 1H2020
Anti-fibrotics	**Porcupine (RXC006)**	Idiopathic pulmonary fibrosis (IPF)				Pre clinical development 1H2019
	GI-targeted ROCK	Crohn's Related Fibrosis				Pre clinical development 1H2019
	ROCK-2 selective	Non-alcoholic Steatohepatitis (NASH)				Pre clinical development 2H2019
Research	**SHP2, AZ collaboration, validated targets**	Cancer & Fibrosis				Lead Optimisation 1H2020

Source: REDX, 2018 FY results presentation

In the near term, two programmes are emerging from the pre-clinical pipeline:

- **RXC004:** This porcupine inhibitor will re-enter the clinic in 1H'19 with a Phase I/IIa trial in colorectal cancer.
- **RXC006:** This differentiated porcupine inhibitor that has been selected recently as the development candidate in IPF.

Precedent has been set by the successful disposal of its pre-clinical BTK programme for $40m (£30.5m) to Loxo Oncology in July 2017. The price achieved was in line with the average for pre-clinical small molecule oncology projects, but without the prospect of development milestone or royalty payments. By developing an asset even further along the pipeline to include a clinical data package, even greater fees and milestones could be expected. The management team is open also to partnering programmes at an earlier stage, if considered appropriate.

Oncology assets

RXC004: porcupine inhibitor in solid tumours

Clinical trials and path forward

Following positive discussions with the MHRA, REDX received agreement, in principle, to resume the clinical study with a revised protocol for its lead programme, the porcupine inhibitor RXC004. Management expects to submit the new protocol before the end of the year, which would allow the trial to re-start in 1H'19. Suspension of the Phase I/IIa trial was seen by the market as a setback; however, it is not unusual to pause a clinical study, especially in a phase I oncology patient population in order to adjust the dose, schedule and optimise safety assessments based on emerging data.

RXC004 showed only on-target side-effects and possesses a strong pharmacokinetic profile

The prudent decision to suspend the trial was based on the observation of some clinically significant Wnt related adverse events in the first subject following a 10mg dose of RXC004, such as:

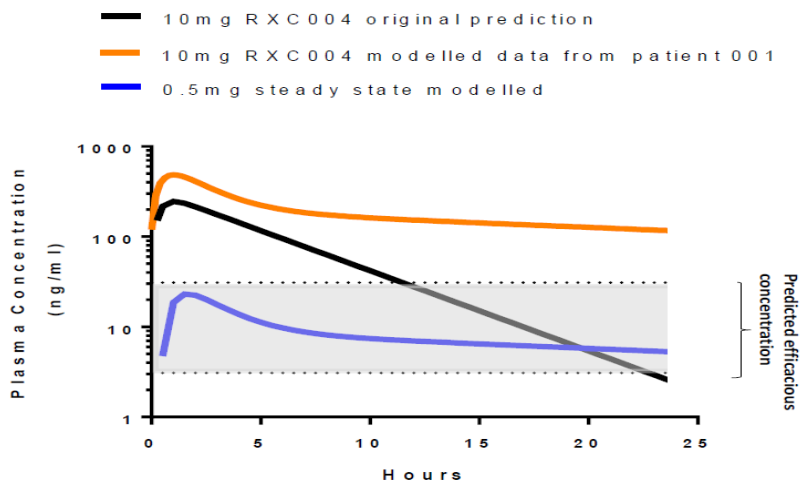
- Dysgeusia (distortion of taste)
- Diarrhoea
- Bone fragility

Such events could be anticipated following inhibition of the Wnt pathway, but at a much higher dose than that used in the trial. Analysis of the data suggested a positive trend with RXC004:

- the drug was well absorbed;
- it had good pharmacokinetic (PK) parameters, such as a long half-life;
- it had only on-target side-effects; and
- it had strong target engagement.

The data also demonstrated that the compound possesses a different pharmacokinetic profile in humans compared with that seen in animal studies, with a slightly higher maximal concentration (C_{max}) in the blood system and an extended plasma half-life. These translate to a significantly higher and prolonged exposure of RXC004 than predicted, leading to levels of the compound above the therapeutic window.

RXC004 – Plasma concentration



Source: Redx Investor Presentation Sept 2018

A final version of the protocol has been submitted to the MHRA; this includes a much lower starting dose of RXC004, and is expected to start in 1H'19

On the basis of this clinical information, REDX intends to re-start the clinical study with a new protocol at a much lower dose with the aim that safety, tolerability and efficacy can be achieved. The company has submitted a revised protocol of the Phase I/IIa trial, and its clinical investigators believe that the required RXC004 exposures can be achieved at lower doses. Following MHRA and Ethics approval, the company aims to re-start in 1H'19 with a reformulated starting dose 20-fold lower, at 0.5mg per day compared with the original protocol. Safety will be the driver of the first part of the study with enhanced monitoring. In the meantime, REDX has prepared a reformulated product that will allow dose escalation from 0.5mg/day up to 3mg/day.

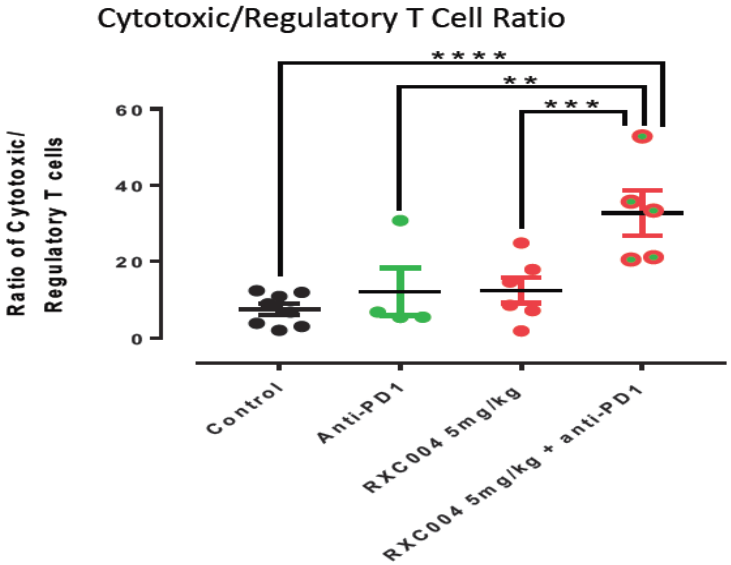
Scientific rationale

The porcupine enzyme is a key protein required for the function of the Wnt pathway that is implicated in many cellular processes including cell proliferation, survival, migration, cell death and polarity. There is also evidence to show that the enzyme is involved in the maintenance of cancer stem cells (CSC) and in the immune tumour micro-environment, which results in the recurrence and emergence of cancer resistance. Porcupine is a validated drug target that is believed to play a key role in the field of immuno-oncology when it is combined with a checkpoint inhibitor (CPI).

Immuno-oncology

An increasing number of scientific publications have demonstrated the implication of activating the Wnt signalling pathway in creating an immuno-suppressive micro-environment in tumours, allowing immune evasion. Also, REDX has confirmed in pre-clinical studies that RXC004 enhances immune system activation, which could reverse immune evasion in patients that do not respond to CPI. In other words, the mechanism of action of RXC004 and the effect of enhancing the immune response, when combined with a PD(L)-1 inhibitor, may turn the 'cold' immune-suppressive tumour environment to 'hot'.

RXC004 – combination efficacy



Source: REDX, 2018 FY presentation

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

RXC004 can demonstrate potentially an anti-tumour effect by an immuno-oncology mechanism either as monotherapy and/or in combination with immune CPI (anti-PD(L)-1). The RXC004 Phase I/IIa trial, therefore, will explore both the immune effect and anti-tumour activity, both as a single agent and in combination with immune CPI.

The second part of the trial (Phase IIa) aims to potentiate the effect of anti-PD(L)-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). This should represent an attractive feature to companies working in the immuno-oncology space.

Targeted therapy

Pre-clinical experiments have demonstrated also that RXC004 alone could inhibit tumour growth in a variety of cancer models. 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.

Novartis's Wnt programme

Regarding the safety profile and clinical relevance of a porcupine inhibitor, Novartis leads the way with WNT974/LGK974, which is in early trials for solid tumours. Results to date suggest that WNT974 affects the immune cell signatures in the tumour microenvironment, an effect observed also with RXC004 in pre-clinical models. In addition, Novartis indicated at the 2018 AACR meeting that a second arm of the study is currently running using WNT974 in combination with its anti-PD-1 antibody, spartalizumab. The study expects to recruit 170 patients and head line data are expected during 2020. Although Novartis is leading the field, REDX remains a close follower with a compound that seems to have greater exposure (longer half-life) compared with WNT974.

Curegenix and A*Star

Both private companies are separately progressing a Phase I trial in several cancer indications. It is worth noting that Curegenix started a Phase I trial with its small molecule CGX1321 in combination with pembrolizumab (Keytruda, a PD-1 checkpoint inhibitor). On the other hand, the Singaporean organisation A*Star is evaluating the safety and tolerability of ETC-159 in advanced solid tumour patients.

Phase I/IIa clinical trial

The new trial will enrol a total of ca.50 patients at three sites (Manchester, Oxford and Newcastle), with the possibility of adding two further sites, with Natalie Cook, at the NHS Foundation Trust in Manchester as the Principal Investigator. This first-in-man study represents a major milestone for the company, being the first programme that REDX has advanced since incorporation in 2010 from discovery to the clinic.

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

- **Phase I:** a multi-arm dose-escalating study, from 0.5mg to 3mg (estimated), 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 safety and tolerability data. It is also possible that early data could be made available during 2019.
- **Phase IIa:** an expansion arm of RXC004 in combination with immuno-oncology agents such as anti-PD(L)-1 (CPI) in colorectal cancer, for example.

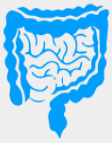
Anti-fibrotic assets

Fibrotic diseases

The second area of focus is the large spectrum of fibrotic disease with high unmet medical needs. With three programmes, REDX is aiming to encompass a vast range of fibrotic conditions that severely affect the quality of life and could also be life threatening, for example IPF.

Targeting fibrotic diseases

Idiopathic Pulmonary Fibrosis (IPF)
Product: Porcupine



Crohn's related fibrosis
Product: GI-targeted-ROCK

Non-alcoholic Steatohepatitis (NASH)
Product: ROCK2

Source: adapted from Redx Pharma

It is worth noting that the fibrotic mechanism that affects different organs usually follows the same pathway. This means that by having a potent and effective compound targeting the fibrotic pathway may have the same effect in multiple organs affected by the scaring. This is what REDX disclosed in its ROCK2 selective programme where the lead compounds provide anti-fibrotic features in both the liver and the kidney.

RXC006: porcupine inhibitor in IPF

Development candidate nomination

REDX has nominated its first development candidate from its fibrosis programmes. RXC006 is a porcupine inhibitor and a potential first-in-class treatment for IPF. This announcement came slightly ahead of schedule – originally expected 1H'19. RXC006 is an orally bioavailable and once/twice daily administered small molecule porcupine inhibitor that acts upstream in the Wnt pathway, which is known to be involved in the fibrosis process in the lung, liver and kidney.

Distinct porcupine inhibitor

REDX is developing a new series of porcupine inhibitor compounds that are distinct from the RXC004 series for colorectal cancer and protected by a different patent family. RXC006 was selected because it had shown encouraging results in suppressing the Wnt pathway involved in fibrosis in different *in vivo* disease models. It has the potential to be first-in-class with the aim of treating IPF, a progressive and life-threatening condition with very poor prognosis. Animal studies have demonstrated RXC006 to be safe and well tolerated and with a pharmacokinetic (PK) profile that will allow flexibility in dosing and dose increases. REDX believes that its porcupine inhibitor may be effective in patients with more severe IPF, where current therapy is ineffective. The company is aiming to enter a first-in-man clinical trial during 2020.

Additional information might be available to the market on Thursday 29 November when the pre-clinical data will be presented by Dr Peter Bunyard, REDX's Head of Fibrosis, at the 2nd anti-fibrotic drug development summit in Cambridge, MA.

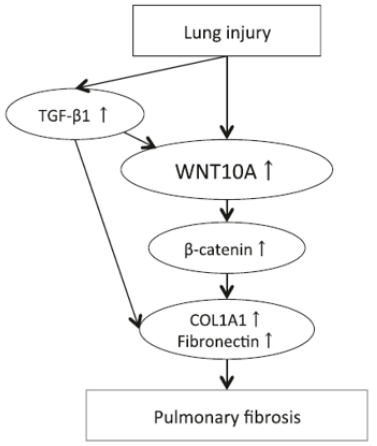
Porcupine programme for IPF

IPF is a chronic, progressive, fibrotic disorder of the lower respiratory tract that typically affects adults over the age of 40. It is the most common interstitial lung disease seen by pulmonologists. There is currently no cure for IPF and the five-year survival rate is around 20% according to the UK's National Health Service (NHS), and the median survival in the US is estimated at 3-4 years after diagnosis (National Institute of Health). The standard-of-care is just to relieve the symptoms as much as possible (oxygen mask) and slow down the scarring of the lungs – i.e. simply slow down progression of the disease. In addition to a healthy diet, fitness and eventually oxygen support and lung transplant, the current treatment includes the use of medications such as:

- **Esbriet** (pirfenidone, Roche), approved in the US (2014) and Europe (2011) and expected to have sales in 2018 of $950m, giving cumulative sales since launch of ca.$3.3bn. This drug helps to slow the development of scarring in the lungs by reducing the activity of the immune system and the lung fibrosis through down-regulation of the production of growth factors and procollagens I and II.
- **Ofev/Vargatef** (nintedanib, Boehringer Ingelheim) was approved in the US (2014) and Europe (2015) and has generated cumulative sales in excess of $3.2bn to end 2018. It works by targeting the vascular endothelial growth factor receptor, fibroblast growth factor receptor and platelet derived growth factor receptor.

Several pulmonary and non-pulmonary comorbidities are associated with IPF, including emphysema, lung cancer, cardiovascular disease, gastroesophageal reflux disease, and depression.

Lung fibrosis



Source: Oda et al, 2016[1]

Market

The National Institute of Health indicates that IPF has an estimated prevalence of 13 to 20 per 100,000 people worldwide. About 100,000 people are affected in the US, and 30,000 to 40,000 new cases are diagnosed each year. Because age is a major risk factor and predictor of IPF, the disease prevalence is expected to rise with the aging population. Because there is no medication that stops or reverses the scaring of the lung tissue, there is clearly a high unmet medical need. There are currently several companies that are progressing treatment for IPF and, to our knowledge, REDX is at the forefront in the porcupine inhibitor option.

When the programme progresses to the clinic, we expect REDX to gain further rights and patent protection through the orphan drug designation programme run by the major regulatory bodies.

ROCK2 programme

The ROCK2 programme is at a late lead optimisation stage, and as ROCK2 has a central role in fibrotic and inflammatory pathways that are conserved across organs, REDX's ROCK2 inhibitors could potentially treat a large spectrum of diseases. The benefit of having a potent selective ROCK2 inhibitor is that systemic anti-fibrotic effects can be achieved without the cardiovascular side effects seen with pan-ROCK1/2 inhibition. While the prime focus of the ROCK2 programme is on NASH, REDX is also building up *in vivo* efficacy evidences of its ROCK2 inhibitor in kidney fibrosis. REDX expects to enter the clinic in 2020 in NASH.

[1] Oda et al, *Respiratory Research*, 2016, 17:39.

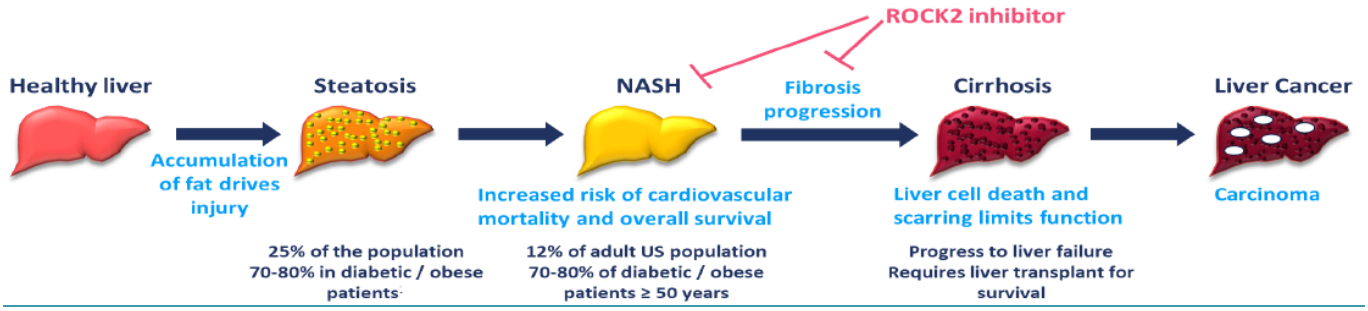
REDX is also developing a ROCK2 selective inhibitor for NASH

ROCK2 inhibitor in NASH

NASH is the main focus for the ROCK2 programme where there are currently no approved therapies to stop the progression of, and then potentially reverse, liver fibrosis. NASH stems from the steady build-up of fat in the liver, which can trigger inflammation and, eventually, scarring and cirrhosis.

Current treatments are more about diet and medications to reduce cholesterol and triglycerides, blood pressure and to control diabetes. The main complication is the progression of NASH into liver cirrhosis that results in permanent scarring and hardening of the liver, which can ultimately lead to liver cancer.

Liver disease progression



Source: Redx, Investor presentation 2018

The ROCK2 inhibitor demonstrated a good pre-clinical profile

Existing treatments are limited, targeting diet intervention and medications to reduce cholesterol, triglycerides and blood pressure, and to control diabetes. There are only a few therapies currently in clinical development that aim to target the fibrosis process and ROCK2 inhibition is one of them. The main complication of liver fibrosis is the progression of NASH into liver cirrhosis. Patients with liver cirrhosis have permanent scarring and hardening of the liver, complete loss of function, and require transplantation. In addition, cirrhosis can ultimately lead to liver cancer.

REDX has indicated that its orally available ROCK2 inhibitor demonstrated a good pre-clinical profile showing improvement compared with Kadmon's ROCK2 inhibitor KD025, currently in Phase II trials in multiple indications: chronic graft-versus-host disease, IPF and scleroderma. Kadmon has indicated in its Phase II study that KD025 slowed the decline in lung function over 24 weeks of treatment and that it is well tolerated with no drug-related serious adverse event. This represents a great endorsement for REDX in treating fibrotic conditions with ROCK2 inhibition. REDX aims to enter into the pre-clinical development stage in 2H'19, with a view to being in the clinic in 2020.

Snapshot of the NASH market

The overall NASH prevalence in the adult population of developed countries has been estimated as high as 12% and is linked with obesity. Also, a consensus of several market research reports indicated that the NASH market is expected to reach $25bn by 2025. As yet, no drug has been approved and R&D activity to find a treatment for NASH is crowded, with an estimated 158 companies investigating 195 pipeline products. While four companies are progressing Phase III trials, many believe that the key in NASH therapy will reside in the combination of drugs.

Phase III products for the treatment of NASH

Company	Product	Target	Result expected
Allergan	Cenicriviroc	CCR2 and CCR5 inhibitor	? / expected by market: 2021
Genfit	Elafibranor	PPARα/δ agonist	Around end 2019
Gilead	Selonsertib	ASK1 inhibitor	1Q'19 and 2Q'19
Intercept	Obeticholic acid	Farnesoid X receptor	1H'19

Source: Company documents, Hardman & Co Life Sciences Research

In November 2016, Allergan acquired Tobira Therapeutics for an up-front payment of $570m for its NASH and other liver disease experimental therapies, with up to a further $1,101m based on successful completion of specific development, regulatory and commercial milestones, of which $303m was paid in Dec 2017 for the initiation of the Phase III trials.

On the other hand, Intercept's product, obeticholic acid, has received accelerated approval by the US FDA for the treatment of primary biliary cirrhosis and is in the clinic for several indications: NASH (Phase III), primary sclerosing cholangitis (Phase II), biliary atresia (Phase II) and other fibrotic conditions (Phase I).

ROCK2 inhibitor in kidney fibrosis

REDX presented a poster at the American Society of Nephrology (ASN) Kidney Week 2018 in San Diego, CA, on 25 October, entitled "*ROCK2 inhibitors for the treatment of chronic kidney disease*", which provided an update on its ROCK2 programme. While the prime focus of the ROCK2 research programme is on NASH, the poster provides the first disclosure of REDX's ROCK2 selective compounds, with *in vitro* and *in vivo* data demonstrating the inhibition of pro-fibrotic factors in a model of acute kidney injury, engaging pathways also associated with chronic disease. Chronic kidney disease (CKD) is a potential second opportunity for the ROCK2 programme. REDX presented a direct comparison between its two lead molecules – REDX10178 and REDX10325 – with KD025 in *in vitro* assays. We note that Kadmon's ROCK2 inhibitor KD025 is currently in Phase II trials in multiple indications, including idiopathic pulmonary fibrosis (IPF).

The key messages from REDX's ROCK2 inhibitors are:

- potent inhibition of ROCK2 with an excellent selectivity against ROCK1 and other kinases;
- REDX's ROCK2 inhibitors have a superior *in vitro* profile compared with Kadmon's product;
- bioavailable, with a suitable pharmacokinetic and cardiovascular safety profile;
- inhibition of the expression of pro-inflammatory and pro-fibrotic factors in an *in vitro* kidney model;
- suppression *in vivo* of the inflammatory, fibrosis and kidney injury pathways; and
- potential for a best-in-class product.

GI-targeted ROCK inhibitors for Crohn's disease

REDX's ROCK1/2 inhibitor has a locally acting and targeted approach to the gut, making it an attractive asset for the treatment of Crohn's-related fibrosis

REDX has developed a novel series as a potent GI-targeted ROCK1/2 inhibitor with potential to be first-in-class. The limited systemic exposure and the selective targeting of the gut is possible through two important factors:

- poor absorption through the gut; and
- rapid degradation by specific blood esterases.

These mean that the ROCK inhibitor has a locally acting and targeted approach to the gut and is rapidly metabolised if absorbed, avoiding the known hypotensive side effect of systemic dual ROCK1/2 inhibition.

With the GI-targeted ROCK1/2 inhibitors, REDX targets primarily the population of patients affected by Crohn's disease that will develop intestinal wall fibrosis, a complication that occurs in 50% of Crohn's patients. There is currently no approved pharmaceutical treatment for Crohn's-related fibrosis and REDX believes that it could be the first to reach the clinic for this indication.

REDX has disclosed that a lead product has demonstrated efficacy in a range of animal IBD fibrosis models already and the company is expecting to announce choice of pre-clinical candidate for development in 2019. REDX believes that it has the opportunity to develop a product that has the potential to not only stop, but also to eventually reverse the formation of fibrotic tissues.

Research programmes

REDX's ambition is to progress biologically validated targets in oncology and fibrosis and, in order to maintain its pipeline, several targets are being evaluated. Among them, only the SHP2 programme has been disclosed publicly.

SHP2 for multiple indications

The non-receptor protein tyrosine phosphatase SHP2 is an emerging cancer target due to its role in signal transduction downstream of growth factor receptor signalling.[2] Activating mutations of SHP2 are found in multiple cancer types, including leukaemia, breast cancer and neuroblastoma. Evidence also suggests a role of SHP2 in immune tumour microenvironment and immune checkpoint signalling.

By inhibiting the SHP2 protein, REDX aims to break the resistance mechanisms associated with receptor tyrosine kinase treatments, therefore improving cancer patient survival. REDX indicates that its SHP2 programme has made good progress and is now at the Lead Optimisation stage, with the identification of potent compounds with an improved safety profile.

Other businesses

Following the decision to shut down its anti-infective unit, REDX has progressed with partnering the assets. In March 2018, the company granted an option for a licence agreement on its NBTI programme to Deinove, a French drug discovery company. REDX indicated that Deinove has invested a significant amount of effort in evaluating the antibiotic programme. According to the terms of the contract, Deinove has until the end of December to exercise the option and licence-in the entire project.

[2] Ying-Nan P. et al, *Nature*, 2016, 535, 148-152.

Financial forecasts

Fiscal 2018 was an eventful year for REDX, given that the asset disposal allowed it to emerge from administration with a clean balance sheet and a new strategy. The full-year 2018 results set a new benchmark with respect to costs and cashflows.

Profit & Loss

- **SG&A:** Net reduction of 80% in the corporate overhead at -£1.5m following the restructuring of the company compared with the same period last year, this translates into a 50% reduction in SG&A to -£2.8m (-£5.7m).
- **R&D:** Drastic reduction of 43% in R&D cost at -£7.4m following the change in focus of the pipeline compared to the same period last year (-£13.0m). Investment will increase as products enter clinical trials, and for additional pre-clinical and regulatory work.
- **Option fee:** In August 2017, REDX received £0.13m from Deinove, corresponding to the option licence fee, and included in "other income".
- **EBIT:** As a consequence, REDX reported a big reduction in its underlying EBIT loss, at -£8.9m (1H'17: -£17.4m).

Profit & Loss account

Year-end Sep (£m)	2016	2017	2018	2019E	2020E	2021E
Sales	0.00	0.00	0.00	0.00	0.00	0.00
SG&A	-2.21	-5.70	-2.81	-2.59	-2.74	-2.88
R&D	-14.32	-13.00	-7.42	-11.06	-11.29	-13.54
Depreciation	-0.26	-0.33	0.16	-0.16	-0.16	-0.16
Licensing/Royalties	0.00	0.00	0.00	0.00	0.00	0.00
Other income	2.38	1.29	1.32	1.00	1.00	1.00
Underlying EBIT	**-14.15**	**-17.41**	**-8.92**	**-12.65**	**-13.03**	**-15.42**
Share-based costs	-0.25	-0.01	-0.28	-0.30	-0.32	-0.34
Exceptional items	-0.56	-7.52	-0.97	0.00	0.00	0.00
Statutory EBIT	-14.95	-24.94	-10.17	-12.95	-13.35	-15.76
Net interest	-0.28	-0.33	0.02	0.01	0.00	0.00
Net financials	-0.46	-3.89	0.02	0.01	0.00	0.00
Underlying pre-tax profit	**-14.61**	**-17.74**	**-8.90**	**-12.64**	**-13.02**	**-15.42**
Extraordinary items	0.00	30.47	0.00	0.00	0.00	0.00
Statutory pre-tax profit	-15.41	1.65	-10.15	-12.94	-13.35	-15.76
Reported taxation	-0.11	-0.12	1.30	1.94	1.98	2.03
Underlying net income	**-13.97**	**-17.86**	**-7.60**	**-10.70**	**-11.05**	**-13.05**
Statutory net income	-15.52	1.53	-8.85	-11.01	-11.37	-13.73
Ordinary 1p shares:						
Period-end (m)	93.6	126.5	126.5	426.5	426.5	426.5
Weighted average (m)	78.4	113.0	126.4	276.5	426.5	426.5
Fully-diluted (m)	82.3	117.3	131.0	281.1	431.1	431.1
Underlying basic EPS (p)	**-17.8**	**-15.8**	**-6.01**	**-3.87**	**-2.59**	**-3.06**
Statutory basic EPS (p)	-19.8	1.4	-7.0	-4.0	-2.7	-3.2
Underlying fully-dil. EPS (p)	-17.0	-15.2	-5.8	-3.8	-2.6	-3.0
Statutory fully-dil. EPS (p)	-18.9	1.3	-6.7	-3.9	-2.6	-3.2
DPS (p)	0.0	0.0	0.0	0.0	0.0	0.0

Source: Hardman & Co Life Sciences Research

Balance sheet

- **Net cash:** At 30 September 2018, REDX had net cash of £6.5m on its balance sheet.
- **Unspent cash:** £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 has extended the company's cash runway.
- **Trade payables:** The new management team has adopted a rapid payment of all invoices, significantly reducing the level of trade payables in the balance sheet.

Balance sheet						
@30 September (£m)	2016	2017	2018	2019E	2020E	2021E
Shareholders' funds	1.72	14.33	5.76	8.86	-2.51	-16.24
Cumulated goodwill	0.00	0.00	0.00	0.00	0.00	0.00
Total equity	1.72	14.33	5.76	8.86	-2.51	-16.24
Share capital	0.94	1.27	1.27	1.93	1.93	1.93
Reserves	0.78	13.06	4.50	6.93	-4.44	-18.17
Capitalised R&D	30.10	36.05	38.09	37.20	38.09	40.58
Provisions/liabilities	0.00	0.00	0.61	0.00	0.00	0.00
Long-term loans	0.00	0.00	0.00	0.00	0.00	0.00
Short-term debt	2.00	0.00	0.00	0.00	0.00	0.00
less: Cash	5.76	23.81	6.47	8.95	-2.56	-16.73
Invested capital	**27.46**	**26.57**	**37.99**	**37.10**	**38.14**	**41.07**
Fixed assets	0.53	0.22	0.19	0.16	0.14	0.13
Intangible assets	0.31	0.43	0.42	0.42	0.42	0.42
Capitalised R&D	30.10	36.05	38.09	37.20	38.09	40.58
Inventories	0.00	0.00	0.00	0.00	0.00	0.00
Trade debtors	*0.00*	*0.00*	*0.00*	*0.00*	*0.00*	*0.00*
Other debtors	*1.55*	*2.59*	*2.02*	*2.02*	*2.02*	*2.02*
Tax credit/liability	*0.64*	*0.64*	*1.21*	*1.94*	*1.98*	*2.37*
Trade creditors	*-1.60*	*-3.81*	*-1.69*	*-1.77*	*-1.86*	*-1.95*
Other creditors	*-4.07*	*-9.55*	*-2.27*	*-1.69*	*-1.81*	*-2.30*
Debtors less creditors	-3.49	-10.13	-0.72	-0.68	-0.52	-0.06
Invested capital	**27.46**	**26.57**	**37.99**	**37.10**	**38.14**	**41.07**
Net cash/(debt)	**3.76**	**23.81**	**6.47**	**8.95**	**-2.56**	**-16.73**

Source: Hardman & Co Life Sciences Research

Cashflow

- **Fiscal 2018:** The movement in cash during fiscal 2018 does not reflect the underlying position since it included repayment of all creditors when the company came out of administration. At 30 September 2018, REDX had £6.5m cash.
- **Cash burn:** The ongoing underlying operational cash burn is ca.£0.65m per month (nearer -£1.0m per month including out-sourced clinical trial costs).
- **Payables:** The large working capital outflow was related directly to creditor payments due when the company was handed back by the administrators, which were all settled in the first half of fiscal 2018. The new management team have resolved all legacy issues with the balance sheet now representing business as usual payables.
- **Capital increase:** Taking account of the Phase I/IIa RXC004 trial re-start, our cashflow forecasts suggest that the company will need to raise more capital in fiscal 2019, which we believe would need to be ca.£15m (gross).
- **Fiscal 2020:** Further funds will be required also in fiscal 2020 and, while equity funding is certainly one option, there is also the possibility that new capital could come from a licensing deal for RXC004.

Cashflow

Year-end Sep (£m)	2016	2017	2018	2019E	2020E	2021E
Underlying EBIT	-14.15	-17.41	-8.92	-12.65	-13.03	-15.42
Depreciation	0.26	0.33	0.16	0.16	0.16	0.16
Amortisation	0.00	0.00	0.00	0.00	0.00	0.00
Inventories	*0.00*	*0.00*	*0.00*	*0.00*	*0.00*	*0.00*
Receivables	*-0.12*	*-1.19*	*0.57*	*0.58*	*0.60*	*0.61*
Payables	*1.27*	*8.87*	*-9.51*	*-0.80*	*-1.04*	*-1.35*
Change in working capital	1.15	7.69	-8.94	-0.22	-0.44	-0.74
Exceptionals/provisions	-0.56	-4.99	-0.22	0.00	0.00	0.00
Disposals	0.00	0.00	0.00	0.00	0.00	0.00
Other	0.00	0.00	0.00	0.00	0.00	0.00
Company op. cashflow	**-13.29**	**-14.38**	**-17.91**	**-12.70**	**-13.31**	**-16.00**
Net interest	0.04	-1.55	-0.03	0.01	0.00	0.00
Tax	0.75	0.00	0.73	1.21	1.94	1.98
Operational cashflow	**-12.51**	**-15.93**	**-17.21**	**-11.48**	**-11.37**	**-14.02**
Capital expenditure	-0.44	-0.03	-0.13	-0.14	-0.14	-0.15
Sale of fixed assets	0.00	0.12	0.23	0.00	0.00	0.00
Free cashflow	**-12.95**	**-15.84**	**-17.11**	**-11.62**	**-11.51**	**-14.17**
Dividends	0.00	0.00	0.00	0.00	0.00	0.00
Acquisitions	0.00	-0.12	0.00	0.00	0.00	0.00
Disposals	0.00	30.47	-0.02	0.00	0.00	0.00
Other investments	0.00	-3.56	0.00	0.00	0.00	0.00
Cashflow after invests.	**-12.95**	**10.96**	**-17.13**	**-11.62**	**-11.51**	**-14.17**
Share repurchases	0.00	0.00	0.00	0.00	0.00	0.00
Share issues	9.30	11.07	0.00	14.10	0.00	0.00
Cash/(debt) acquired	-0.03	-1.98	0.00	0.00	0.00	0.00
Change in net debt	**-3.68**	**20.05**	**-17.13**	**2.48**	**-11.51**	**-14.17**
Opening net cash	7.44	3.76	23.81	6.47	8.95	-2.56
Closing net cash	**3.76**	**23.81**	**6.68**	**8.95**	**-2.56**	**-16.73**
Hardman FCF/share (p)	-16.0	-14.1	-13.6	-7.2	-5.9	-7.3

Source: Hardman & Co Life Sciences Research

Company matters

Registration

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Tel: +44 1625 469 900

www.redxpharma.com

Board of Directors

Board of Directors

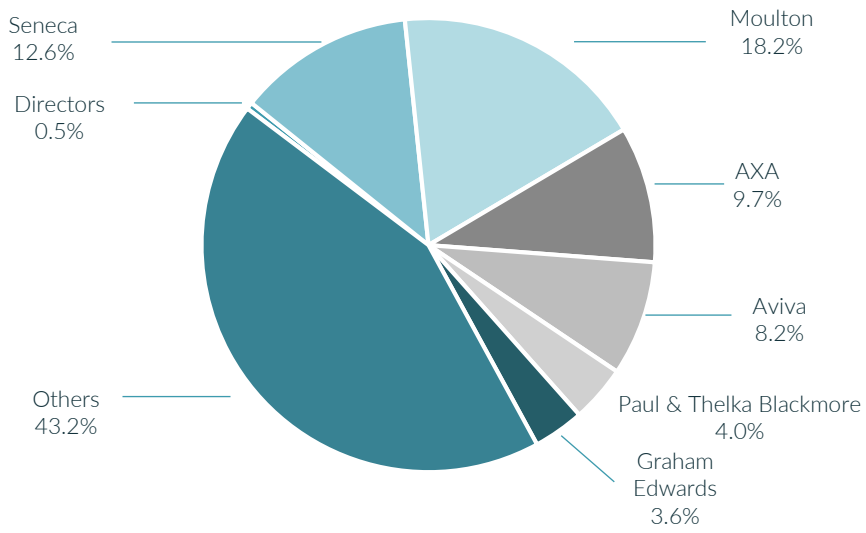
Position	Name	Remuneration	Audit
Chairman	Iain Ross	M	M
Chief Executive Officer	Lisa Anson		
Chief Financial Officer	Dominic Jackson*		
Non-executive director	Dr Bernard Kirschbaum	C	M
Non-executive director	Peter Presland	M	C

M = member; C = chair
** Dr James Mead from February 2019*
Source: Company reports

Share capital

REDX has 126,477,914 Ordinary 1p shares in issue. The company also has 4.25m options outstanding.

Key shareholders



Source: Hardman & Co Life Sciences Research

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