Trinity Delta

Redx Pharma

Initiation of coverage

Proof is in the pipeline

14 September 2020

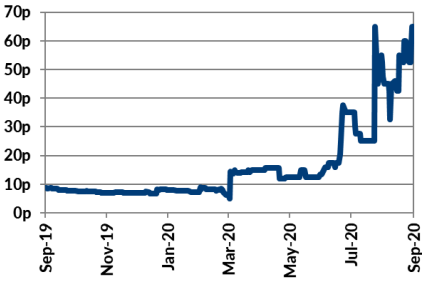
Redx Pharma is a UK-based clinical stage drug discovery company that specialises in developing highly specific small molecules based on its proven medicinal chemistry expertise and research platform. These are either "best-in-class" or "first-in-class" and target existing unmet needs in large oncology and fibrosis indications. A driven management team is implementing a focussed and ambitious strategy that should be transformative for the business over the medium term. The approach has been validated by a series of out-licensing and partnering deals. Knowledgeable and supportive shareholders have rebuilt the balance sheet, but further funding is, in our view, required to capitalise on the existing opportunities. Our valuation, based on conservative assumptions, is £296m, equivalent to 152p/share, and 92p fully diluted.

Year-end: September 30	2018	2019	2020E	2021E
Revenues (£m)	0.1	3.1	12.7	1.6
Adj. PBT (£m)	(10.5)	(7.5)	(2.6)	(27.9)
Net Income (£m)	(8.8)	(4.3)	(2.0)	(27.4)
Adj.EPS (p)	(7.2)	(4.0)	(1.2)	(14.2)
Cash (£m)	6.5	(3.7)	27.1	3.1
EBITDA (£m)	(10.0)	(6.2)	(1.3)	(27.3)

Source: Trinity Delta Note: Adjusted numbers exclude share-based payments and exceptionals.

- **Right team, right assets, attractive indications** Redx's portfolio is well-balanced and focussed on genetically defined cancers and on fibrotic diseases. The strategy is to develop and progress "best in class" or "first-in-class" compounds to sizeable value-inflection points. Recent outlicensing deals, struck on attractive terms, have reduced Redx's risk profile and allow the in-house development of the two lead assets to Phase II proof of concept stage: these are porcupine inhibitor RXC004 in oncology and ROCK2 inhibitor RXC007 for fibrosis indications.
- **A track record of innovation and delivery** Redx has a proven model based on the excellence of its medicinal chemistry expertise, with its discovery platform having generated several promising assets. These include RXC004 and RXC007, as well as two early-stage programmes that have been recently partnered with AstraZeneca (RXC006) and Jazz Pharmaceuticals (pan-RAF) for meaningful downstream success-based payments. However, the most advanced Redx-derived asset is BTK inhibitor LOXO-305 which Eli Lilly is progressing through trials. Unfortunately, this was sold to Loxo Oncology for $40m in 2017 to facilitate Redx's exit from administration.
- **Ambitious, albeit realistic, goals** Management is high quality, with a track record of execution. The near- and medium-term strategic goals are ambitious but realistic. The backing of knowledgeable and supportive shareholders, Redmile and Sofinnova, and an experienced and well-connected board, means the foundations are now in place to support the next chapter of growth. Nevertheless, the share price suggests that markets have yet to catch up with events. The shares appear undervalued when viewed in isolation, but even more so when compared to international peers. We value Redx at £296m, or 152p per share (92p fully diluted).

Price	65p
Market Cap	£127m
Enterprise Value	£120m
Shares in issue	195.3m
12 month range	4.5-93.75p
Free float	6.8%
Primary exchange	AIM London
Other exchanges	N/A
Sector	Healthcare
Company Code	REDX
Corporate client	Yes



Company description

Redx Pharma specialises in the discovery and early clinical development of small molecule therapeutics, with an emphasis on oncology and fibrotic disease. Typically, these are progressed through proof-of-concept studies and then partnered for further development. The strategy has been validated by several collaborations.

Analysts

Lala Gregorek
lgregorek@trinitydelta.org
+44 (0) 20 3637 5043

Franc Gregori
fgregori@trinitydelta.org
+44 (0) 20 3637 5041

Investment case

Defined by its medicinal chemistry expertise and track record of productivity

Redx Pharma is a clinical-stage biopharmaceutical company focused on oncology and fibrosis. The strategy is to identity and develop small molecules that are either "best-in-class" or "first-in-class", with the emphasis on scientifically validated targets. The lead candidates are progressed to Phase II proof of concept trials before being outlicensed, with an element of commercial revenues retained; however, assets can be outlicensed earlier if the proposed returns are sufficiently attractive. Redx listed on AIM in March 2015, raising £15m; with a further £10m in April 2016 and £12m in March 2017. Other financing events include MGL capitalising its £2.5m June 2019 loan in January 2020, and share subscriptions by Redmile for £1.3m (March 2020) and Sofinnova for £0.8m (July 2020). The latter two investors also hold $29m in convertible loan notes. Redx is based near Manchester (in Alderley Edge, Cheshire), and has c 50 full-time employees.

Valuation

The discovery platform has an enviable track record and its inherent value is not appreciated

We value Redx using an rNPV of the known development programmes together with an estimate of the inherent worth of the now well-proven drug discovery platform. These are then netted out against the cost of running the business and net cash. The success probabilities in each indication are based on standard industry criteria for each stage of the development process but flexed to reflect the characteristics of the differing indications. We have employed conservative assumptions throughout; for example, erring on the cautious side with factors such as the timing of clinical studies, market launches, adoption curves, and patient penetration. Despite such a deliberately cautious approach we value Redx at £296m or 152p/share, equivalent to 92p per share (fully diluted).

Financials

Poised for growth again, after an amazing comeback from administration in 2017

Redx's $30m (gross) fund raise in June 2020 provided a cash runway into Q321. Subsequent milestone/licensing receipts from AstraZeneca and Jazz Pharmaceuticals could extend this/or fund additional R&D activities. We forecast a rise in operating expenses, particularly to fund R&D activities as the proprietary pipeline advances, while G&A will grow at a more modest pace. There is potential for further milestones to be received in FY21e contingent on progress in the underlying programmes, although in our view, further funding is advisable to capitalise on the quality and number of platform and pipeline opportunities.

Sensitivities

Drug development is inherently risky but active management is employed to contain risks

Redx seeks to either address validated molecular targets and create a "best-in-class" or, if a target is particularly attractive, to create a "first in class" compound. Arguably, developing small molecules is less risky than an equivalent biological compound. Irrespective of the merits of this point, the typical industry risks associated with clinical trial results, navigating regulatory hurdles, ensuring sufficient financing is in place, partnering discussions and, eventually, pricing and commercialisation still apply. Our main sensitivities are detailed later (in the body of the note), with particular emphasis on each individual programme.

Redx Pharma: Ambitious and focussed

Redx Pharma is best known for being forced into administration and then rapidly exiting it as one of its preclinical assets, a BTK inhibitor, was sold to Loxo Oncology for $40m. Yet this episode encapsulates the value of Redx's discovery engine and, importantly, the strength of its medicinal chemistry expertise. The validation was tangible as two years later Eli Lilly acquired Loxo for $8bn, in no small part because of this BTK programme. A revitalised Redx, with fresh management and clear strategy, is aiming to show this was no fluke. The pipeline is well-balanced; two in-house programmes (RXC004 and RXC007) are progressing well, two have been successfully partnered, and the earlier stage assets are showing promise. Together with supportive and knowledgeable shareholders, a respected board, and a rich news flow, we believe Redx's investment case is not reflected in the share price.

Defined by its medicinal chemistry expertise and track record of productivity

Redx Pharma is emerging as a respected creator of innovative small molecule drugs. It has established a laudable industry-wide reputation for its medicinal chemistry expertise, which underpins its discovery activities. Given its size, the research productivity has been impressive, both in quality and quantity, and an expectation of an average of one lead candidate entering the clinic annually is, in our view, realistic. The focus is on oncology and fibrotic diseases, where there are multiple large and attractive indications that are poorly served with existing therapies. The aim is to address validated receptors as well as novel targets, generating "best-in-class" or "first-in-class" programmes. These are progressed quickly to key evaluation points, with rapid assessments to continue or not.

Professional management, knowledgeable shareholders, and notable non-execs

The quality of the science is complimented by an impressive management team, which brings big pharma professionalism and expertise. A key aspect has been to retain swift decision making and development speed, but to temper this with active risk minimisation. The outlicensing of RXC006 to AstraZeneca in August 2020 is a pertinent example; this commercially attractive deal brings in welcome funds and reduces the weight of the porcupine inhibitor class as a development risk for Redx. A further validation is the involvement of knowledgeable specialist shareholders such as Redmile and Sofinnova; these bring valuable expertise and, importantly, investor credibility. New additions to the Board include two non-executive directors: Sarah Gordon-Wild and Tom Burt.

Poorly understood, underappreciated, and undervalued

Underappreciation of the intrinsic value of a drug discovery company is commonplace in the pharmaceutical industry. It is, after all, the tenet behind how many drug majors replenish their pipelines. In Redx's case the reasons are more complex; clearly the past plays a role, but there is also poor awareness that this is a real company, as opposed to a virtual business, undertaking real science in its own laboratories. And, tellingly, these scientists are "cracking the chemistry" on validated targets that have eluded other, better funded teams. In our view the existing pipeline of optimised compounds provides demonstrable evidence of this working in practice and history helps underpin our belief that the process is reproducible.

£296m company valuation ahead of various catalysts

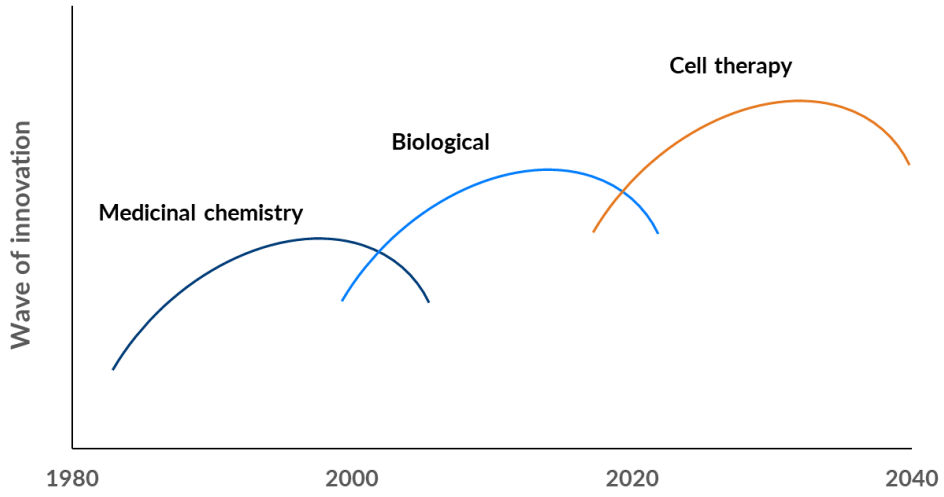
Redx has turned a corner; the scientific, operational, and personnel foundations are now in place to generate material value. Ahead of a steady stream of newsflow into 2022, our valuation is £296m or 152p/share (92p fully diluted).

Singing the praises of medicinal chemistry

Medicinal chemistry underpins a large element of the drug industry

Seldom do we begin one of our in-depth reports with a journey back through history, but the importance of high-quality medicinal chemistry in today's drug industry needs some context. From its inception, pharmaceutical innovation was driven by advances in the understanding of biological processes and their role in any given disease. Drug discovery and development has always been a multi-disciplinary effort, but it was the prowess of the medicinal chemist that converted fascinating insights into a medicinal product. It was debatable if it was astute marketing that produced "blockbuster" drugs, but the importance of visionary medicinal chemists was unquestionable.

Exhibit 1: Waves of technological innovation driving medical advances



Source: Trinity Delta

It fell out of the spotlight as other innovative technologies came to the fore

It was said drug companies' market valuations reflected the relative abilities of their medicinal chemistry departments; but they lost their lustre as the need to replenish ageing product portfolios meant techniques such as combinatorial chemistries and high-throughput screening (HTS) transformed it into a numbers game. Effectively the "art" of the chemistry was, arguably, gone. This coincided with the advent of the new breakthroughs that saw the onset of the "biological" age of innovation, which can be typified by monoclonal antibodies. Both the pharmaceutical industry and financial markets seized the opportunities and whole new business empires were created.

Yet the need for high-quality, value-adding medicinal chemistry is as high as ever

The genomics revolution sparked the next wave of innovation and the results are clear to see. We now have potentially curative treatments for a number of previously intractable diseases; understandably, these advances attract market attention and command premium pricing to recoup sizeable research and manufacturing investments. Whilst these may be acceptable for "orphan indications", economic realities mean that common diseases will increasingly require treatments that are not only effective but also affordable. This will be particularly important in areas such as oncology, where biomarker selected combination treatment is surely the way forward.

The time for medicinal chemistry to shine again?

The benefits of small molecules are manifold

It is against this backdrop that the benefits of a medicinal chemistry approach to discovery are once more becoming better appreciated. New drug approvals continue to be skewed towards small molecules, which generally have lower technical risk as well as attractive clinical and commercial features. As an example, the advances in understanding even complex biological pathways mean that targets which are currently addressed solely by biologic drugs will likely be supplemented with novel receptors and nodes that prove more amenable to addressing with small molecules.

The increasingly targeted nature of small molecule drugs also means that they potentially have a central role in addressing the development of acquired resistance, and their use in defined populations could support premium pricing. AstraZeneca's third-generation EGFR inhibitor Tagrisso provides an interesting case study. It was designed as a treatment option for EGFR-resistant T790M+ NSCLC patients, and since first approval in 2017 has rapidly achieved blockbuster status (FY19 sales of $3.19bn).

Small molecules tend to be easier to produce, easier to administer, and easier to afford

A key benefit for patients and clinicians is that small molecule drugs tend to be easier to administer, often being orally available, but their usually easier synthesis would typically result in lower manufacturing costs, with a consequent benefit to both company margins and to the payor(s). Small molecules also lend themselves to combination therapy approaches, especially where they are highly specific and have a clean safety profile. Thus, they could be a central feature of life cycle management strategies for key franchises of large pharma players.

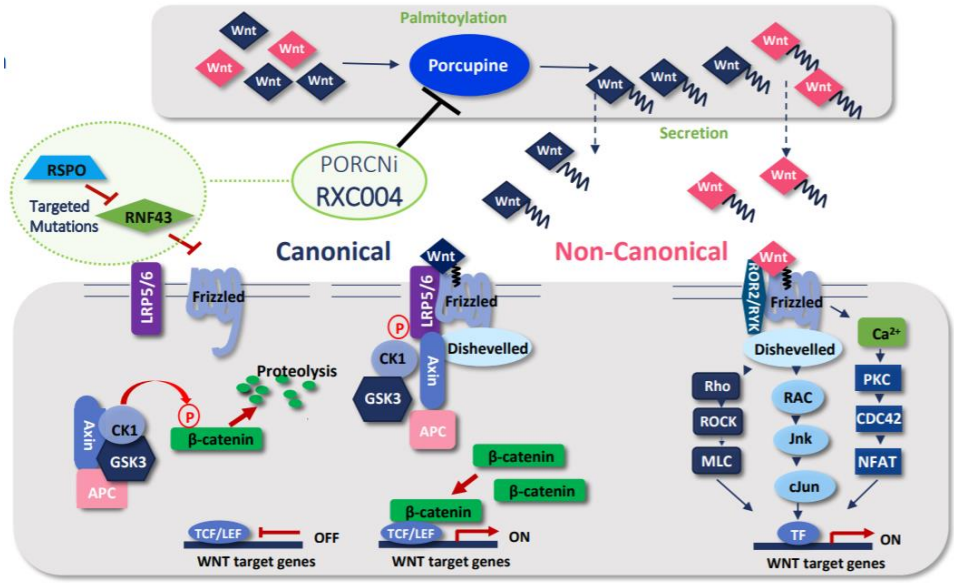
The Wnt pathway has been a prized pharmaceutical target for decades…

The Wnt/β-catenin pathway provides an apt example of a biological pathway where small molecules should play an important part. Wnt was first described in 1982 and in the intervening years the pathway has become recognised as being linked to a wide range of conserved biological processes. Wnt signals, in both the canonical and non-canonical (non-β-catenin) systems, impinge on multiple developmental decisions through the control of cell–cell communication and play a key role in tissue homeostasis and repair. Wnt has long been known as a crucial oncogenic pathway in various cancers and can regulate diverse biological processes necessary for cancer progression, including tumour initiation, tumour growth, cell senescence, cell death, differentiation, and metastasis.

…but has only become truly druggable once the complexities were elucidated with new tools

Yet, despite a clear recognition that the various Wnt pathways offer valuable targets for pharmaceutical intervention, the complex interactions could not be elucidated until the research tools underlying the genomic revolution became available. It is now known that, despite the multitude of cellular responses that they elicit, all 19 secreted Wnt family members are dependent upon the same biosynthetic enzymes, such as Porcupine to supply a single fatty acid adduct (palmitoylation), that is required to enable their transport, secretion, and activity. Understanding the importance of the Porcupine node has meant that medicinal chemistry has been employed to create small molecules that can address and carefully modulate the responses.

Exhibit 2: The Wnt signalling pathway



Source: Redx Pharma

Developing "first in class" or "best in class" compounds

The "administration paradox" – proof of the inherent value of the discovery platform

Redx's pipeline has a clear focus on selective small molecules for the treatment of oncology and fibrotic diseases. Management is applying the acknowledged in-house expertise to develop both first-in-class molecules addressing novel targets, and best-in-class drugs directed at already known and validated targets. The first tangible validation of the approach was, somewhat ironically, demonstrated by a $40m (£30.2m) deal struck with Loxo Oncology in 2017 that effectively brought Redx out of administration (forced by Liverpool City Council to recover a £2m development loan). The administrators sold the leading programme RXC005, a Bruton's tyrosine kinase (BTK) inhibitor, that was ready to enter clinical development. This became LOXO-305 and, interestingly, when Loxo was acquired two years later by Eli Lilly for $8bn, LOXO-305 was cited as one of the key desired programmes.

A diverse and well-balanced development pipeline, which is progressing well

Redx currently has a portfolio of four proprietary programmes, two of which are being developed in-house, likely to Phase II, and two have been outlicensed/sold. Of these, one (RXC004) is in the clinic and two (RXC007 and RXC006) are in the late preclinical stages (see Exhibit 3). RXC004 is a porcupine inhibitor being studied as both monotherapy and in combination with checkpoint inhibitors in various solid tumours. RXC007 is a selective ROCK2 inhibitor being explored in several fibrotic indications and is set to enter the clinic in H221. RXC006 is also a porcupine inhibitor, but being developed for lung fibrosis, that was recently subject to a licensing agreement with AstraZeneca. A further programme, a pan-RAF inhibitor being explored at the research stage for oncology indications, is partnered with Jazz Pharmaceuticals. A number of earlier research programmes for oncology and fibrosis indications are also ongoing. Timelines for anticipated pipeline newsflow is presented in Exhibit 4.

Exhibit 3: Redx Pharma pipeline

Target / Product	Indication(s)	Research	Preclinical	Clinical Phase 1/2	Targeted Milestones
Porcupine Inhibitor (RXC004)	Monotherapy in solid tumours (genetically selected MSS mCRC and pancreatic cancer; biliary cancer) Combination with anti-PD-(L)1 (genetically selected MSS mCRC)				Phase 1 mono safety completion – **H2 2020 - H1 2021 (dependent on Covid-19 impact)** Phase 2 start – **H1 2021**
ROCK2 Selective Inhibitor (RXC007)	Lung fibrosis (IPF) Liver fibrosis (NASH)				GLP toxicity studies – **H2 2020** Entering clinic – **H1 2021**
Porcupine Inhibitor (RXC006)	Lung fibrosis (IPF)				Licensed to AstraZeneca
Pan-RAF Inhibitor Collaboration	Oncology				Partnered with Jazz Pharmaceuticals
GI-targeted ROCK Inhibitor	Fibrosis associated with Crohn's disease				Preclinical development candidate – **2021**
Research Targets	Oncology and Fibrosis				In-house Research Teams investigating oncology and fibrosis targets

Source: Redx Pharma Note: Navy – Redx development, red = partnered programme, blue = Redx research. MSS mCRC = microsatellite stable metastatic colorectal cancer, IPF = idiopathic pulmonary fibrosis, NASH = non-alcoholic steatohepatitis

Exhibit 4: Key milestones and value drivers to 2022

	2020	2021	2022
PORCN (RXC004)	✓ **H1** Ph 1 complete first two dose-escalation cohorts **H2** Ph 1 monotherapy safety completion*	**H1** Ph 2 mono expansion start (mCRC, biliary, pancreatic) **H1** Ph 1 start - IO combo safety **H2** Ph 2 start - IO combo MSS mCRC	Ph 2 data mono MSS mCRC Ph 2 data mono biliary cancer Ph 2 interim data mono pancreatic and combo MSS CRC
ROCK2 (RXC007)	✓ **H1** Development Candidate selected **H2** GLP toxicity studies	**H1** Ph 1 start	**H1** Ph 1 safety data readout **H2** Ph 2 start
PORCN (RXC006)	Out licensing agreement with AstraZeneca	AstraZeneca responsible for development	AstraZeneca responsible for development
Pan-RAF inhibitor	Progress collaboration with Jazz	Progress collaboration **with Jazz**	Progress collaboration **with Jazz**
GI-targeted ROCK	Ongoing research	Development Candidate selected	Ph 1 start
Research	Progress discovery activities for Research programmes	Progress discovery activities for Research programmes	Progress discovery activities for Research programmes

Source: Redx Pharma Note: * potential delay to H121 dependent on COVID19 impact

RXC004: a leading porcupine inhibitor in the clinic

Porcupine is critical for the release and activity of all Wnt ligands

RXC004 is a highly selective and potent small molecule that targets the Porcupine (Porcn) enzyme on the Wnt (Wingless type) signalling pathways. Wnt is increasingly recognised as an attractive albeit challenging drug target, with a growing interest in these pathways. Gradients of diverse Wnt proteins regulate fundamental processes such a cell development, renewal, and differentiation, hence their important roles in oncology and fibrosis indications. Porcupine is a membrane-bound enzyme (MBOAT) that enables a key step (supplying a palmitoyl

group to serine) required for the secretion, transportation, and activity of Wnt ligands. There are multiple porcupine inhibitors in clinical phases which have now demonstrated the ability to block Wnt signalling in cancer patients and retain a suitable safety profile.

The actual effect of the porcupine enzyme is dependent on the cell type and the physiological context. For instance, inhibiting porcupine impacts growth of tumours carrying specific gene mutations such as RNF43 and fusions in the RSPO gene family. Such mutations are found in a number of solid tumours, most notably in difficult to treat colorectal, biliary, and pancreatic cancers. Head and neck squamous cell carcinoma (HNSCC) cell lines carrying related mutations also appear particularly sensitive to porcupine inhibition.

Major side-effect is expected to be with bone metabolism and can be easily countered

As porcupine is an important element of tissue homeostasis, its inhibition could result in undesired effects. In rodent models inhibition of the Wnt pathway is linked to effects on the GI tract, but in humans the main safety concern would be the disruption of bone metabolism. This effect has been successfully managed by prophylactic use with existing treatments for osteoporosis. These are safe and effective therapies that are frequently used in cancer patients to treat bone fragility associated with bone metastasis. Key opinion leaders (KOLs) are supportive of their use in cancer patients and see no detriment to the future development of porcupine inhibitors with this co-medication.

RXC004 is highly specific and shows promising anti-tumour activity

RXC004 selectively targets porcupine and comprehensive preclinical studies have shown it to have promising direct anti-tumour activity in cancer lines with these genetically defined alterations. A blood-based biomarker assay, colloquially known as a liquid biopsy, is being developed (working with NewGene) to identify these treatment sensitive tumours and guide patient selection for future clinical use. However, the Phase II trials are expected to employ traditional, and well characterised, solid tumour biopsies. Accurately selecting patients most likely to benefit from treatment will clearly improve the probability of success of these clinical studies.

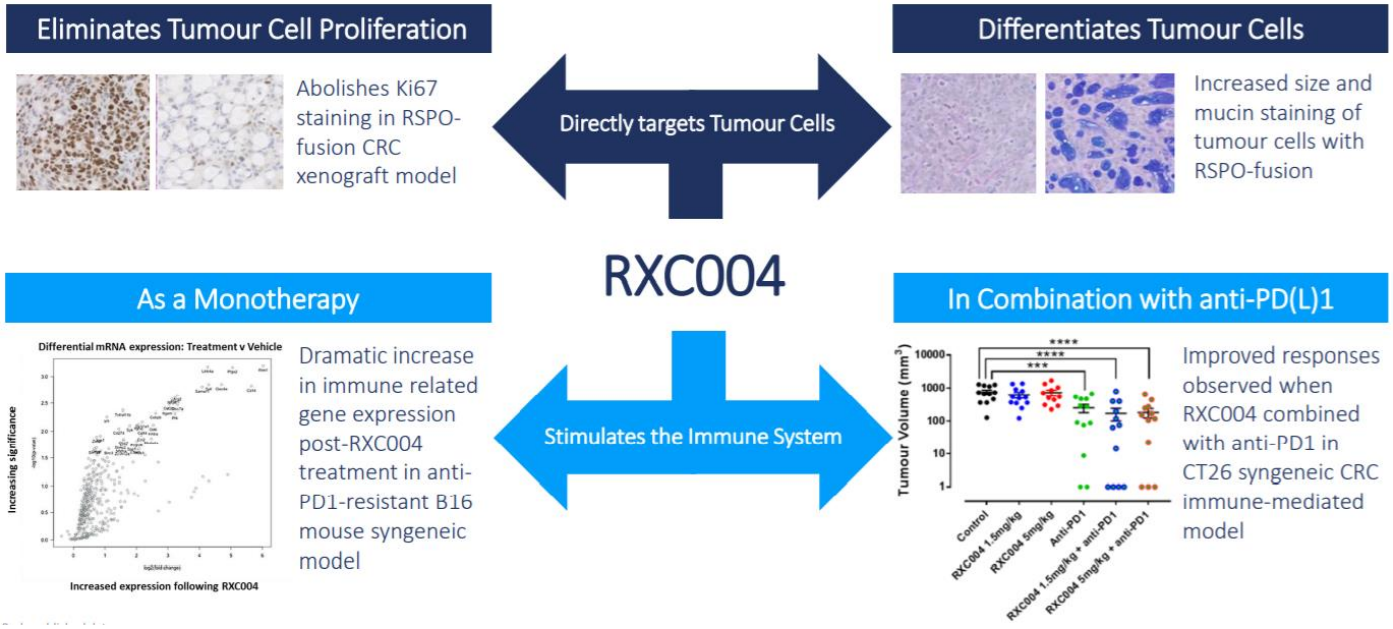
Wnt pathway plays key role in immune evasion and linked to checkpoint inhibitor resistance

Immuno-oncology (IO) therapies, typically checkpoint inhibitors (CPI) such pembrolizumab (Merck's Keytruda) and nivolumab (Bristol Myers Squibb's Opdivo), have become the backbone for many cancer treatments, however, they only tend to work well in around a third of patients due to either innate or acquired resistance. As well as a key role in driving tumour growth the Wnt pathway also plays an important role in tumour immune system evasion. Blockade of Wnt pathways by porcupine inhibitors like RXC004 could remove this brake on the immune system. Wnt pathway activation has also been linked to both innate and acquired resistance to CPIs and so combination of a porcupine inhibitor plus a CPI could lead to both an increase in response to the CPI and a delayed resistance in those patients who already respond.

Animal models suggest it enhances the immune response directly

Preclinical studies have shown that RXC004 enhances the immune response in the tumour microenvironment, and hence has a dual mechanism of action (Exhibit 5). A poster describing the improvement in immune responses in two mouse models, CT26 colon and B16F10 melanoma, was presented at the American Association of Cancer Research (AACR) meeting (Bhamra 2018). Further work on human dendritic cells has corroborated the role of Wnt pathway and tumour immune evasion. The use of RXC004 in combination with CPIs will be explored in future clinical studies.

Exhibit 5: RXC004 dual mechanism of action

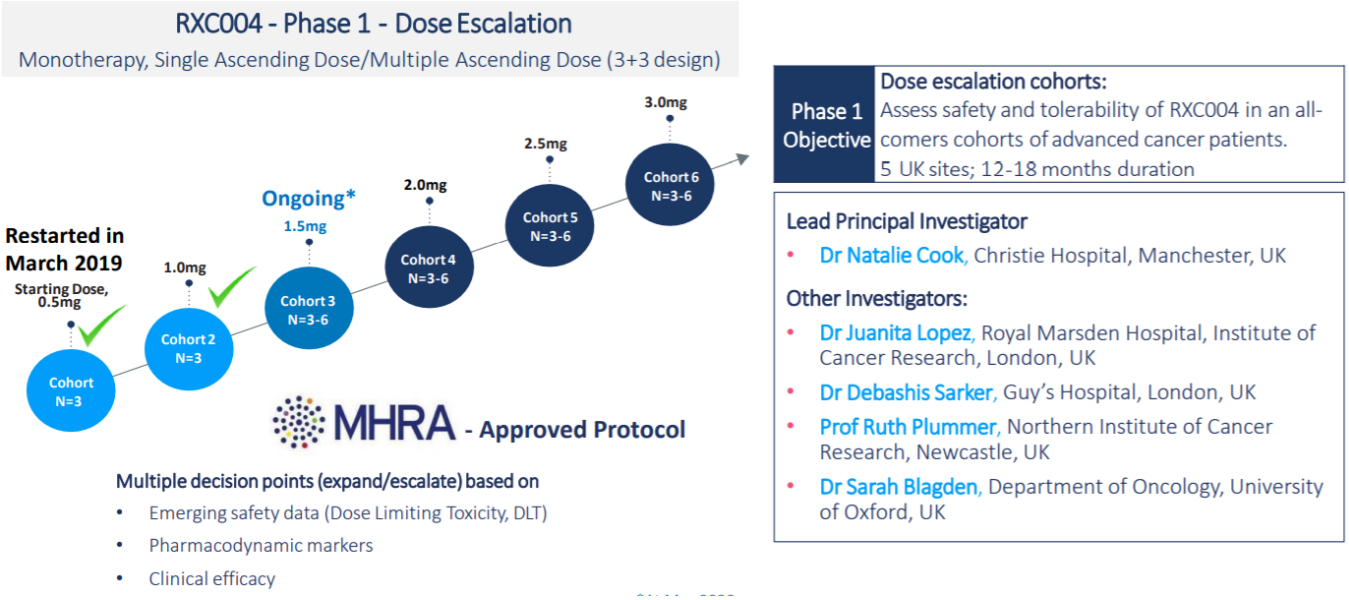


Source: Redx Pharma

Phase I data expected by end-2020 and its quality will define future clinical development

RXC004 is currently in a dose escalation Phase I trial to examine its safety and tolerability (Exhibit 6). The study is set to enrol up to 30 patients across five centres in the UK. Initial results from the 0.5mg and 1mg cohorts showed no dose limiting toxicities (DLTs) and there was strong target engagement detected in markers in skin tissue. The pharmacokinetics showed good oral absorption and bioavailability and support a once daily dosing. A third patient cohort at a 1.5mg dose was initiated in 2019 and, despite a pause in patient recruitment due to COVID-19 restrictions, the full data are still expected to be available before end-2020. A move into Phase II trials is planned for early 2021 but, along with most similar clinical studies, timings may be impacted by COVID-19 factors.

Exhibit 6: RXC004 Phase I dose escalation design



Source: Redx Pharma Note: * at September 2020

Four other porcupine inhibitors known to be in clinical development

Four other porcupine inhibitors are known to be in clinical development for oncology indications:

- Novartis has been the leading player for some time, with WNT974 (previously known as LGK974) having successfully completed Phase I monotherapy trials in various solid tumours. A more recent 32 patient Phase I study in combination with the monoclonal antibody spartalizumab (a PD-1 checkpoint inhibitor) showed promising signs of efficacy and a manageable side-effect profile. A Phase II monotherapy study in head and neck squamous cell carcinoma appears to have been withdrawn. Novartis lists WNT974 as an active programme on its Global Pipeline website.
- CGX1321 is the lead programme of Curegenix, a clinical-stage company based in San Francisco and Guangzhou, China. It has successfully completed a single-agent dose-escalation Phase I study programme, with a Phase Ia single agent China study in gastric tumours and a Phase Ib US trial in combination with pembrolizumab in colorectal tumours still underway. There is little information in the public domain on CGX1321.
- ETC-1922159 is a small molecule being developed by A*STAR, Singapore's Agency for Science, Technology and Research. It is listed as undergoing Phase I dose escalation trials both as a single agent and in combination with pembrolizumab in Singapore and the US in various advanced solid tumours. Interestingly, ETC-1922159's long half-life necessitates dosing on alternate days.
- XNW7201, Sinovent's lead programme, is in Phase I trials in solid tumours in Australia. This will explore pharmacokinetics, safety, tolerability and seek to establish a maximum dose. Sinovent is a Chinese company, founded in 2017 and based in Suzhou, that has three programmes in the clinic, with five more at earlier stages of development.

The results seen with WNT974 are a useful indicator of the likely clinical profile and utility of a porcupine inhibitor and help shape our view of RXC004.

Novartis' WNT974 may not have optimal dosing

A total of c 162 patients have been evaluated with WNT974 as monotherapy, with no MTD (maximum tolerated dose) established, a benign safety profile, and no unexpected adverse effects. Interestingly, the AXIN2 inhibition data was stated as not being dose dependent, yet the mixed results suggest the 10mg daily dose selected may be insufficient to achieve optimal inhibition in the tumour. This could reflect WNT974's relatively short half-life and that, at least in preclinical models, the 10mg dose does not achieve the 24-hour efficacy that may be required for direct tumour targeting.

Better genetic screening of study patients could improve outcomes

Also, a small number of patients in the Phase I expansion trial of WNT974 were genetically selected for "Wnt pathway activation"; it is unknown if downstream mutations such as APC were excluded. The expectation is that tumours with downstream mutations in the pathway will be resistant to porcupine inhibition. These factors suggest efficacy of WNT974 as monotherapy could be greater than reported, particularly with guided genetic targeting of susceptible tumour types.

Combination with a PD-1 inhibitor suggests ability to turn a "cold" tumour "hot"

Looking at the findings of WNT974 in combination with spartalizumab, Novartis' Phase III PD-1 inhibitor, shows that the MTD and RDE (recommended dose for expansion) have not been determined and that the combination was well

tolerated. There was a spinal compression fracture, but this was due to trauma, suggesting concerns about porcupine inhibition's role on bone metabolism are containable. Again, there was evidence of porcupine inhibition, assessed by skin AXIN2 suppression, at all dose levels albeit not at optimal levels. A key finding was that WNT974 did appear to improve response to PD-1 inhibition, suggesting that it could turn a "cold" tumour "hot". This was borne out by improvement in the immune signature, suggesting that it helped promote T-cell recruitment into the tumour. Interestingly, A*Star appears to have shown similar effects with ETC-1922159.

Admittedly early data suggests RXC004 could be a "best-in-class" compound

The known clinical experience with WNT974 provides valuable insights for formulating the next stage of the clinical development programme for RXC004. Preclinical evidence does offer the potential for RXC004 to be a better compound in terms of expected efficacy and, possibly, side-effect profile than WNT974. The pharmacokinetics suggest a useful half-life and activity that support a direct tumour targeting effect as well as the cover to work in combination with CPIs. Clearly the data from the Phase I study is awaited keenly, particularly early signals of direct efficacy. Assuming positive outcomes, we expect RXC004 to be progressed to Phase II trials, with that data used for outlicensing discussions.

RXC007: a disease altering approach for fibrosis?

RXC007 highlights Redx's skills in medicinal chemistry

RXC007 is a particularly promising programme. It is a novel and highly specific small molecule that selectively targets the ROCK2 (Rho Associated Coiled-Coil Containing Protein Kinase 2) receptor. Successfully tackling the ROCK receptors is recognised as a difficult task by all medicinal chemists.

ROCK is a key pathway in several major indications, including oncology and fibrosis

The ROCK pathways mediate a broad range of cellular responses that involve the actin cytoskeleton and are important regulators of cellular growth, migration, metabolism, and apoptosis. Aberrant downstream signalling is shown to have important roles in cardiovascular diseases, CNS disorders (including Alzheimer's and Parkinson's), as well as diabetes (including insulin resistance and nephropathy) and a range of fibrotic dysfunctions. There are two kinase forms, ROCK1 and ROCK2, which have broadly similar functions (especially in fibrosis) but the simultaneous targeting of both forms appears to be more closely associated with cardiovascular effects (notably hypotension).

Fibrosis is surprisingly common, with numerous debilitating conditions in need of therapies

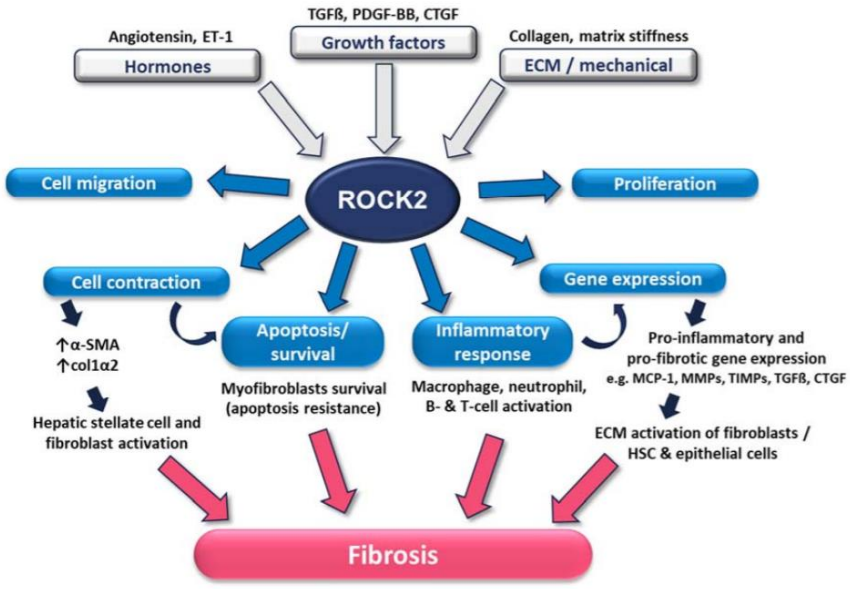
Fibrosis occurs when the normal healing process goes awry, with the formation of excessive scarring. It develops because of aberrant wound healing responses to repetitive injury. Tissue responses to injury involve coordinated activities of multiple cell types that, when appropriate in duration and magnitude, restore normal tissue structure and function. Fibrosis can occur in most tissues, and severely impairs the function of the affected organ. The initial causes of fibrosis are manifold, and while the precise disease process is not fully understood. It typically involves a common series of events, including secretion of cytokines which provoke a pro-fibrotic, chronic inflammatory immune response that leads to production of excessive extracellular matrix (ECM) proteins (eg collagen) and the tissue becoming fibrous in nature.

ROCK plays a central role but has been difficult to target

Pro-fibrotic signals are delivered to cells after injury by both biochemical mediators and mechanical forces, and ROCK activation is central to many cellular responses to both types of signals (Exhibit 7). LPA (lysophosphatidic acid),

thrombin, and TGF-β (Transforming Growth Factor-β), are important mediators that appear to act through ROCK and inhibition of the ROCK receptors can block the pro-fibrotic progression. There is mounting evidence that the behaviours of the cells involved in these wound healing responses, particularly epithelial cells, endothelial cells, and fibroblasts, are fundamentally regulated by ROCK signalling. ROCK activation has been implicated in the development of fibrosis in multiple organs including the lungs, heart, liver, kidneys, peritoneum, and skin.

Exhibit 7: ROCK is a central node in fibrosis-associated signalling pathways

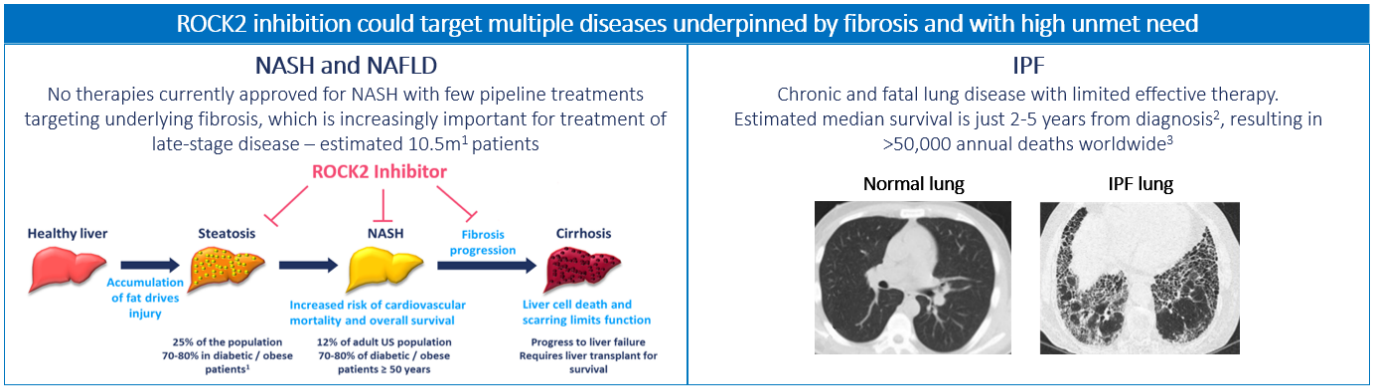


Source: Redx Pharma

RXC007 is highly selective, has good pharmacokinetics, and promising preclinical data

Redx explored a series of highly selective and orally active ROCK2 inhibitors in *in vivo* preclinical models of multiple diseases with underlying fibrosis, including liver, lung, and kidney. Good ADME profiles and robust anti-fibrotic effects were seen and suggest a benefit is diseases such as idiopathic pulmonary fibrosis (IPF), non-alcoholic steatohepatitis (NASH), and diabetic nephropathy (DN). In H120 RXC007 was selected as the lead candidate and is expected to enter Phase I studies, most likely in IPF initially, in H121 with a subsequent clinical trial plan being developed. RXC007 is a programme that we expect will be progressed to Phase II proof-of-concept trials before being prepared for outlicensing.

Exhibit 8: RXC007 potential to treat multiple fibrotic diseases



*Preclinical efficacy in murine bleomycin-induced lung fibrosis model and murine CCl_4-induced liver fibrosis model demonstrated with RXC007. Preclinical efficacy in murine UUO kidney fibrosis model demonstrated with close RXC007 analogue REDX10843. 1. Calculated from GlobalData Opportunity Analyser Report, Hagstrom et al (2017), Jnl of Hepatology based on patients at F3/F4 stage, "GlobalData: NASH – Current and Future Trends, October 2018"; 2. Clinical Estimates from Hyun 2015, Ley 2012, Raghu 2006; 3. GlobalData IPF Opportunity Analyser and Forecast to 2025 report, Hutchinson et al. (2014), Natsuizaka et al. (2014), Navaratnam et al. (2011), Raghu et al. (2006)

Source: Redx Pharma

Sizeable indications, some with a particularly poor prognosis

The fibrosis indications are sizeable and poorly addressed by currently available therapies:

- **Idiopathic pulmonary fibrosis** (IPF) involves irreversible scarring of the interstitial cells in the lungs. There are no effective treatment, although drugs such as pirfenidone and nintedanib have shown slowing of disease progression. Palliative care includes the use of steroids, oxygen therapy, and pulmonary rehabilitation. Lung transplants are often the only resort. Life expectancy from diagnosis is typically three to five years. Over 50,000 new cases are seen per annum in the seven largest markets. Estimates of market size vary between $2bn-$3bn pa but fail to include the non-pharmaceutical treatment costs and impact on quality of life.
- **Non-alcoholic steatohepatitis** (NASH) is a progressive inflammatory and fibrotic disease of the liver. It sits on a pathway starting with non-alcoholic fatty liver disease (NAFLD) and often ends with hepatocellular carcinoma (HCC). It is linked with obesity, diabetes, and sedentary lifestyles. Incidence is rising globally, and the current prevalence of 1.5% to 6.5% is expected to rise significantly. There are no approved products as yet, but promising approaches range from Vitamin E to liraglutide (GLP-1 agonist). Addressing the fibrotic challenge remains the pressing need. Estimates of likely market size range from $18bn to $37bn.
- **Diabetic nephropathy** is a complication of diabetes that will affect between 20% and 40% of all patients. It is the leading cause of chronic kidney disease and end-stage renal failure. Given 8-10% of the global population is expected to develop diabetes, the magnitude of the issue will become material. Tight blood glucose control and the lowering of hypertension are known to delay progression, as have angiotensin II receptor blockers (ARBs) and angiotensin-converting enzyme (ACE) inhibitors. Newer therapies such as SGLT2 inhibitors and GLP1 agonists are beginning to make a difference too. However, there remains a clear need for novel treatments that address the structural changes that are happening within the kidney.

Kadmon is the only other player with advanced programmes in the ROCK space

Currently there is one other ROCK2 inhibitor in clinical development. Kadmon is developing belumosudil (KD025) for chronic graft-versus-host disease (GVHD), where it is in pivotal Phase II trials, and systemic sclerosis (SSc), where a Phase II study is underway. Belumosudil met its primary endpoint in the ROCKstar (KD025-213) study with impressive data and has been granted FDA Breakthrough Therapy designation and Orphan Drug status, with an NDA planned for Q420. A 60-patient double-blind Phase II trial in diffuse cutaneous SSc has been initiated but enrolment has been delayed due to COVID-19. A second 12-15 patient open label study is now planned for Q121 with the aim of demonstrating likely efficacy more rapidly. Belumosudil is an orally active small molecule, with dosing of 200mg daily or twice daily, that has been studied in over 550 patients.

Kadmon is also developing a second ROCK inhibitor, KD045. The IND is in preparation following positive preclinical results in lung, kidney, and liver fibrosis models. KD045 is a pan-ROCK inhibitor, opening concerns about possible hypotension due to inhibiting ROCK1 and ROCK2 simultaneously (see earlier).

RXC007 has a promising profile in what could become a hot, and desirable, therapeutic class

RXC007's preclinical data package is very promising and suggests it has the potential to be a best-in-class compound. The ADME, toxicology profiles (notably with liver enzymes), and on-receptor activity are well suited for fibrosis indications. The clinical programme is expected to be directed, at least initially, towards the more serious indications, such as IPF, where the medical need is greatest. We would expect RXC007 to be taken through to Phase II trials before outlicensing discussions take place.

RXC006: scooped up by AstraZeneca

RXC006 is the second porcupine programme and targets fibrosis

RXC006 is a potent small molecule of the porcupine receptor that is being developed for fibrosis indications. The Wnt pathways are critical elements in maintaining adult cell homeostasis, which includes wound healing and repair functions. Aberrant wound healing causes increased proliferation and attenuated apoptosis of myofibroblasts, which results in the excessive synthesis, remodelling, and contraction of extracellular matrix that characterises fibrosis. Myofibroblasts are the key cells in the pathophysiology of fibrotic disorders and their differentiation can be triggered by multiple stimuli, with Wnt being one of the three key elements (the others being TGF-β and YAP/TAZ signalling). As in oncology indications, porcupine inhibition may be useful here.

Outlicensed to AstraZeneca in an attractive preclinical deal

RXC006 belongs to a different chemical class to RXC004, with an independent family of patents. It showed promising efficacy and tolerability in a number of preclinical fibrosis models (including lung, liver and kidney), with a poster presented at European Respiratory Society (ERS) 2019. A Phase I trial programme in IPF has been prepared but this will now be progressed by AstraZeneca which licenced RXC006 in August 2020. Deal terms include an upfront fee and early development milestones totalling $17m, further development milestones worth up to $360m, and mid-single digit royalties on any eventual sales. If the early IPF studies are positive, AstraZeneca will seek to broaden the development programme into other fibrosis indications.

Jazz Pharmaceuticals: a clearly working partnership

Pan-RAF programme outlicensed to focus on in-house porcupine and ROCK projects

Redx is working with Jazz Pharmaceuticals to develop a pan-RAF inhibitor programme for RAS and RAF mutant tumours. The sale of this asset was agreed in July 2019, with Jazz paying an upfront fee of $3.5m, with a further $203m in development, regulatory, and commercial milestones, and mid-single digit royalties on eventual sales. The next milestones are triggered by successfully initiating IND enabling studies and an IND submission to the FDA. Jazz is funding the necessary preclinical work to prepare the IND submission, although Redx has a separate collaboration agreement, signed in parallel, to perform research and preclinical development services to completion of IND-enabling studies. The first milestone, likely due on initiation of regulatory toxicology studies, is expected within around 12 months.

Avoids issues seen with first-generation selective RAF inhibitors

The MAPK (mitogen-activated protein kinase) pathway plays a critical role in the proliferation of numerous cancers, being seen as a growth driver in over a third of all solid tumours. The main downstream cascade involves the RAS protein family, and, in turn, the RAF kinase groups. There are three RAF enzyme members - A-RAF, B-RAF, and C-RAF - with B-RAF currently seen as particularly clinically relevant as it is mutated in 50%-70% of malignant melanomas, 40% of thyroid

carcinomas, 30% of ovarian tumours, and nearly 100% of hairy cell leukaemias. Within this, the V600 mutation is the most prevalent and active, so became a key target and led to the introduction of initially highly effective first-generation compounds, such as vemurafenib and dabrafenib.

Early data suggests a better profile than competing compounds in development

However, not only did treatment resistance surface quickly but, in what has become known as the RAF inhibitor paradox (or RAF dimer dilemma), the drugs activated the MAPK pathway elsewhere. These targeted first-generation products actively triggered compensatory feed-back loops in tumour cells and in the components of the tumour microenvironment. A number of approaches are being explored, including the use of pan-RAF inhibitors, with promising efficacy as monotherapy in animal and preclinical models. Several pan-RAF inhibitors are in Phase I development, including LXH254 (Novartis), TAK-580 (Takeda/Sunesis), which appears to have a poor profile, and HM95573 (Genentech/Hamni). LY3009120 (Eli Lilly) was too toxic at therapeutic doses, hence failed to show a benefit and was terminated.

A further deal extends the relationship...

Redx's strong working relationship with Jazz has been further reinforced in a research collaboration to discover and develop drug candidates for two oncology targets on the Ras/Raf/MAPK pathway. Deal economics include a $10m upfront payment and a further $10m in year two (contingent on continued progress), with up to a further $400m in development, commercial, and regulatory milestones split equally between the two programmes, and tiered mid-single digit royalties on net sales. Redx will be responsible for research and preclinical development up to IND submission, which will trigger the first milestone.

...and helps validate the strength and quality of Redx's discovery expertise

The collaborations with Jazz validate Redx's expertise in medicinal chemistry and drug design, and its capabilities as a research partner. They also highlight the potential of the discovery platform to generate a stream of additional drug candidates to add to its pipeline. Indeed, Redx has several other undisclosed discovery and early preclinical development programmes targeting oncology and fibrosis underway. The productivity of the discovery engine is proven, with four drug candidates in little more than four years. Now that Redx has returned its research base to full strength, we believe that the expectation of an average of one lead candidate entering the clinic annually as realistic. The current early-stage proprietary research programmes are largely undisclosed, although Redx has provided some information on one of these: GI-targeted ROCK.

GI-targeted ROCK inhibitor: a novel approach to Crohn's

Redx has a second ROCK programme, referred to as GI-targeted ROCK, which is at the research stage but has shown interesting preliminary data that lends itself to inflammation/fibrosis of the gastrointestinal tract.

A clear medical need to address surprisingly common and severe issues

The gastrointestinal tract has a remarkable ability for self-regeneration following short-lived and mild insults, as in peptic ulceration, infectious enteritis, or mild diverticulitis. However, if inflammation becomes chronic and severe, as in Crohn's disease, inflammatory mechanisms drive the excessive production of extracellular matrix (ECM) components and activate intestinal stromal cells that produce fibrosis. Even in the absence of inflammation, tissue damage and fibrosis continue to progress with increased accumulation and crosslinking of ECM.

Existing treatments work best in earlier stages of disease progression

Once fibrosis is established, control of inflammation with even biologicals is not sufficient to halt fibrosis progression as matrix stiffness can drive fibrosis independently of intestinal inflammatory activity. Hence anti-inflammatory treatment is best suited for early-stage disease, as fibrosis might become self-perpetuating once ECM activity has become established.

Currently surgery is one of the best options and that is sub-optimal

In ulcerative colitis the fibrosis is located mainly in rectal mucosa and submucosa, but in Crohn's disease it can be seen in all regions of the intestinal wall. Between a third and a half of Crohn's disease patients develop clinically relevant fibrostenosis that leads to hospitalisations and endoscopic interventions or surgery. Between 70-90% of patients will require at least one surgical resection within their lifetime, with a recurrence rate of up to 70%. The patient, and economic, burden of fibrotic strictures in Crohn's disease is significant.

Preclinical models are very encouraging, demonstrating both prevention and reversal

The ROCK receptors are expressed in fibroblastic, epithelial, endothelial, and muscle cells of the human intestinal tract and are activated in inflamed and fibrotic tissue. Redx has evaluated pan-ROCK inhibitors, which address both ROCK1 and ROCK2 pathways, in several preclinical and animal models. These have shown inhibition prevented myofibroblast accumulation, expression of pro-fibrotic factors, and accumulation of fibrotic tissue; repeated administration resulted in the prevention and reversal of the fibrotic damage.

Works locally and avoids any issues with systemic effects

Redx has taken a very interesting, and innovative, approach. The pan-ROCK inhibitor selected is designed to work locally in the gut wall and, as it is quickly degraded by metabolic enzymes, to have a short half-life once absorbed. The aim is to avoid the systemic side-effects, notably cardiovascular, that are associated with simultaneous inhibition of ROCK1 and ROCK2. A poster of the preclinical data for REDX08087 was presented at ECCO (European Crohn's and Colitis Organisation) 2018. Preclinical work to select a lead compound is underway and a candidate is expected to be chosen in 2021. The novelty of the approach will likely need the clinical programme, and endpoints, to be discussed with the regulatory agencies.

Sensitivities

Main risks centre on clinical progress, commercial execution, and adequate funding

Typically, with innovative healthcare companies the three main sensitivities relate to the clinical and regulatory aspects, commercial execution, and the financial resources required to accomplish these. More specifically for Redx, the key near- and medium-term sensitivities are directed to the clinical and partnering progress with the four lead programmes.

Targeting difficult to address but well characterized receptors

The strategy is to focus on small molecules that are either first-in-class or best-in-class. Addressing highly novel targets clearly carries a greater risk, however the scientific validity and clinical relevance of the mechanism has been elucidated. Importantly, the novelty of the compound, while making the development process more challenging, means that it is likely to be commercially attractive to prospective partners. Creating a best-in-class molecule carries less risk as learnings from the leading players are applied. However, the timeliness of the development becomes paramount as speed of development is a critical factor.

Developing to Phase II data is a recognised strategy to optimise value

The risks of clinical development are well known and documented. Less than 8% of preclinical programmes ultimately reach the market. The success probabilities improve as a programme progresses through clinical development, with a key inflection point seen at the Phase II proof-of-concept stage. This is often viewed as an attractive point for value optimisation as the risk profile improves materially but the most expensive, and pivotal, Phase III trials lie ahead.

Proven record of developing desirable compounds and striking attractive deals

The partnering process is the key test of a management's strategy. A well-struck deal validates not simply the attractiveness of the proprietary technology and scientific skills, but the commercial terms are a tangible insight into management acumen. Given its size and history, Redx has an impressive track record of developing commercially attractive targets. Three preclinical assets have been successfully outlicensed, which suggests that the aim to develop a number of programmes to the Phase II proof-of-concept stage is well founded.

Validated business model, respected management, and supportive shareholders

Financing is a perennial element to any innovative research-based company and Redx is no exception. We believe the strategy to develop selected assets to a greater value creation point is sound, the inherent scientific expertise is proven, and the current management is well respected. The real question is whether investors can appreciate the investment case and support Redx through to the next phase of its journey. The presence of industry specialists such as Redmile and Sofinnova on the register is reassuring and the opportunist approach by Samuel Waksal (via Yesod BioSciences) suggests that canny industry players can see the inherent value. This background suggests that funding will become available when the need arises.

Valuation

Lassic rNPV model fails to capture all the inherent value

Redx is a classic discovery and development play, hence would appear well suited to using an rNPV model to value the business. However, such models tend to attribute most value to later stage clinical compounds and underplay earlier stage programmes. To counter this a value has to be included for the discovery platform and, understandably, this requires more subjective considerations than a simple rNPV calculation. In Redx's case the track record of generating attractive compounds and management history of striking commercially sound licensing deals gives a satisfying degree of comfort that our valuation remains realistic but, in line with our philosophy, still errs on the side of caution.

rNPV model is applied to the pipeline using tailored success probabilities and assumptions…

The rNPV of the individual development projects are assessed and success probabilities adjusted for the inherent clinical, commercial, and execution risks each carry. These are summed and netted against the costs of running the operation and net cash. We also include risk-adjusted development milestones for actual and assumed licensing deals, which are benchmarked against similar deals. The success probabilities are based on standard industry criteria for the respective stage of clinical development but, importantly, flexed to reflect the inherent risks of the individual programme, the indication targeted, and the trial design.

…that are conservative and err on the side of caution

Even though the strategy envisages the outlicensing of at least some of the programmes before the later, and more expensive, stages of clinical development, we allow for the commercial and execution risks as we view these as integral to any programme's intrinsic value. As always, we employ conservative assumptions throughout our modelling, particularly regarding market sizes and growth rates, net pricing, adoption curves, and peak market penetration.

Valuing the discovery platform is more subjective but proven historical delivery is reassuring

For the discovery platform we examined the historical output, particularly its quality and commercial attractiveness, and assessed the likely sustainable future output. As mentioned, the track record is impressive; the BTK programme that was sold to Loxo (sadly as a distressed sale) has progressed well and provides tangible evidence of Redx's ability to produce high-worth assets. Similarly, the AstraZeneca and Jazz Pharmaceuticals deals provide reassurance that Redx's output is desirable and reproducible. The aim of generating an average of one lead drug candidate per annum may appear ambitious but, when placed into historical context, is realistic and achievable. It is against this framework that we attribute a value of between $160m (£123m) and $240m (£185m) for the discovery engine. Again, being conservative, we have opted to use £123m in our modelling. At present, the Jazz Ras/Raf/MAPK collaboration is included within the discovery platform, although we intend to break this out with an explicit value once there is more clarity on timelines and indication(s).

The pipeline contributes around half of the calculated value, which feels intuitively right

Our model ascribes a valuation for Redx of £296m, equivalent to 152p per share (92p fully diluted). The outputs and underlying assumptions of our model are presented in Exhibit 9. Looking at the elements of our valuation in greater detail:

- RXC004 is the most advanced programme and its valuation of £63m (32p per share) reflects its clinical stage and likelihood of successful progression. We have not modelled its use in an explicit oncology patient population, an exercise we would normally perform in the later stages of development, but we do highlight our expectation that development in

relevant genetically defined cancers will be pursued. However, even a cursory exploration of its potential use in selected cancers, which could support pursuit of accelerated regulatory approval pathways and attractive pricing, suggests that our assumptions are justifiable.

- RXC007, valued at £54m (28p/share) is a material contributor to our model despite being deliberately cautious; we flag that this programme could surprise on the upside. Fibrosis is an attractive area due to the poor treatment options currently available and the number of debilitating conditions where it is a key element. We expect development to focus initially on more severe indications, such as IPF, but if efficacy and, importantly, tolerability is appropriate then larger indications such as NASH and diabetic nephropathy could become accessible.
- The RXC006 valuation of £28m (14p/share) is based on risk-adjusted estimates for the development, registration, and commercial milestones from AstraZeneca together with an assumed 5% sales royalty. We assume typical timelines in terms of development progression and approval.
- The Jazz Pharmaceuticals Pan-RAF collaboration is treated similarly, with milestones for the usual inflection points and 5% royalties on eventual sales. The value is £20m or 10p/share.
- The GI pan-ROCK programme is an appealing concept that could be truly attractive both clinically and commercially. However, we temper this with the possible difficulties of performing timely clinical trials that would satisfy regulators. Hence, we attribute a value of £25m, or 13p/share.

Exhibit 9: rNPV-based valuation of Redx Pharma

Programme	Total NPV ($m)	Total NPV (£m)	Likelihood of approval	rNPV ($m)	rNPV (£m)	rNPV/ share (p)	Notes
RXC004 (porcupine inhibitor - oncology)	700.4	538.8	18%	82.0	63.1	32.3	Peak sales: $2.55bn (£1.96bn) Launch year: 2027
RXC007 (ROCK2 inhibitor - IPF/NASH)	983.4	756.4	10%	70.0	53.9	27.6	Peak sales: $3.13bn (£2.41bn) Launch year: 2028
RXC006 (AstraZeneca: porcupine inhibitor - IPF)	273.5	210.4	7%	36.3	28.0	14.3	Peak sales: $1.66bn (£1.28bn) Launch year: 2028
Pan-RAF (Jazz Pharma: oncology)	139.5	107.3	7%	26.2	20.2	10.3	Peak sales: $707m (£544m) Launch year: 2029
GI-targeted ROCK (ROCK1/2 - Crohn's disease)	137.3	105.6	5%	32.6	25.1	12.8	Peak sales: $1.61bn (£1.24bn) Launch year: 2029
Discovery engine				160.0	123.1	63.0	
Operating costs	(31.6)	(24.3)		(31.6)	(24.3)	(12.4)	
Net cash	9.1	7.0		9.1	7.1	3.6	At FY20e
Total	2,211.6	1,701.2		384.8	296.0	151.6	
Total (fully diluted)				389.1	299.3	91.5	Based on all options and convertible loan notes

Source: Trinity Delta Note: The rNPV of RXC004 and RXC007 includes a deal success factor of 80%, and of 75% for GI-targeted ROCK; other valuation assumptions include a 12.5% discount factor, £/$ FX rate of 1.30, and 10% taxation from 2028 (UK patent box).

Our model results in a valuation of £296m, equivalent to 152p per share and 92p when fully diluted

Our conservative approach yields a valuation of £296m (152p/share or 92p fully diluted). To provide context we have collated data from peers (Exhibit 10) with similar business models and a comparable small molecule R&D pipeline in terms of disease focus, size, and maturity. All are publicly listed and, except for Inventiva, are US based. Their stock market valuations range from c$450m to $1.9bn.

Exhibit 10: Small molecule discovery and development peers

Company	Market cap (EV) $m	Description
Black Diamond Therapeutics (NASDAQ: BDTX)*	1,246 (901)	Focus: small molecule precision oncology Platform: Mutation-Allostery-Pharmacology (MAP) Platform Pipeline: one Phase I (BDTX-189), one in lead optimisation IPO details: $201m in Jan 2020 ($471m pre-money valuation)
Inventiva (Euronext / NASDAQ: IVA)*	454 (393)	Focus: small molecules for fibrosis, lysosomal storage disorders, oncology Platform: chemical library of over 240,000 molecules Pipeline: Two Phase III, one Phase II, two discovery programmes IPO details: $108m in July 2020 ($444m pre-money valuation)
Kadmon (NYSE: KDMN)	744 (574)	Focus: immune disorders, fibrotic diseases, cancer Platform: structure-based drug design platform (also monoclonal antibody platform) Pipeline: two small molecule assets - NDA pending for ROCK2 inhibitor (also in Phase II in second fibrosis indication) and one preclinical asset
Oric Pharmaceuticals (NASDAQ: ORIC)*	688 (492)	Focus: small molecules targeting cancer resistance mechanisms Platform: internal medicinal chemistry team Pipeline: one Phase Ib asset, two preclinical, three in lead identification IPO details: $138m in April 2020 ($373m pre-money valuation)
Pliant Therapeutics (NASDAQ: PLRX)*	923 (709)	Focus: tissue-specific inhibition in fibrosis (integrins, TGF-β pathway) Platform: translational -74809medicine and drug discovery platform Pipeline: one Phase IIa asset, one Phase I (partnered with Novartis), two preclinical IPO details: $165.6m coupled with $10m private placement with Novartis in June 2020 ($446m pre-money valuation)
Revolution Medicines (NASDAQ: RVMD)*	1,890 (1,565)	Focus: precision oncology focused on RAS and mTOR pathways Platform: structure-based drug discovery Pipeline: one Phase I (partnered with Sanofi), three preclinical assets IPO details: $238m in Feb 2020 ($762m pre-money valuation)
Zentalis Pharmaceuticals (NASDAQ: ZNTL)*	1,148 (915)	Focus: small molecules targeting fundamental biological cancer pathways Platform: integrated discovery engine Pipeline: three Phase I/II assets, and one in IND-enabling studies IPO details: $190m in April 2020 ($455m pre-money valuation)

Source: Trinity Delta, Company websites Note: * indicates a 2020 IPO; pricing as of close of business September 10, 2020

The peer group, notably US comparables, are on much higher valuations

Several of these peers listed on NASDAQ during 2020, raising gross proceeds of $108-238m at IPO, on an average pre-money valuation of slightly below $500m. Two of these, Zentalis Pharmaceuticals and Revolution Medicines have also closed significant follow-on offerings at higher prices than at IPO. In our view, these NASDAQ IPOs, at attractive valuations, provide compelling evidence for the appeal of medicinal chemistry approaches to investors. Equally, for more mature companies, there is also significant corporate interest as shown by the 2019 acquisitions of Loxo Oncology (by Eli Lilly for $8bn) and Array BioPharma (by Pfizer for $11.4bn).

Financials

A brief historical recap provides useful insights of likely future…

Colourful is a useful word to describe Redx's financial history. Headlines were made when, in May 2017, the administrators were called in at the behest of Liverpool City Council over the repayment of a loan. The £2m loan, which accrued interest at 12%, had been made five years earlier to enable Redx to expand its operations in the city. In 2016 the corporate headquarters and Oncology business was moved to the current site near Manchester, where the Anti-infectives and Immunology businesses were already based. Some observers believe this transfer caused discontent and sowed the seeds for the dramatic move.

…as BTK programme rescues company and strikes it rich for the acquirer (Loxo)

Within weeks the BTK inhibitor programme was sold to Loxo Oncology for $40m (£30m) and all creditors were paid in full. The business was deemed to be a going concern and in November the company shares resumed trading on AIM. New management was appointed, notably Lisa Anson as CEO in June 2018 and James Mead as CFO in February 2019. At the time, the scientific staff had been downsized, but is being rebuilt to support the discovery and development plans that are in place.

The past is now history and the focus, strategy, and ambition are reassuring

Redx has emerged from this period of restructuring; all associated costs and exceptionals are now legacy issues, with its focused strategy now more clearly reflected in its financials. Revenues will consist of milestones and collaboration income from partners, while investment in both discovery and development activities is expected to rise. Our forecasts are presented in our financial summary (Exhibit 11).

Revenues are solely from licensing-out of early stage programmes

The company booked £3.13m of revenues in FY19, which were solely derived from the Jazz Pharmaceuticals pan-RAF inhibitor partnership (£2.79m from the upfront payment and £341k under the preclinical collaboration agreement). For FY20e, we expect further collaboration revenues from Jazz Pharmaceuticals and receipt of the $10m upfront payment, in addition to revenue under the AstraZeneca RXC006 deal. The latter includes $17m in early payments; we assume that this is structured with an upfront payment (broadly equivalent to that paid by Jazz) with the remainder back-end weighted and expected to be paid by the start of the first clinical trial. Our forecasts only include our assumption of the upfront, given limited visibility on the RXC006 preclinical development timeline and payment schedule.

At present our FY21e revenue forecast only includes pan-RAF collaboration revenue; however, contingent on progress with the underlying programmes there is potential for receipt of the second $10m payment from Jazz and further AstraZeneca milestone(s).

R&D is the bulk of spend and we expect it to rise as investment builds up

R&D expenses for FY19 were £6.2m, with G&A of £4m. We anticipate a significant ramp up in the former during FY21e as the discovery engine research activities and staffing return to pre-administration levels, and the pipeline progresses through late preclinical (RXC007) and early clinical (RXC004) development. We forecast R&D spend of £9.6m and £23.9m in FY20e and FY21e respectively. G&A will also rise to support the growing research organisation, but we expect these costs (around £5-6m pa) to be controlled with a more modest rate of increase.

Financing has turned a corner, with 2020 being a busy year

2020 has been a busy year on the financing front. At end-H120 (March 31, 2020), Redx had £1.9m of cash and equivalents, but had also announced a £5m short-term debt facility from Redmile (received in April 2020). In June 2020, the company announced a $30m financing, which closed on July 20th; use of proceeds was earmarked for repayment of the Redmile loan, progression of the pipeline (including RXC004 into Phase I), and general working capital purposes.

The financing was structured as $29m (equivalent to £20.1m) in convertible loan notes (CLNs) issued to Redmile ($19m) and Sofinnova ($10m), and a further $1m (£812k) direct subscription in 5.24m new ordinary shares by Sofinnova at 15.5p per share. The CLNs are subject to a single drawdown and have a three-year term with 0% interest, no early repayment, an option for annual extension, and a 15.5p per share conversion price.

New milestones extend the cash runway, but additional funding could accelerate progress

Management had previously guided that these new funds provided Redx with a cash runway into Q321. We note that milestone receipts under the subsequently announced AstraZeneca RXC006 outlicensing deal and Jazz Pharmaceuticals Ras/Raf/MAPK collaboration could extend this and/or fund additional R&D activities. In our view, the quality and number of opportunities that are presenting would suggest that further funding is required to capitalise on these, both in the pipeline and platform.

Exhibit 11: Summary of financials

Year-end: Sept 30	£'000s	2017	2018	2019	2020E	2021E
INCOME STATEMENT						
Revenues		**30,474**	**129**	**3,131**	**12,729**	**1,575**
Cost of goods sold		0	0	(350)	0	0
Gross Profit		**30,474**	**129**	**2,781**	**12,729**	**1,575**
R&D expenses		(8,168)	(5,732)	(6,166)	(9,557)	(23,893)
G&A expenses		(7,600)	(4,874)	(4,004)	(5,240)	(5,349)
Underlying operating profit		**14,706**	**(10,477)**	**(7,389)**	**(2,069)**	**(27,668)**
Share-based payments		(13)	(282)	(45)	(91)	(92)
Exceptionals		(14,008)	(596)	948	69	0
Other revenue/expenses		1,291	1,186	241	386	393
EBITDA		**2,303**	**(10,005)**	**(6,154)**	**(1,350)**	**(27,296)**
Operating Profit		**1,976**	**(10,169)**	**(6,245)**	**(1,705)**	**(27,367)**
Financing costs/income		(330)	23	(90)	(507)	(240)
Profit Before Taxes		**1,646**	**(10,146)**	**(6,335)**	**(2,212)**	**(27,607)**
Adj. PBT		**14,376**	**(10,454)**	**(7,479)**	**(2,576)**	**(27,908)**
Current tax income		(118)	1,301	2,017	256	239
Net Income		**1,528**	**(8,845)**	**(4,318)**	**(1,956)**	**(27,368)**
EPS (p)		**1.4**	**(7.0)**	**(3.4)**	**(1.0)**	**(14.0)**
Adj. EPS		**(12.4)**	**(7.2)**	**(4.0)**	**(1.2)**	**(14.2)**
DPS (p)		**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Average no. of shares (m)		113.0	126.4	126.4	192.6	195.2
BALANCE SHEET						
Current assets		**27,037**	**9,705**	**5,807**	**27,603**	**3,432**
Cash and cash equivalents		23,806	6,471	3,704	27,117	3,103
Accounts receivable		2,588	2,023	1,232	1,371	1,232
Other current assets		643	1,211	871	(885)	(902)
Non-current assets		**652**	**614**	**551**	**4,248**	**3,880**
Property, plant & equipment		222	191	134	111	69
Intangible assets		430	423	417	409	405
Other non-current assets		0	0	0	3,728	3,406
Current liabilities		**(13,362)**	**(3,950)**	**(4,867)**	**(23,414)**	**(26,472)**
Short-term debt		0	0	(468)	(20,100)	(20,100)
Accounts payable		(13,362)	(3,803)	(3,445)	(2,676)	(5,734)
Other current liabilities		0	(147)	(954)	(638)	(638)
Non-current liabilities		**0**	**(605)**	**0**	**(3,320)**	**(2,998)**
Long-term debt		0	0	0	0	0
Other non-current liabilities		0	(605)	0	(3,320)	(2,998)
Equity		**14,327**	**5,764**	**1,491**	**5,117**	**(22,158)**
CASH FLOW STATEMENTS						
Operating cash flow		**14,098**	**(17,177)**	**(4,668)**	**139**	**(23,990)**
Profit before tax		1,646	(10,146)	(6,335)	(2,212)	(27,607)
Non-cash adjustments		4,436	656	(782)	880	404
Change in working capital		7,686	(8,391)	(265)	(452)	3,197
Interest paid		330	(23)	13	(134)	(240)
Taxes paid		0	727	2,701	2,057	256
Investing cash flow		**(30)**	**(109)**	**32**	**(19)**	**(24)**
CAPEX on tangible assets		(154)	(132)	(28)	(23)	(24)
Acquisitions/disposals		124	23	60	4	0
Other investing cash flows		0	0	0	0	0
Financing cash flow		**3,980**	**(49)**	**1,869**	**23,294**	**0**
Proceeds from equity		11,066	0	0	2,099	0
Increase in loans		(1,975)	0	1,000	21,600	0
Other financing cash flow		(5,111)	(49)	869	(405)	0
Net increase in cash		**18,048**	**(17,335)**	**(2,767)**	**23,413**	**(24,015)**
Cash at start of year		5,758	23,806	6,471	3,704	27,117
Cash at end of year		**23,806**	**6,471**	**3,704**	**27,117**	**3,103**
Net cash at end of year		**23,806**	**6,471**	**3,236**	**7,017**	**(16,997)**

Source: Company, Trinity Delta

Company information

Contact details

Block 33
Mereside, Alderley Park
Alderley Edge
Macclesfield
SK10 4TG
United Kingdom

Tel: 01625 469900

www.redxpharma.com

Top institutional shareholdings

	% holding
Redmile Group LLP	90.5
Sofinnova Partners	2.7
Top institutional investors	**93.2**
Other shareholders	6.8
Total shareholders	**100.0**

Source: Redx Pharma Note: Post CLN conversion, Redmile's holding would be 79.0% and Sofinnova's would rise to 16.6%.

Key personnel

Person	Position	Biography
Iain Ross	Non-Executive Chairman	Appointed May 2017. Also Interim Executive Chairman of Silence Therapeutics and Chairman of Kazia. Previously with multinational companies (Sandoz, Hoffman La Roche, and Celltech Group). CEO of Quadrant Healthcare and Chairman/CEO of Allergy Therapeutics. Former Vice Chairman of the Council of Royal Holloway, London University.
Lisa Anson	CEO	Appointed June 2018. Significant leadership experience, including 20-year career at AstraZeneca including Global VP, Oncology and VP of emerging brands. President of AstraZeneca UK since 2012. Joined Zeneca Pharmaceuticals (USA) in 1998 as business development manager. Previously with Salick Health Care (now Aptium) and KPMG. Past President of the ABPI until 2018, then elected to the BIA board. Holds an MBA (distinction) from INSEAD and a First Class honours degree in Natural Sciences from University of Cambridge.
James Mead	CFO	Appointed February 2019. Extensive finance roles in a 16-year career with AstraZeneca, including CFO AstraZeneca Netherlands, R&D Portfolio Finance Director, Finance Director of multiple clinical development project teams, and in Investor Relations and Corporate Finance. Holds PhD a in Molecular Biology and First Class honours degree in Biochemistry (Cardiff University). Associate Member of Chartered Institute of Management Accountants.
Richard Armer	CSO	Joined in 2012, becoming CSO in 2014. Significant experience in small biotech and large pharma (via roles within Pfizer, Organon, Ardana, Oxagen, and Lectus Therapeutics) and in drug discovery. Experience across many therapeutic areas and notable success in generating and progressing multiple clinical candidates.
Andrew Saunders	CMO	Joined in February 2018. Extensive industry experience including at Eli Lilly and Hoffman-La Roche. Former founder and MD of Linden Oncology, a strategic and clinical development consultancy. Has a medical degree (Trinity College Dublin) and a Fellow of the Faculty of Pharmaceutical Medicine, Royal College of Physicians, UK.

Lala Gregorek lgregorek@trinitydelta.org
+44 (0) 20 3637 5043

Franc Gregori fgregori@trinitydelta.org
+44 (0) 20 3637 5041

Disclaimer

More information is available on our website: www.trinitydelta.org