Trinity Delta

Redx Pharma

Update

Ready to ROCK as RXC008 enters the clinic

28 February 2024

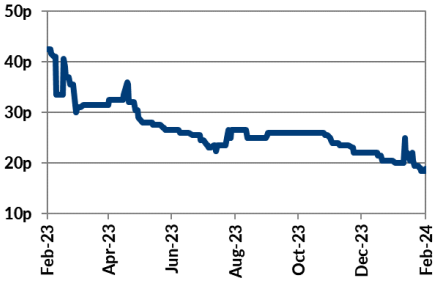
Redx Pharma's differentiated ROCK inhibitor assets hold much promise in the treatment of a variety of serious and intractable fibrotic conditions. Hence, the start of a Phase I trial with second ROCK programme RXC008 is an important milestone. The preclinical data for RXC008 are extensive and, if replicated in the clinic, suggest that RXC008 could have a unique role in the treatment of fibrostenotic Crohn's disease, a debilitating condition that requires repeated surgical interventions. Meanwhile, data for lead ROCK asset zelasudil for IPF (idiopathic pulmonary fibrosis), which are a key catalyst for Redx, continue to be expected during H124. Redx also continues to execute on business development opportunities within its pipeline, with a third deal signed with Jazz; further deal(s) could be catalysed once RXC004 data become available in H124. Our updated rNPV valuation is £386m, or 99p per share.

Year-end: September 30	2022	2023	2024E	2025E
Revenues (£m)	18.7	4.2	15.0	2.5
Adj. PBT (£m)	(17.3)	(28.8)	(22.1)	(36.2)
Net Income (£m)	(18.0)	(33.2)	(23.9)	(38.0)
Adj.EPS (p)	(5.9)	(8.7)	(5.3)	(7.3)
Cash (£m)	53.9	18.1	50.0	21.1
EBITDA (£m)	(15.4)	(32.9)	(21.3)	(34.9)

Source: Trinity Delta Note: Adjusted numbers exclude share-based payments and exceptionals. Our cash forecasts assume receipt of £40m in additional funding

- **Second ROCK programme starts clinical development** The first subject has been dosed in the Phase I trial for RXC008, a potential first-in-class GI-targeted pan-ROCK inhibitor for fibrostenotic Crohn's disease, which is anticipated to be used in combination with standard-of-care anti-inflammatories (anti-TNF). The first part of the Phase I study includes healthy volunteers and will primarily assess safety, with initial data expected by end-2024; the second part will include fibrostenotic Crohn's patients and will also assess target engagement and biomarkers.
- **Extensive preclinical data support Phase I development** Preclinical data and pre-IND studies have established RXC008's GI-restriction. Complete fibrosis reversal has been seen in a therapeutic preclinical model. In addition, RXC008 could have a synergistic effect with anti-TNFs in the treatment of fibrostenotic CD.
- **Third deal with Jazz highlights pipeline optionality** The recent KRAS deal with Jazz is another example of Redx's ability to execute on partnering opportunities. These contribute non-dilutive funding, with Redx eligible for remaining potential milestones of up to c $1.2bn from Jazz alone, in addition to milestones from partner AstraZeneca. RXC004 (zamaporvint) has been earmarked for partnering, hence clinical data in H124 in combination with checkpoint inhibitors will be important.
- **rNPV increased to £386m or 99p/share; cash runway into 2025** Incorporation of the Jazz KRAS deal and slightly de-risking RXC008 result in an increased valuation of £386m/$463m (from £367m/$441m previously), or 99p per share. The $10m upfront from Jazz extends the cash runway into 2025, well beyond key H124 value inflection points (Phase II zelasudil and RXC004 data).

Price	18.50p
Market Cap	£72.0m
Enterprise Value	£69.6m
Shares in issue	389.0m
12 month range	18.0-46.0p
Free float	15.4%
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 development of small molecule therapeutics, with an emphasis on oncology and fibrotic diseases. It aims to progress them through proof-of-concept studies, before evaluating options for further development and value creation.

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Redx Pharma: Focus ROCK pipeline advances

Redx Pharma's unique and differentiated ROCK inhibitor portfolio, targeting diverse and underserved fibrosis indications, is central to its investment case. The Phase IIa trial of its lead asset, selective ROCK2 inhibitor zelasudil (RXC007) in idiopathic pulmonary fibrosis (IPF), is due to read out top-line data in H124 and will inform subsequent clinical development plans. This potentially includes expansion into broader interstitial lung diseases (ILDs) and cancer-associated fibrosis. Its second ROCK asset, GI-targeted pan-ROCK inhibitor RXC008 for fibrostenotic Crohn's disease has now started a Phase I study, with initial safety data in healthy volunteers expected by end-2024. Other key data points in 2024 include Phase II checkpoint inhibitor combination data for porcupine inhibitor RXC004 in Wnt-ligand dependent tumours, expected H124, which will be a prelude to partnership discussions. Continued execution on business development opportunities within the pipeline has led to a third deal with Jazz Pharmaceuticals, focused on KRAS, and bringing in a $10m upfront payment, which has extended the cash runway into 2025. Our updated rNPV-based valuation is £386m ($463m), equivalent to 99p per share.

Focus is firmly on fibrosis, with novel ROCK programmes showing real promise

Redx Pharma's pipeline prioritisation review has put the focus firmly on advancing its differentiated ROCK inhibitor portfolio, and the second wholly-owned ROCK asset recently entered clinical development. Another outcome of the review was the decision to partner porcupine inhibitor RXC004 for future development; key data expected H124 could catalyse discussions, in our view. Redx's core medicinal chemistry expertise to discover novel drug candidates provides optionality for pipeline expansion or future partnerships, and this was recently demonstrated with a third collaboration with Jazz Pharmaceuticals. Redx also has a partnership deal with AstraZeneca and these agreements bring in non-dilutive funding that can be used to advance the pipeline (which is shown in Exhibit 1).

Exhibit 1: Redx Pharma pipeline

	Target/ Product	Indication(s)	Research	Preclinical	Phase 1	Phase 2	Upcoming Milestones
ROCK Portfolio	**ROCK2 Selective Inhibitor** Zelasudil (RXC007)	Idiopathic pulmonary fibrosis (IPF)					Phase 2a topline data **H1 2024**
		Pancreatic cancer*					Phase 1b commencement **H2 2024**
		cGvHD*					Phase 2a commencement **H2 2024**
	GI-targeted pan-ROCK Inhibitor (RXC008)	Fibrostenotic Crohn's disease					Phase 1 healthy volunteers data **H2 2024**
Pipeline Assets	**Porcupine Inhibitor** Zamaporvint (RXC004)	Wnt-ligand driven GI-tumours – combination					Report data **H1 2024** Potential partnership
	Discoidin Domain Receptor (DDR) Inhibitor (RXC009)	Kidney Fibrosis					IND / CTA Submission **2025**
Partnered	**KRAS Inhibitors** (G12D selective and pan-KRAS)	Oncology					Sold to Jazz Ongoing collaboration
	Porcupine Inhibitor (RXC006/AZD5055)	Idiopathic pulmonary fibrosis (IPF)					Licensed to AstraZeneca
	Pan-RAF Inhibitor (JZP815)	Oncology					Sold to Jazz
	MAPK Pathway Target	Oncology					Licensed to Jazz Ongoing collaboration

Source: Redx Pharma Note: GI = gastrointestinal; IND = investigational new drug application; MAPK = mitogen-activated protein kinase; MSS mCRC = microsatellite stable metastatic colorectal cancer; RAF = rapidly accelerated fibrosarcoma. ROCK: Rho associated protein kinase; cGvHD: Chronic Graft Versus Host Disease; KRAS: Kirsten rat sarcoma virus. *Would require additional funding

RXC008: first participant dosed in Phase I trial

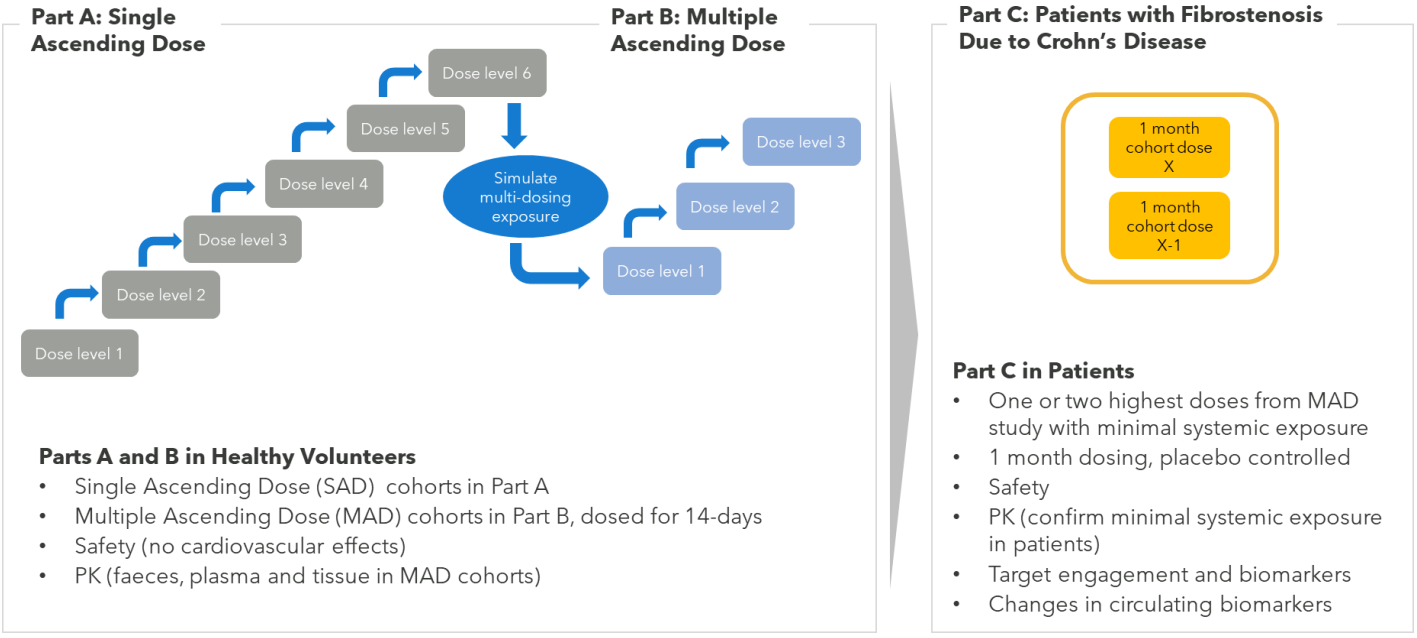
RXC008 is the second wholly-owned ROCK asset to enter clinical development

RXC008 is a novel GI-targeted pan-ROCK (Rho Associated Coiled-Coil Containing Protein Kinase) inhibitor in development as a potential first-in-class therapy for patients with fibrostenotic Crohn's disease (CD). With the dosing of the first participant in its Phase I study, it has become Redx's second wholly-owned ROCK asset to enter clinical development.

Maximal GI activity, negligible systemic exposure, and thus avoidance of hypotension

RXC008 is a potent, oral, small molecule inhibitor of both ROCK1 and ROCK2 pathways that has been specifically designed to act only locally at sites of CD-associated fibrosis within the gastrointestinal (GI) tract. Low permeability and high efflux mean it localises to the gut, and in the event of any residual absorption it is rapidly metabolised by paraoxonase enzymes in the blood. This GI-restricted effect allows the targeting of both ROCK receptors while avoiding the cardiovascular side-effects (hypotension, tachycardia) associated with systemic pan-ROCK inhibition. We note that no pharmacologically significant systemic exposure to RXC008 has been seen in any animal model despite much greater than efficacious doses being tested.

Exhibit 2: Phase I Study Protocol in Healthy Volunteers and Fibrostenotic Crohn's Disease Patients



Source: Redx Pharma

Phase I trial includes healthy volunteers to assess safety, and will then move to fibrostenotic CD patients

The Phase I trial (Exhibit 2) is a three-part study evaluating the safety and pharmacokinetic (PK) profile of RXC008 in healthy volunteers (Part A and B) and fibrostenotic CD patients (Part C). The healthy volunteer cohorts include single ascending dose (SAD) and multiple ascending dose (MAD) over 14 days, with safety as the primary endpoint and secondary endpoints evaluating PK to confirm the target profile (including data on faeces, plasma, and tissue in the MAD cohort). The third part of the study, Part C, involves a one-month dosing period of patients with fibrostenotic CD to investigate safety, confirm minimal systemic exposure in patients (as absorption may differ from healthy volunteers), explore evidence of target engagement, and changes in circulating fibrotic biomarkers. Data from the healthy volunteer cohorts are expected by end-2024.

Targeting an unmet need in Crohn's disease

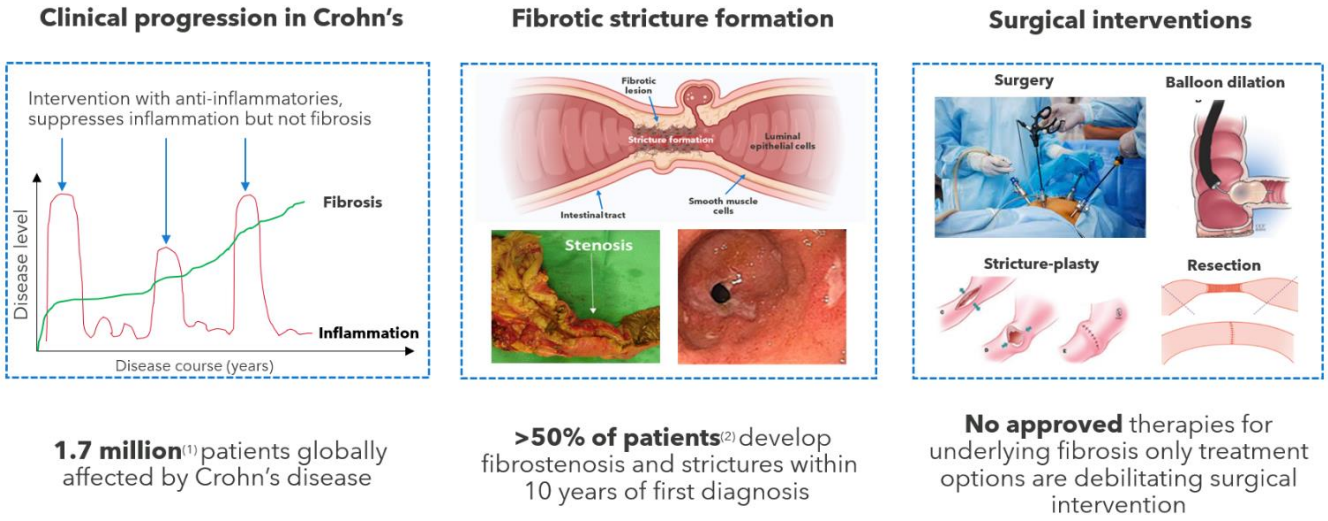
Crohn's disease causes chronic inflammation of the GI tract; it typically starts in young adults

Crohn's disease is a chronic inflammatory condition which, along with ulcerative colitis (UC), is one of the two main subtypes of inflammatory bowel disease (IBD). CD typically follows a relapsing-remitting course and at initial diagnosis, typically at a young adult age, most CD patients present with chronic and persistent inflammation, which over time leads to tissue damage. The GI tract usually has a remarkable ability to self-regenerate following short-lived or mild insults, however, with recurring and severe inflammation, the inflammatory mechanisms drive an 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.

Fibrostenotic complications occur in c 50% of CD patients

Intestinal fibrosis is a common, chronic, and debilitating complication of IBD with c 50% of CD patients developing structural complications within 10 years of diagnosis. These include fibrostenosis and strictures, resulting from the excessive build-up of collagen and fibrotic ECM narrowing the GI tract, both of which result in potentially life-threatening bowel obstruction. The unmet medical need in fibrostenotic CD is high as while treatment with anti-inflammatory drugs (eg steroids or targeted biologics) can successfully suppress the episodic inflammation it has little to no effect on inhibition of fibrosis and there are currently no drugs approved to target the underlying fibrosis in IBD. This leaves invasive hospital interventions such as surgical resection or endoscopic dilation (EBD) as the only current treatment options, and these are often associated with high rates of recurrence and repeat procedures. Up to 80% of such patients will require at least one surgical resection, with a recurrence rate of up to 70%. Longer-term, successive surgeries can lead to progressive loss of GI function and significant complications, such as short bowel syndrome, severely impacting quality of life. Thus, the patient, and economic, burden of fibrostenotic CD is significant.

Exhibit 3: Fibrostenotic Crohn's disease



Source: Redx Pharma Notes: (1) GlobalData Crohn's Disease Dynamic Market Forecast to 2026 report; (2) Chan et al, 2018

Comprehensive preclinical package

RXC008 preclinical data suggest it could be a first-in-class option for fibrostenotic CD

Redx had extensively evaluated its pan-ROCK inhibitor programme in several preclinical and animal models before selecting RXC008 as its development candidate. These have shown that pan-ROCK 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. The RXC008 preclinical package, across multiple therapeutic models, provides management with added comfort that it could be a first-in-class treatment option for fibrostenotic CD patients, with disease modifying potential.

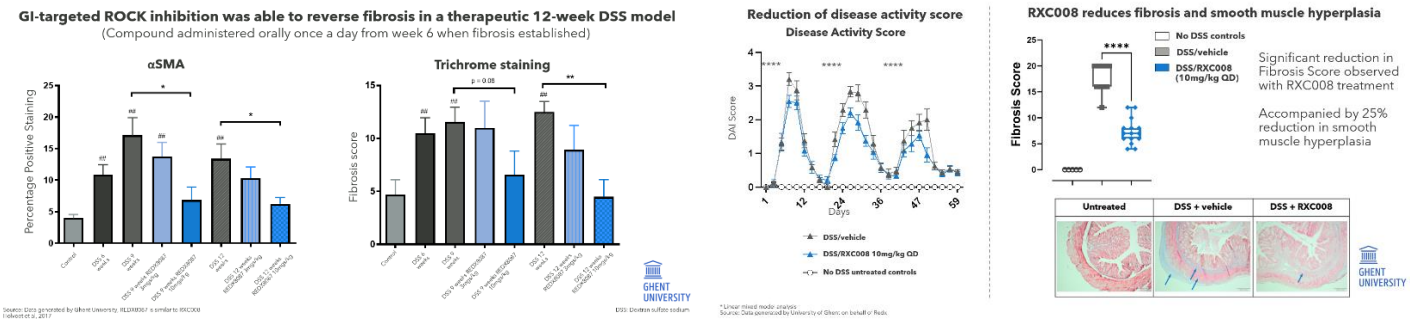
More comprehensive pre-clinical package than usual underpins comfort with Phase I

The supportive preclinical package and further pre-IND work carried out at Redx, which focused on establishing RXC008's GI-restriction and extensively characterising the therapeutic window to define human dosing, has significantly de-risked this programme. The latter has included evaluation of GI-tissue PK as well as standard plasma PK assessments, and toxicology work around different routes of administration (including IV) to further investigate systemic exposure and model PK/PD safety margins. The fact that the Phase I trial has now started, following CTA filing in Q423, suggests that the MHRA was comfortable with the RXC008 preclinical data package which supported Redx's Phase I trial design.

RXC008 led to complete fibrosis reversal in preclinical models…

Preclinical data in both chemically induced (chronic DSS) and mechanistic (adoptive T-cell transfer) models were presented at the 2022 Inflammatory Bowel Disease (IBD) Nordic Conference (poster). These studies demonstrated the ability of a closely related GI-targeted ROCK inhibitor to completely reverse fibrosis to baseline levels in a therapeutic 12-week DSS model (Exhibit 4, left), and the ability of RXC008 to reduce fibrosis and smooth muscle hyperplasia, an important contributing factor to stricture development (Exhibit 4, right) in a nine-week DSS colitis model. Analyses of gene expression in the DSS colitis model also indicated that RXC008 induces changes in gene expression in the colon, upregulating genes involved in tissue repair (AhR and IL-22Ra), and down regulating expression of pro-fibrotic genes (collagen, Wisp2, TGFß, CCR10).

Exhibit 4: Impact of ROCK inhibition in preclinical Crohn's model

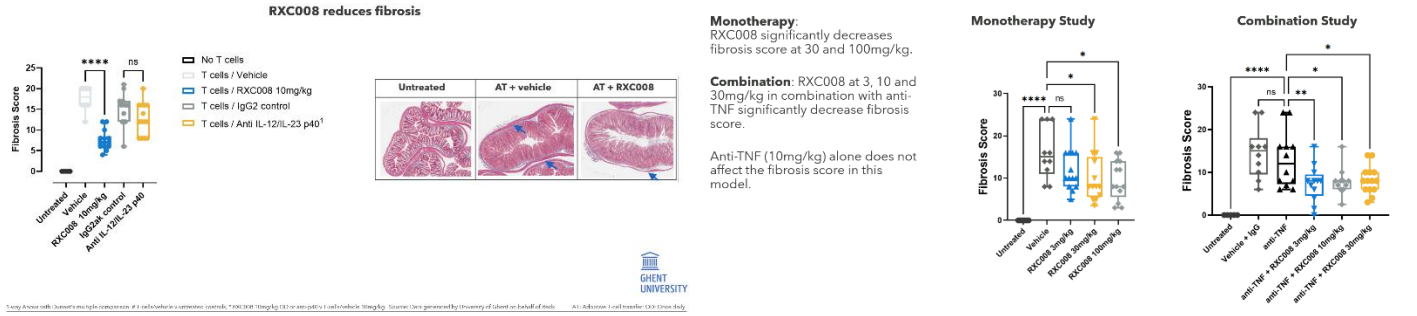


Source: Redx, Ghent University

…and could have a synergistic effect with anti-TNFs

RXC008 was shown to have a therapeutic effect in an adoptive T-cell transfer model (where inflammation and tissue remodelling have been induced and established), demonstrating reduced fibrosis and tissue damage (Exhibit 5, left). Further studies (Exhibit 5, right) with both RXC008 monotherapy and its combination with an anti-TNF demonstrated synergies in the combination with a lower minimally efficacious RXC008 dose (3mg/kg) vs RXC008 monotherapy (30mg/kg), while the anti-TNF alone had no impact on the fibrosis score.

Exhibit 5: RXC008 efficacy in adoptive T-cell transfer models



Source: Redx, Ghent University

Extensive collaboration with Ghent University taps into specialist skills

Ghent University is an important collaborator on Redx's GI-restricted pan-ROCK programme with respect to translational research. Professor Debby Laukens' group has generated data from human cells where RXC008 was shown to inhibit phospho-MYPT1 (myosin phosphatase target subunit 1) in stenotic fibroblasts isolated from resected bowel segments of CD patients; pMYPT1 is the proximal biomarker for ROCK activity. In addition, Ghent University is investigating the development of non-invasive monitoring methods such as MRI scans with the aim of using these translationally in clinical trials. MRI image analysis has successfully detected tissue remodelling in the GI tract of a mouse model of disease, with non-invasive measurement mirroring the RXC008 induced efficacy signal observed from the fibrotic pathology scoring of stained tissue sections.

Anti-fibrotic profile suggests a broad activity, with disease altering potential

Disclosures indicate Redx is positioning RXC008 as an add-on therapy that can be used in conjunction with the current standard of care for CD (anti-inflammatories or other symptomatic therapies). As previously highlighted, anti-inflammatory drugs have limited to no impact on chronic fibrosis, so a therapy which addresses the underlying fibrosis in fibrostenotic CD would meet a significant unmet need. RXC008 is the first anti-fibrotic we are aware of that has demonstrated the potential to reverse established fibrosis, in addition to slowing new fibrotic development. This suggests that RXC008 ultimately could have both a therapeutic and preventative effect, although the latter can only be determined in the clinic.

Indication is gaining academic and industry attention

STAR consortium is developing more clinically relevant end-points for regulatory use

A crucial aspect in designing clinical trials for fibrostenotic CD centres is applying standardised clinically relevant endpoints that are accepted by the regulatory agencies. However, typical CD clinical endpoints consider the anti-inflammatory aspects eg the Crohn's disease activity index is primarily an assessment of quality of life and inflammatory symptoms. This challenge is currently being tackled by the Stenosis Therapy and Anti-Fibrotic Research (STAR) consortium, coordinated by Dr Florian Rieder at the Cleveland Clinic, which is working on validating clinical endpoints.

Fibrostenosis is gaining wider academic and industry interest

Developments such as these indicate that there is growing support for the concept of treating fibrostenosis as a disease, and undoubtedly there is a clear need for more effective treatments that address the fibrotic aspects of CD, not just the inflammatory symptoms.

Agomab raised $100m to progress AGMB-129 in Phase IIa studies

The only other programme to our knowledge specifically targeting fibrostenotic CD is Agomab Therapeutics' AGMB-129, a small molecule GI-restricted inhibitor of ALK5 (TGFβR1) currently under evaluation in the STENOVA Phase IIa trial.

AGMB-129 has FDA Fast Track Designation and showed good tolerability, a favourable safety profile, and no clinically relevant systemic exposure in Phase I studies in healthy volunteers. STENOVA is evaluating two active arms (low and high dose) vs placebo and is expected to complete early-2025. We highlight that Agomab raised $100m in a Series C round in October 2023 led by Fidelity Investments. AGMB-129 is its lead programme and it has a second clinical asset, AGMB-447, an inhaled small molecule lung-restricted inhibitor of ALK5, in Phase I studies for IPF.

GI inflammation and stenosis have featured as key aspects in a number of deals

However, considering novel therapeutic modalities more broadly across IBD, several recent M&A and licensing transactions centred on monoclonal antibodies (mAbs) directed to TL1A (tumour necrosis factor [TNF]-like ligand 1A) have attracted both industry and investor attention. TL1A is a target associated with inflammation, playing a role in amplification and modulation of the immune response. Preclinically in addition to being anti-inflammatory these antibodies have demonstrated an anti-fibrotic effect. Current clinical trials for these agents however seem to be focused on well-established anti-inflammatory endpoints. These anti-TL1A deals and key trials for the underlying mAbs include:

- the c $10.8bn acquisition of Prometheus Biosciences by Merck & Co in April 2023 for its lead candidate PRA023, now known as MK-7240, or tulisokibart. MK-7240's lead indication is ulcerative colitis: it recently began enrolment into a Phase III study in UC, following positive data from the Phase II ARTEMIS-UC trial. The Phase IIa APOLLO-CD open label trial also read out positively and a Phase II study (ATHENA-SSc-ILD) for systemic sclerosis associated with interstitial lung disease is ongoing.
- the October 2023 Sanofi/Teva Pharmaceuticals co-development and co-commercialisation collaboration for TEV'574, under which Teva received a $500m upfront and is eligible for up to $1bn in development and launch milestones. TEV'574 is currently under evaluation in the Phase IIb RELIEVE UCCD basket study in moderate-to-severe IBD; and
- Roche's December 2023 acquisition of Televant, a Roivant/Pfizer vehicle created to develop and commercialise RVT-3101 (formerly PF-06480605), for c $7.1bn upfront plus $150m in cash upon completion of a near-term milestone. Note: Televant held US and Japan rights, with Pfizer continuing to hold the rights in other territories. A Phase III study is in planning following positive data from the Phase IIb TUSCANY-2 trial.

RXC008 appears well placed to augment the potential therapies undergoing clinical evaluations

Initial clinical data on remission rates and endoscopic improvement from these anti-TL1A programmes vs placebo appear promising and if borne out in larger and longer studies, could provide additional new therapeutic options for hard-to-treat IBD patients. Aside from addressing both UC and CD, these mAbs are also targeting anti-TNF failures, a sicker and different patient population to RXC008. RXC008 theoretically could be an oral add-on therapy at any stage that a CD patient presents provided they have fibrosis. Additionally, the potential for anti-TL1As to provide greater efficacy by hitting inflammatory pathways as well as fibrotic pathways could mean the regulatory pathway is more convoluted/complex as it may be difficult to separate the inflammatory and fibrosis effects, particularly as the trials have anti-inflammatory endpoints.

Partnered assets: All that Jazz, and AstraZeneca too

Medicinal chemistry expertise is validated by a history of successful partnerships

Blue-chip partnerships are a key aspect of Redx's strategy. Its impressive track record of executing sale/licensing deals with attractive economics, especially given the early, research/preclinical stage of development, has provided external validation of Redx's medicinal chemistry expertise and drug design capabilities. Importantly, these deals have facilitated continued pipeline progress and provided non-dilutive funding to support the wholly-owned priority ROCK portfolio.

Three agreements with Jazz and one with AstraZeneca

Following the February 2024 KRAS licensing deal, Redx now has four partnership agreements: three with Jazz and one with AstraZeneca. Exhibit 6 summarises the respective deals. To date, upfront/milestone receipts total $58.5m, with potential future success-based milestones of c $1.6bn in aggregate plus royalties on sales.

Exhibit 6: Redx Pharma partnerships

Partner	Asset	Deal structure	Deal terms
Jazz Pharmaceuticals	KRAS programme (preclinical, oncology)	Global licensing & commercialisation deal covering two KRAS targets (G12D selective and pan-KRAS), with separate collaboration agreement (signed February 2024)	**Licensing deal**: $10m upfront payment, plus cumulative potential development, regulatory, and commercial milestones of up to $870m, and tiered mid-single digit percentage royalties on future net sales. Jazz bears responsibility for clinical development, regulatory, manufacturing and commercialisation activities. **Collaboration deal**: Jazz to pay Redx to carry out research and preclinical development to support IND-enabling studies. **Redx milestones received**: $10m upfront. IND application clearance, which we expect in 2026, will trigger the first development milestone. Up to $870m in remaining potential milestone payments.
	Ras/Raf/MAPK programme (preclinical, oncology)	Oncology research collaboration to discover and develop drug candidates for two targets on the RAS/RAF/MAPK pathway (signed September 2020)	**Collaboration**: Upfront payment of $10m 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 percentage royalties on net sales. Redx leads discovery and preclinical development up to IND submission, after which Jazz assumes responsibility for further development, manufacturing, regulatory activities and commercialisation. Note: one of these targets was discontinued in 2022 due to pipeline prioritisaton at Jazz. **Redx milestones received**: $20m received to date ($10m upfront in September 2020, $10m in December 2021). IND submission would trigger the first development milestone. Up to $200m in remaining potential milestone payments.
	JZP815 (Phase I, oncology)	Sale of preclinical pan-RAF inhibitor programme, with separate collaboration agreement (signed July 2019)	**Sale economics**: Upfront fee of $3.5m, plus up to $203m in cumulative potential development, regulatory, and commercial milestones, and mid-single digit percentage royalties on future net sales. Jazz funds all development, and is responsible for all post-IND development, regulatory, manufacturing, and commercial activities. **Collaboration deal**: Jazz funded Redx to carry out research and preclinical development to completion of IND-enabling studies. **Redx milestones received**: $3.5m upfront and $8m in further cumulative milestones received to date ($3m on initiation of IND-enabling studies in September 2021; $5m on IND clearance in June 2022). Up to $195m in remaining potential milestone payments.
AstraZeneca	AZD5055 (previously RXC006, Phase I, IPF)	Global licensing deal for the development & commercialisation of porcupine inhibitor RXC006 in fibrotic diseases (signed August 2020)	**Licensing deal:** Upfront fee and early development milestones totalling $17m between deal signing and Phase I start, plus up to $360m in development, regulatory, and commercial milestones, and mid-single digit percentage royalties on future net sales. **Redx milestones received:** Cumulative receipt of $17m to date including $4m in June 2021, and $9m in December 2021 on the initiation of Phase I studies. Up to $360m in remaining potential milestone payments.

Source: Trinity Delta, Redx Pharma Note: IPF = idiopathic pulmonary fibrosis

Clinical risks have been actively managed, with non-dilutive funding a welcome benefit

Redx's deals have had both a financial and risk management angle. The sale or outlicensing of assets, including of previously under the radar discovery programmes, has enabled the company to realise immediate value while also sharing in material potential upside as programmes progress into and beyond the clinic funded by partners. In the case of AZD5055, its outlicensing was a strategic move to lessen Redx's exposure to the porcupine class. The non-dilutive funding generated by Redx's business development activities has been directed towards advancing its priority assets, and while future potential milestone receipts are significant there is limited visibility on timings. Milestones are linked to the clinical development progress of the underlying programmes, which are under the control of their respective licensors. We note that for the clinical stage assets, JZP815 and AZD5055, future milestone receipts are expected to be triggered less frequently as partnered candidates advance to later, and therefore longer, studies.

The first Jazz deal was for JZP815; the second was focused on the MAPK pathway…

Existing partnerships validate Redx's expertise in generating differentiated and relevant drug candidates that address unmet needs. Redx's expanding relationship with Jazz appears to be mutually beneficial with Redx making an important contribution to Jazz's growth plans for its haematology/oncology R&D pipeline. The first agreement covers JZP815, a precision pan-RAF inhibitor now in Phase I, which was designed to overcome the acquired resistance mechanisms associated with currently approved B-RAF selective drugs. Around one-third of cancers involve mutations that result in uncontrolled signalling in the RAS-RAF-MAPK pathway. The second Jazz collaboration addresses an undisclosed target on the MAPK pathway, although this is programme is at an earlier pre-IND stage.

…followed by the KRAS deal, including both G12D selective and pan-KRAS candidates

The most recent licensing deal between the two parties covers KRAS (Kirsten rat sarcoma virus), a well-validated oncology target that is one of the most frequently mutated oncogenes across many different cancer types. To date, targeting specific KRAS mutations, with the exception of G12C, has proved challenging. Developing oral molecules with optimised target coverage and therapeutic windows is a focus area given this unmet need. The Jazz/Redx KRAS programme includes both G12D selective and pan-KRAS candidate molecules.

AstraZeneca's AZD5055 is in Phase I for fibrosis indications

Redx's licence agreement with AstraZeneca centres on AZD5055 (formerly RXC006), a potent, highly selective small molecule of the porcupine receptor that is currently in development for fibrosis indications. AZD5055 targets the Wnt pathways that are critical elements in maintaining adult cell homeostasis, which includes wound healing and repair functions. It is currently under evaluation in a 60-patient two-part Phase I trial, with IPF as the initial indication. If this early study is supportive, we expect AstraZeneca to seek to broaden the development programme into other fibrosis indications.

RXC004, Redx's lead compound, is being prepared for partnering

Redx's lead oncology programme, RXC004 (zamaporvint), also targets Wnt pathways but belongs to a different chemical class to AZD5055. RXC004 is a highly potent, selective porcupine inhibitor in development for Wnt-ligand dependent cancers in combination with immunotherapies. A partner is sought for further development post-Phase II data (anticipated in H124) as preclinical data suggest that there is a broader opportunity for RXC004 in potentially synergistic combinations with other therapeutic agents, including chemotherapies and MAPK inhibitors. However, evaluating this is beyond the scope of Redx's current resources, and outside its priority focus on its ROCK portfolio in fibrosis, but could be an attractive proposition for a larger partner.

Valuation and Financials

rNPV valuation of £386m, or 99p per share

We value Redx Pharma as a classic drug discovery and development play, using a sum of the parts rNPV-based model that includes a pipeline rNPV (risk-adjusted net present value) and a discovery platform valuation based on Redx's output/track record. These are summed and netted against central costs and cash. Our valuation has been updated to reflect the $10m upfront from Jazz for the recent KRAS collaboration, leading to an increase in currently available cash, in addition to start of the Phase I trial with RXC008, which we have slightly de-risked to a 10% probability (from 5%) reflecting the extensive preclinical data package and progress into first-in-human studies. Our other assumptions are unchanged.

The changes to RXC008 and to cash drive an increase in our valuation to £386m/$463m (from £367m/$441m), equivalent to 99p per share (from 94p). An overview of our valuation and key assumptions are summarised in Exhibit 7.

Exhibit 7: rNPV-based valuation of Redx Pharma

Programme	NPV ($m)	NPV (£m)	Approval likelihood	rNPV ($m)	rNPV (£m)	rNPV/ share (p)	Notes
Zelasudil (ROCK2 inhibitor - IPF/NASH/oncology)	1,285.7	1,071.4	15%	155.1	129.3	33.2	Peak sales: $4.1bn; Launch: 2029
RXC008 (ROCK1/2 - Crohn's disease)	478.7	398.9	10%	53.4	44.5	11.4	Peak sales: $1.6bn; Launch: 2030
RXC004 (porcupine inhibitor - oncology)	537.9	448.2	30%	86.8	72.3	18.6	Peak sales: $1.9bn; Launch: 2028
AZD5055 (AstraZeneca: porcupine inhibitor - IPF)	291.3	242.8	15%	36.0	30.0	7.7	Peak sales: $1.7bn; Launch: 2029
JZP815 (Jazz Pharma: pan-RAF - oncology)	165.7	138.1	10%	13.8	11.5	3.0	Peak sales: $707m; Launch: 2029
Discovery engine				101.3	84.4	21.7	
Operating costs	(30.8)	(25.7)		(30.8)	(25.7)	(6.6)	
Cash	47.6	39.7		47.6	39.7	10.2	Includes $10m from Jazz
Total	**2,776.1**	**2,313.4**		**463.3**	**386.1**	**99.2**	
Total (fully diluted)				479.9	399.9	74.1	All options and CLNs

Source: Trinity Delta Note: The rNPVs of RXC004 includes a deal success factor of 65%, with 80% for zelasudil, and of 75% for GI-targeted ROCK; other valuation assumptions include a 12.5% discount factor, £/$ FX rate of 1.20, and 10% taxation from 2030 (UK patent box).

Jazz KRAS deal boosts cash and revenues

We have also incorporated the recent KRAS deal with Jazz in our financial forecasts. There are two main elements that have led to increases in our FY24e and FY25e revenue forecasts, described below. Our other key P&L forecasts, including R&D and G&A, are unchanged; more details on these are available in our December 2023 Update:

- **Upfront of $10m:** We assume this is recognised in full, hence our FY24 revenue forecast has been boosted by c £7.9m. There are significant future development, regulatory, and commercial milestones of up to $870m as part of the deal with Jazz. However, given that the first will be triggered by FDA IND application clearance, which we believe will be in around two years (thus not within our current forecast period), we do not include any other milestones from this deal in our current revenue forecasts.

- **Research collaboration:** A separate collaboration agreement has been signed under which Jazz will pay Redx to carry out research and preclinical development to support IND-enabling studies. We assume Redx will receive c £2-3m per annum until successful IND submission, which is broadly in-line with prior research collaboration income from Jazz as part of the pan-RAF deal. We therefore include £1.2m in FY24e (reflecting around seven months of work) and £2.5m in FY25e.

Current cash runway extended into 2025 well beyond H124 value inflection points

Receipt of the $10m upfront from Jazz has extended Redx's cash runway into 2025 (from September 2024 previously), well beyond key value inflection points, most notably zelasudil Phase IIa IPF data, plus the RXC004 Phase II combination data, both of which are expected in H124. Potential milestone receipts from existing partners, further business development activity, or other options including equity financing(s), could extend the runway further. Note that we include illustrative placeholder milestones totalling £5m in FY24e but there could be upside to this given Redx has highlighted there could be near-term potential milestones of $15m due under existing collaborations. Our updated financial forecasts (shown in Exhibit 8) continue to include a placeholder £40m financing (in short-term debt) in FY24e.

Exhibit 8: Summary of financials

Year-end: Sept 30	£'000s	2021	2022	2023	2024E	2025E
INCOME STATEMENT						
Revenues		**10,035**	**18,690**	**4,202**	**14,963**	**2,503**
Cost of goods sold		0	0	0	0	0
Gross Profit		**10,035**	**18,690**	**4,202**	**14,963**	**2,503**
R&D expenses		(24,445)	(28,563)	(29,117)	(30,573)	(31,490)
G&A expenses		(6,492)	(10,229)	(8,069)	(8,160)	(8,241)
Underlying operating profit		**(17,117)**	**(15,737)**	**(29,790)**	**(20,512)**	**(33,906)**
Share-based payments		(3,785)	(4,365)	(3,194)	(3,258)	(3,323)
Exceptionals		0	0	(2,393)	0	0
Other revenue/expenses		1,157	3,836	1,557	1,588	1,620
EBITDA		**(19,112)**	**(15,380)**	**(32,860)**	**(21,309)**	**(34,909)**
Operating Profit		**(19,745)**	**(16,266)**	**(33,820)**	**(22,182)**	**(35,609)**
Financing costs/income		(1,698)	(1,538)	1,032	(1,596)	(2,250)
Profit Before Taxes		**(21,443)**	**(17,804)**	**(32,788)**	**(23,777)**	**(37,859)**
Adj. PBT		**(18,815)**	**(17,275)**	**(28,758)**	**(22,107)**	**(36,156)**
Current tax income		(133)	(201)	(368)	(153)	(157)
Net Income		**(21,576)**	**(18,005)**	**(33,156)**	**(23,930)**	**(38,016)**
EPS (p)		**(8.4)**	**(6.1)**	**(9.9)**	**(5.7)**	**(7.6)**
Adj. EPS		**(7.4)**	**(5.9)**	**(8.7)**	**(5.3)**	**(7.3)**
DPS (p)		**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Average no. of shares (m)		256.4	294.2	334.9	417.1	499.3
BALANCE SHEET						
Current assets		**35,815**	**59,378**	**23,302**	**55,339**	**22,168**
Cash and cash equivalents		29,552	53,854	18,092	50,010	21,139
Accounts receivable		6,231	5,498	5,210	5,329	1,028
Other current assets		32	26	0	0	0
Non-current assets		**3,730**	**3,099**	**2,334**	**16**	**(2,869)**
Property, plant & equipment		3,325	2,699	1,940	1,272	787
Intangible assets		405	400	394	394	394
Other non-current assets		0	0	0	(1,650)	(4,050)
Current liabilities		**(9,592)**	**(27,205)**	**(21,007)**	**(43,680)**	**(44,717)**
Short-term debt		0	(15,731)	(15,731)	(40,000)	(40,000)
Accounts payable		(4,699)	(5,958)	(3,756)	(3,057)	(4,094)
Other current liabilities		(4,893)	(5,516)	(1,520)	(622)	(623)
Non-current liabilities		**(16,821)**	**(1,951)**	**(1,274)**	**376**	**2,776**
Long-term debt		(14,247)	0	0	0	0
Other non-current liabilities		(2,574)	(1,951)	(1,274)	376	2,776
Equity		**13,132**	**33,321**	**3,355**	**12,051**	**(22,642)**
CASH FLOW STATEMENTS						
Operating cash flow		**(21,379)**	**(8,470)**	**(34,747)**	**(21,515)**	**(28,655)**
Profit before tax		(21,443)	(17,804)	(32,788)	(23,777)	(37,859)
Non-cash adjustments		6,116	6,776	3,122	5,727	6,272
Change in working capital		(6,065)	2,038	(7,673)	(1,662)	5,337
Interest paid		13	187	1,160	(1,596)	(2,250)
Taxes paid		0	333	1,432	(207)	(156)
Investing cash flow		**(754)**	**(241)**	**(195)**	**(205)**	**(215)**
CAPEX on tangible assets		(754)	(262)	(195)	(205)	(215)
Acquisitions/disposals		0	21	0	0	0
Other investing cash flows		0	0	0	0	0
Financing cash flow		**24,143**	**32,982**	**(816)**	**53,638**	**0**
Proceeds from equity		24,929	33,798	0	13,638	0
Increase in loans		0	0	0	40,000	0
Other financing cash flow		(786)	(816)	(816)	0	0
Net increase in cash		**2,010**	**24,271**	**(35,758)**	**31,918**	**(28,870)**
Cash at start of year		27,513	29,552	53,854	18,092	50,010
Cash at end of year		**29,552**	**53,854**	**18,092**	**50,010**	**21,139**
Net cash at end of year		**15,305**	**38,123**	**2,361**	**10,010**	**(18,861)**

Source: Company, Trinity Delta Note: Short-term debt in CY23/FY24e includes receipt of £40m in additional funding. The Redmile/Sofinnova Convertible Loan Note revised conversion date is 4 August 2024, with a conversion price of 15.5p, equating to a potential 110.3m of new shares.

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