Redx
Discovering Targeted Medicines

Interim Results Presentation

For Period Ended 31 March 2022

23 June 2022

AIM:REDX

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Redx – Discovering Targeted Medicines

Speakers

Lisa Anson
CEO

Richard Armer
CSO

Peter Collum
CFO

Agenda

- Business progress during H1 2022
- Portfolio overview
- Financials
- Outlook
- Q&A

Redx – Discovering Targeted Medicines

Novel, small molecule, highly targeted medicines for cancer and fibrotic disease, including the emerging area of cancer-associated fibrosis

Clinical-stage biotech with two wholly-owned clinical assets and Discovery Engine fuelling pipeline

2 Clinical Assets

Ambitious, experienced leadership/scientific team with distinct approach and track record for consistently generating differentiated drug candidates

70 Scientists

Supported by blue-chip specialist biotech investors, with cash runway through 2023 to deliver multiple value-inflection points

Redmile Group
POLAR CAPITAL
Platinum ASSET MANAGEMENT
SOFINNOVA PARTNERS
INVUS

Strong Momentum on All Fronts

Redx

Clinical

Positive progress on both wholly-owned clinical assets

RXC004 - First wholly-owned Redx asset to enter Phase 2 clinical trials
- Initiated both Phase 2 trials - PORCUPINE & PORCUPINE2

RXC007 - Phase 1 study showed excellent safety and pharmacokinetic profile
- Data presented at the Interstitial Lung Disease Drug Development Summit March 2022

Discovery Engine

Discovery Engine continues to deliver

- **RXC008**, a GI-targeted ROCK inhibitor for fibrostenotic Crohn's disease, nominated as development candidate
- **Discoidin Domain Receptors** (DDR) progressed to lead optimisation
- **Partnered pan-RAF** IND clearance - will represent **5th** clinical programme discovered by Redx

Corporate

Strengthened balance sheet

- Post period - successful fundraise of **£34.3m** (gross)
- **$19m** partnership milestones received in period
- **$5m** partnership milestone triggered post-period

GI: Gastrointestinal; ILD: Interstitial Lung Disease; IND: Investigational news drug application; ROCK: Rho associated protein kinase

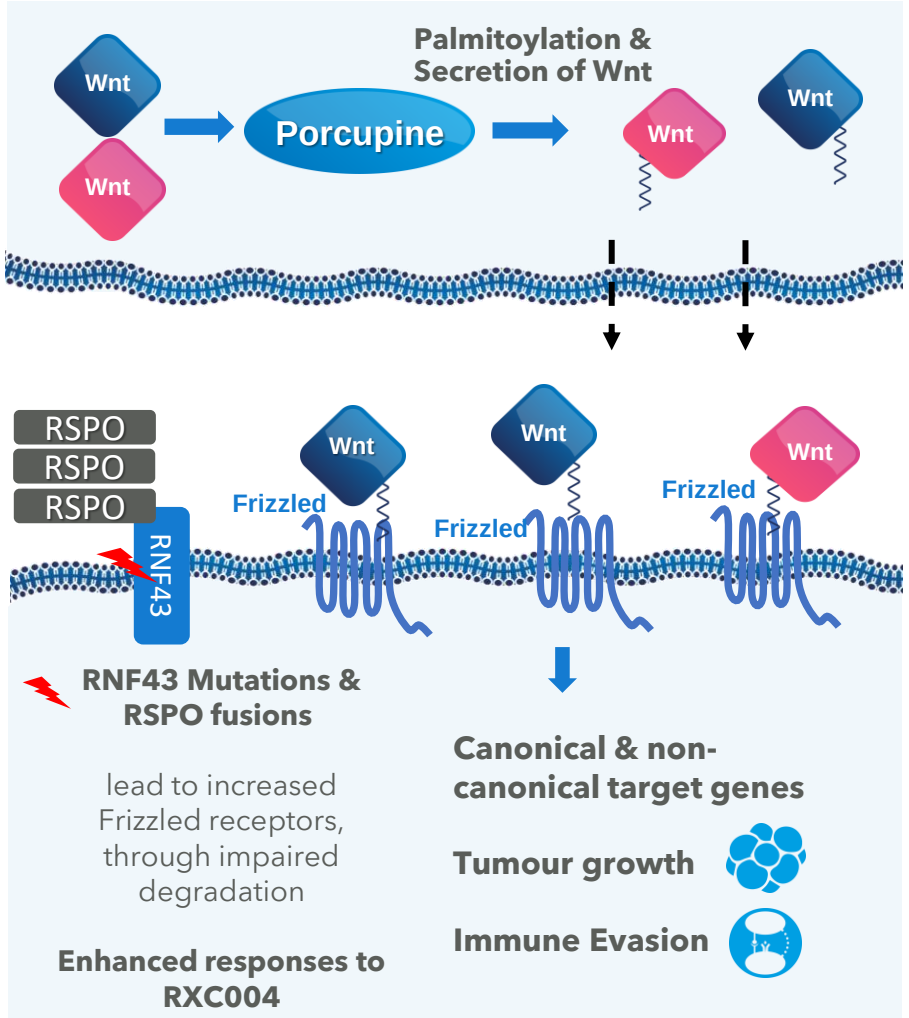
Advancing a Robust Pipeline Built In-House

Redx

	Target/ Product	Indication(s)	Research	Preclinical	Phase 1	Phase 2	Phase 3	Upcoming Milestones
Oncology	**Porcupine Inhibitor** (RXC004)	Genetically selected MSS mCRC mono + nivolumab combo	PORCUPINE					Initiate combo arms – **H2 2022** Topline data – **From H1 2023**
		Genetically selected pancreatic cancer Unselected biliary cancer mono + PD1 combo	PORCUPINE2					
Fibrosis	**ROCK2 Selective Inhibitor** (RXC007)	Idiopathic pulmonary fibrosis (IPF)						Initiate Phase 2a - **2022**
Discovery Engine	**GI-targeted ROCK Inhibitor** (RXC008)	Fibrostenotic Crohn's Disease						Progress programmes – **3 IND's by 2025** • RXC008 IND submission – **end 2023**
	DDR Inhibitor (Discoidin Domain Receptor)	Fibrosis, Cancer-associated fibrosis						
	Research Targets (Wholly-owned)	Oncology & Fibrosis						
Partnered	**Porcupine Inhibitor** (RXC006/AZD5055)	Idiopathic pulmonary fibrosis (IPF)						Licensed to AstraZeneca
	Pan-RAF Inhibitor (JZP815)	Oncology						Sold to Jazz Pharmaceuticals
	MAPK Pathway (undisclosed target)	Oncology						Progress towards IND

DDR: Discoidin Domain Receptor; IND: Investigational new drug application; GI: Gastrointestinal; MAPK: Mitogen-activated protein kinase; MSS mCRC: Microsatellite-Stable Metastatic Colorectal Cancer; RAF: Rapidly accelerated fibrosarcoma; ROCK: Rho associated protein kinase

RXC004 : Clinically Validated Porcupine Inhibitor in Phase 2



Blue and red Wnt ligands denote canonical and non-canonical signalling pathways, respectively

RXC004 is a potent, once-daily, orally active Porcupine Inhibitor

- Differentiated vs. competitors
- Encouraging Phase 1 monotherapy data reported at ESMO 2021, differential clinical efficacy in Wnt-ligand dependent tumours

Porcupine is a key enzyme in the Wnt pathway

- Wnt pathway is well established as a critical driver of cancer
- Inhibition of Porcupine blocks the release of all Wnt ligands from cells, **preventing both tumour growth** and **tumour immune evasion**
- Clear patient selection - targeting **Wnt-ligand dependent** tumours

Phase 2 programme data expected from H1 2023

- **Monotherapy and combination** in genetically-selected MSS metastatic colorectal cancer
- Genetically selected pancreatic cancer
- **Monotherapy and combination** unselected biliary cancer

ESMO: European Society for Medical Oncology; MSS: Microsatellite-stable; RNF43: Ring finger protein 43; RSPO: R-spondin; Wnt: Wingless/integrated

RXC004

Clinical Efficacy Data Supports Development in Wnt-Ligand Dependent Tumours

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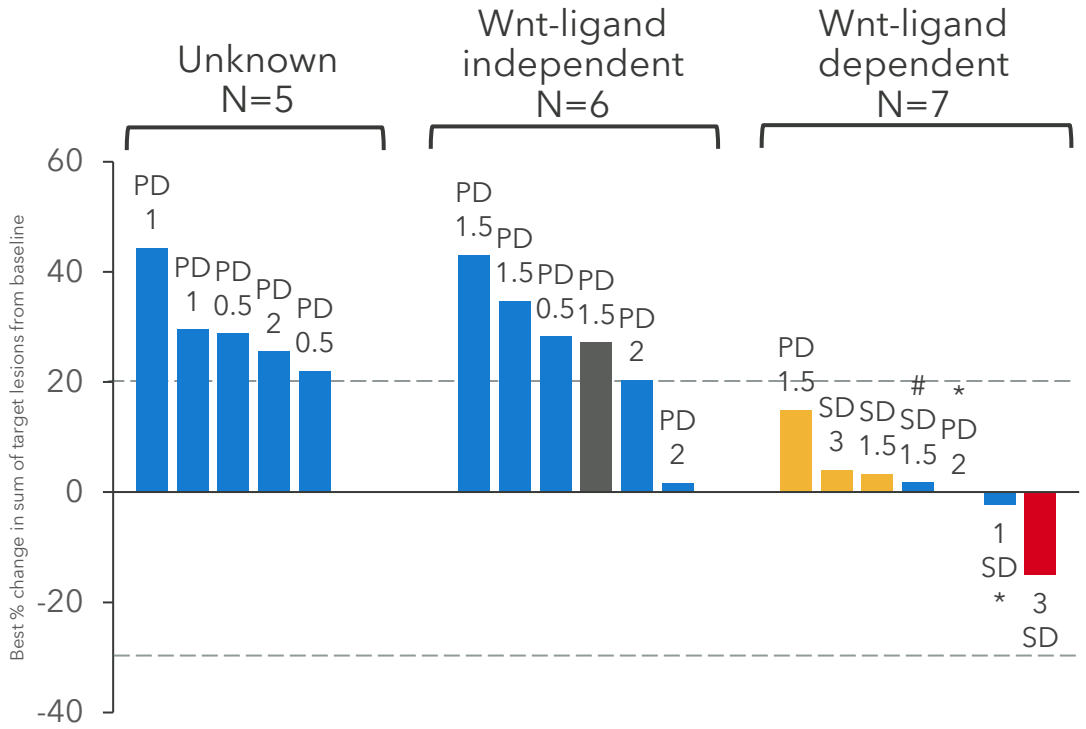
Clinical activity by Wnt-ligand dependence†



Numbers= dose in mg
† Study was in unselected patients; retrospective analysis
* RNF43 LoF mutation
# RSPO Fusion

18 patients had RECIST - evaluable disease

5/7 patients with Wnt-ligand dependent tumours had durable RECIST Stable Disease (SD)

- In addition, 2/7 patients with Wnt-ligand dependent tumours had SD in target lesions but disease progression overall
- 0/11 patients with unknown or Wnt-ligand independent tumours had SD

Median treatment duration higher in patients with Wnt-ligand dependent tumours

- 13.1 weeks in Wnt-ligand dependent tumours
- 6.6 weeks in unknown or Wnt-ligand independent tumours

APC: Adenomatous polyposis coli gene; CRC: Colorectal cancer; LoF: Loss of function; PD: Progressive disease; RECIST: Response evaluation criteria in solid tumours; RNF43: Ring finger protein 43; RSPO: R-spondin; SD: Stable disease; Wnt: Wingless/integrated

Data cut-off date 30 July 2021

RXC004

Phase 2 Programme in Wnt-ligand Dependent Tumours Expected to Deliver Topline Data from H1 2023

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	PORCUPINE MSS Metastatic Colorectal Cancer		PORCUPINE2		
	Monotherapy Genetically Selected RXC004 (n=20)	Combination Genetically Selected RXC004 + PD1 (n=20)	Monotherapy Genetically Selected Pancreatic Cancer (n=15)	Monotherapy Unselected Biliary Cancer (n=15)	Combination Unselected Biliary Cancer RXC004 + PD1 (n=15)
Patient Selection	**8% of patients** (RNF43 mutations 3%[1] + RSPO fusions 5% of patients[2]) MSS is 95% of all mCRC cases[6]		RNF43 mutations in **7% of patients**[7]	**>70% of patients** have high Wnt-ligand expression[3]	
5-Year Survival [4]	14%		3%	2%	
Annual Target Market [5]	14,000		9,000	>51,000	

(1) RNF43 mutation frequency determined from all relevant studies published on cBioPortal for cancer genomics (updated Jan 2018). Only mutations resulting in functional impairment (LoF) were considered. Gao et al. 2013 & Cerami et al. 2012. (2) RSPO fusion prevalence in CRC is a combination of studies (Shesagiri, 2012; Shinmura, 2014; Kleeman, 2019); Redx notes the combined figure is an approximate figure calculated on the basis of RNF43 mutations and RSPO fusions based on the studies indicated and these studies included a limited dataset of samples.; (3) Loilome et al. 2014, Boulter et al. 2015; (4) www.cancer.net (5) Incidence data sourced from GlobalData Epidemiology data (Major Markets: US, EU5, Japan, China) (6) Gong et al. March 21, 2017 (ASCO JCO) (7) Witkiewicz 2015.

MSS mCRC: Microsatellite-stable metastatic colorectal cancer; RNF43: Ring finger protein 43; RSPO: R-Spondin; Wnt: Wingless/integrated

RXC007

RXC007 : A Selective ROCK2 Inhibitor for Fibrotic Diseases – Phase 1 Topline Data Confirms Drug-like Profile

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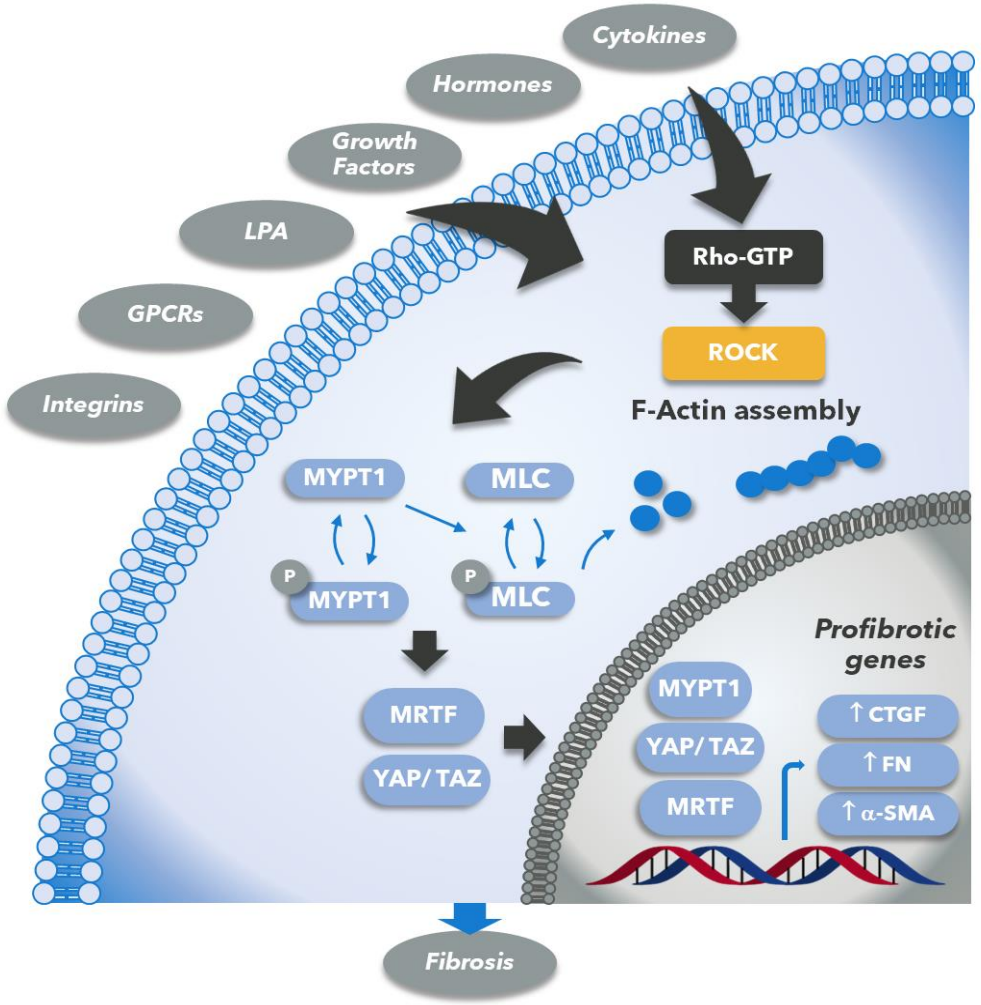


RXC007 is a highly selective oral ROCK2 Inhibitor

- Robust preclinical efficacy demonstrated across fibrotic disease models
- Phase 1 topline data confirms safety and PK profile

ROCK2 is a compelling fibrosis target

- ROCK sits at a key junction in cell signalling pathways central to fibrosis
- Systemic inhibition of ROCK1&2 results in hypotension, not seen with ROCK2 selective inhibition
- Validated target with a product approved by FDA for cGvHD
- Extensive growth potential to be developed broadly across various disease areas associated with fibrosis:
  - Pulmonary, hepatic, metabolic, cardiovascular, neuromuscular, CNS and cancer
- Heavily upregulated in IPF

Phase 2a in IPF expected to commence 2022

- Idiopathic Pulmonary Fibrosis (IPF) high unmet need - median survival 3-5 years [1] with approximately 170,000+ patients [2]
- IPF market projected to reach $3.6 bn by 2029[2]*

1. Clinical Estimates from Hyun 2015, Ley 2012, Raghu 2006
2. Patient numbers (diagnosed prevalence) & market size forecast data sourced from Global Data (US, EU5, Japan)

** Global Data (US, EU5, Japan)*

cGvHD: Chronic graft versus host disease; CNS: Central Nervous System; IPF: Idiopathic pulmonary fibrosis; PK: Pharmacokinetic; ROCK: Rho associated protein kinase

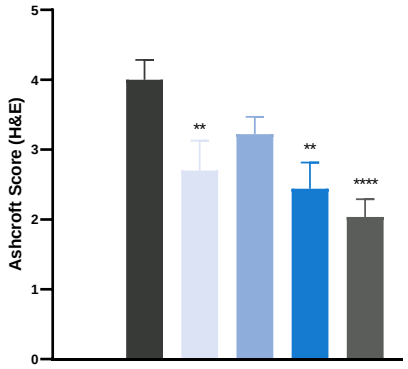
RXC007

Preclinical Efficacy Data in Lung Fibrosis Models Support IPF as a Lead Indication

Fibrosis reduction in IPF therapeutic model (Bleomycin)

Mouse 21-day therapeutic model (dosing from day 7)

Ashcroft Score

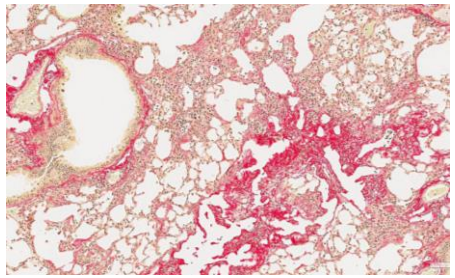


- Vehicle
- Bleomycin Vehicle
- RXC007 (5 mg/kg BID)
- RXC007 (20 mg/kg BID)
- RXC007 (50 mg/kg BID)
- Pirfenidone (100 mg/kg BID) (as a positive control)

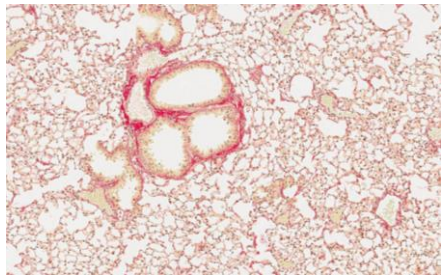
Representative images

Lung histology Sirius red

Vehicle

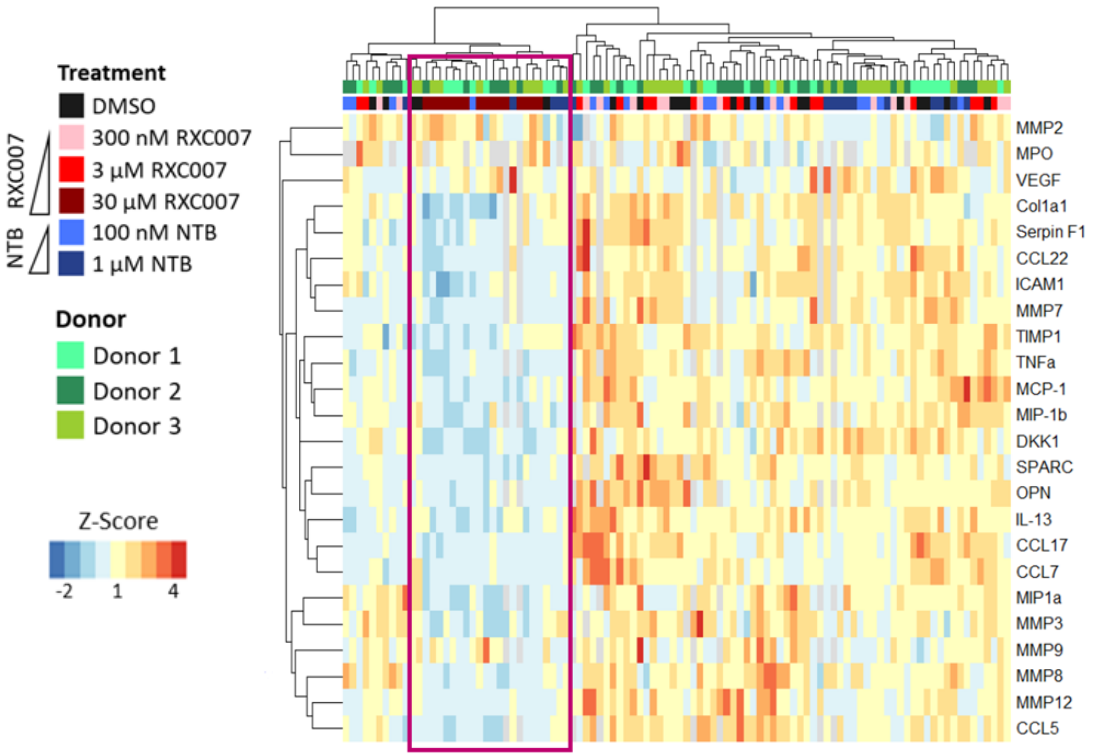


RXC007 50 mg/kg BID



Modulation of key gene signals in IPF lung tissue

Protein expression heatmap comparison to nintedanib (NTB)

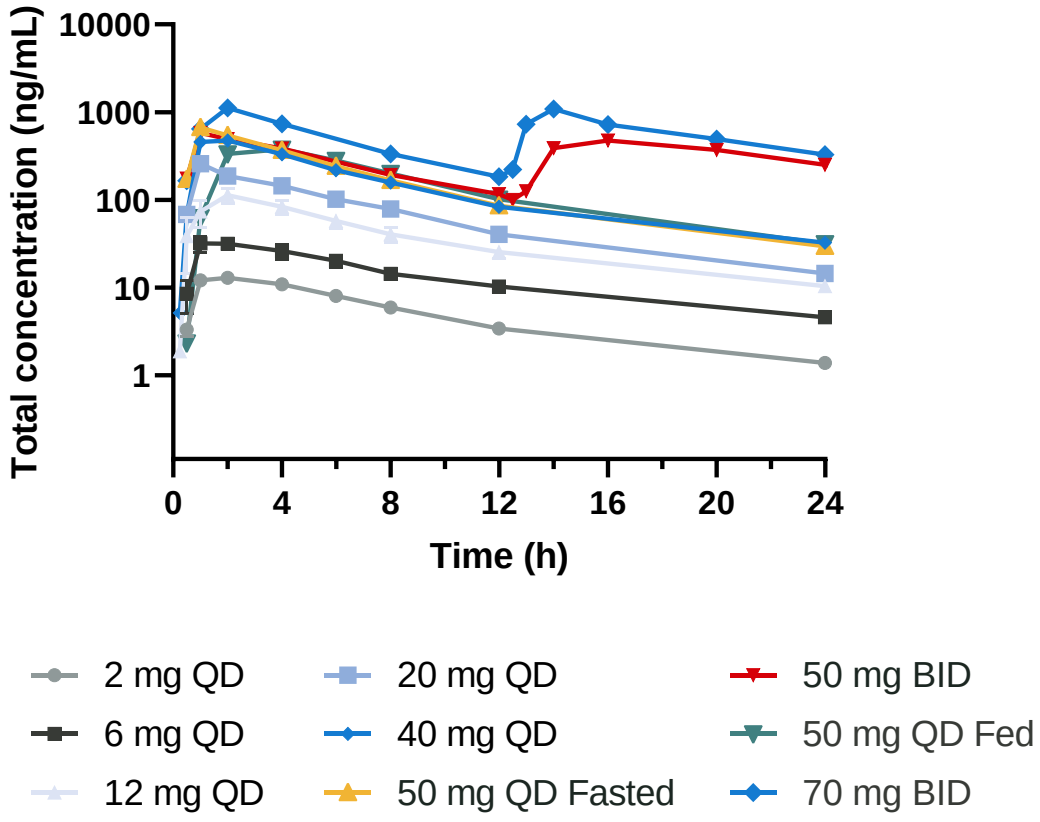


BID: Twice daily; IPF: Idiopathic pulmonary fibrosis

RXC007

Strong Safety and Pharmacokinetic Profile in Phase 1* in Healthy Volunteers

Total plasma concentration over time; single dose



- No adverse events observed to date following single oral dose of 2 mg QD to 70 mg BID
- Pharmacokinetics as predicted from preclinical data
- Essentially linear exposure 2-70 mg
- Achieved biologically relevant exposures based on preclinical models
- No significant differences between 50 mg QD fasted and fed cohorts
- Half-life 9-11 hours, potentially suitable for once-daily dosing

- Safe and well tolerated in 50 mg BID multi dose cohort with few treatment-emergent adverse events reported

*Data to 3 March 2022

BID: Twice daily; QD: Once daily; SAD: Single ascending dose

RXC007

Differentiated Phase 2 Programme in IPF Expected to Commence in 2022

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Phase 2a Dose Ranging Study to inform Phase 2b dose; 3 cohorts of 16 patients each

- Provides early efficacy readouts, safety and tolerability in IPF patients, with or without standard IPF therapy
- Assigned dosing period of 3 months. Patients may potentially continue for longer if no signs of disease progression

Cohort 1
Dose Level 1
12:4 RXC007:pbo

Cohort 2
Dose Level 2
12:4 RXC007:pbo

Cohort 3
Dose Level 3
12:4 RXC007:pbo

Translational Science Sub-Study with 2 cohorts of 8 patients each

To evaluate target and disease marker engagement

Endpoints include changes from baseline in blood biomarkers, proteins and genes from broncho-alveolar lavage (BAL) fluid, BAL-fluid cells and bronchial epithelial cells

Key Endpoints

- Safety, PK Profile
- Changes from baseline in lung function - FVC and DLCO
- Changes from baseline in Quantitative Lung Fibrosis Score, airway volume and resistance on HRCT Scan

DLCO: Carbon monoxide diffusion coefficient; FVC: Forced vital capacity; HRCT: High resolution computerized tomography; Pbo: Placebo; PK: Pharmacokinetics

RXC008 : GI-targeted ROCK Inhibitor Planned to Enter Phase 1 Clinical Trial End 2023

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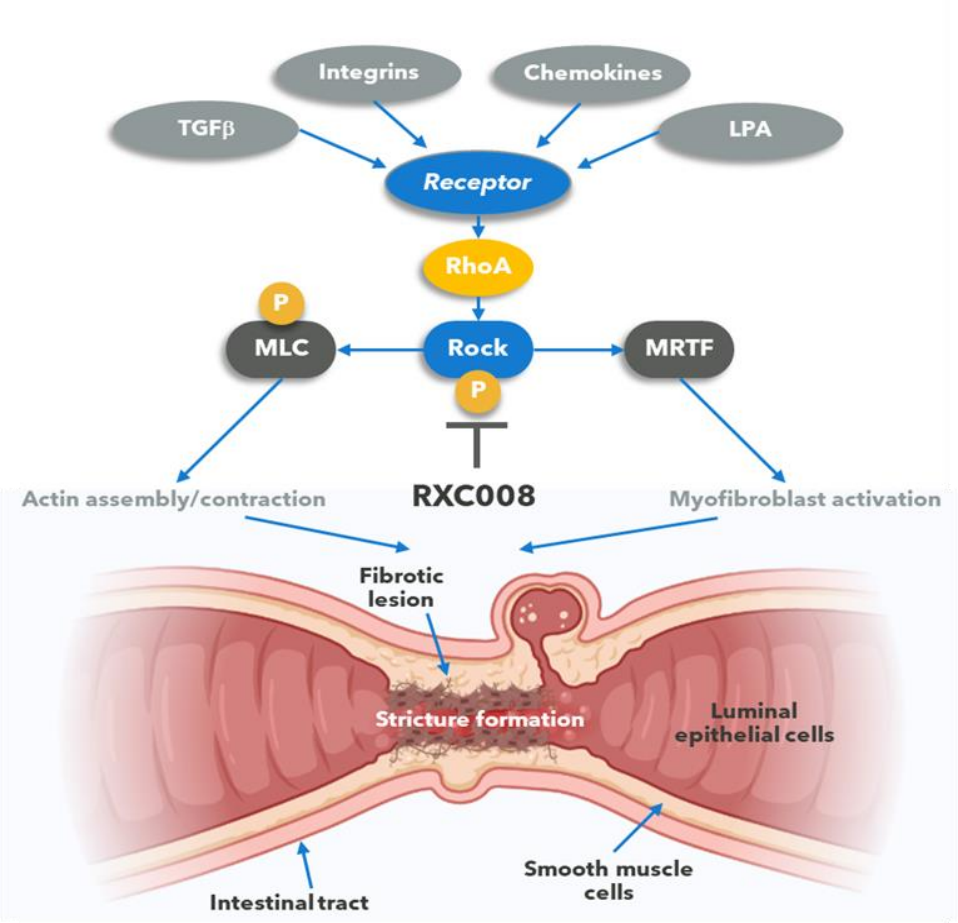
ROCK: nodal point for fibrotic signalling



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

Potent, oral small molecule non-systemic ROCK 1/2 inhibitor

- ROCK is a key target involved in fibroblast activation
- Selectively active in gut without risking systemic exposure
- *In vivo* efficacy in models and *ex vivo* using tissue from Crohn's patients

Potential first-in class treatment for fibrostenotic Crohn's disease

- Crohn's disease affects 1.5m[1] people globally, of which 50% will develop strictures or complications leading to fibrostenosis[2]
- No curative treatment currently available
- No approved therapies for underlying fibrosis

IND enabling work underway - Phase 1 target start end 2023

IND: Investigational new drug application

RXC008 Reduces Fibrosis in the Adoptive T-cell Transfer Model

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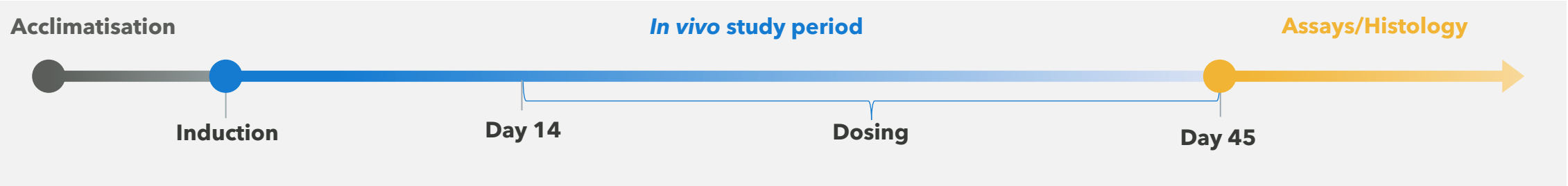
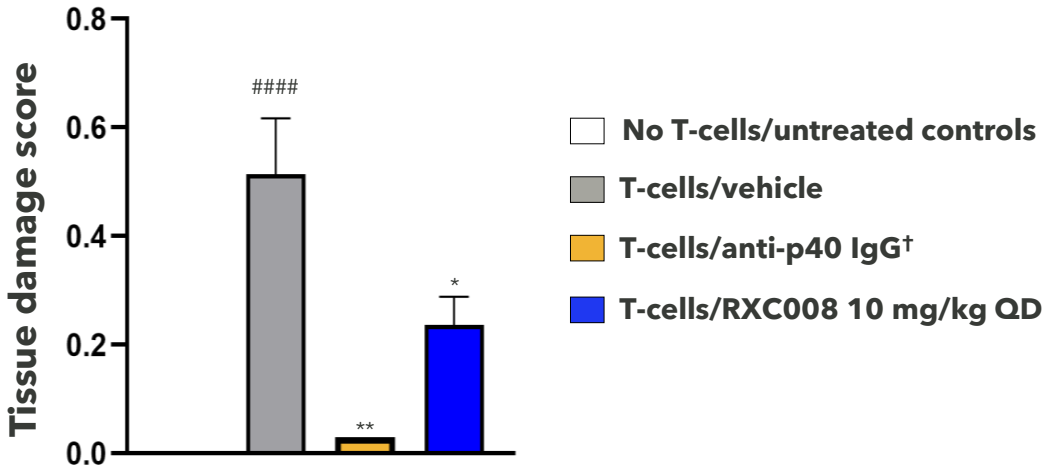
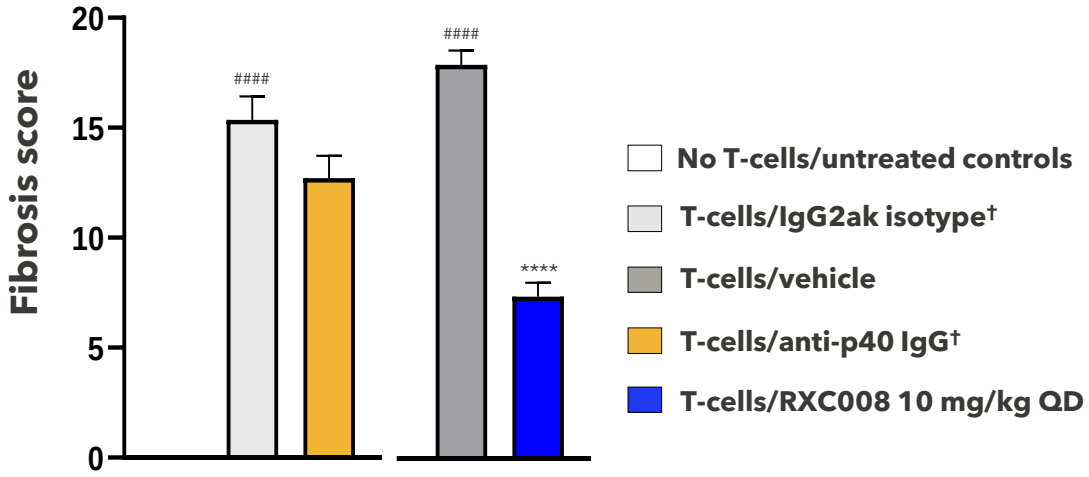


RXC008 reduces tissue damage



RXC008 reduces fibrosis

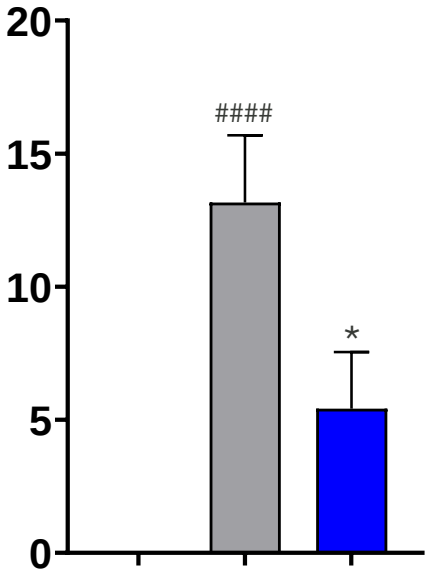


p40 data has been modified for the purpose of graphical representation
Colon damage could not be detected in the p40 treated animals.

AT: Adoptive T-cell transfer; QD: Once daily

RXC008 Reduces Fibrosis in the Chronic DSS Model

Reduction in fibrosis measured by histology



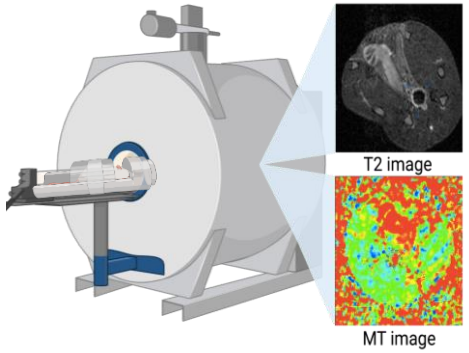
- No DSS untreated controls
- DSS/vehicle
- DSS/RXC008 10mg/kg QD

25% reduction in smooth muscle hyperplasia observed

1-way Anova with Dunnet's multiple comparison, # Vehicle day 0 v day 61 * vehicle day 61 v RXC008 day 61

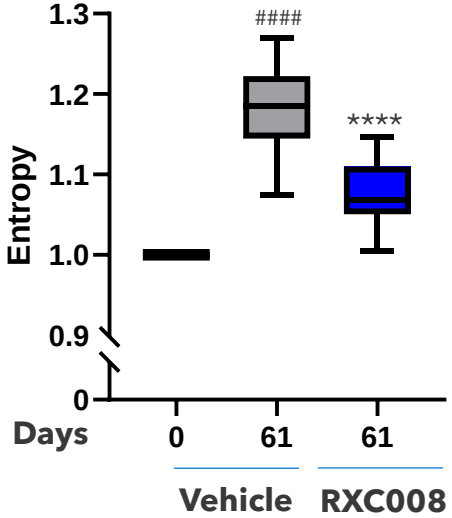
Reduction in fibrosis measured by MRI*

Analysis using MT imaging



Murine sized MRI scanner

Entropy fibrosis score



*Research in collaboration with Ghent University

DSS: Dextran sulfate sodium; GI: Gastrointestinal; MRI: Magnetic resonance imaging; MT: Magnetization transfer; QD: Once daily

Funded Through 2023 to Continue Pipeline Progression

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Post Period

Cash at end of period £31.6m
at 31 March 2022

Including $19m in milestones

£34.3m funding

- Strong support from all existing institutional investors
- New specialist investor, Invus
- Priced at market

$5m milestone triggered

Potential future milestones remain available

Current cash £59.7m*

Funds through important clinical data milestones

Supported by top tier Specialist Investors

Redmile Group

SOFINNOVA PARTNERS

POLAR CAPITAL

Platinum ASSET MANAGEMENT

INVUS

AIM (UK) listed Ticker: REDX
Total shares in issue: 333,353,161
Fully diluted: 481,893,777**

* Estimation as at completion of funding on 8 June 2022
** Assuming full conversion of loan notes and exercise of employee share options. Updated 7 June 2022

Financials Reflect Continued Progress Across Pipeline

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Statement of Financial Position, £'000	H1'22	FY'21
Cash	31,583	29,552
Other current assets	4,907	6,263
Non-current assets	3,450	3,730
Total assets	**39,940**	**39,545**
Contract liabilities	11,044	4,318
Other current liabilities	6,277	5,274
Borrowings (non-current)	14,971	14,247
Lease liabilities (non-current)	2,268	2,574
Total liabilities	**34,560**	**26,413**
Net assets	**5,380**	**13,132**

Statement of Comprehensive Income £'000	H1'22	H1'21
Revenue	8,353	2,101
Research & development expenses	(12,913)	(10,463)
General & administrative expenses	(4,905)	(3,797)
Net finance costs	(842)	(999)
Tax credits, operating income & other items	552	443
Total comprehensive loss for period	**(9,755)**	**(12,715)**

H1 2022 Highlights

- **Cash balance -** £31.6m on 31 March 2021 providing cash runway through 2022
- **Increased R&D investment –** £12.9 million (H1 2021: £10.5 million) reflecting the consistent growth and progress of our pipeline
- **Milestone payments from partnerships** - $19 million in cash received from partnered programmes during the period

Post Period Highlights

- **Financing completed in June 2022-** raising £34.3m (gross), further bolsters the cash position and extends cash runway through 2023
- **$5 million milestone –** triggered by Jazz pan-RAF program IND clearance

IND: Investigational new drug application

Significant Potential Clinical Validation Points Expected Over Next 18 Months

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Selective Porcupine Inhibitor (RXC004)

- Data from **Phase 1** combination study with nivolumab (anti-PD1)
- Initiation of PORCUPINE **combination arm** in genetically selected MSS mCRC

Data readout expected to commence H1 2023

Selective ROCK2 Inhibitor (RXC007)

- Initiation of **Phase 2a** study in IPF
- US **IND** application

Topline data readout H2 2023

Discovery Engine

- **RXC008** to commence preclinical **IND** enabling work
- Progress **DDR** inhibitor for fibrosis
- Advance **multiple programmes** in early discovery

RXC008 IND end 2023

Progress three wholly-owned INDs by 2025

DDR: Discoidin Domain Receptor; IND: Investigational New Drug application; IPF: Idiopathic Pulmonary Fibrosis; MSS mCRC: Microsatellite-Stable Metastatic Colorectal Cancer

Redx
Discovering Targeted Medicines

Q&A

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