Redx
Discovering Targeted Medicines

Developing Novel, Targeted Therapeutics for Cancer and Fibrotic Diseases

Corporate Presentation

November 2022

AIM:REDX

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Strong Leadership Team with Extensive Industry Experience

Our ambition:
To create world leading medicines to transform patients' lives

Lisa Anson
CEO

High profile general manager, former President of AstraZeneca UK, with >25 years in biotech and pharma

Dr Richard Armer
CSO

Accomplished drug discovery executive, with >25 years in biotech and pharma

Dr Jane Robertson
CMO

Oncologist with >18 years in biotech and pharma drug development. Led the successful clinical development of Lynparza

Peter Collum
CFO

Experienced finance and strategy executive with >25 years in biopharma

Developing Novel Targeted Medicines for High Unmet Medical Needs

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

Clinical-stage biotech with two Phase 2 assets against compelling clinical targets, and Discovery Engine fuelling pipeline

Porcupine **ROCK**

Experienced scientific team leveraging distinct approach. Track record of consistently generating differentiated drug candidates

5 **clinical molecules discovered**

Backed by blue chip specialist biotech investors. Cash runway into 2024 to deliver multiple value-inflection points

Redmile Group

SOFINNOVA PARTNERS

POLAR CAPITAL

Platinum ASSET MANAGEMENT

INVUS

Validated Discovery Engine Fuels Pipeline

TARGET
Select validated "druggable" targets

- Biologically or clinically validated
- *In vivo* PoC achieved on target / pathway
- High unmet medical need
- Focus on commercially attractive markets
- Clear regulatory path to approval
- Opportunity to be best-in-class

DESIGN
Leverage medicinal chemistry and translational biology

- Apply Redx small molecule design framework using multi-parameter optimisation
- Select chemical start point to develop IP
- Improve on frontrunner e.g.
  - Overcome resistance
  - Improve side-effect profile
  - Fix ADME / PK for dosing or overcome drug-drug interaction (DDI) liability

DELIVER
Strong track record

- Generated 5 clinical molecules including pirtobrutinib
- 1 molecule targeting IND/CTA end 2023
- Targeting 2 additional wholly-owned INDs by 2025
- Deals undertaken with AstraZeneca and Jazz - $48.5m earned since 2019

ADME: Absorption, distribution, metabolism and excretion; IND: Investigational new drug application; PoC: Proof of concept; PK: Pharmacokinetic

Advancing a Robust Pipeline Built In-House

	Target/ Product	Indication(s)	Research	Preclinical	Phase 1	Phase 2	Phase 3	Upcoming Milestones
Oncology	**Porcupine Inhibitor** (RXC004)	Genetically selected MSS mCRC monotherapy + anti-PD-1 combination			PORCUPINE			Topline data – **from H1 2023**
		Genetically selected pancreatic cancer monotherapy Biliary cancer monotherapy + anti-PD-1 combination			PORCUPINE2			
Fibrosis	**ROCK2 Selective Inhibitor** (RXC007)	Idiopathic pulmonary fibrosis (IPF)						Phase 2a topline data – **H2 2023**
	GI-targeted ROCK Inhibitor (RXC008)	Fibrostenotic Crohn's disease						IND/CTA submission – **end 2023**
Discovery Engine	**DDR Inhibitor** (Discoidin Domain Receptor)	Fibrosis, cancer-associated fibrosis						Progress programmes – **target of 2 INDs by 2025**
	Research Targets (Multiple Programmes)	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 Target	Oncology						Progress Jazz collaboration

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

RXC007

RXC007: A Selective ROCK2 Inhibitor for Fibrotic Diseases – Lead Indication is IPF with Phase 2 Data Expected H2 2023

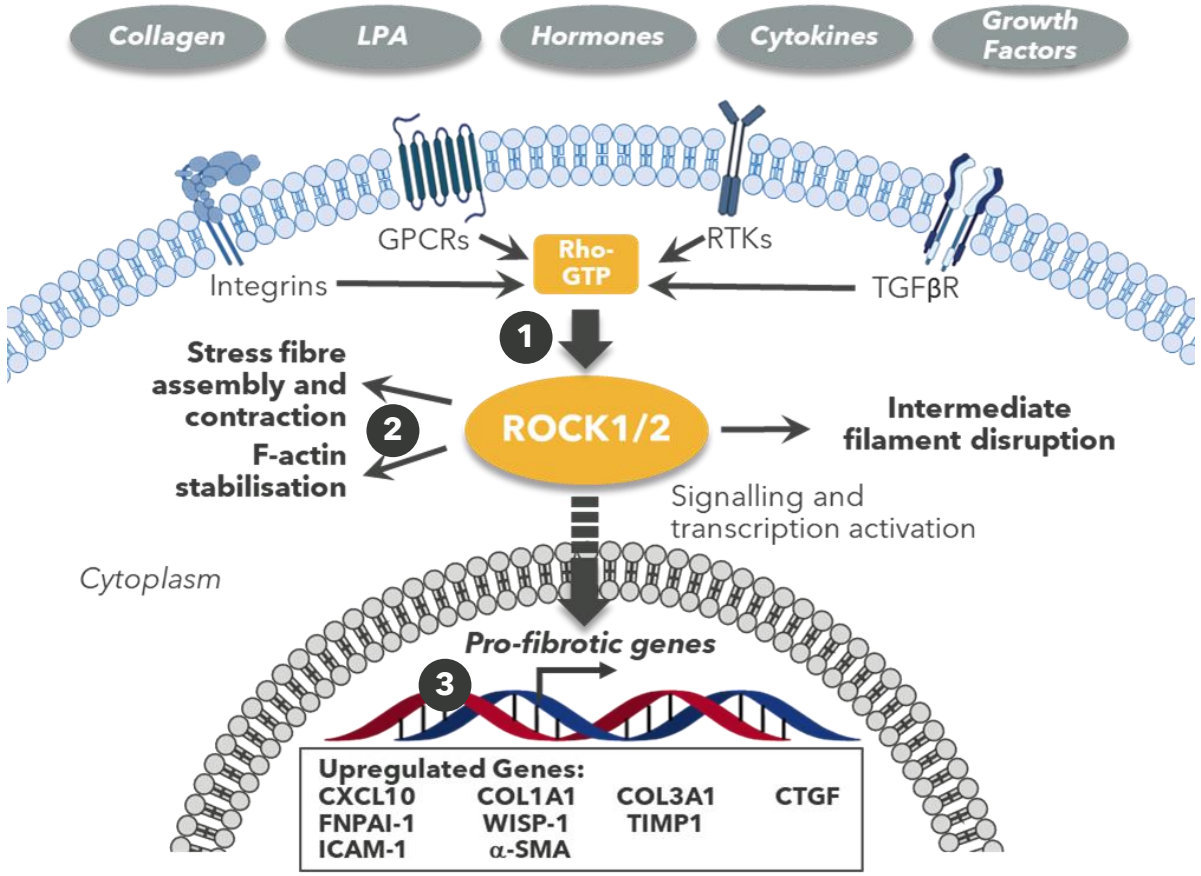
Highlights

- RXC007 is a highly potent, selective and orally-active ROCK2 inhibitor
- ROCK2 is a validated, compelling target at a key junction in cell signalling pathways central to fibrosis
- Robust preclinical efficacy data across disease models supports clinical development plan in lung fibrosis – IPF and CF-ILD
- Phase 1 data in SAD and multi-dose cohorts confirms drug like profile for safety and PK
  - No significant adverse events observed in healthy volunteers and predictable PK profile
- **Phase 2a in IPF, expected to report H2 2023**, is a dose-ranging study to inform Phase 2b dose
  - Initial 12-week Phase 2a study for early efficacy readouts, safety and tolerability in IPF patients +/- SoC, in addition to target and disease biomarker engagement
- Phase 2b planned for RXC007 plus SoC over 12 months with lung function (FVC) as primary endpoint

CF-ILD: Chronic fibrosing interstitial lung disease; FVC: Forced vital capacity; IPF: Idiopathic pulmonary fibrosis; PK: Pharmacokinetic; ROCK: Rho associated protein kinase; SAD: Single ascending dose; SoC: Standard of care

RXC007

ROCK is a Compelling, Nodal Target for Fibrotic Diseases



Why ROCK

1. RhoA/ROCK/ROCK2 downstream of many major profibrotic factors
2. ROCK is involved in diverse cellular processes
3. ROCK upregulates key profibrotic genes. Upregulation of these genes leads to actin cytoskeleton organisation, cell adhesion and motility, proliferation, and extra cellular matrix remodeling

Why ROCK2

- The role of ROCK2 in a diverse range of cellular process allows RXC007 to have pleiotropic effects
- Systemic inhibition of ROCK1&2 results in hypotension, not seen with selective ROCK2 inhibition
- ROCK2 inhibition alone is sufficient to protect from pulmonary fibrosis in mouse models[1]

(1) Knipe, 2018

RXC007

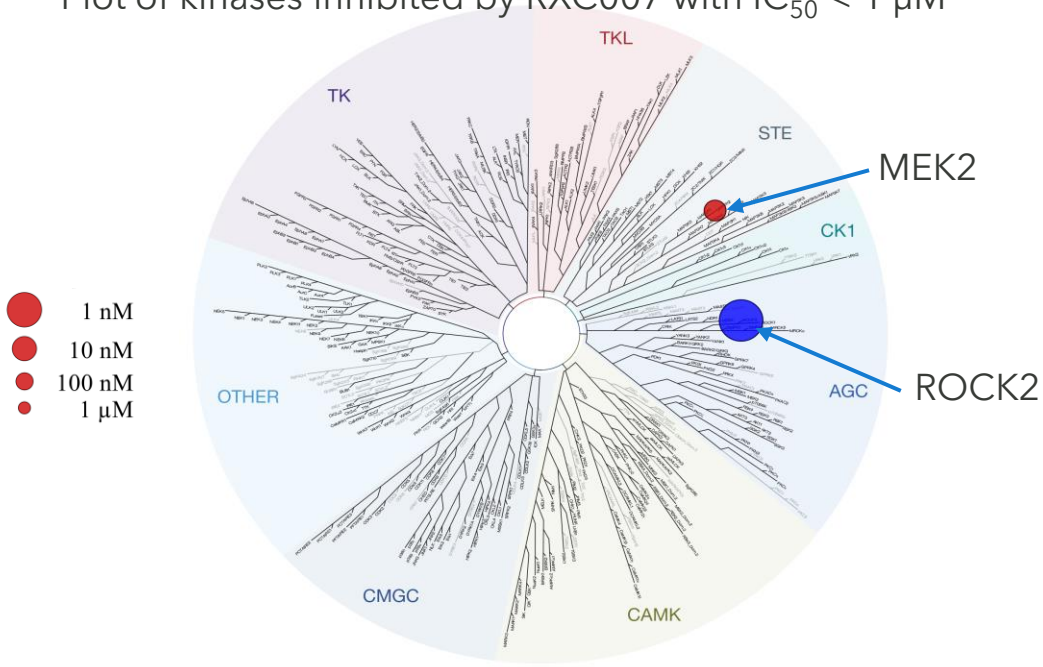
Highly Selective ROCK2 Inhibition Avoids Hypotension and Limits Off-target Toxicity

- Selectively inhibiting ROCK2 has been notoriously challenging
- High target selectivity desirable to limit off target toxicity
- RXC007 is potent and highly selective
  - >100-fold versus ROCK1 in biochemical assays
  - >100-fold selectivity against 468 kinases
- RXC007 Phase 1 in healthy volunteers showed
  - No SAEs
  - All AEs transient, mild and reversible with no dose changes required
  - No evidence of hypotension

Data generated by Redx

RXC007 is highly selective against ROCK1 and other kinases

Plot of kinases inhibited by RXC007 with IC_{50} < 1 µM



- IC_{50} determination at Km ATP of the 20 kinases inhibited with >50% following 468-kinase panel at 10 µM
- Only 2 kinases inhibited at IC_{50} < 1 µM
  - ROCK2 the most potently inhibited kinase (0.004 µM)
  - MEK2 only off-target below 1 µM (0.428 µM)

RXC007

Lung Fibrosis: A Growing Clinical Need with Limited Treatment Options

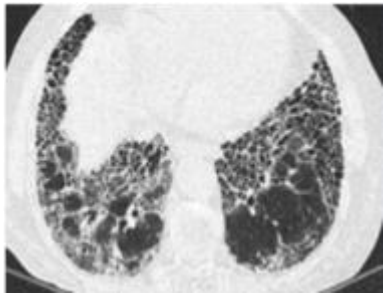
Lead indication is Idiopathic Pulmonary Fibrosis (IPF)

- IPF is a deadly fibrotic lung disease
- Median survival between 3 – 5 years(1)
- High unmet need: over 170,000+ patients in the US, EU5 and Japan alone
- Global IPF market projected to reach $3.6 billion by 2029(2)
- Nintedanib and pirfenidone are the only approved treatments but have significant side effects that limit use

Normal lung

Broader opportunity in Interstitial Lung Disease (ILD)

- IPF represents approx. one third of ILD patients(3)
- Of the two thirds of ILD patients without IPF, up to 40% may develop a progressive fibrosing phenotype(4) (PF-ILD) where new anti-fibrotic treatments are needed
- PF-ILD includes rheumatoid arthritis-ILD (RA-ILD), systemic sclerosis-ILD (SSc-ILD) and mixed connective tissue disease-ILD (mCTD-ILD)
- SSc-ILD market is particularly well-characterized, with this segment alone estimated to surpass $1.1 billion by 2030(5)



Fibrotic lung

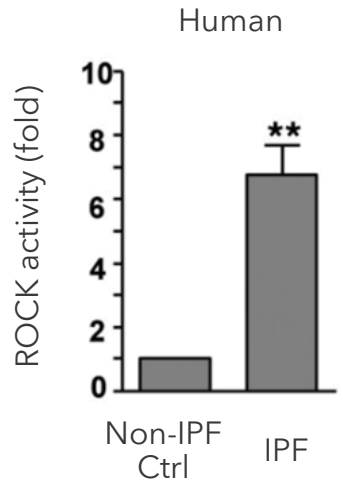
(1); (2) Patient numbers (diagnosed prevalence) & market size forecast data sourced from Global Data (US, EU5, Japan)
(3) Kaul 202Clinical Estimates from Hyun 2015, Ley 2012, Raghu 20061 (4) Olson 2021; (5) Clarivate, Key Findings on Scleroderma (Systemic Sclerosis) Published: September 2021

RXC007

Strong Literature Rationale on ROCK and ROCK2 Supports IPF as a Lead Indication

ROCK as a target in IPF[1]

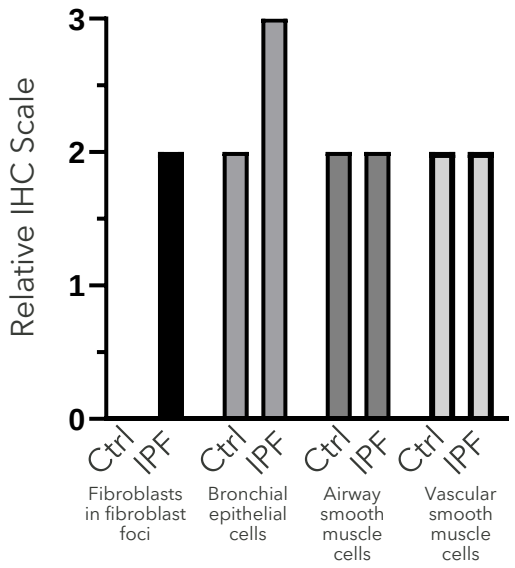
RhoA/ROCK/ROCK2 signalling pathway is upregulated in human IPF patients



(Myo)fibroblasts isolated from lungs of patients with IPF (n = 8), non-IPF control subjects (n = 6) ROCK activity assays using a colorimetric approach. Data are mean ± SD

ROCK2 expression in IPF[2]

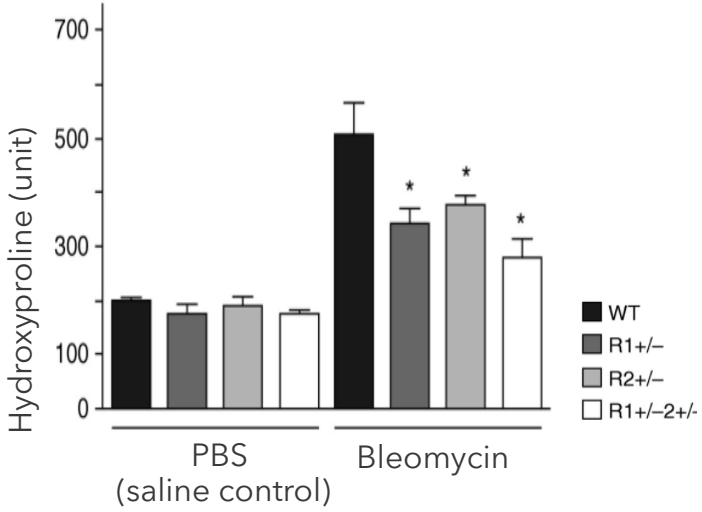
Increased ROCK2 expression in IPF bronchial epithelial cells and fibroblasts



Intensity of immunostaining evaluated on a scale of 0 to 3
N=6 per group; NF: not found

Preclinical validation of selective ROCK2 inhibition[3]

ROCK2+/- knockout mice are protected from bleomycin-induced pulmonary fibrosis



Genetic reduction in either or both ROCK isoforms affords protection from bleomycin-induced pulmonary fibrosis
Significant reduction in hydroxyproline content (lung collagen)

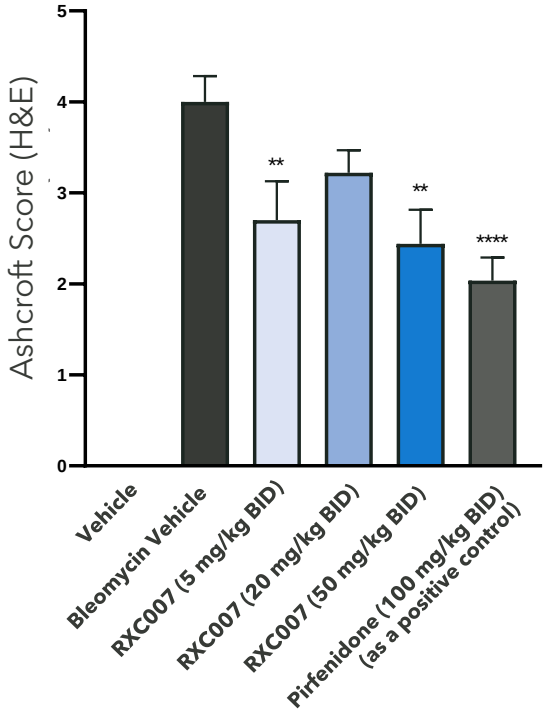
(1) Zhou, 2013; (2) Shimizu, 2014; (3) Knipe, 2018

RXC007

Preclinical Efficacy Data Demonstrates Pleiotropic Effects of Selective ROCK2 Inhibition Supporting IPF as Lead Indication

Therapeutic Murine Bleomycin-induced Lung Fibrosis Model (BLM)

Reduction of collagen deposition

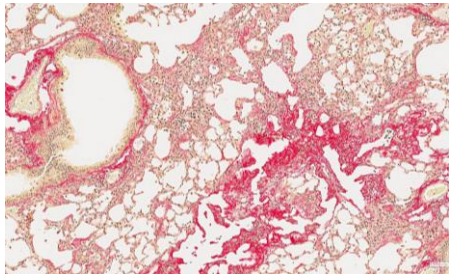


Mouse 21-day therapeutic model (dosing from day 7)
Data generated by Redx

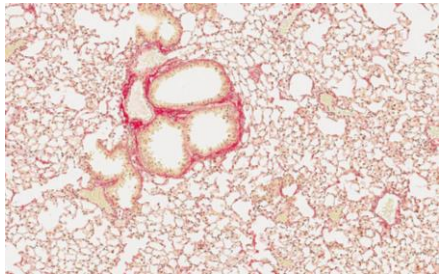
Reduction of fibrosis

Representative images

Lung histology Sirius red

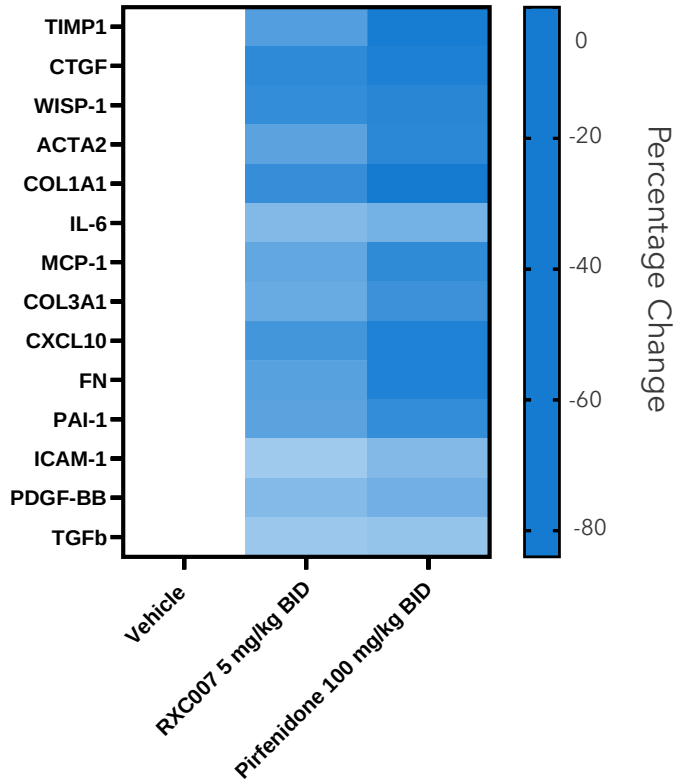


Vehicle



RXC007 50 mg/kg BID

Suppression of the expression of genes strongly associated with fibrosis in IPF



RXC007

RXC007 Modulates Pro-Fibrotic Gene and Protein Expression in *Ex-vivo* Lung Tissue from Patients with Pulmonary Fibrosis

Methodology : Analysis of RXC007 in live IPF tissue samples

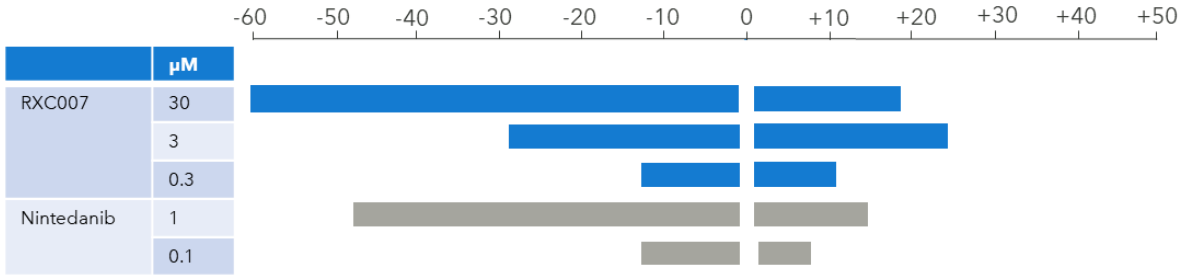
Cores of tissue from 3 resected ILD lungs and cultured *in vitro*

Compound addition to supernatant for 48 hours
- RXC007: 0.3, 3, 30µM
- Nintedanib: 0.1, 1µM

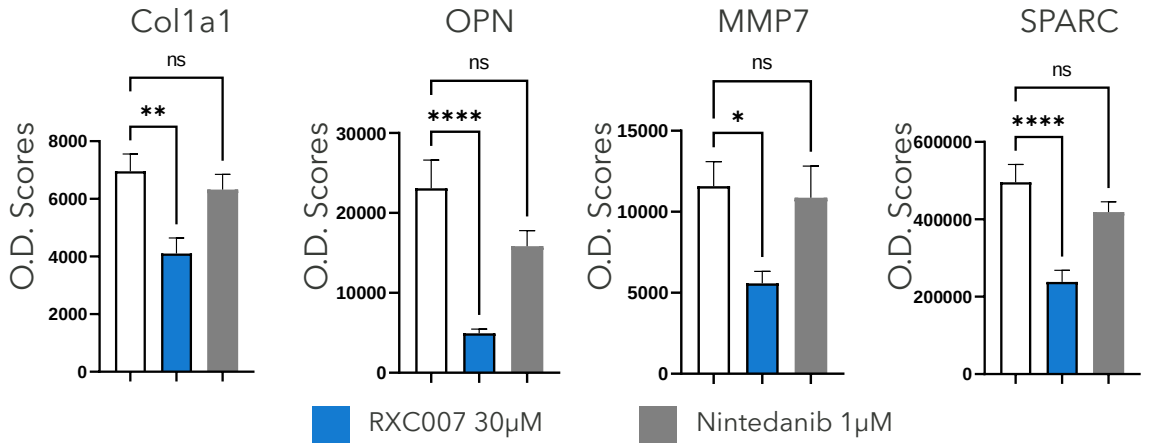
Tissues analysed for pro-fibrotic gene expression
Supernatants analysed for pro-fibrotic proteins
Tissue proven to be live
Compounds shown to be non-toxic

RXC007 modulated inflammation & tissue remodelling gene expression pathways, similar profile to nintedanib

Number of pathways significantly increased or decreased out of 103 measured



RXC007 suppressed expression of pro-fibrotic proteins (examples)



Notes: Gene expression analysis was analysed using KEGG pathway grouping and Z-scores to normalise analysis across donors. RXC007 was shown to suppress expression of 20 out of 24 protein analytes analysed from the supernatant at 30µM but not at 3 or 0.3µM. Nintedanib did not suppress protein analytes at either concentration
Data generated by Redx

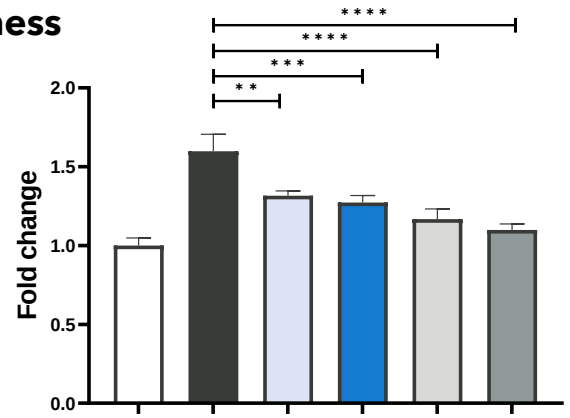
ILD: Interstitial lung disease

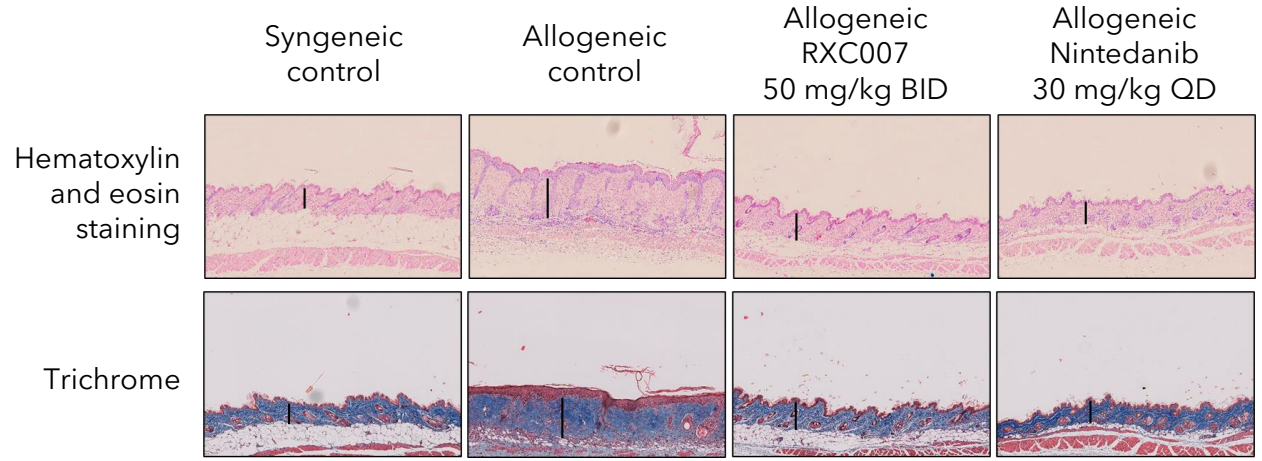
RXC007

Proof-of-Concept Demonstrated in an Immune Mediated Model

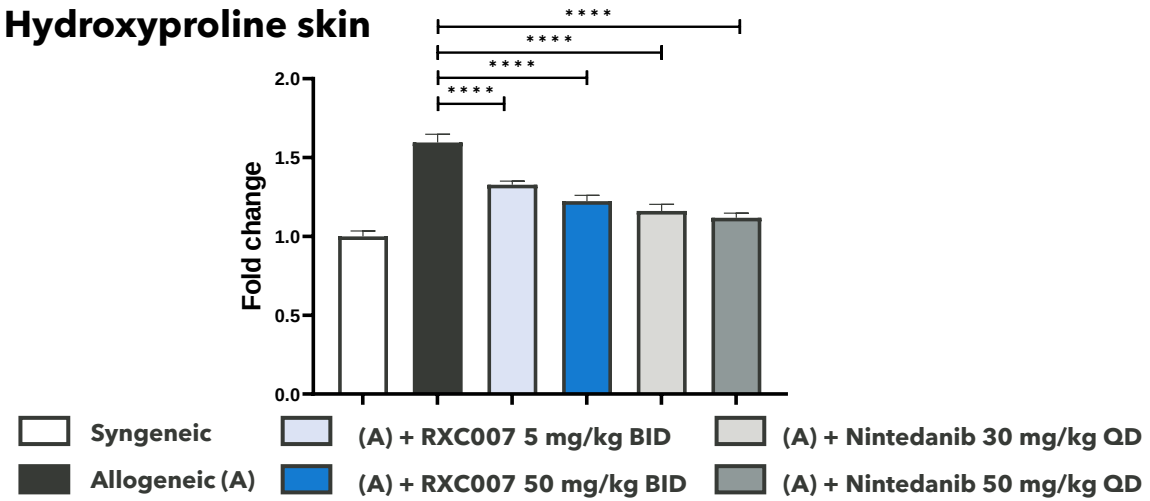
Murine Sclerodermatous chronic Graft versus Host Model

Skin thickness

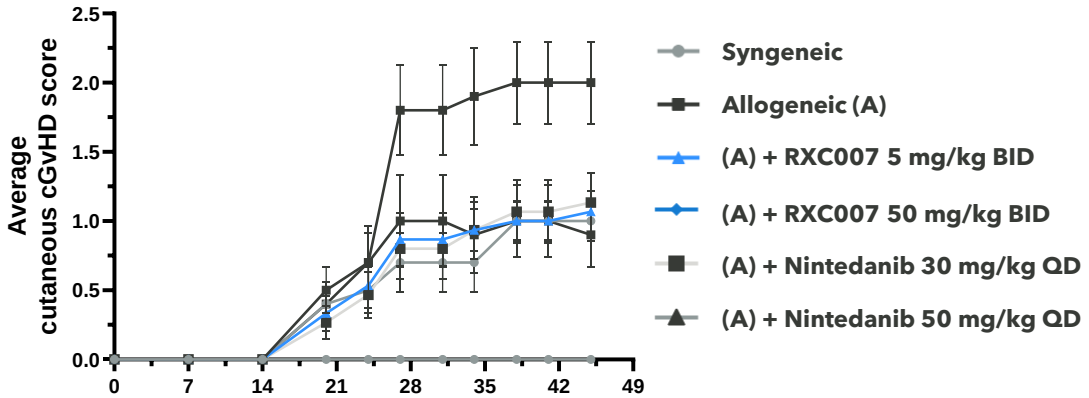




Hydroxyproline skin



Cutaneous cGVHD Score

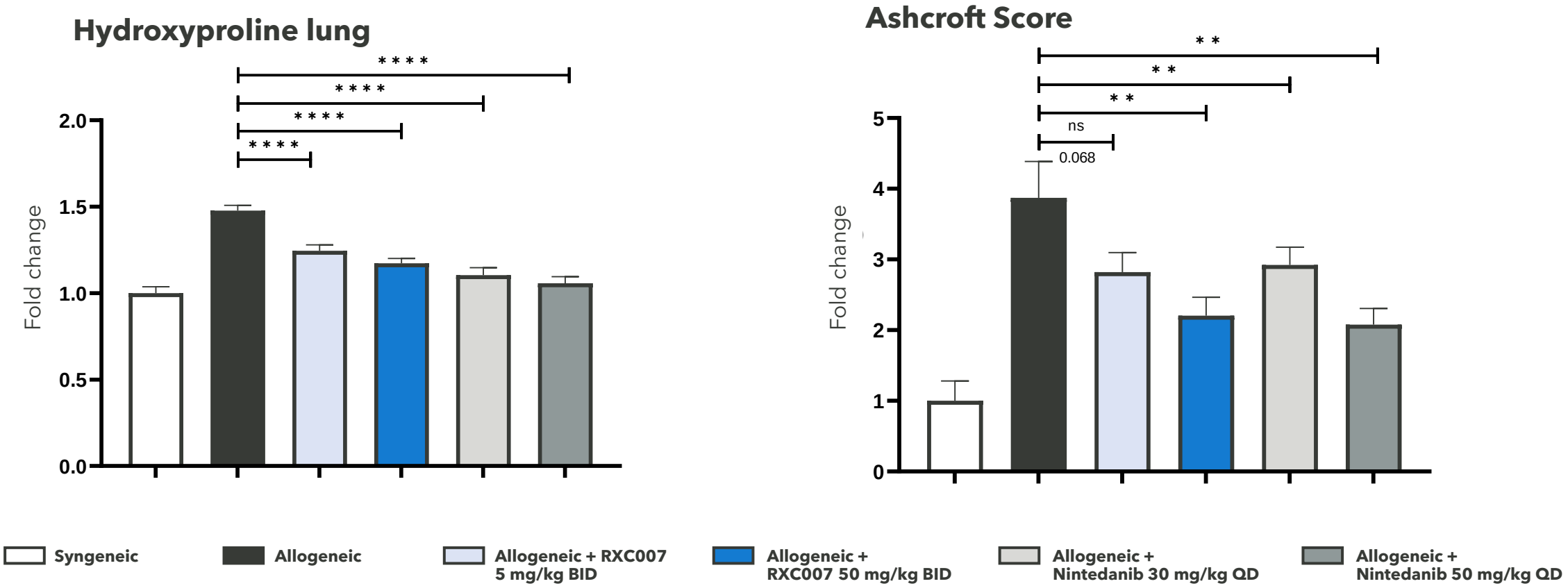


Data generated by Redx, as presented at ICLAF 2022

RXC007

Significant Reduction of Fibrosis Score and Collagen Content in the Lungs Supports Broader Development in Lung Fibrosis

Murine Sclerodermatous chronic Graft versus Host Model

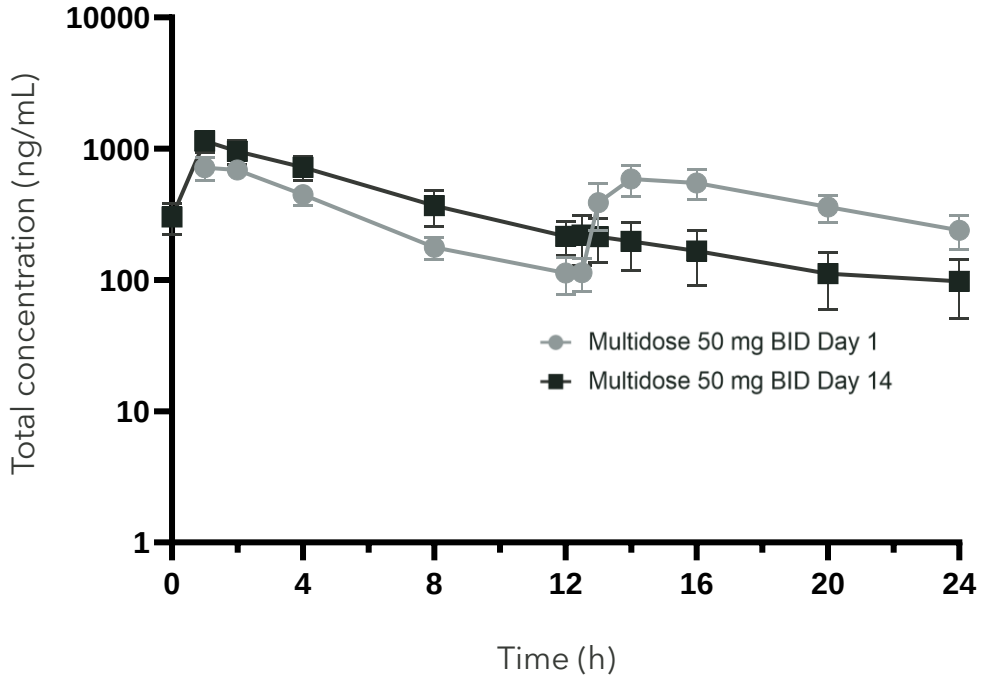


Data generated by Redx, as presented at ICLAF 2022

RXC007

Phase 1 Data in Healthy Volunteers Showed Good Safety and Pharmacokinetic Profile

Multidose cohort 50 mg BID - total plasma concentration over time



Good safety profile

- No SAEs reported in SAD and multidose cohorts
- Safe and well tolerated with few treatment emergent adverse evens reported
- All AEs transient, mild and reversible with no dose changes required
- No evidence of hypotension, validating rationale for selective ROCK2 inhibition

Drug-like pharmacokinetic profile

- Pharmacokinetics as predicted from preclinical data
- Mean half-life 9–11 hours, potentially suitable for once-daily dosing
- Essentially linear exposure in SAD from 2 mg QD to 70 mg BID
- No significant differences between 50 mg fed and fasted cohorts
- Achieved biologically relevant exposures from 20 mg BID and above based on preclinical models

PK sampling up to 72 h; only 0-24 h plotted
Data generated by Redx, as presented at ICLAF 2022

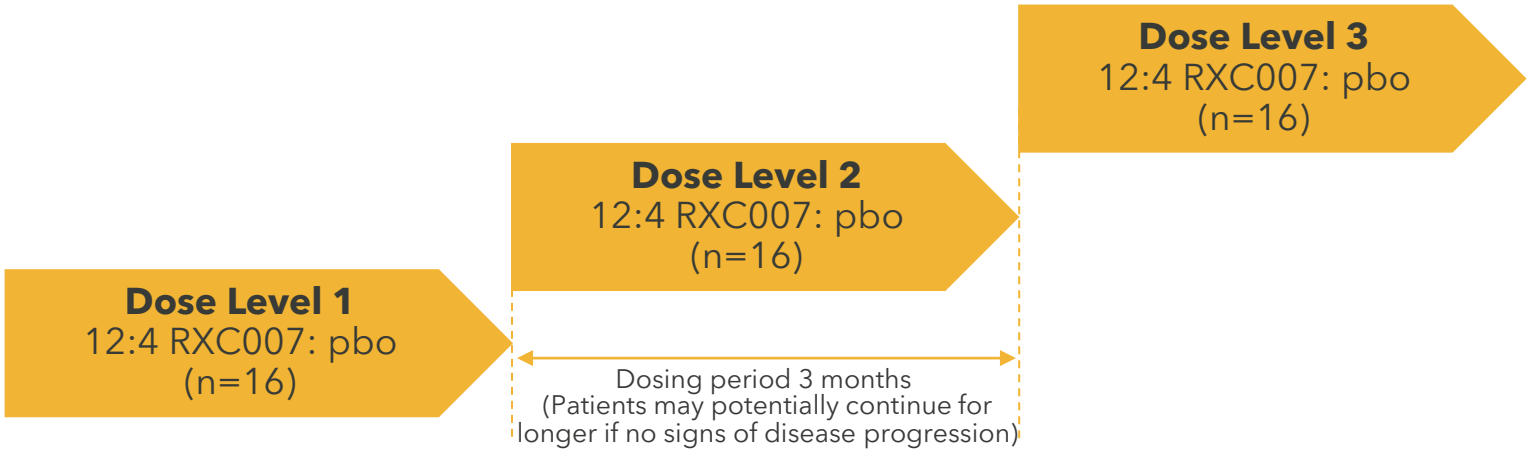
BID: Twice daily; QD: Once daily; SAD: Single ascending dose; SAE: Serious adverse event

RXC007

Phase 2 Programme in IPF Expected to Report H2 2023

Phase 2a dose ranging study to inform Phase 2b dose

Provides early efficacy readouts, safety and tolerability in IPF patients with or without standard IPF therapy



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

Translational Science Sub-Study to evaluate target and disease marker engagement

Cohort 1
8 patients

Cohort 2
8 patients

Endpoints include:

- Changes from baseline in blood biomarkers
- Proteins and genes from broncho-alveolar lavage (BAL) fluid
- BAL-fluid cells and bronchial epithelial cells

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

RXC004

RXC004: Clinically Validated Porcupine Inhibitor in Phase 2

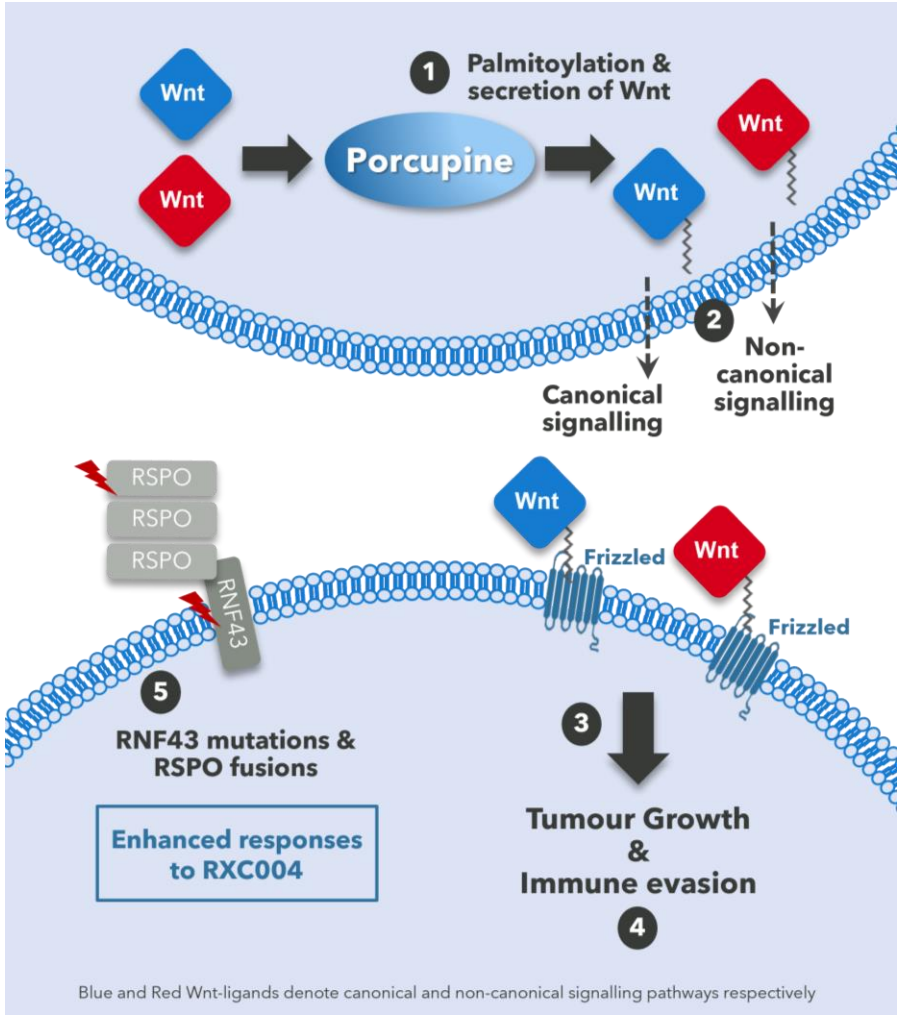
Highlights

- RXC004 is a highly potent, orally active, once daily Porcupine inhibitor
- Porcupine inhibition blocks secretion of all Wnt ligands, preventing both tumour growth and immune evasion
- RXC004 demonstrated clinical target engagement at all doses and has optimal PK profile with once daily, oral dosing
- RXC004 was well tolerated in Phase 1, both monotherapy and in combination with nivolumab, and achieved exposures clinically that demonstrated efficacy in pre-clinical models
- RXC004 demonstrated differential clinical efficacy in Wnt-ligand dependent tumours in Phase 1 monotherapy cohort (ESMO 2021)
- Combination with anti-PD-1 treatment could open new patient segments e.g. MSS mCRC, and anti-PD-1 resistant patients
- Recruitment ongoing, Phase 2 programme in Wnt-ligand dependent tumours – **data expected from H1 2023**
  - In genetically selected Wnt-ligand driven tumours, monotherapy and anti-PD-1 combination settings
  - In tumours with high Wnt-ligand expression, monotherapy and anti-PD-1 combination settings
  - Phase 2 dose selected for monotherapy 2 mg, and 1.5mg in combination with anti-PD-1
  - Media reported single biliary cancer patient partial response at six months

RXC004

Porcupine Inhibition Targets Wnt-Ligand Dependent Tumours

Wnt signalling pathway is well established as a critical driver of cancer



1. Porcupine is a key enzyme upstream in the Wnt pathway, which adds a lipid chain to all 19 Wnt ligands (palmitoylation) enabling secretion

2. Wnt ligands activate both canonical and non-canonical signalling pathways

3. Canonical and non-canonical target genes drive tumour growth and tumour immune evasion

4. By inhibiting Porcupine, RXC004 blocks the release of all Wnt ligands from cells **inhibiting tumour growth** and **reversing immune evasion**

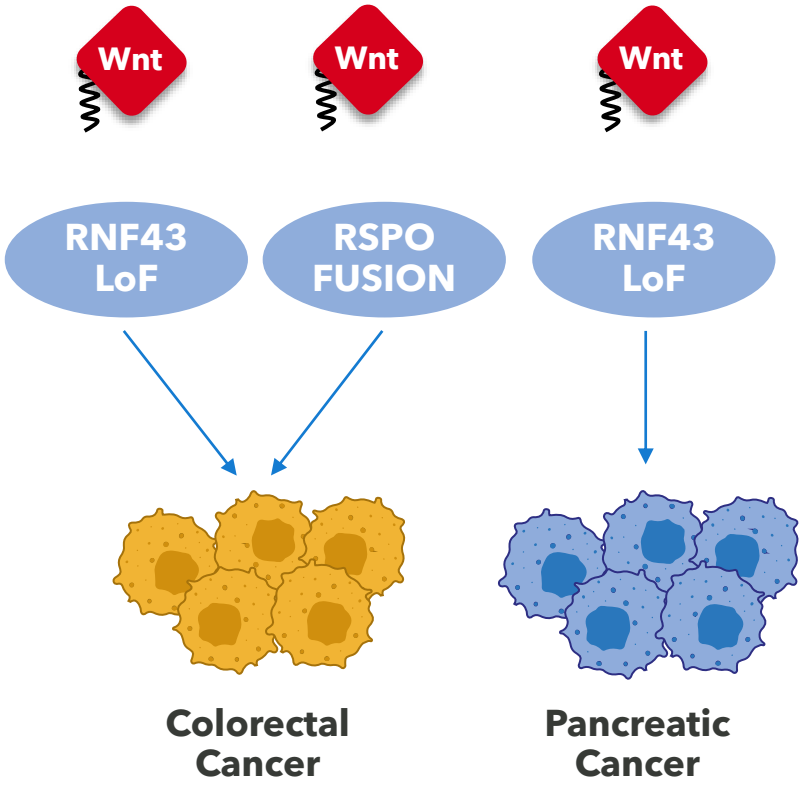
5. Targeting Wnt-ligand dependent tumours provides a clear **patient selection strategy**. Tumours with RSPO fusion or RNF43 mutations see upregulation of the Wnt pathway (increased number of frizzled receptors, through impaired degradation). Beyond genetic mutations, some other tumours display elevated Wnt-ligand expression

RNF43: Ring finger protein 43; RSPO: R-spondin; Wnt: Wingless/integrated

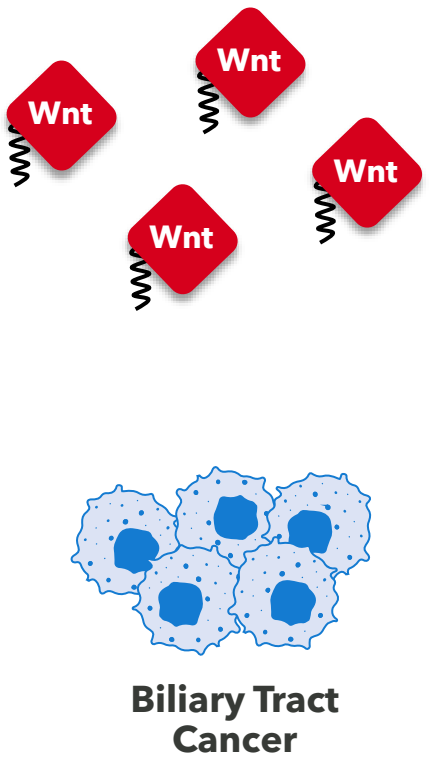
RXC004

Patient Selection Strategy: Wnt-Ligands can Drive Growth and Immune Evasion in the Tumour Microenvironment

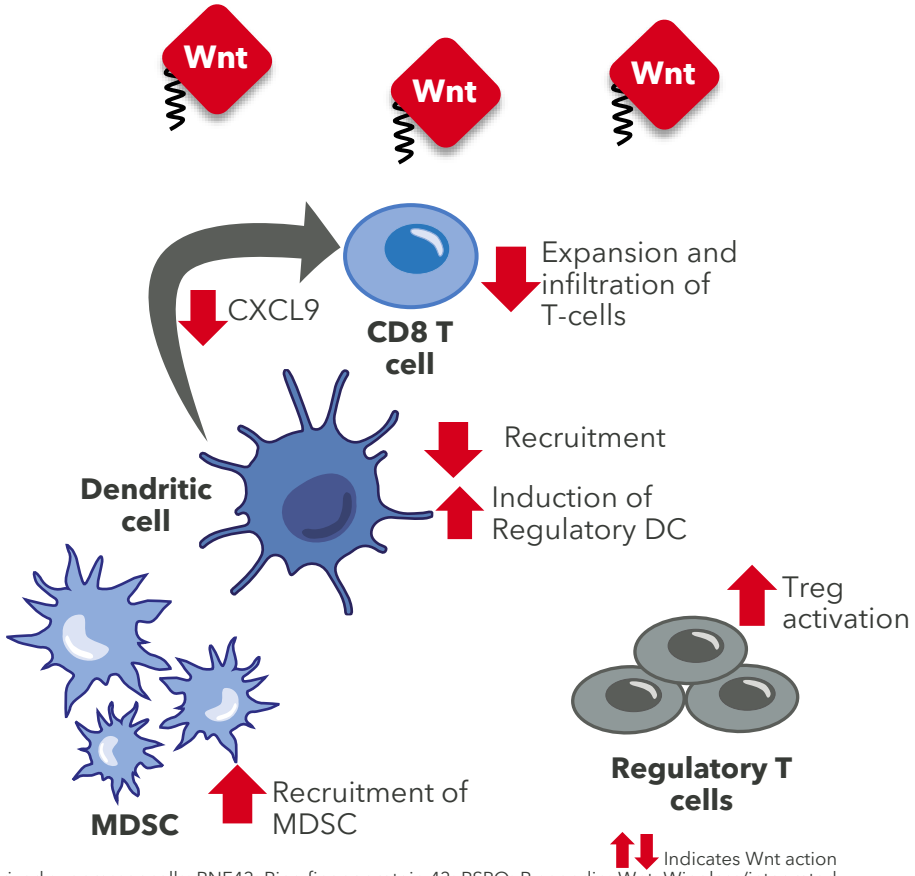
Genetic aberrations lead to Wnt-ligand driven tumour growth



Wnt-ligand expression can drive tumour growth



Wnt-ligands negatively impact immune cell function, resulting in immune evasion and cold tumours

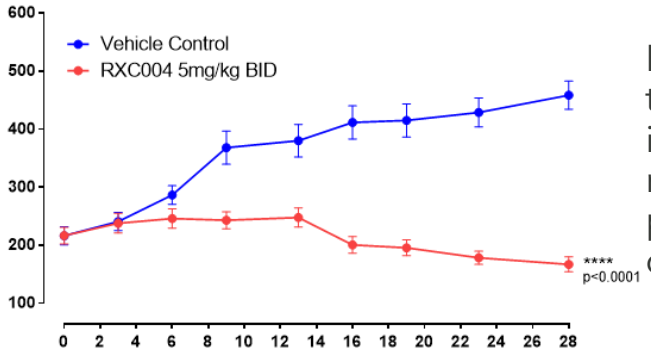


MDSC: Myeloid-derived suppressor cells; RNF43: Ring finger protein 43; RSPO: R-spondin; Wnt: Wingless/integrated

RXC004

Dual Mechanism of Action Demonstrated Preclinically

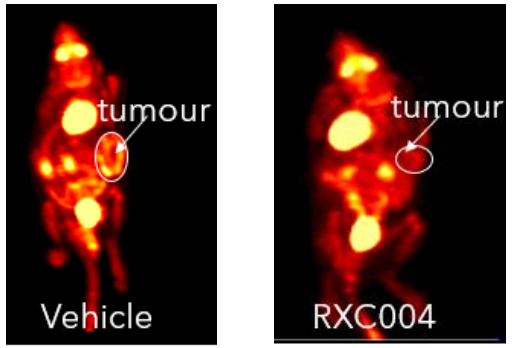
Inhibits tumour cell proliferation



RXC004 inhibits tumour growth in an RNF43 mutant human pancreatic cancer model

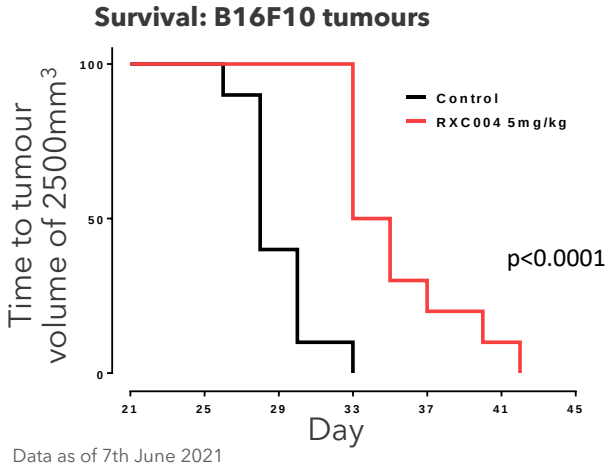
DIRECTLY TARGETS TUMOUR CELL GROWTH

Alters tumour cell metabolism



RXC004 treated tumour cells are less metabolically active. Cells also change morphology and increase mucous secretion

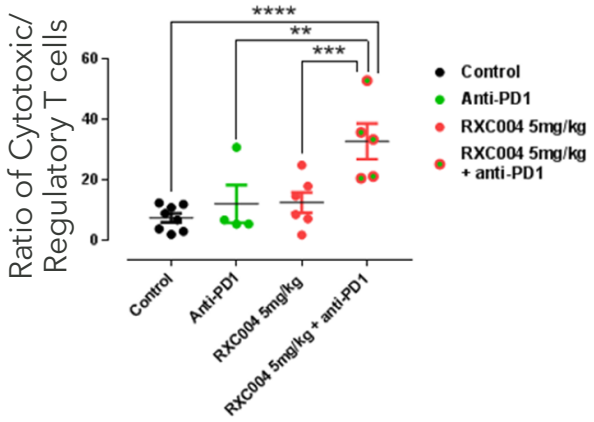
As a monotherapy



Increased survival rate post-RXC004 monotherapy treatment in an anti-PD-1 resistant 'cold' mouse melanoma syngeneic model (B16F10)

REVERSES WNT PATHWAY INDUCED IMMUNE EVASION

In combination with anti-PD-1



Combination of RXC004 + anti-PD-1 showed a statistically relevant change in ratio of Cytotoxic T cells: Regulatory T cells, compared to either monotherapy alone in PD(L)-1 axis dominated CT26 CRC model

Data as of 7th June 2021
Source: Redx posters, https://aacrjournals.org/cancerrescommun/article/2/9/914/708958/The-Wnt-Pathway-Inhibitor-RXC004-Blocks-Tumor

CRC: Colorectal cancer; RSPO: R-Spondin

RXC004

High Unmet Need in Hard-to-Treat Wnt-Ligand Dependent Tumours

Wnt-ligand dependence mechanism	Tumour	5-year survival rate[1]	Prevalence of Wnt-ligand dependence	Annual Wnt-ligand dependence incidence[6]	Approach being tested in Ph2	
					Monotherapy	anti-PD-1 Combo
Wnt-ligand driven	MSS mCRC	14%	8% RNF43 mutation & RSPO fusion[2][3]	14,000 patients	✓	✓
	Pancreatic	3%	7% RNF43 mutation[4]	9,000 patients	✓	✗
Wnt-ligand expressed	Biliary	2%	70% Wnt-ligand expression[5]	51,000 patients	✓	✓

LCM potential in multiple additional tumours

Monotherapy – opportunity to pursue a tumor agnostic approach - RNF43 mutations and RSPO fusions also detected in MSI-H mCRC, CRPC and squamous NSCLC

Combination – opportunity to target any anti-PD-1 resistant tumour with high Wnt-ligand expression (~28 tumour types)

(1) www.cancer.net (2) 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. (3) 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; (4) Witkiewicz 2015; (5) Loilome et al. 2014, Boulter et al. 2015; (6) Incidence data sourced from GlobalData Epidemiology data (Major Markets: US, EU5, Japan, China)

RXC004

RXC004 was Safe and Well Tolerated in Monotherapy and in Combination with anti PD-1 at Phase 2 Doses

Phase 1 Study Data	1.0mg monotherapy N=3	1.0mg nivo combination N=5	1.5mg monotherapy N=7	Phase 2 doses: 1.5mg nivo combination N=8	Phase 2 doses: 2.0mg monotherapy N=6	3.0mg monotherapy N=4	TOTAL N=33*
Any TRAEs*	3 (100)	5 (100)	5 (71)	8 (100)	5 (83)	4 (100)	**30 (91)**
Fatigue	1 (33)	2 (40)	4 (57)	3 (38)	3 (50)	2 (50)	**15 (45)**
Nausea	2 (67)	2 (40)	3 (43)	4 (50)	1 (17)	3 (75)	**15 (45)**
Dysgeusia	0 (0)	1 (20)	2 (29)	4 (50)	4 (67)	3 (75)	**14 (41)**
Decreased appetite	1 (33)	1 (20)	2 (29)	3 (38)	2 (33)	3 (75)	**12 (36)**

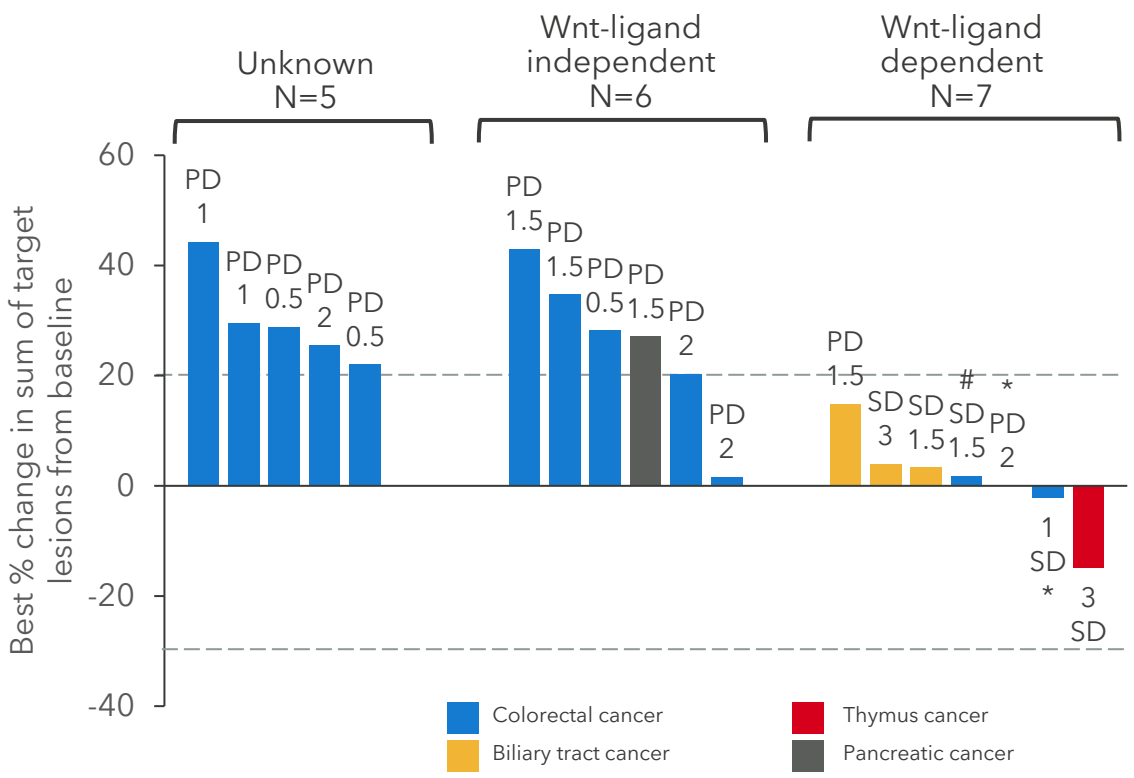
- The recommended Phase 2 dose of RXC004 is 2mg in monotherapy
- Both RXC004 1.0mg and 1.5mg doses were safe and tolerable in combination with nivolumab
  - RXC004 doses higher than 1.5mg were not explored in Module 2 because of the potential for overlapping toxicity of colitis, which was reported in RXC004 monotherapy Module 1 and is a known adverse effect of immune checkpoint inhibitors.

TRAE: Treatment related adverse event

RXC004

Phase 1 Clinical Efficacy Data Supports Development in Wnt-Ligand Dependent Tumours

Phase 1 Monotherapy All Comers Study Clinical Activity by Wnt-Ligand Dependence†



Numbers= dose in mg
† Study was in unselected patients; retrospective analysis
* RNF43 LoF mutation # RSPO Fusion
Data generated by Redx: Monotherapy Data cut-off date 30 July 2021, as presented at ESMO 2021; Combination Data Cut off 18 Oct 2022, as presented at SITC 2022

Phase 1 monotherapy efficacy data

18/25 monotherapy patients had RECIST-evaluable disease

5/7 patients with Wnt-ligand dependent tumours achieved 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

Phase 1 combination efficacy data

10/13 patients had RECIST evaluable disease

- 4/6 patients with unselected tumours in the 1.5mg cohort had RECIST stable disease as best response

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

RXC004

Phase 2 Programme in Wnt-Ligand Dependent Tumours Expected to Deliver Topline Data During 2023

	PORCUPINE – MSS Metastatic Colorectal Cancer		PORCUPINE2 – Pancreatic and Biliary Cancer		
	Monotherapy Genetically Selected (n=20)	Combination Genetically Selected RXC004 + anti-PD-1 (n=20)	Monotherapy Genetically Selected Pancreatic Cancer (n=15)	Monotherapy Biliary Cancer (n=15)	Combination Biliary Cancer RXC004 + anti-PD-1 (n=15)
Endpoints	**DCR** Secondary Tumour size change, ORR, DoR, PFS	**ORR** Secondary DCR, Tumour size change, DoR, PFS	**PFS at 6 months** Secondary – DCR, OS, ORR, DoR and % change in sum of target lesions		**ORR** Secondary DCR, Tumour size change, DoR, PFS
Topline data expected	**H2 2023**	**H2 2023**	**H2 2023**	**H1 2023**	**H2 2023**

Analysis

Key translational endpoints will characterise mechanism of action

- FDG-PET scans to assess metabolic effect of RXC004 on tumours
- Tracking circulating tumour DNA (ctDNA)
- Baseline and on-treatment biopsies to assess changes to tumour and immune microenvironment

DCR: Disease control rate; DoR: Duration of response; ORR: Overall response rate; OS: Overall survival; PFS: Progression free survival

RXC008

RXC008: GI-targeted ROCK Inhibitor for Fibrostenotic Crohn's Disease Planned to Enter Phase 1 Clinical Trial End 2023

Highlights

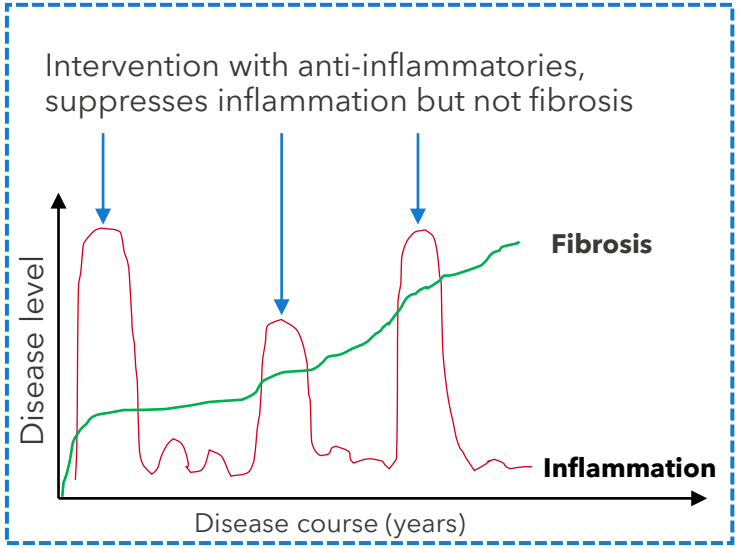
- RXC008 is a potent, oral, small molecule non-systemic ROCK 1/2 inhibitor
- Fibrostenotic Crohn's disease is a significant unmet need - only treatment option for patients is successive surgical intervention
- RXC008 is a potential first-in class treatment - no approved therapies for underlying fibrosis and no curative treatments available
- ROCK is a key target involved in fibroblast activation, and is upregulated in fibrostenosis in Crohn's disease
- RXC008 is GI-targeted, selectively active in gut without risking systemic exposure
- RXC008 has demonstrated robust preclinical efficacy *in vivo*
- IND enabling work underway - **Phase 1 start planned for end 2023**

GI: Gastrointestinal; IND: Investigational new drug application; ROCK: Rho associated protein kinase;

RXC008

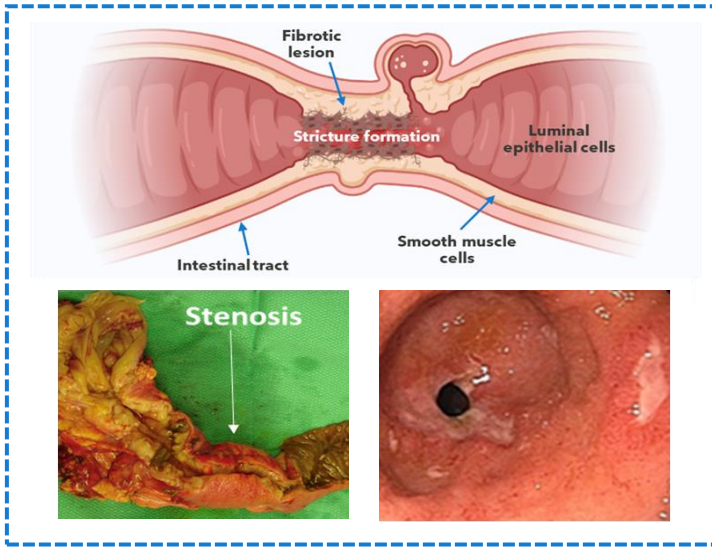
Potential First-in-Class Treatment for Fibrostenotic Crohn's Disease

Clinical progression in Crohn's



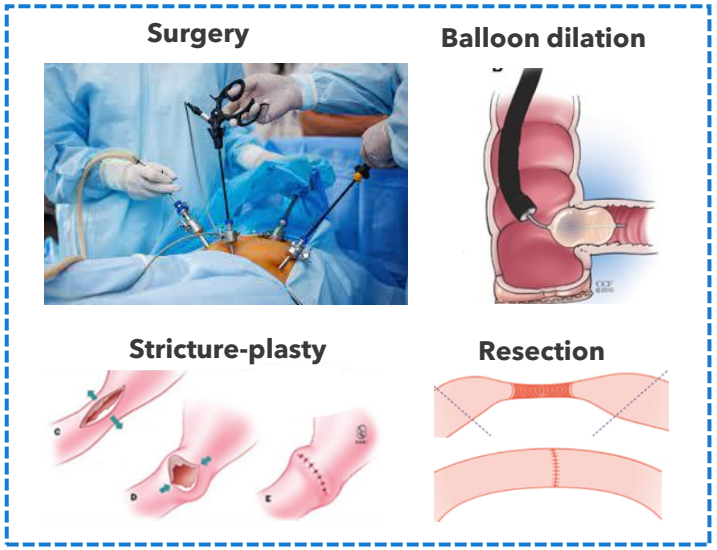
1.7 million(1) patients globally affected by Crohn's disease

Fibrotic stricture formation



>50% of patients(2) develop fibrostenosis and strictures within 10 years of first diagnosis

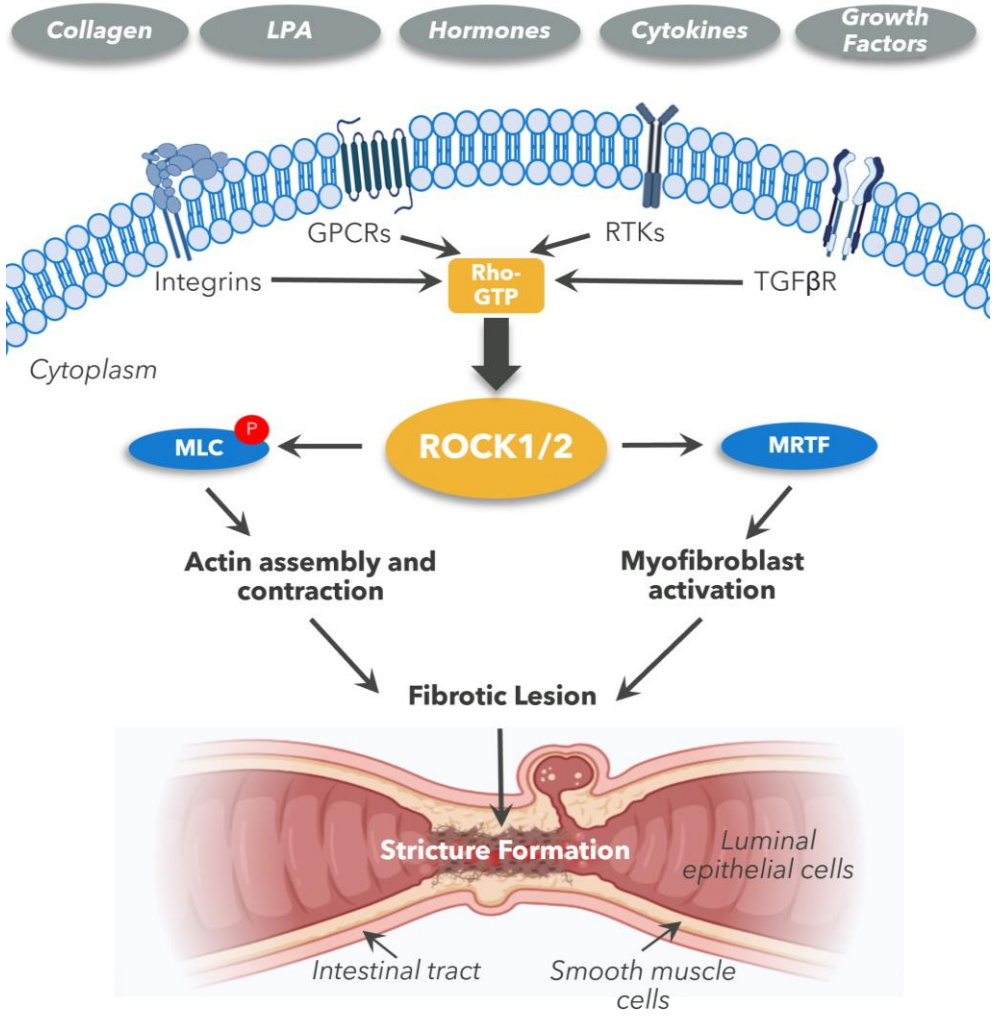
Surgical interventions



No approved therapies for underlying fibrosis only treatment options are debilitating surgical intervention

(1) Clarivate, Crohn's disease disease landscape & forecast pg 39, Published Sep 2022; (2) Chan et al, 2018

RXC008: GI-targeted pan-ROCK Inhibitor Targets a Fibrotic Pathway Nodal Point without Systemic Breakthrough



- ROCK is a nodal point in the fibrotic signalling pathway
- Inhibiting ROCK 1&2 systemically is known to result in hypotension
- GITR inhibitors are specifically designed to avoid hypotensive effects associated with systemic ROCK inhibition
- RXC008 designed to be retained in the GI tract via high efflux and low permeability, rapidly metabolised by paraoxonase enzymes in the plasma
- Result of this is virtually no systemic breakthrough

GI: Gastrointestinal; GITR: Gastrointestinal targeted ROCK; MRTF: myocardin-related transcription factor; MLC: myosin light chain

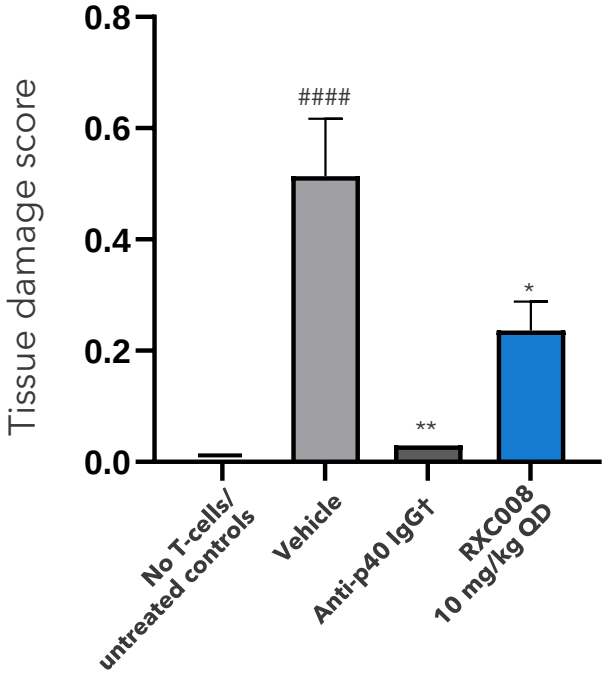
RXC008

RXC008 Reduces Fibrosis in the Adoptive T-cell Transfer Model

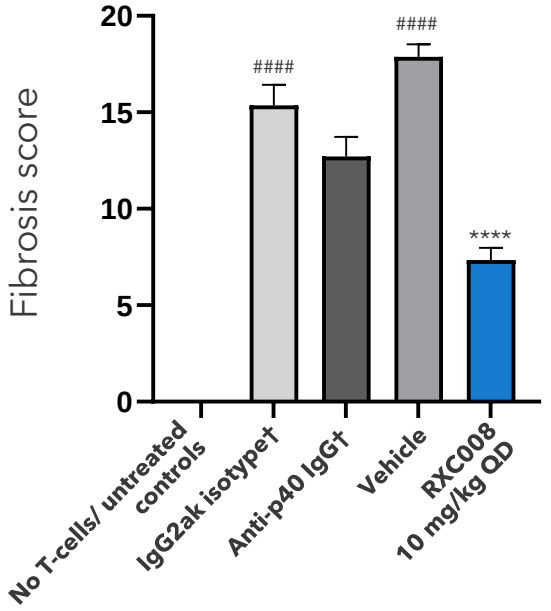
45-day Adoptive T-cell transfer model of Crohn's disease

(with therapeutic oral compound administration from day 14)

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.

Data generated by Redx

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

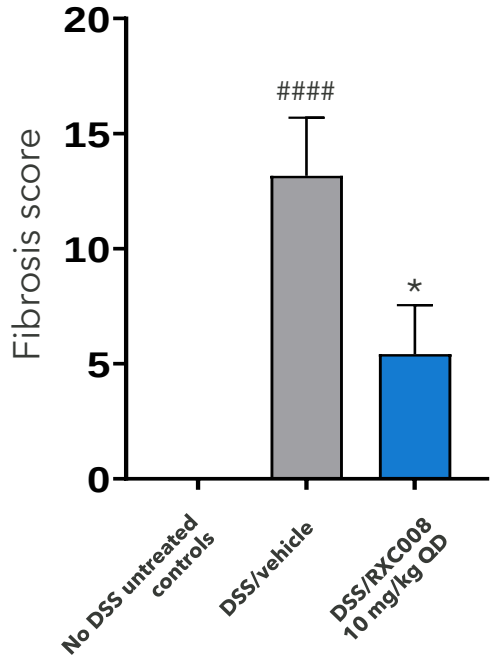
RXC008

RXC008 Reduces Fibrosis in a Translational Model

Chronic DSS GI fibrosis model*

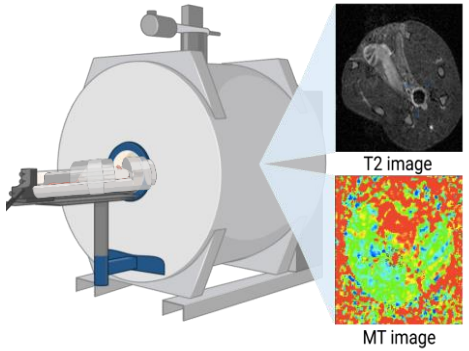
(RXC008 dosed orally, prophylactically for 9 weeks)

Reduction in fibrosis measured by histology



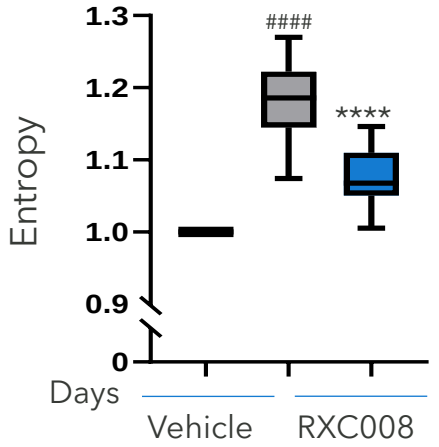
Reduction in fibrosis measured by MRI

Analysis using MT imaging



Murine sized MRI scanner

Entropy fibrosis score



*Research in collaboration with Ghent University
1-way Anova with Dunnet's multiple comparison, # Vehicle day 0 v day 61 * vehicle day 61 v RXC008 day 61
Data generated by Redx

DSS: Dextran sulfate sodium; MT: Magnetization transfer; QD: Once daily

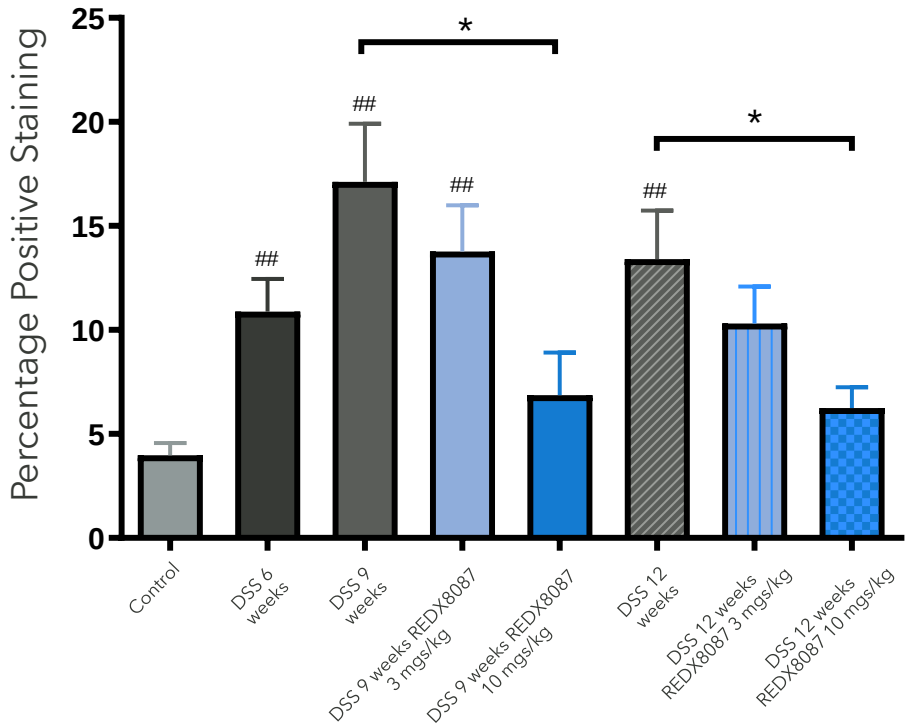
RXC008

ROCK Inhibition Potently Suppressed or Reversed Fibrosis in Preclinical GI Models

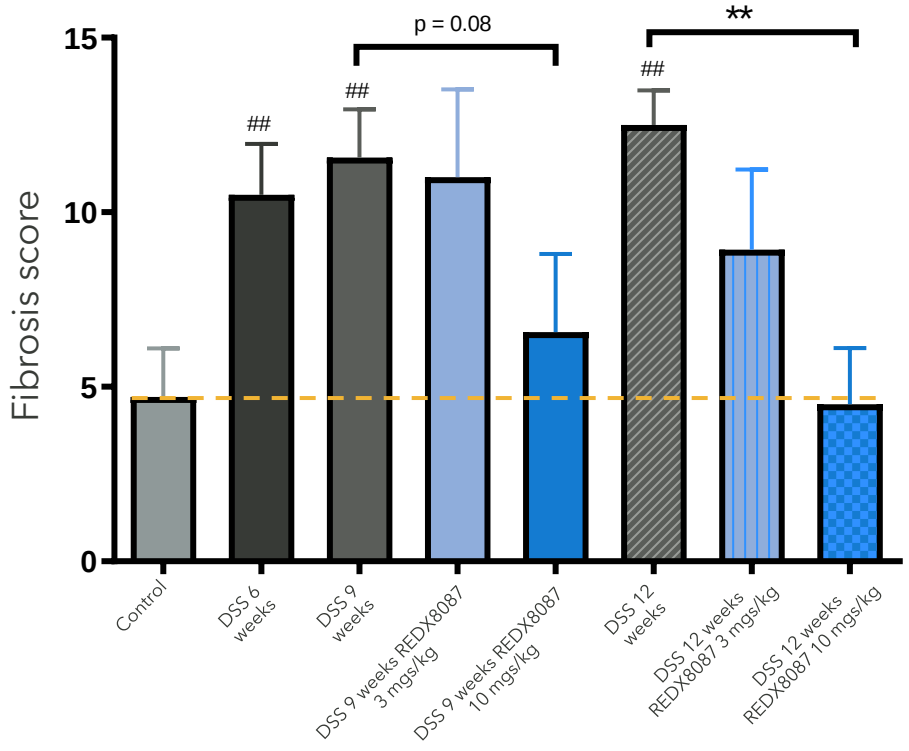
GITR inhibition was able to reverse fibrosis in a therapeutic 12-week DSS model

(Compound administered orally once a day from week 6 when fibrosis established)

αSMA



Trichrome staining



Data generated by Redx, REDX8087 is similar to RXC008

DSS: Dextran sulfate sodium

Redx is Funded into 2024 to Deliver Significant Pipeline Progression

Recent Financing

£34.3m fundraise June 2022

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

Milestone Payments

$24m milestones earned during FY 2022

Potential future milestones remain available

Cash Runway

£60m* in cash

Funds into 2024, enabling delivery of key phase 2 clinical data milestones

Top Tier Specialist Investors

Redmile Group
POLAR CAPITAL
Platinum ASSET MANAGEMENT
SOFINNOVA PARTNERS
INVUS

AIM (UK) listed Ticker: REDX
Total shares in issue: 334,911,458
Fully diluted: 482,210,019**

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

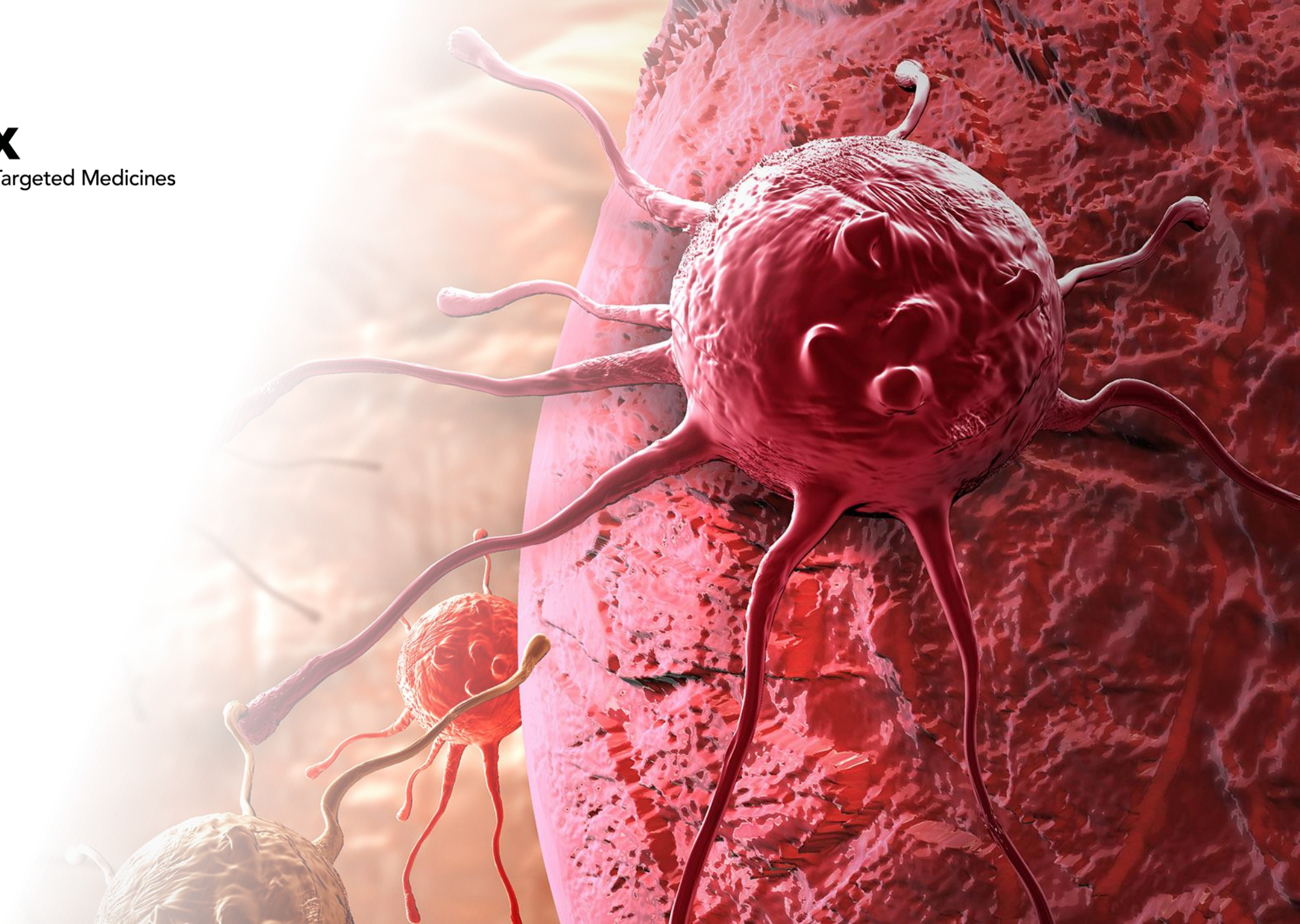
Multiple Potential Milestones During 2022 and 2023

	2022 (CY)	2023 (CY)
Porcupine Inhibitor (RXC004)	✓ Data from Phase 1 combination study with nivolumab (anti-PD-1) ✓ Initiation of PORCUPINE2 monotherapy Phase 2 study in genetically selected pancreatic and biliary cancer ✓ Initiation of anti-PD-1 combination arms	**Ph2 data - from H1 2023** PORCUPINE • **H2** mono & combination - MSS mCRC PORCUPINE2 • **H1** monotherapy - biliary • **H2** combination - biliary • **H2** monotherapy - pancreatic
ROCK2 Selective Inhibitor (RXC007)	✓ **H1** Data from Phase 1 healthy volunteer study ✓ Initiation of Phase 2a study in IPF • **H2** US IND	**H2** Phase 2a topline data read out
GI-targeted ROCK Inhibitor (RXC008)	✓ **H1** Select development candidate	IND/CTA submission – **end 2023**
DDR Inhibitor (Discoidin Domain Receptor) **Research Targets**	• Progress DDR inhibitor for fibrosis • Advance multiple programmes in early discovery	Progress target of two additional wholly-owned INDs by 2025
Porcupine Inhibitor (RXC006/AZD5055) **Pan-RAF Inhibitor** (JZP815) **MAPK Pathway Target**	✓ IND cleared triggering $5m June 2022	Redx remains eligible for regulatory and development milestones

CY: Calendar year; CTA: Clinical trial application

Redx
Discovering Targeted Medicines

Appendix



RXC004

Monotherapy is Safe and Well Tolerated at Phase 2 Recommended Dose

Number of Patients (%)	0.5mg cohort N=4	1.0mg cohort N=3	1.5mg cohort N=7	Phase 2 dose 2.0mg cohort N=6	3.0mg cohort N=4	10.0mg cohort N=1	TOTAL N=25
Any TRAEs*	4 (100)	3 (100)	5 (71)	5 (83)	4 (100)	1 (100)	**22 (88)**
Fatigue	2 (50)	1 (33)	4 (57)	3 (50)	2 (50)	1 (100)	**13 (52)**
Nausea	1 (25)	2 (67)	3 (43)	1 (17)	3 (75)	1 (100)	**11 (44)**
Decreased appetite	1 (25)	1 (33)	2 (29)	2 (33)	3 (75)	1 (100)	**10 (40)**
Dysgeusia	0 (0)	0 (0)	2 (29)	4 (67)	3 (75)	1 (100)	**10 (40)**
Vomiting	0 (0)	1 (33)	2 (29)	1 (17)	1 (25)	1 (100)	**6 (24)**

- Dose limiting toxicities in 4 patients: diarrhoea, colitis and fragility fractures (10 mg); colitis (3 mg); ileitis (3 mg); pancreatitis (2 mg)
- Lower doses and denosumab prophylaxis averted bone toxicity associated with Wnt inhibition – no rises of bone turnover marker βCTX and no spontaneous fractures
- Dysgeusia appears to be dose related and did not lead to discontinuations

Redx internal data
* All treatment related adverse events (any grade) occurring in at least 20% patients

ESMO: European Society for Medical Oncology; TRAE: Treatment related adverse event; Wnt: Wingless/integrated

RXC004

MSS mCRC Patients Have Poor Outcomes with Current Standards of Care

MSI-H metastatic CRC (5% patients) → **Anti-PD-1 approved segment**

MSS metastatic CRC (95% patients)

Wnt-ligand driven tumours

8% tumours RNF43/RSPO

1st Line

5-FU based chemotherapy

Plus anti VEGF or anti EGFR

All patients OS: 30m(1)

BRAF V600E OS: 11m(2)

2nd Line

5-FU based chemotherapy with anti VEGF or anti EGFR

All patients OS: 11m(3)

BRAF V600E Cetuximab + encorafenib

ORR 20% DCR 74% PFS 4.2m OS 8.4m(4)

3rd Line

Single agent TAS-102 or regorafenib, or chemo+cetuximab

All patients: ORR 5% DCR 40% PFS 3m OS 7m(5)

BRAF V600E: ORR 2%, DCR 31%, PFS 1.5m, OS 5.4m(4)

(1) Aparicio et al 2020 (2) Tabernero 2022 (3) (4) Kopetz 2021 (Beacon) Giordano et al, 2021(5) Vegal et al, 2016

DCR: Disease control rate; MSI: Microsatellite-instable
ORR: Overall response rate; OS: Overall survival; PFS: Progression free survival; RNF43: Ring finger protein 43; RSPO: R-spondin; Wnt: Wingless/integrated

RXC004

Currently, 2% Overall Survival Rate for Biliary Tract Cancers, Opportunity in Late Line Settings to Reverse Immune Evasion

Metastatic Biliary Tract Cancers

Intrahepatic Cholangiocarcinoma (IHCCa) 2% 5-yr OS	Gall Bladder 10% 5-yr OS
Extrahepatic Cholangiocarcinoma (EHCCa) 8% 5-yr OS	Ampulla of Vater 14% 5-yr OS

70% have high Wnt-ligand expression

1st Line

Gemcitabine + cisplatin [Likely to become anti-PDL1* or anti-PD-1* combined with gemcitabine + cisplatin*(2)]

Gem-Cis OS: 11.7m(1)
Durvalumab Gem Cis: 12.8m(2)

Targeted Treatment options for tumours with
NTRK fusion (~1% BTC)
MSI-H (~10% BTC)

2nd Line and later

FOLFOX(3) or other chemotherapies

All patients OS: 6.2m(2)

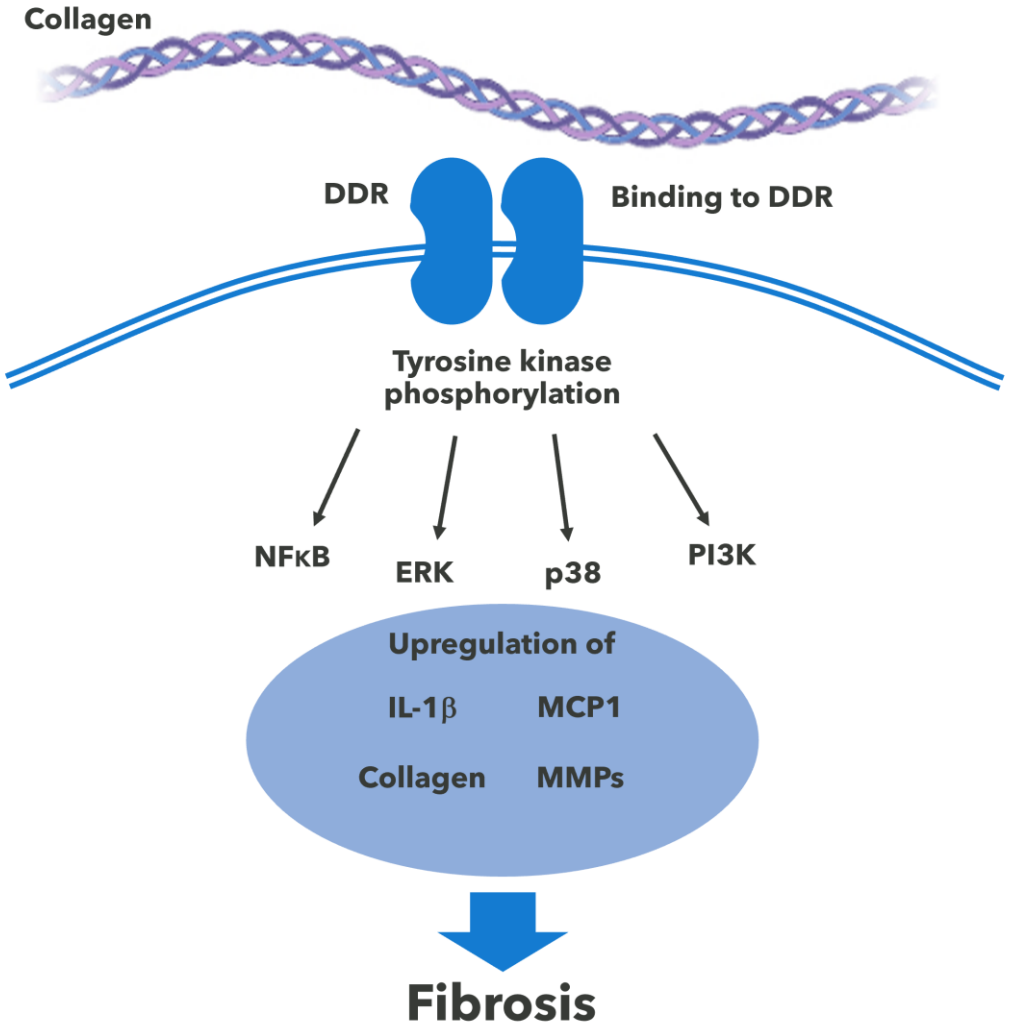
Targeted treatment options for tumours with
BRAF V600E (~3% BTC)
FGFR2 (13% of IHCCa)
IDH-1 (20% of IHCCa)
HER-2 (20% of EHCCa)

*N.B. FDA approval of durvalumab + chemo received by AstraZeneca in September 2022. Pembrolizumab Phase 3 ongoing with commercial use subject to regulatory approval.
(1) Valle et al NEJM 2010; (2) Oh et al NEJM Evidence 2022; (3) Lamarca et al Lancet 2019

BTC: Biliary tract cancer; Wnt: Wingless/integrated

Discovery Engine

Discoidin Domain Receptor (DDR) Inhibition as a Potential Novel Therapeutic Class for Fibrosis



DDR is a collagen target

- Non-integrin tyrosine kinase collagen receptors
- Collagen binding initiates downstream fibrotic signalling pathways

DDR inhibition is a novel approach

- Novel, druggable therapeutic target for fibrosis
- Recent publication of preclinical PoC studies for small molecule inhibitors in models of lung and kidney fibrosis
- Potential for disease modifying efficacy

Redx has a discovery programme

- Potent and selective DDR inhibitors identified
- In lead optimisation phase
- Preclinical PoC ongoing in lung and kidney fibrosis models