Redx
Discovering Targeted Medicines

Developing Novel, Targeted Therapeutics for Cancer and Fibrotic Diseases

Corporate Presentation

March 2023

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

AstraZeneca abpi

Dr Richard Armer
CSO

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

Pfizer ORGANON

Dr Jane Robertson
CMO

Oncologist with >20 years in biotech and pharma drug development. Led the successful clinical development of Lynparza

AstraZeneca NUCANA ACHILLES THERAPEUTICS

Peter Collum
CFO

Experienced finance and strategy executive with >25 years in biopharma

Bank of America MTS Health Partners Roche

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 FDA approved Jaypirca™ (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

*the asset was subsequently sold outright to Loxo Oncology, now part of Eli Lilly, Redx has no remaining economic interest
Jaypirca™ is a trademark owned by or licensed to Eli Lilly and Company, its subsidiaries, or affiliates
ADME: Absorption, distribution, metabolism and excretion; IND: Investigational new drug application; PoC: Proof of concept; PK: Pharmacokinetic

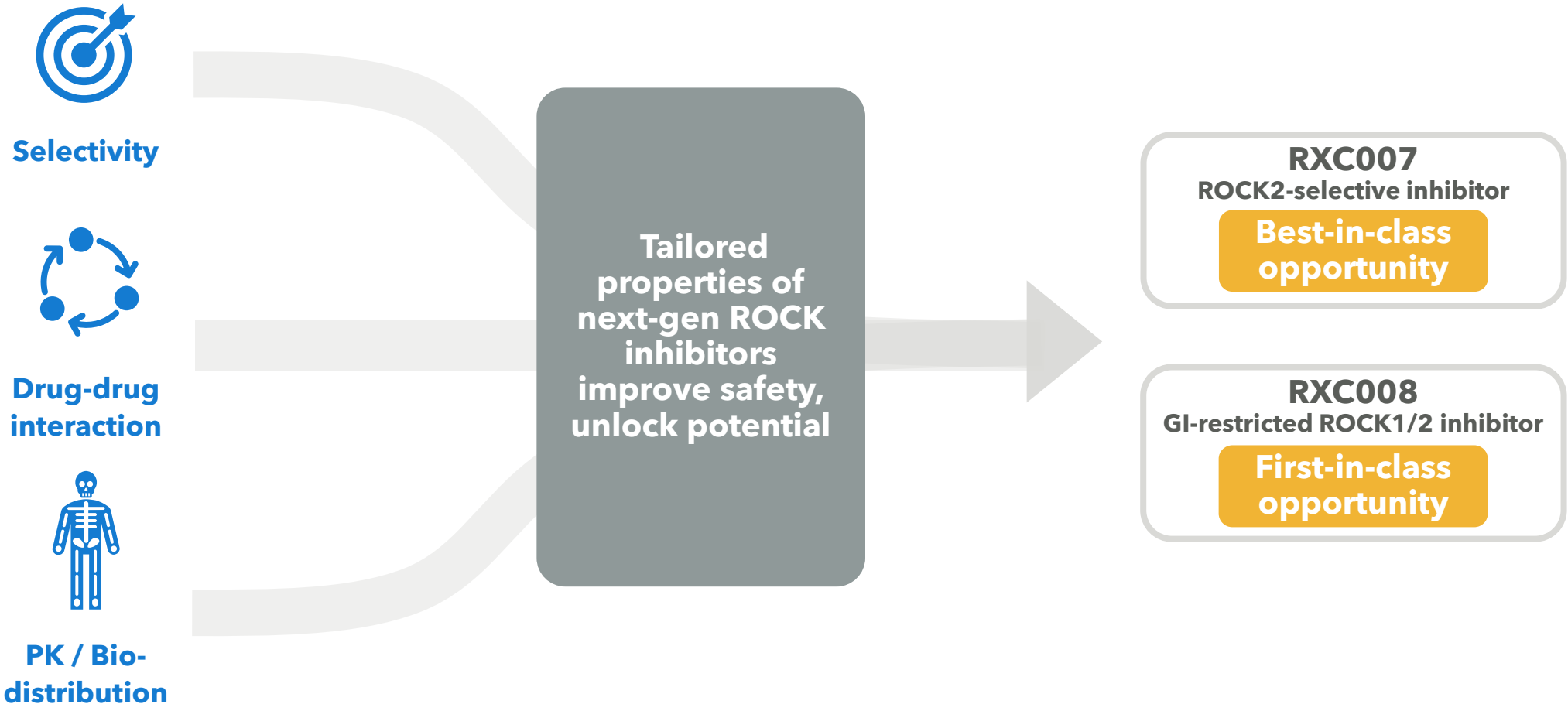
Advancing a Robust Pipeline Built In-House

	Target/ Product	Indication(s)	Research	Preclinical	Phase 1	Phase 2	Phase 3	Upcoming Milestones
Fibrosis	**ROCK2 Selective Inhibitor** (RXC007)	Idiopathic pulmonary fibrosis (IPF)						Phase 2a topline data – **Q1 2024**
Fibrosis	**GI-targeted ROCK Inhibitor** (RXC008)	Fibrostenotic Crohn's disease						CTA/IND submission – **end 2023**
Oncology	**Porcupine Inhibitor** (RXC004)	Genetically selected MSS mCRC monotherapy + anti-PD-1 combination Genetically selected pancreatic cancer monotherapy Biliary cancer monotherapy + anti-PD-1 combination			PORCUPINE PORCUPINE2			Topline data: – monotherapy from **H1 2023** – combination **H2 2023**
Discovery Engine	**DDR Inhibitor** (Discoidin Domain Receptor)	Fibrosis, cancer-associated fibrosis						Progress programmes – **target of 2 INDs by 2025**
Discovery Engine	**Research Targets** (Multiple Programmes)	Oncology & fibrosis						
Partnered	**Porcupine Inhibitor** (RXC006/AZD5055)	Idiopathic pulmonary fibrosis (IPF)						Licensed to AstraZeneca
Partnered	**Pan-RAF Inhibitor** (JZP815)	Oncology						Sold to Jazz Pharmaceuticals
Partnered	**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

Next Generation ROCK Inhibitor Portfolio

Redx combines unique ROCK expertise and medicinal chemistry strength



RXC007

RXC007: A Selective ROCK2 Inhibitor for Fibrotic Diseases – Lead Indication is IPF with Phase 2 Data Expected Q1 2024

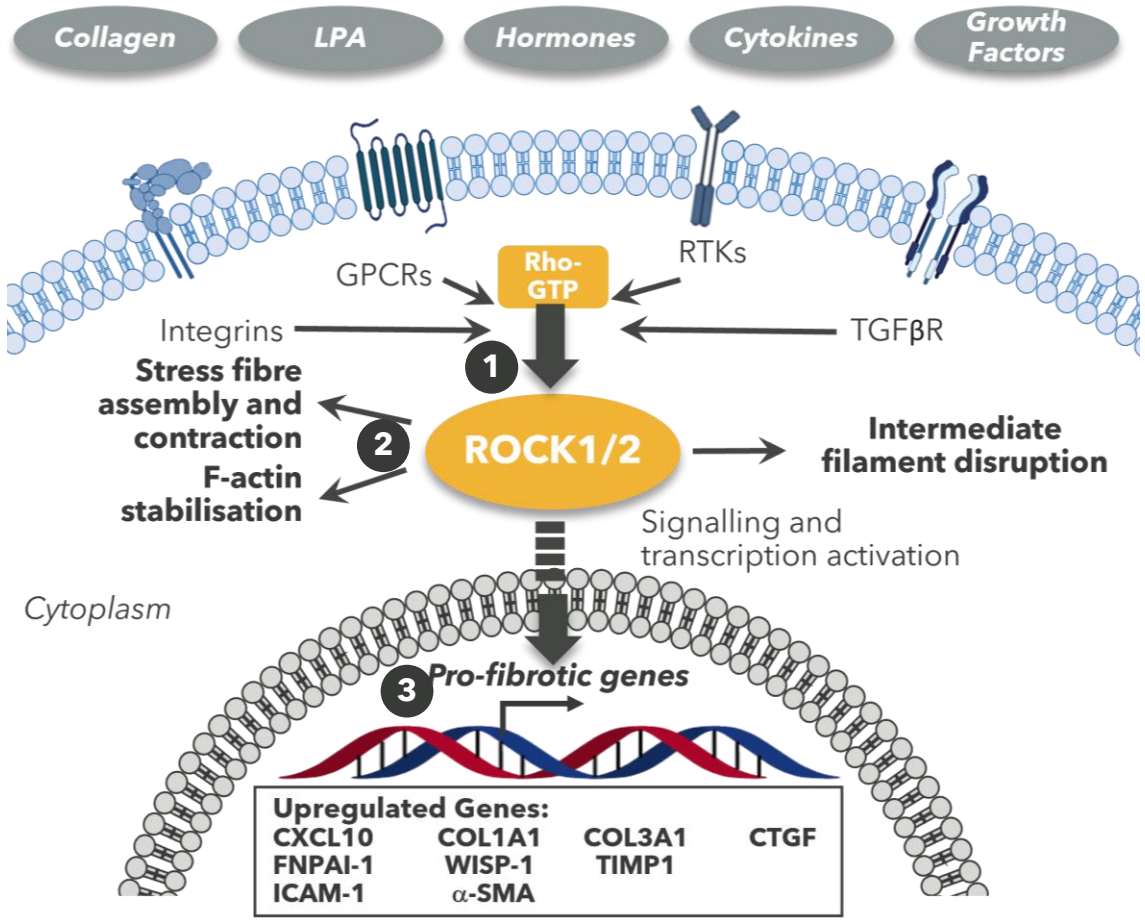
Highlights

- 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 Q1 2024**, 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
  - Effect not seen with selective ROCK2 inhibition
- ROCK2 inhibition alone is sufficient to protect from pulmonary fibrosis in mouse models(1)

(1) Knipe et al., 2018

ROCK: Rho-associated protein kinase

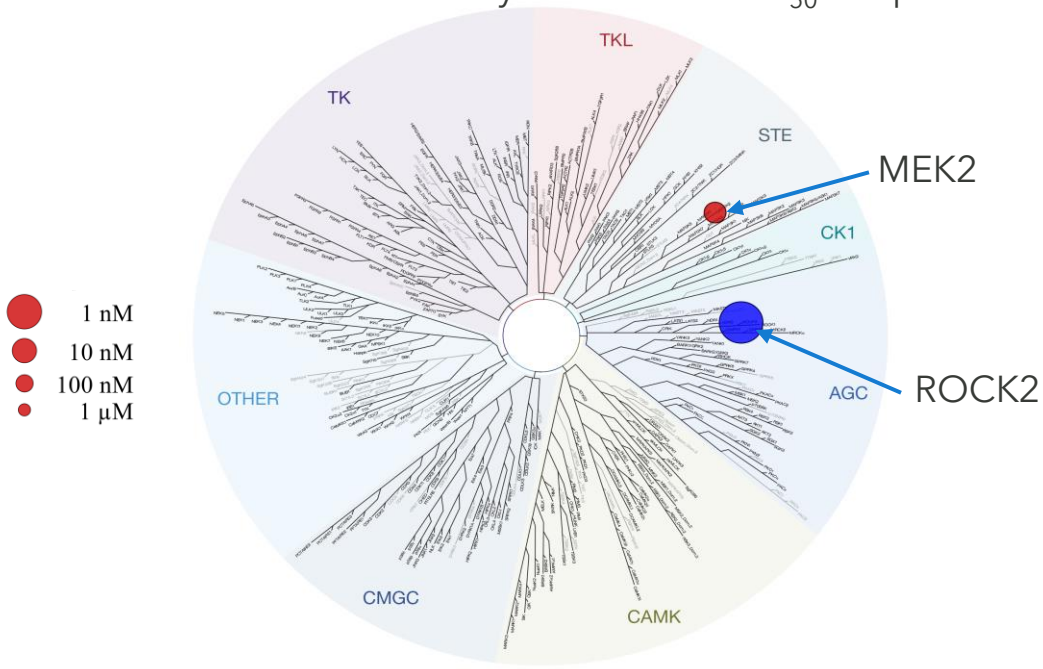
RXC007

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

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)

Data generated by Redx

RXC007

Lung Fibrosis: A Growing Clinical Need with Limited Treatment Options

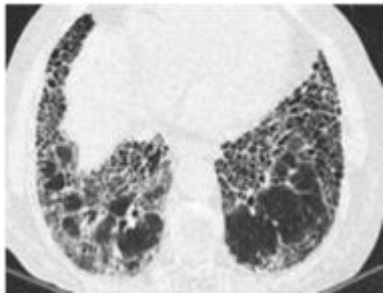
Lead indication is Idiopathic Pulmonary Fibrosis (IPF)

- 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(2)
- Global IPF market projected to reach $3.6 billion by 2029(3)
- 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(4)
- Of the two thirds of ILD patients without IPF, up to 40% may develop a progressive fibrosing phenotype(5) (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(6)



Fibrotic lung

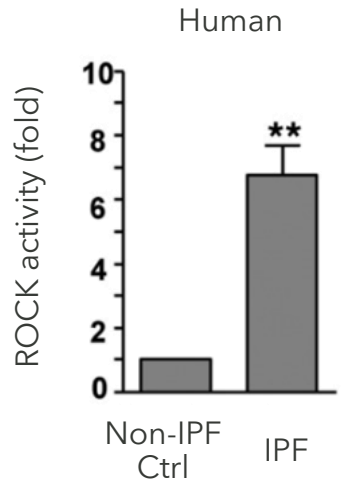
(1) Clinical Estimates from Hyun 2015, Ley 2012, Raghu 2006; (2)(3) Patient numbers (diagnosed prevalence) & market size forecast data sourced from Global Data (US, EU5, Japan); (4) Kaul 2021 (5) Olson 2021; (6) Clarivate, Key Findings on Scleroderma (Systemic Sclerosis) Published: September 2021

RXC007

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

ROCK as a target in IPF[1]

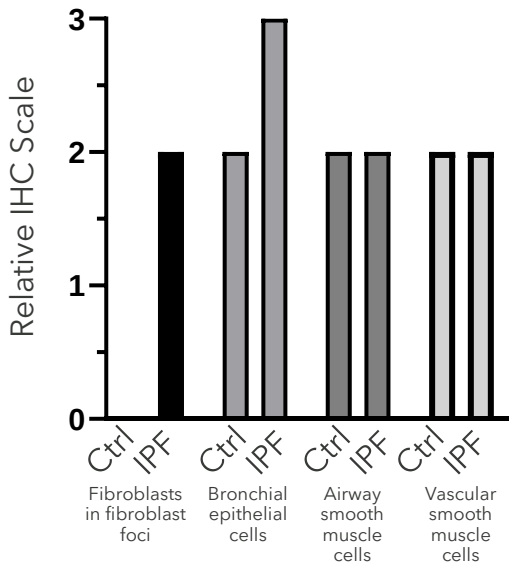
RhoA/ROCK/ROCK2 signalling pathway is upregulated in human IPF patients



(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]

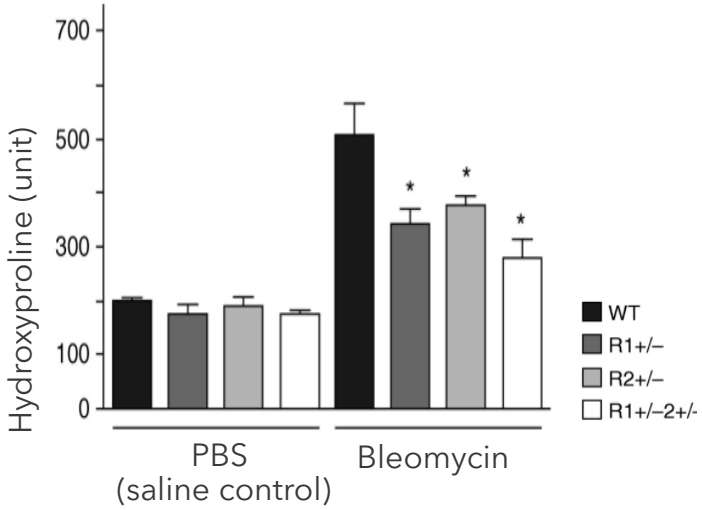
Increased ROCK2 expression in IPF bronchial epithelial cells and fibroblasts



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

RXC007 Unlocks ROCK as Key Fibrosis Target Across Indications

Redx

- Murine & Rat Bleomycin-Induced IPF Models
- PCLS from Patients with IPF
- Murine Sclerodermatous chronic Graft versus Host Model

Fibrosis
- IPF
- ILD

Supportive preclinical ROCK2 inhibitor data available

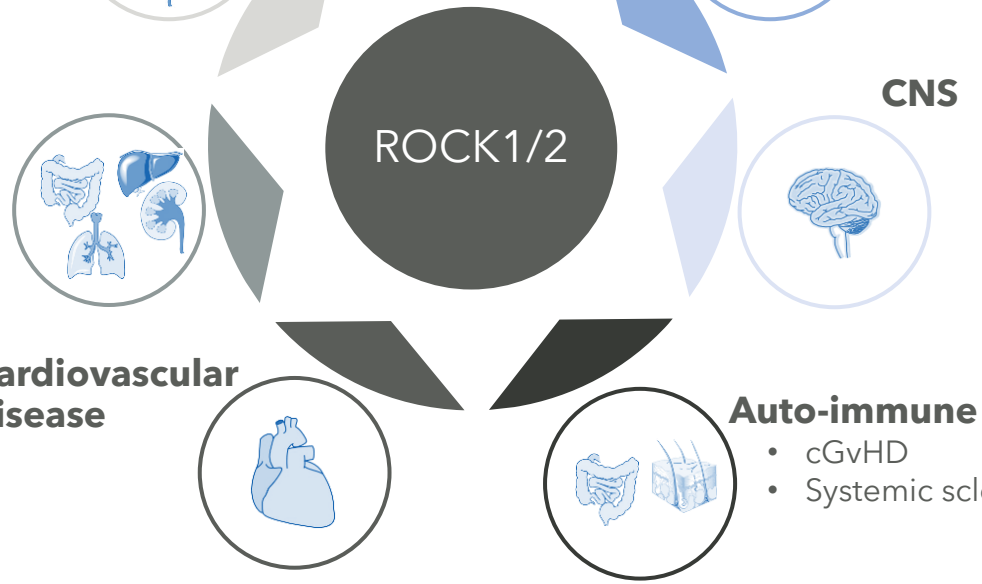
- DIO NASH murine model
- CCl_4-induced murine liver model
- Kidney Murine UUO model

Metabolic diseases
- NASH
- Kidney fibrosis

Neuromuscular

Oncology
- Pancreatic

- Pancreatic metastatic patient-derived PDAC (PDX-05) murine xenograft
- FOLFIRINOX resistant PDX-08 model
- Murine KPC syngeneic model



CNS

Cardiovascular disease

Auto-immune
- cGvHD
- Systemic sclerosis

Murine Sclerodermatous chronic Graft versus Host Model

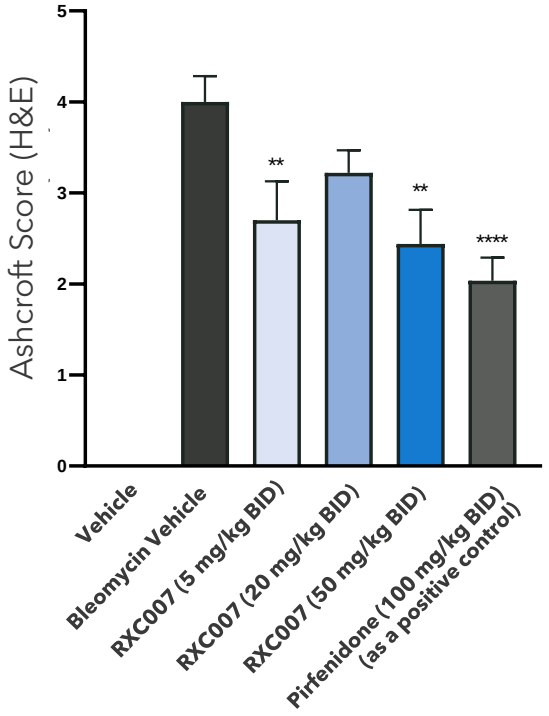
ALS: Amyotrophic lateral sclerosis; DMD: Duchenne muscular dystrophy; DN: Diabetic nephropathy; HCC: Hepatocellular carcinoma; IPF: Idiopathic pulmonary fibrosis; NAFLD: Nonalcoholic fatty liver disease; NASH: Nonalcoholic steatohepatitis; OSCC: Oral squamous cell carcinoma; RCC: Renal cell carcinoma

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

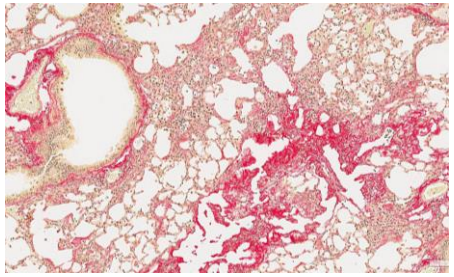


Mouse 21-day therapeutic model (dosing from day 7)
Data generated by Redx

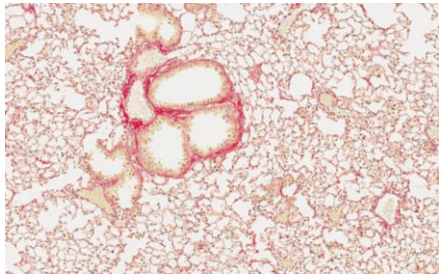
Reduction of fibrosis

Representative images

Lung histology Sirius red

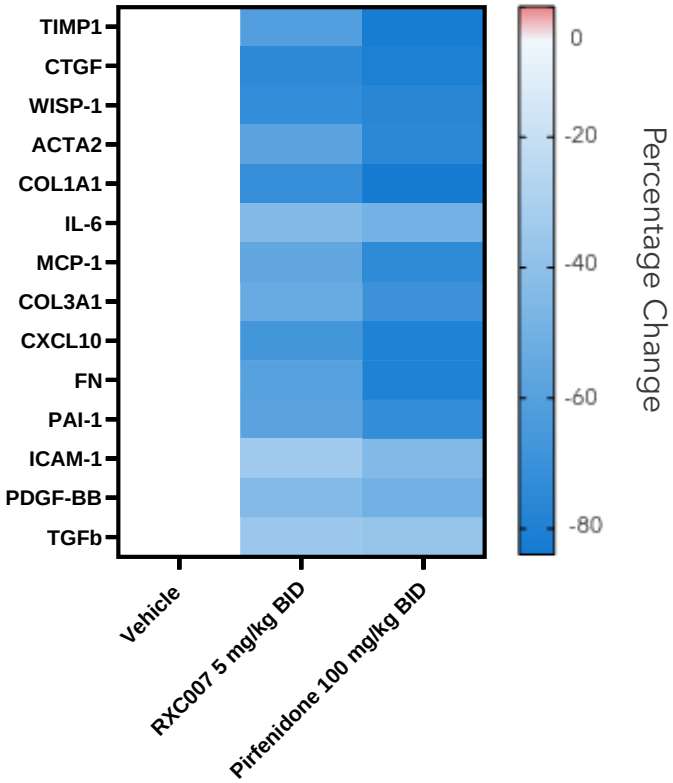


Vehicle



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

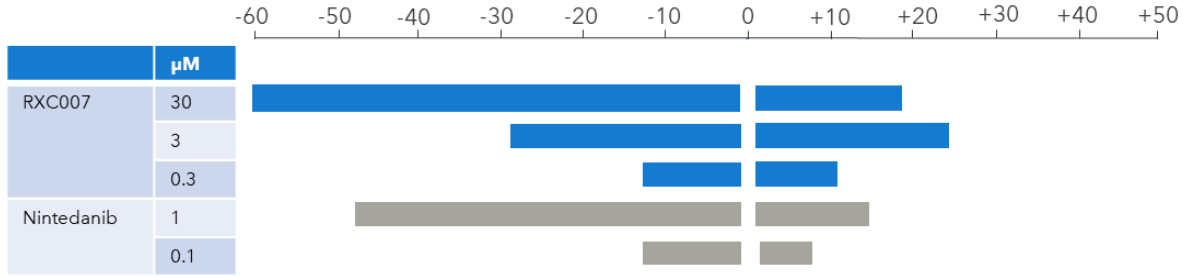
Supernatants analysed for pro-fibrotic proteins

Tissue proven to be live

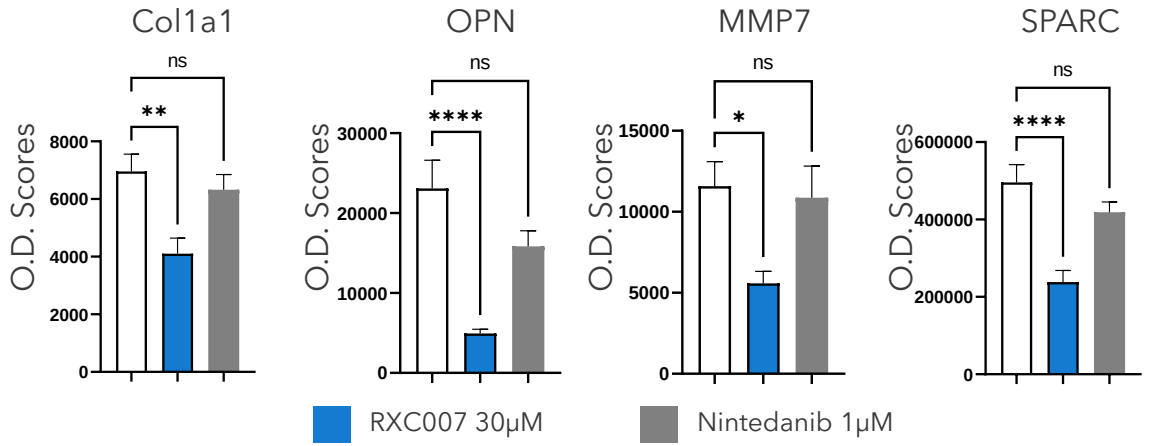
Compounds shown to be non-toxic

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

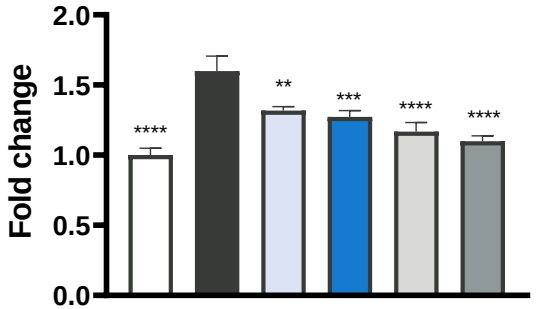
RXC007

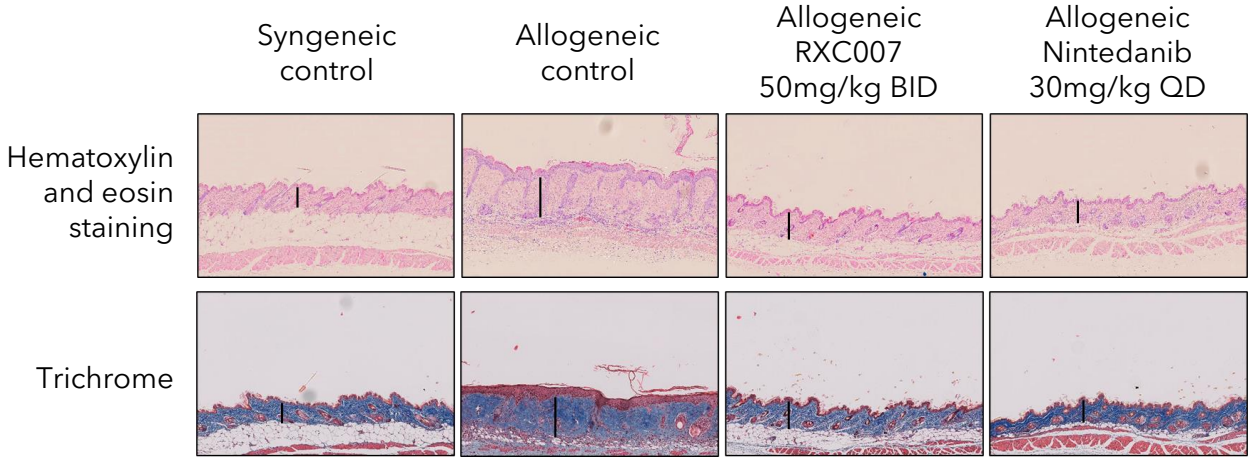
Proof-of-Concept in an Immune Mediated Model Demonstrates Potential for Broader ILD Indications

New Data

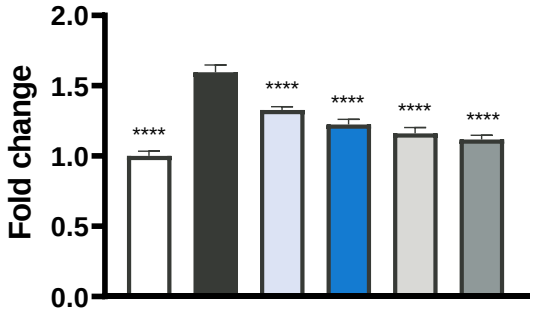
Murine Sclerodermatous chronic Graft versus Host Model

Skin thickness



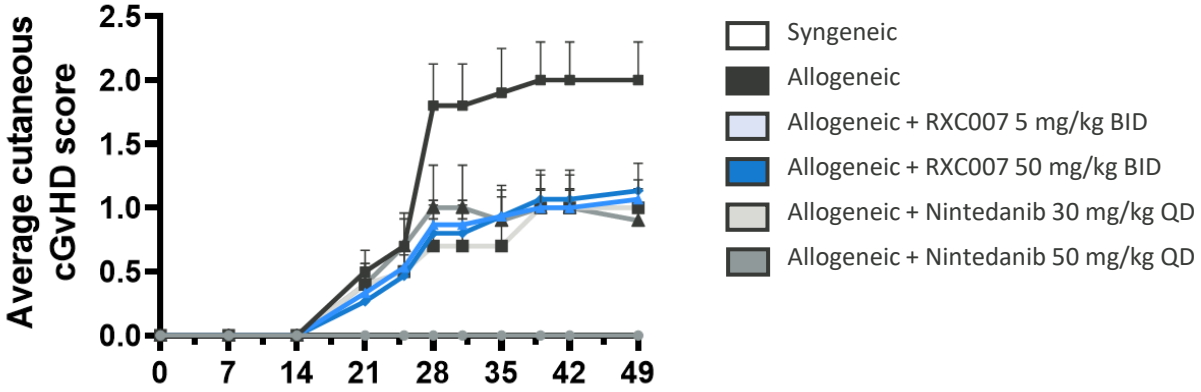


Hydroxyproline skin



Syngeneic
Allogeneic (A)
(A) + RXC007 5mg/kg BID
(A) + RXC007 50mg/kg BID
(A) + Nintedanib 30mg/kg QD
(A) + Nintedanib 50mg/kg QD

Cutaneous cGVHD Score



Data generated by Redx, as presented at ICLAF 2022

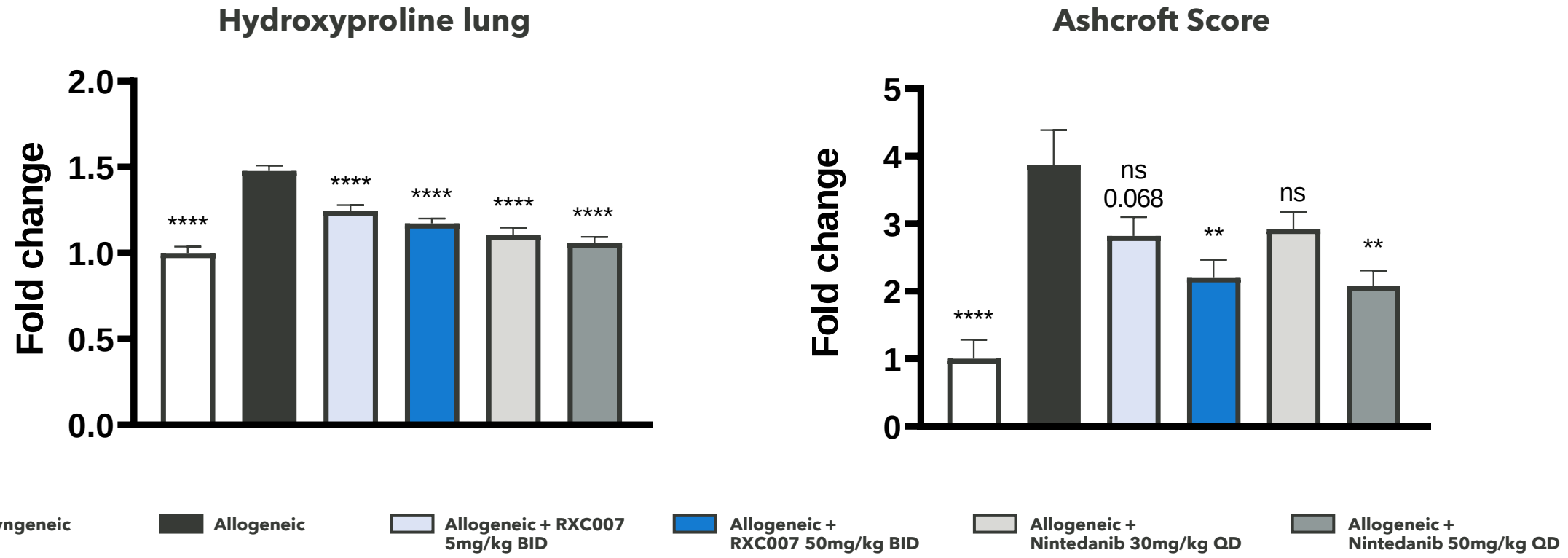
RXC007

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

Redx

New Data

Murine Sclerodermatous chronic Graft versus Host Model



Data generated by Redx, as presented at ICLAF 2022

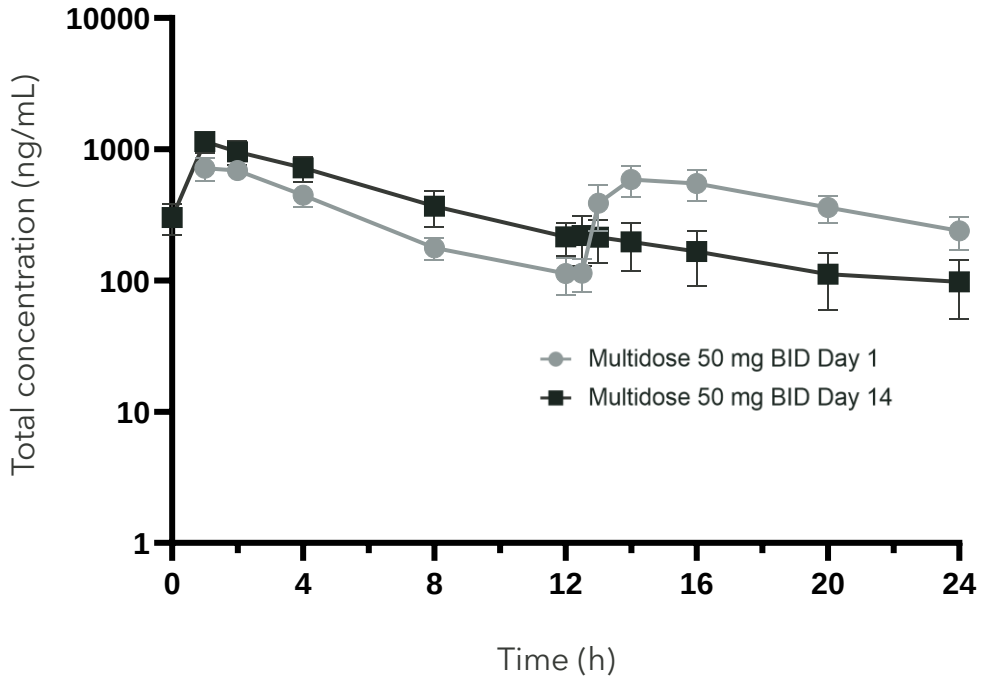
RXC007

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

New Data

Presented at ICLAF 2022

Multidose cohort 50mg 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 events 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 2mg QD to 70mg BID
- No significant differences between 50mg fed and fasted cohorts
- 20mg BID selected as starting dose for Phase 2a, which achieved biologically relevant exposures 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 Q1 2024

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

Dose Level - 20mg BID
12:4 RXC007: pbo
(n=16)

Dose Level - 50mg BID
12:4 RXC007: pbo
(n=16)

Dose Level – 70mg BID tbc
12:4 RXC007: pbo
(n=16)

Dosing period 3 months
(Patients may elect to continue for longer if no signs of disease progression)

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 demonstrate effects on disease biomarkers e.g., α-SMA, TIMP-1, ICAM-1, and target engagement biomarkers e.g., pMYTP1 and pMLC2

Cohort 1
8 patients

Cohort 2
8 patients

Dosing Evaluation period 28 days
(Patients may elect to continue for longer)

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

Status: *Six countries approved US IND open for 28-day dosing; further information required for three-month dosing*
Plan for 40 sites to be active in Q2 2023

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

RXC008

RXC008: GI-targeted ROCK Inhibitor for Fibrostenotic Crohn's Disease Planned to Enter Phase 1 Clinical Trial H1 2024

Highlights

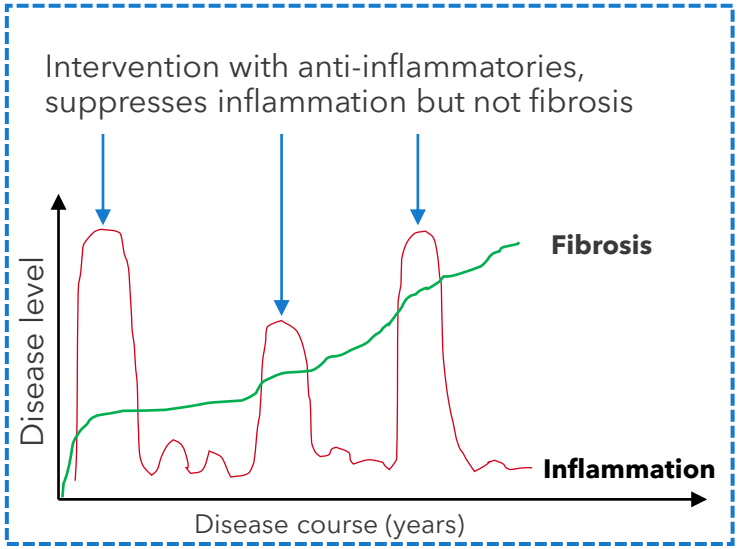
- RXC008 is a potent, oral, small molecule non-systemic ROCK 1/2 inhibitor
- Fibrostenotic Crohn's disease is a significant unmet need - only treatment option for patients is successive surgical intervention
- RXC008 is a potential first-in class treatment - no approved therapies for underlying fibrosis 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*
- CTA/IND enabling work underway – **submission planned for end 2023**
  - CMC API manufacture complete
  - Toxicology studies initiated

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

RXC008

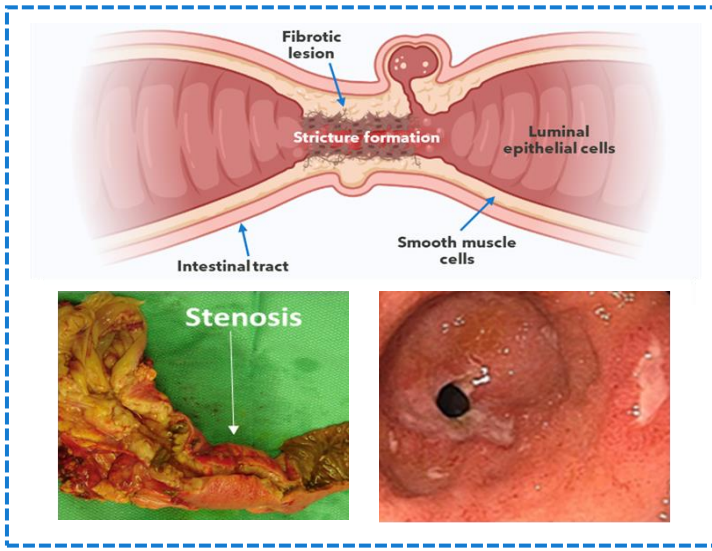
Potential First-in-Class Treatment for Fibrostenotic Crohn's Disease

Clinical progression in Crohn's



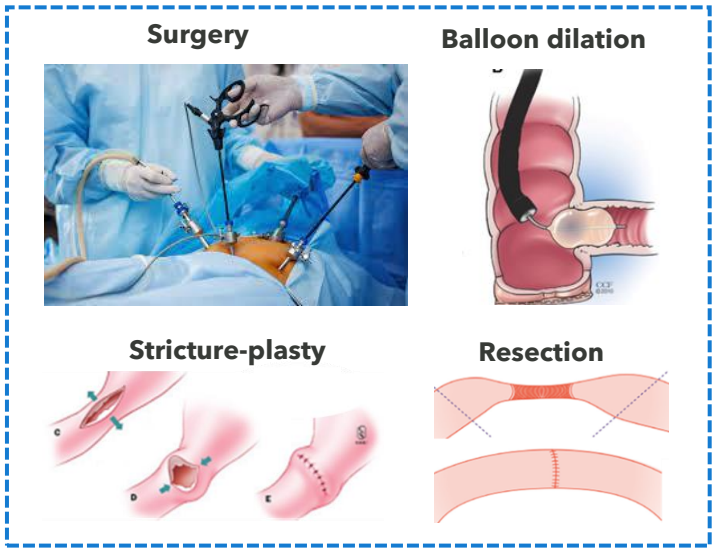
1.7 million(1) patients globally affected by Crohn's disease

Fibrotic stricture formation



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

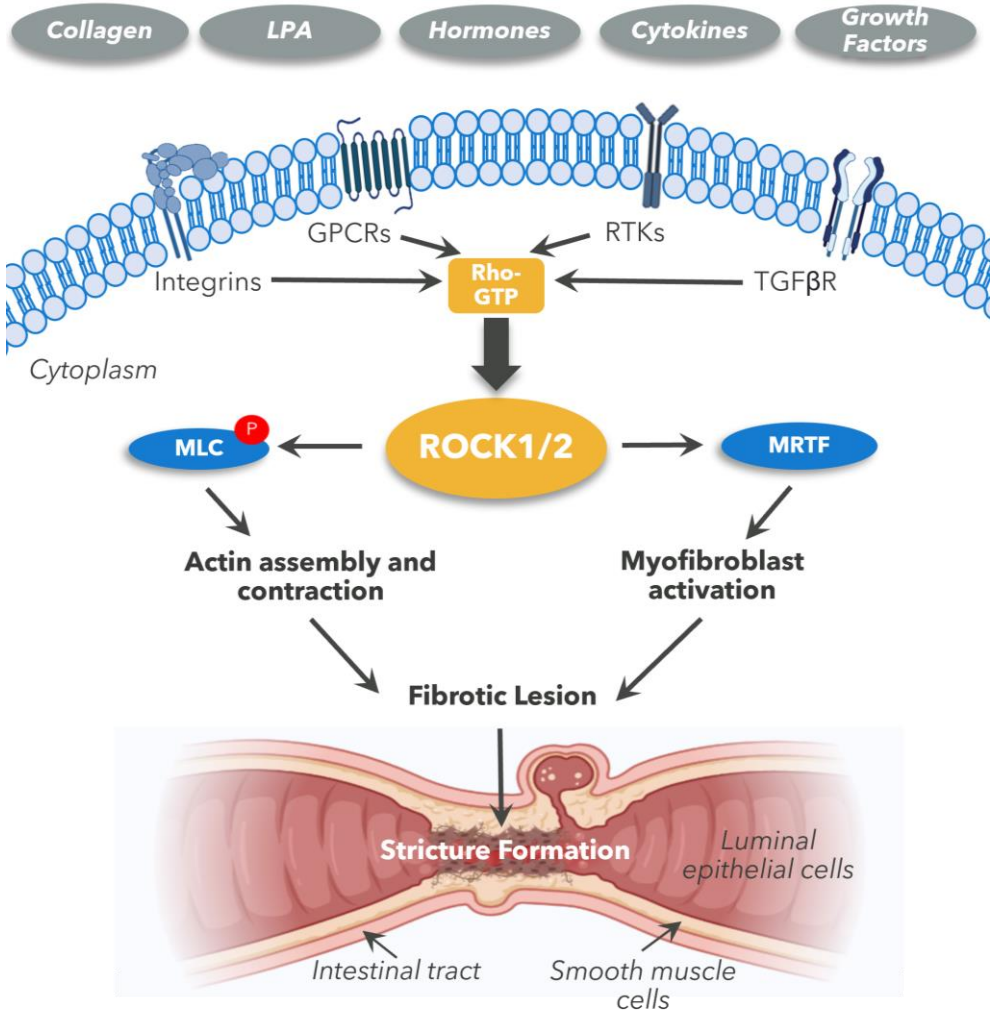
Surgical interventions



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

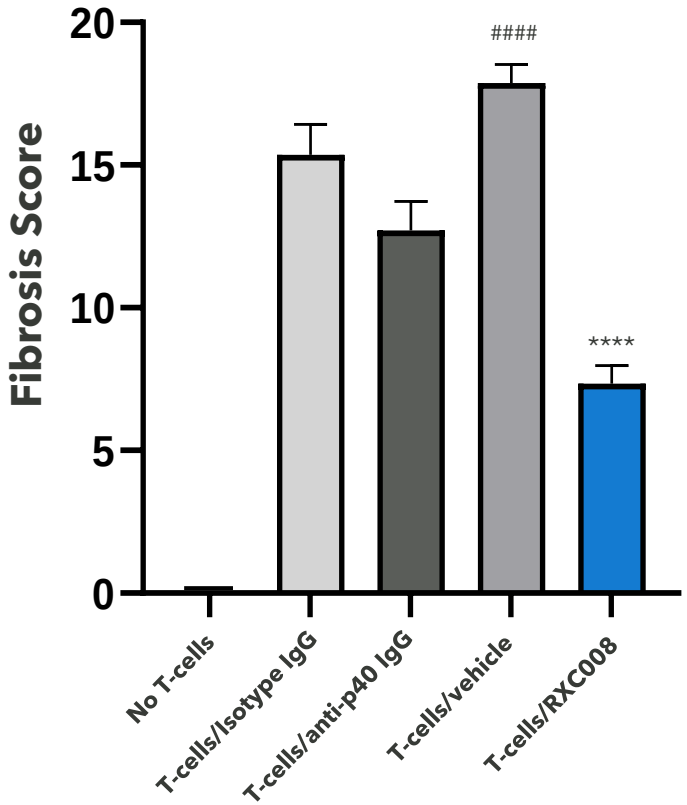
GI: Gastrointestinal; GITR: Gastrointestinal targeted ROCK; MRTF: myocardin-related transcription factor; MLC: myosin light chain

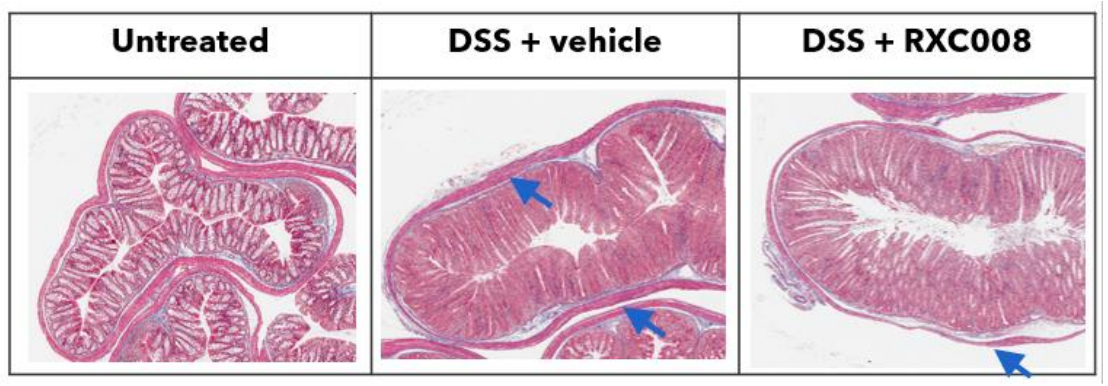
RXC008

RXC008 is Efficacious in Adoptive T cell Transfer Model

GHENT UNIVERSITY

RXC008 reduces fibrosis and smooth muscle hyperplasia





Significant reduction in Fibrosis Score observed with RXC008 treatment

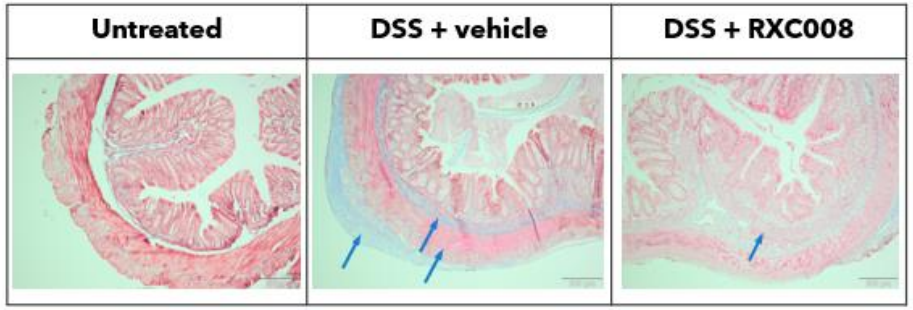
Anti-P40 does not significantly alter fibrosis score

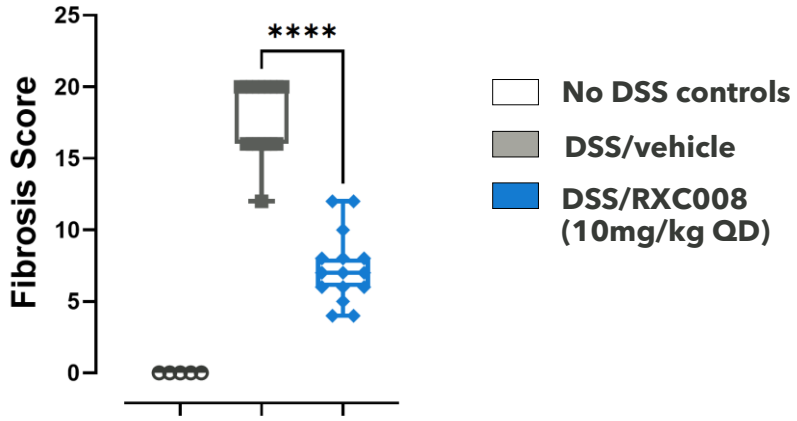
1-way Anova with Dunnet's multiple comparison, # T-cells/vehicle v untreated controls, * RXC008 10mg/kg QD or anti-p40 v T-cells/vehicle.
Data generated by Redx

DSS: Dextran sulfate sodium

RXC008

RXC008 Reduces Fibrosis in the Chronic DSS Model





Significant reduction in Fibrosis Score observed with RXC008 treatment. Accompanied by 25% reduction in smooth muscle hyperplasia

* Linear mixed model analysis
Data generated by Redx

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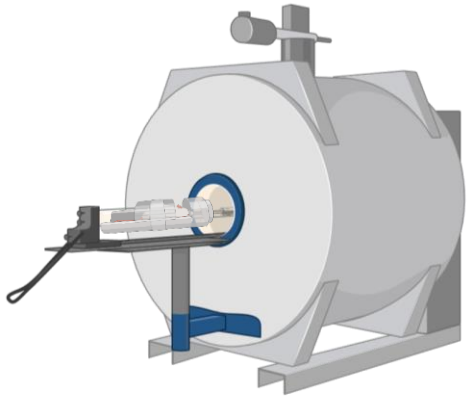
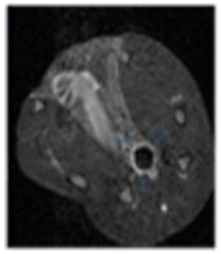
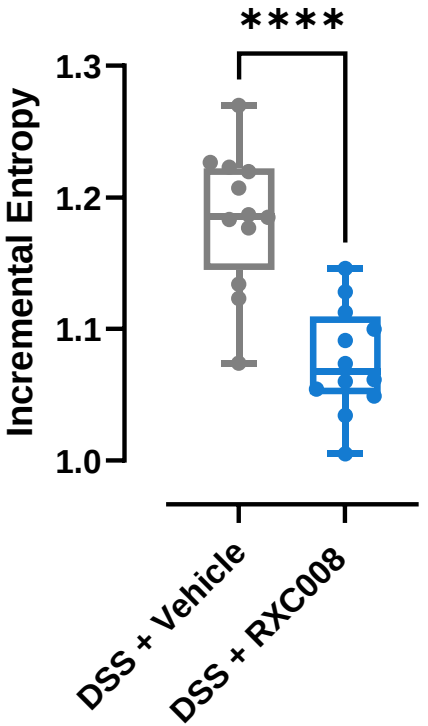
Entropy changes correlate with progression of IHC confirmed fibrosis in the DSS model and patient samples





T2 image



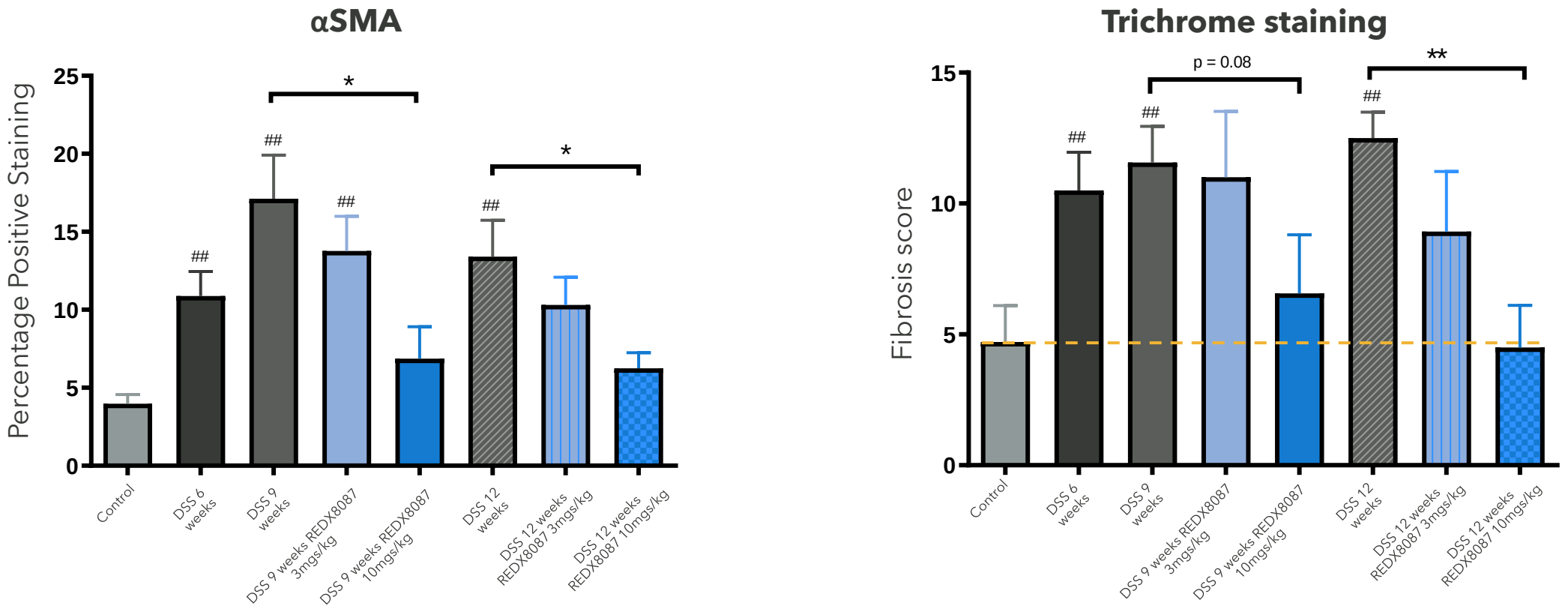
DSS: Dextran sulfate sodium

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)



Data generated by Redx, REDX8087 is similar to RXC008

DSS: Dextran sulfate sodium

RXC004

RXC004: Clinically Validated Porcupine Inhibitor in Phase 2

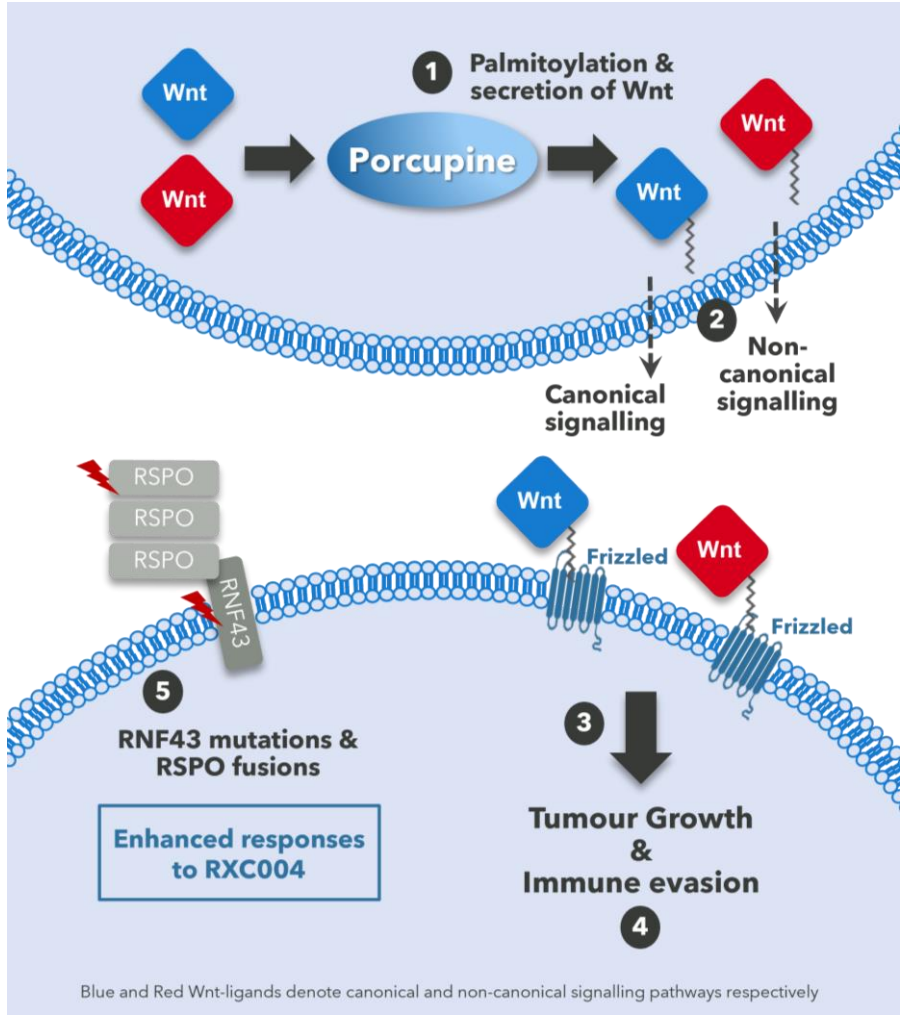
Highlights

- 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 is active as monotherapy in Phase 1 – with differential clinical efficacy in Wnt-ligand dependent tumours (ESMO 2021)
- Primary efficacy hypothesis is that combination with anti-PD-1 treatment can overcome anti-PD-1resistance, which could open new patient segments (SITC 2022)
- Recruitment ongoing, Phase 2 programme in Wnt-ligand dependent tumours – **data expected H2 2023**
  - Phase 2 dose in selected for combination with anti-PD-1 is 1.5mg and modules now open
  - Phase 2 dose selected for monotherapy 2mg, and recruitment nearing completion
  - Biliary tract cancer module: single agent activity reported supports combination hypothesis whilst insufficient to develop as a monotherapy in this setting

RXC004

Porcupine Inhibition Targets Wnt-Ligand Dependent Tumours

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



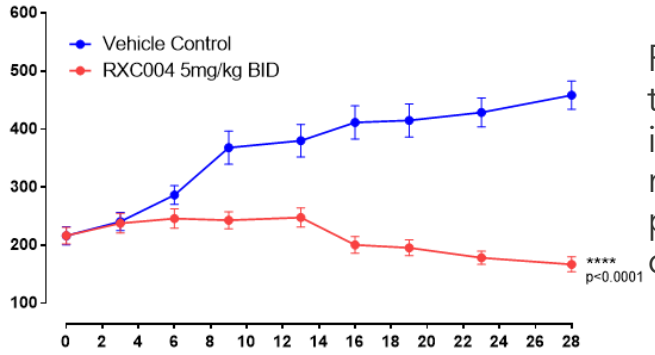
1. Porcupine is a key enzyme upstream in the Wnt pathway, which adds a lipid chain to all 19 Wnt ligands (palmitoylation) enabling secretion
2. Wnt ligands activate both canonical and non-canonical signalling pathways
3. Canonical and non-canonical target genes drive tumour growth and tumour immune evasion
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

Dual Mechanism of Action Demonstrated Preclinically

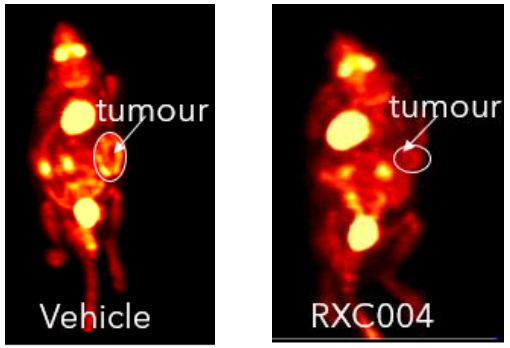
Inhibits tumour growth



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

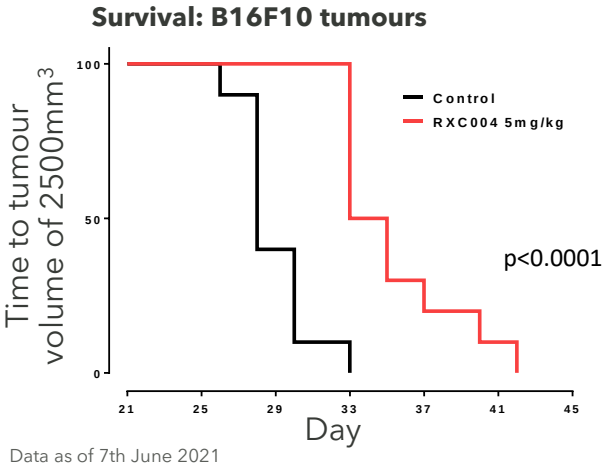
DIRECTLY TARGETS TUMOUR CELL GROWTH

Decreases tumour metabolism



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

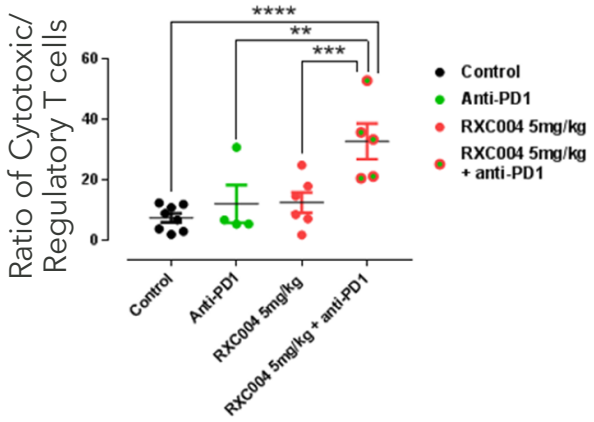
As a monotherapy



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

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)**

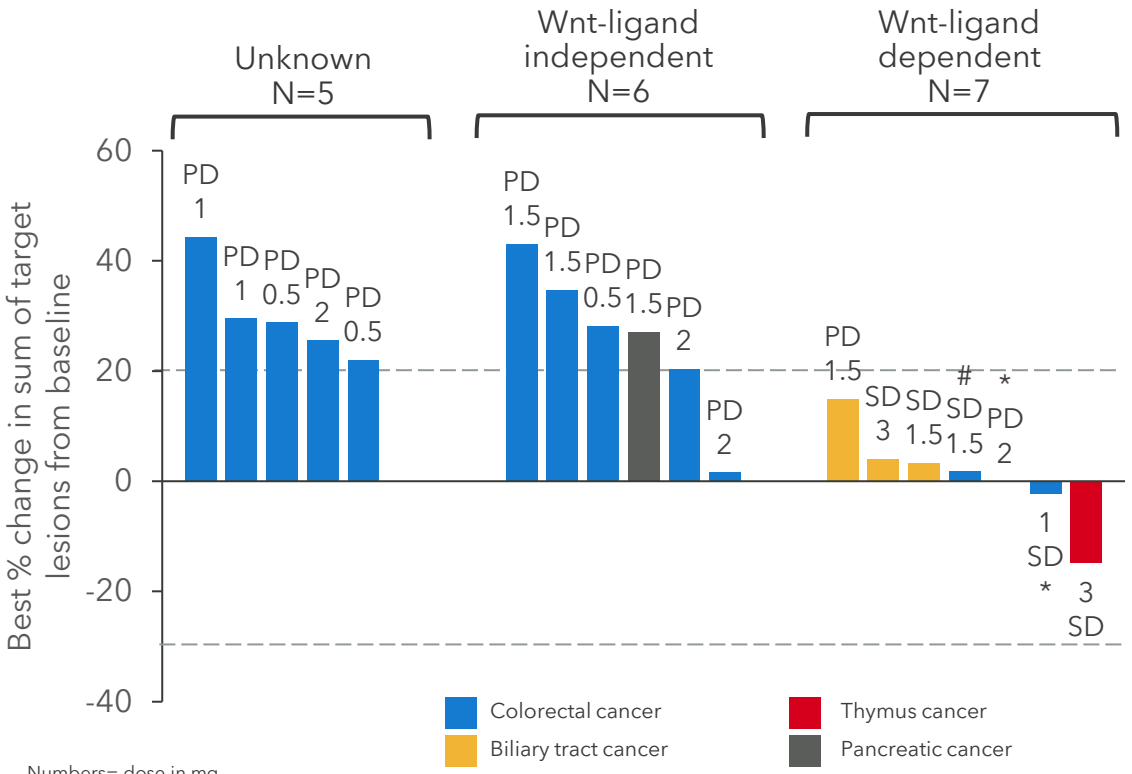
- The recommended Phase 2 dose of RXC004 is 2mg in monotherapy
- Both RXC004 1.0mg and 1.5mg doses were safe and tolerable in combination with nivolumab
  - RXC004 doses higher than 1.5mg were not explored in Module 2 because of the potential for overlapping toxicity of colitis, which was reported in 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 cut-off date 30 July 2021, as presented at ESMO 2021
Data generated by Redx

Phase 1 monotherapy data presented at ESMO 2021

18/25 monotherapy patients had RECIST-evaluable disease

Disease stabilisation observed in Wnt-ligand dependent tumours

- 5/7 patients with Wnt-ligand dependent tumours
- 0/11 pts with Wnt-ligand unknown or independent tumours

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

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

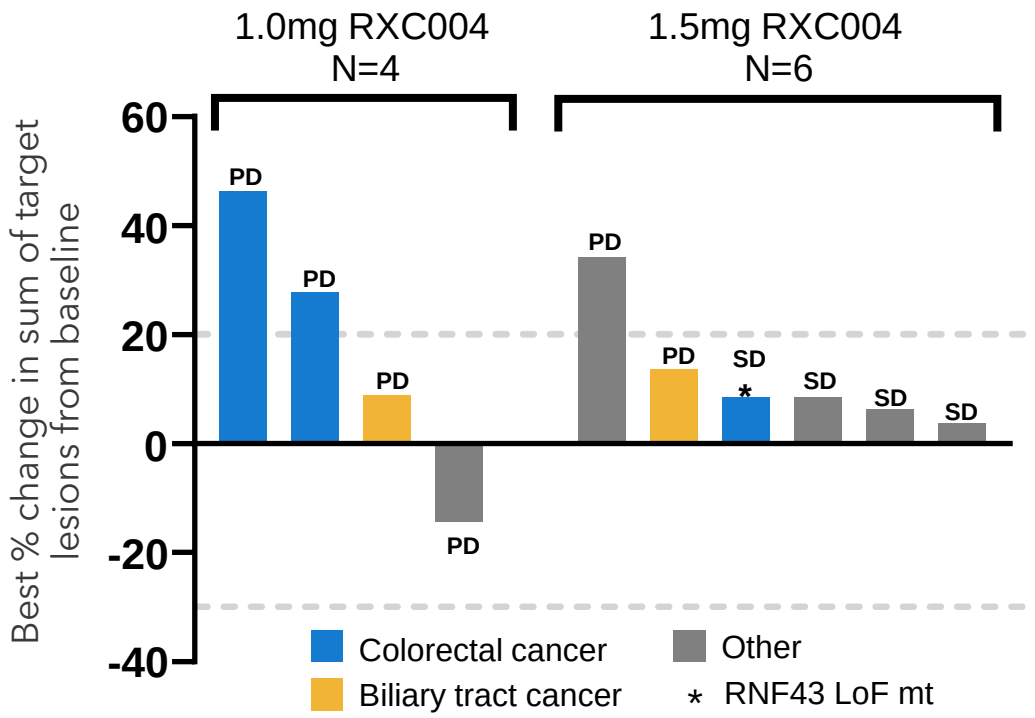
APC: Adenomatous polyposis coli gene; CRC: Colorectal cancer; LoF: Loss of function; PD: Progressive disease; RECIST: Response evaluation criteria in solid tumours; RNF43: Ring finger protein 43; RSPO: R-spondin; SD: Stable disease; Wnt: Wingless/integrated

RXC004

Phase 1 Clinical Data supports the Anti-PD-1 Combination Hypothesis

New Data

Clinical Activity by Dose Cohort



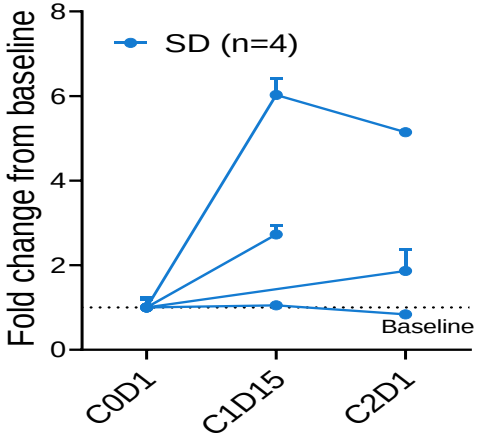
RNF43 LoF mt: loss of function mutation in Ring finger protein 43;
M-MDSCs: monocytic myeloid derived suppressor cells
PD: Progressive disease;
RECIST: Response evaluation criteria in solid tumours;
SD: Stable disease
Source: RedX internal data

Data presented at SITC, November 2022

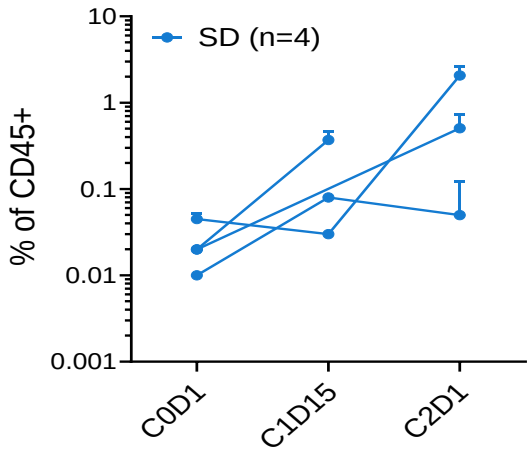
- **4/6** patients in the 1.5mg cohort had RECIST stable disease as best response

Changes in peripheral immune cell compartments are consistent with pre-clinical data and suggest an anti-tumour immune response

Ki67+ CD8+ T cells



M-MDSCs



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 + Nivolumab (n=20)	Monotherapy Genetically Selected Pancreatic Cancer (n=15)	Monotherapy Biliary Cancer (n=15)	Combination Biliary Cancer RXC004 + Pembrolizumab (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**	**Reported**	**H2 2023**

Analysis

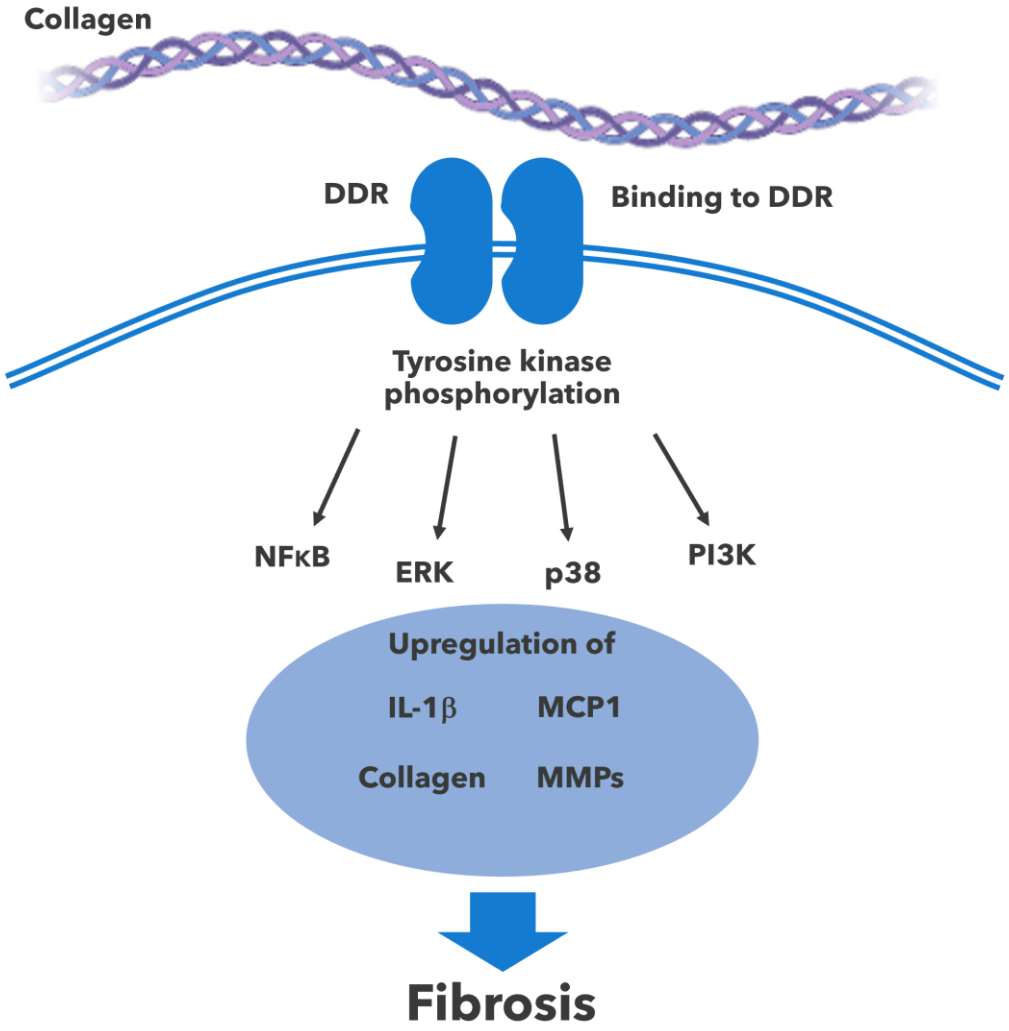
Key translational endpoints will characterise mechanism of action

- 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

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 pre-clinical PoC studies for small molecule inhibitors in models of lung and kidney fibrosis
- Potential for disease modifying efficacy

Redx has a discovery programme

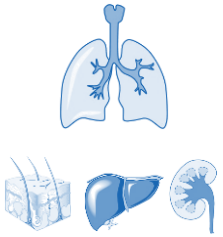
- Potent and selective DDR inhibitors identified
- In lead optimisation phase
- Pre-clinical PoC in lung and kidney fibrosis models

DDR: Discoidin domain receptor; PoC: Proof of concept

Financed through Next-Generation ROCK Portfolio Key Catalysts in '23/'24

ROCK2 Selective Inhibitor — RXC007

Best-in-class ROCK2 inhibitor opportunity in fibrotic diseases



IPF Phase 2a topline data readout	**Q1 2024**
Exploring development in ILD, oncology, cGvHD and other fibrotic disease areas including liver and kidney	

GI-targeted ROCK Inhibitor — RXC008

First-in-class opportunity in fibrostenotic Crohn's disease

CTA/IND submission	**Q4 2023**

Porcupine Inhibitor — RXC004

Combination Oncology opportunity in MSS mCRC, PDAC, BTC

Ph2 monotherapy data	**H2 2023**
Ph 2 Combination efficacy modules	**H2 2023**

* As of 30 September 2022
** Assuming full conversion of loan notes and exercise of employee share options. Updated 30 March 2023

Redx track record presents compelling value proposition

Recent Financing

£34.3 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

£54m in cash (at Sept 2022)
Funds into 2024, enabling delivery of key phase 2 clinical data

Top Tier Specialist Investors

Redmile Group · POLAR CAPITAL · INVUS · SOFINNOVA PARTNERS · Platinum ASSET MANAGEMENT

AIM (UK) listed Ticker: REDX
Total shares in issue: 334,911,458
Fully diluted: 487,776,686**

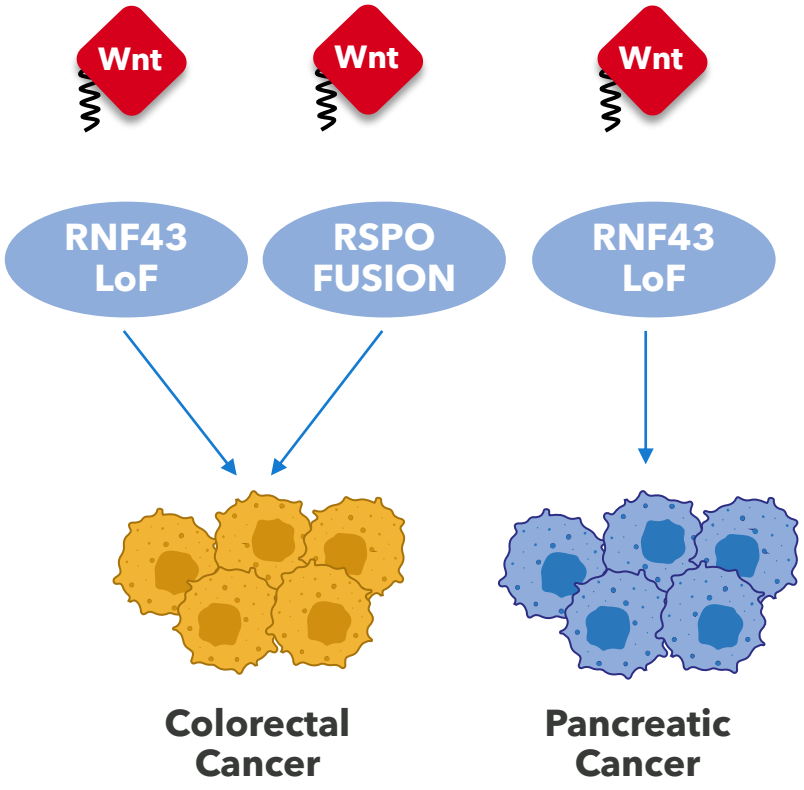
Redx
Discovering Targeted Medicines

Appendix

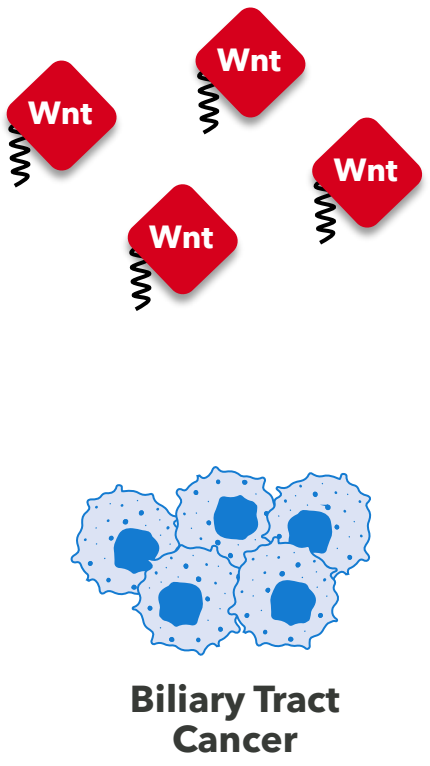
RXC004

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

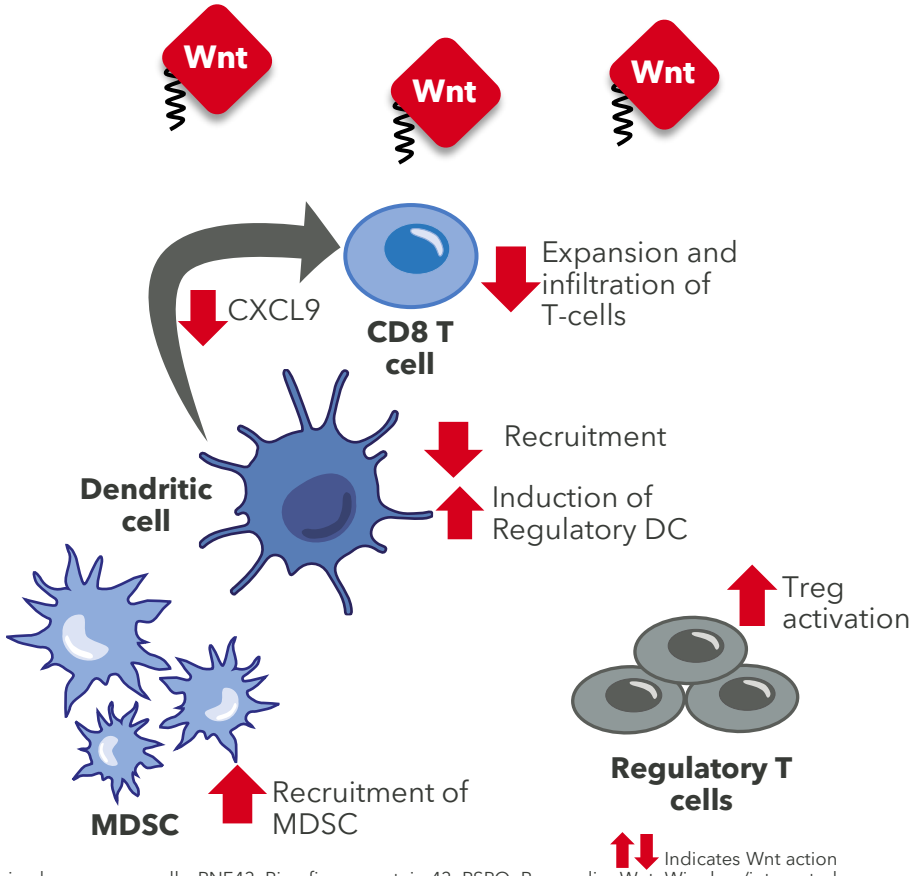
Genetic aberrations lead to Wnt-ligand driven tumour growth



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

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)