Redx
Discovering Targeted Medicines

Corporate Presentation

June 2022

AIM:REDX

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Ambitious Leadership Team with Deep Industry Experience

Lisa Anson, CEO

Experienced General Manager, Former President of AstraZeneca UK with >25 years biotech and pharma

Dr Richard Armer, CSO

Accomplished drug discovery executive, ex Pfizer, Organon, Ardana, Oxagen, Lectus Therapeutics with >25 years biotech and pharma

Peter Collum, CFO

Experienced biopharma finance and strategy executive with >24 years in biopharma as CFO, CBO and healthcare investment banking

Dr Jane Robertson, CMO

Expert oncology drug developer ex AstraZeneca, Achilles, Nucana. Led the successful clinical development of Lynparza with >18 years in biotech and pharma

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

SOFINNOVA PARTNERS

POLAR CAPITAL

Platinum ASSET MANAGEMENT

INVUS

A Clinical Stage Biotech with Three Value Drivers

Selective Porcupine Inhibitor (RXC004)

- Targeting Wnt-ligand dependent tumours
- Differential activity in Ph1 monotherapy
- Ph1 combo ongoing with nivolumab
- Ph 2 (PORCUPINE) initiated: genetically selected MSS mCRC
  - Open IND in the US
- Ph 2 (PORCUPINE2) initiated: genetically selected pancreatic/ unselected biliary cancer

Selective ROCK2 Inhibitor (RXC007)

- Targeting a master switch in fibrosis
- Clinically validated target, with first ROCK2 inhibitor approved by FDA in 2021 for cGvHD
- Ph1 data: confirms safety and PK profile
- Biologically relevant exposures
- Lead indication IPF – Ph2 start in 2022

Discovery Engine

- Targeting 3 wholly-owned INDs by 2025
- RXC008 for fibrostenotic Crohn's disease in pre-IND stage
- Strong track record:
  - Generated four molecules now in clinic incl. pirtobrutinib
  - Partnership deals with Jazz and AstraZeneca
- Partnered programmes: $48.5m milestones since 2019 with further potential milestones

*Calendar year

IND: Investigational new drug application; IPF: Idiopathic pulmonary fibrosis; MSS mCRC: Microsatellite-stable metastatic colorectal cancer; Rho associated protein kinase; Wnt: Wingless/integrated; cGvHD: Chronic Graft vs. Host Disease

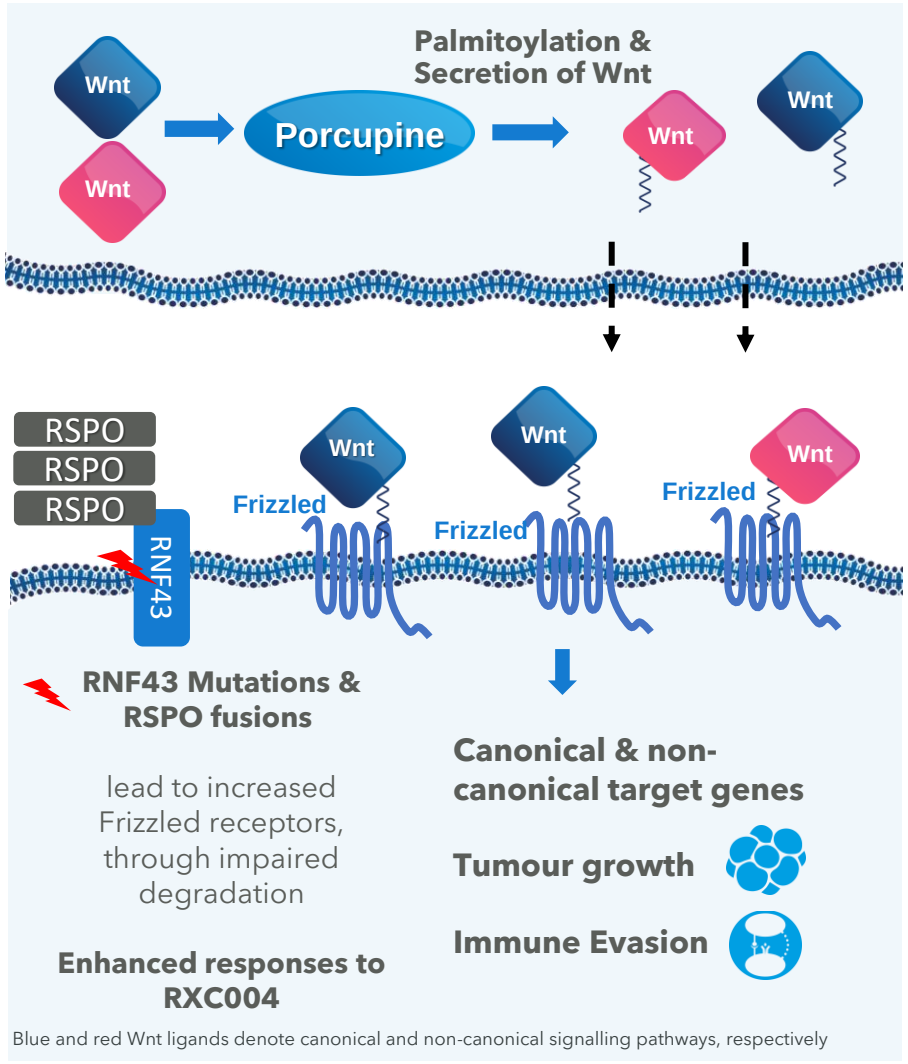
Advancing a Robust Pipeline Built In-House

	Target/ Product	Indication(s)	Research	Preclinical	Phase 1	Phase 2	Phase 3	Upcoming Milestones
Oncology	**Porcupine Inhibitor** (RXC004)	Genetically selected MSS mCRC mono + nivolumab combo Genetically selected pancreatic cancer Unselected biliary cancer mono + PD1 combo			PORCUPINE PORCUPINE2			Initiate combo arms – **H2 2022** Topline data – **From H1 2023**
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 Jazz collaboration

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

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

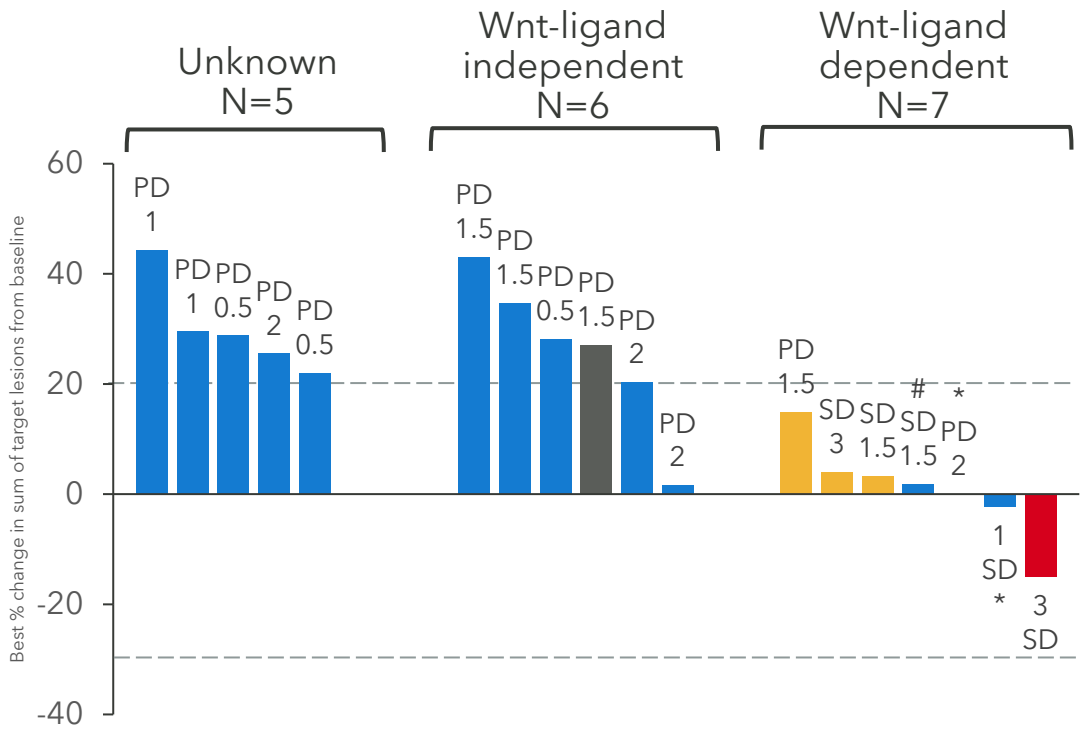
- **Monotherapy and combination** in genetically-selected MSS metastatic colorectal cancer
- Genetically selected pancreatic cancer
- **Monotherapy and combination** unselected biliary cancer

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

RXC004

Clinical Efficacy Data Supports Development in Wnt-Ligand Dependent Tumours

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

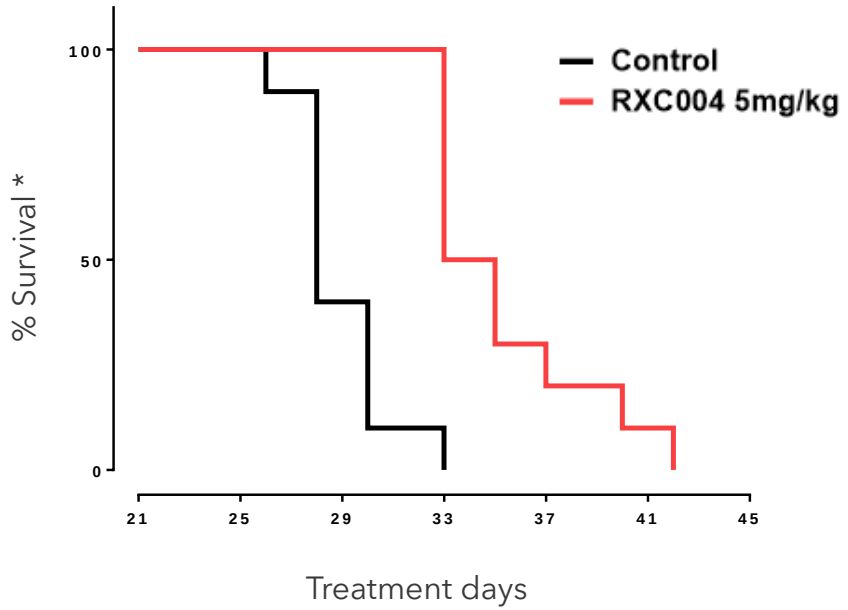
APC: Adenomatous polyposis coli gene; CRC: Colorectal cancer; LoF: Loss of function; PD: Progressive disease; RECIST: Response evaluation criteria in solid tumours; RNF43: Ring finger protein 43; RSPO: R-spondin; SD: Stable disease; Wnt: Wingless/integrated

Data cut-off date 30 July 2021

RXC004

Preclinical Data Supports Potential For Wnt Pathway Blockade to Enhance Immune Related Survival

RXC004 is efficacious in a "cold" tumour model



Improved survival rate observed as monotherapy in B16F10 syngeneic melanoma immune mediated model

Anti-PD1 had no monotherapy effect on this immunologically "cold" model

- Immune-checkpoint inhibitors (ICI) ineffective in MSS mCRC (~95% MSS mCRC[1])
- Wnt driven tumour immune evasion: Wnt activation leads to ICI resistance across 28 cancer types[2,3]
- RXC004 potential to initiate immune responses in "cold" tumours, where anti-PD1 ineffective, and "hot" tumours to improve ICI responses[4]
- Porcupine inhibitor (WNT974, Novartis) in combination with ICI in ongoing clinical trial demonstrates acceptable safety and early proof of concept[5]

(1) Gong et al. March 21, 2017 (ASCO JCO); (2) Spranger et al., 2015; (3) Luke et al., 2019; (4) Phillips et al 2019; (5) Janku et al. (2020) AACR, CT034 - Phase I study of WNT974 + spartalizumab in patients with advanced solid tumors;
* Survival data calculated from the point at which mice were sacrificed when they reached 2500mm^3 tumour volume
ICI: immune-checkpoint inhibitor, mCRC: Metastatic colorectal cancer; MSS: Micro satellite stable

Redx internal data

RXC004

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

	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

RXC004

RXC004 Showed Clinical Efficacy in Wnt-Ligand Dependent Tumours and Manageable Toxicity in Phase 1

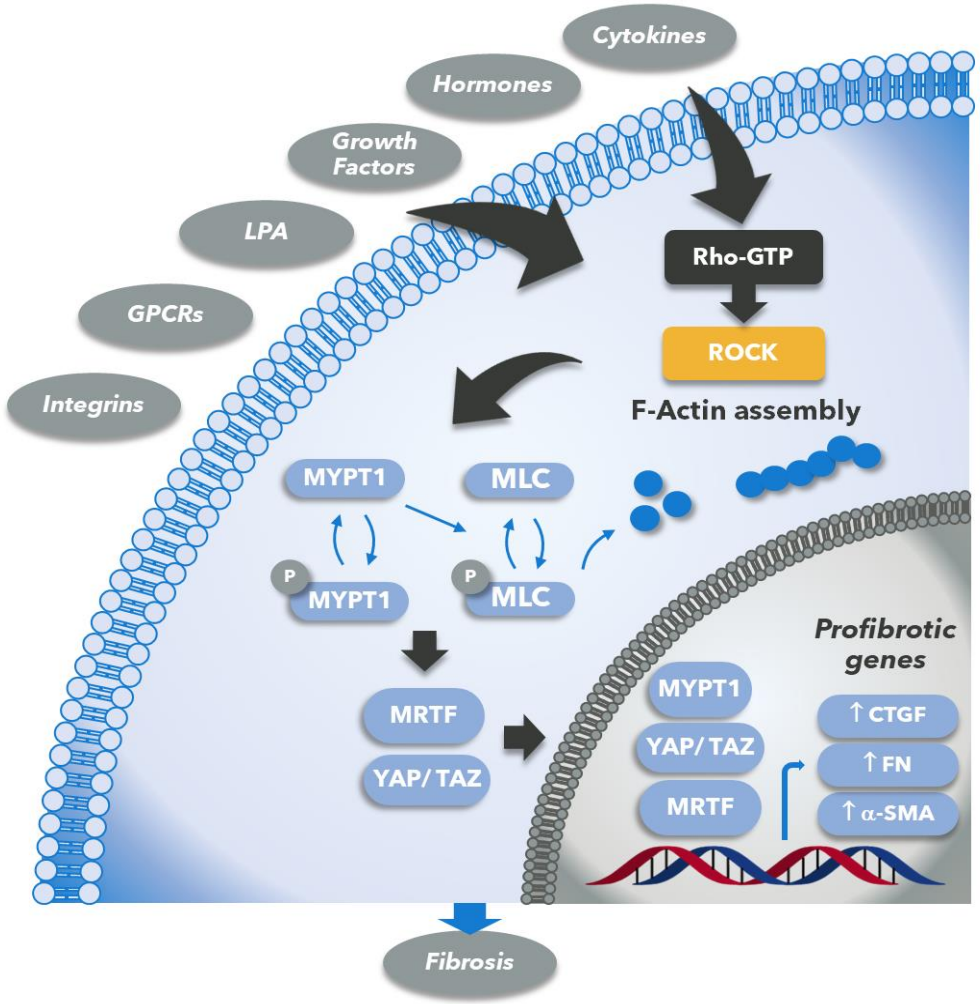
Highlights

- Porcupine inhibition blocks all Wnt ligands, preventing tumour growth and immune evasion
- RXC004 is a highly potent, orally active, once daily Porcupine inhibitor
- RXC004 demonstrated differential clinical efficacy in Wnt-ligand dependent tumours in Phase 1 monotherapy cohort
- RXC004 monotherapy was well tolerated at doses up to 2 mg
- Target engagement evident at all doses, with doses ≥1.5 mg achieving exposures that demonstrated efficacy in all preclinical models tested
- Selected dose for Phase 2 monotherapy studies is 2 mg
- Phase 2 monotherapy programme in Wnt-ligand dependent tumours recruiting; combination arms to commence in H2 2022

Wnt: Wingless/integrated

RXC007

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



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

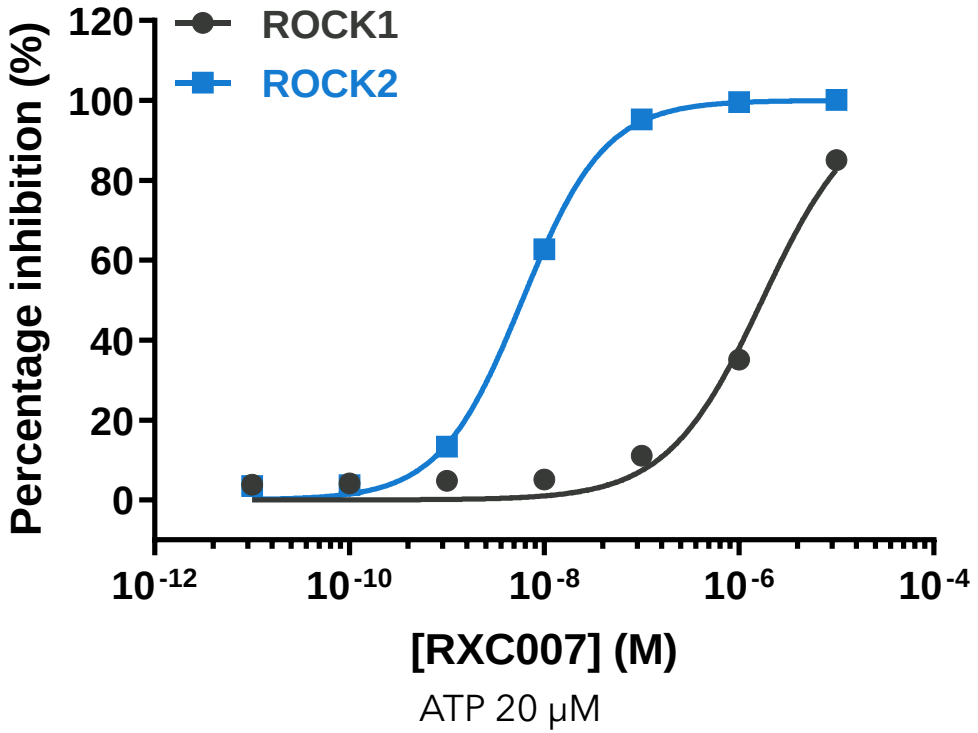
- Idiopathic Pulmonary Fibrosis (IPF) high unmet need - median survival 3-5 years
- IPF market projected to reach $3.6 bn by 2029*

** 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

Selective Inhibition of ROCK 2 Critical to Systemic Safety



- ROCK has been a notoriously difficult target
- Systemic inhibition of ROCK1&2 results in hypotension, not seen with ROCK2 selective inhibition
- Need high selectivity for safety
- RXC007 is potent and highly selective, >100-fold versus ROCK1 in biochemical assays

Redx internal data

ATP: Adenosine triphosphate; Rho associated protein kinase

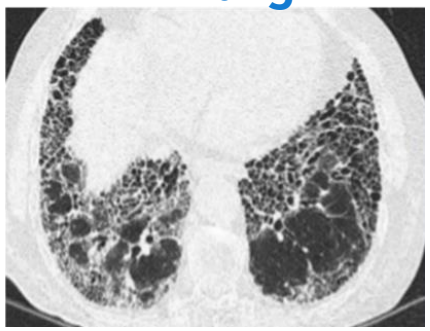
RXC007

Significant Market Opportunity in IPF, where ROCK2 is Implicated

- IPF is a deadly fibrotic disease, median survival 3 – 5 years (1)
- 170,000+patients (2)
- IPF market projected to reach $3.6 billion by 2029 (2)
- Nintedanib and pirfenidone are the only approved treatments for IPF
  - Slow the progression of the disease
  - Side effects that limit use
  - Clear opportunity to improve on standard of care

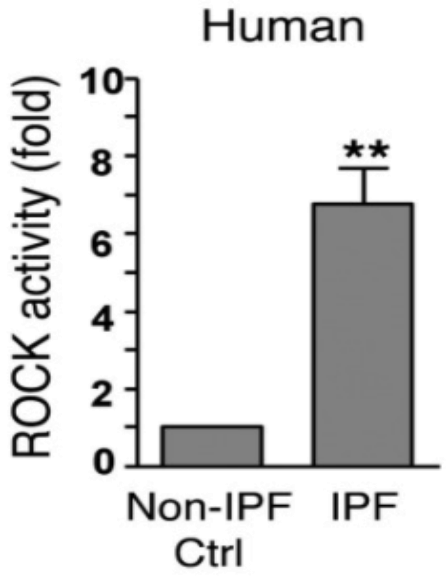
Normal Lung

IPF Lung



ROCK is upregulated in IPF

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



Adapted from Zhou2013

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)

IPF: Idiopathic pulmonary fibrosis

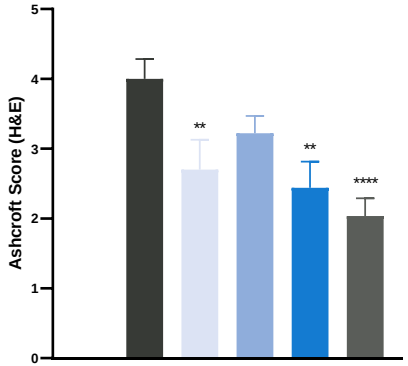
RXC007

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

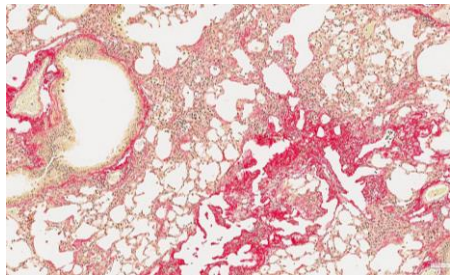


- Vehicle
- Bleomycin Vehicle
- RXC007 (5 mg/kg BID)
- RXC007 (20 mg/kg BID)
- RXC007 (50 mg/kg BID)
- Pirfenidone (100 mg/kg BID) (as a positive control)

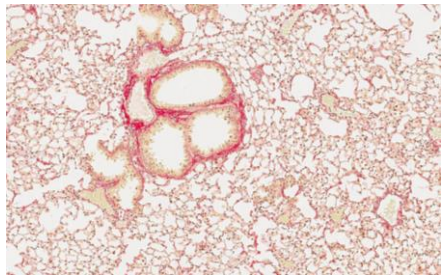
Representative images

Lung histology Sirius red

Vehicle

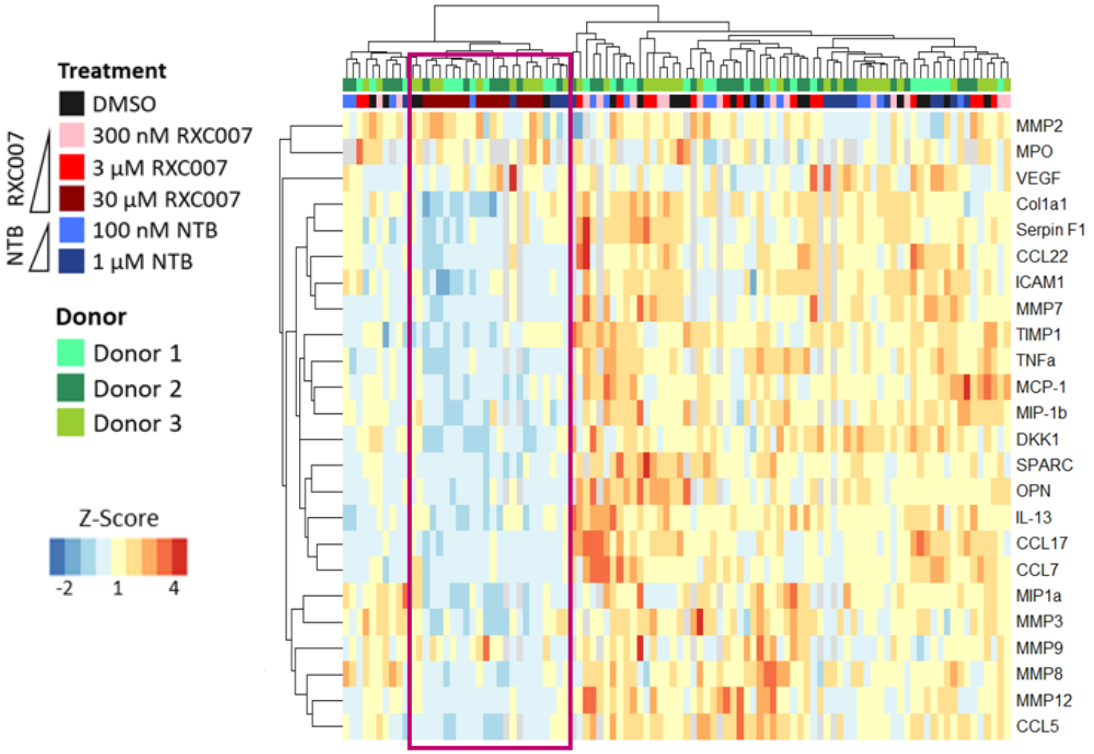


RXC007 50 mg/kg BID



Modulation of key gene signals in IPF lung tissue

Protein expression heatmap comparison to nintedanib (NTB)

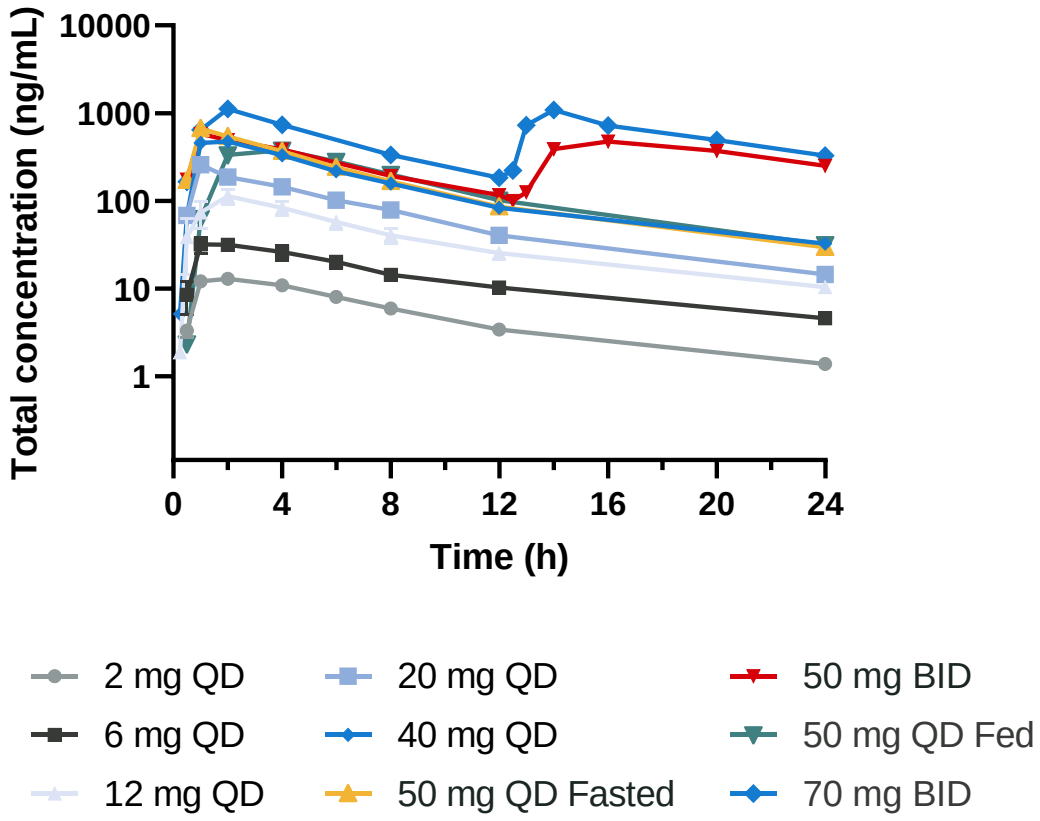


BID: Twice daily; IPF: Idiopathic pulmonary fibrosis

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

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

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 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

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

RXC007

Lead Indication is IPF with Phase 2 Start Expected 2022

Highlights

- ROCK is a validated compelling target at a key junction in cell signalling pathway central to fibrosis
- RXC007 is a highly potent, selective and orally active ROCK2 inhibitor
- Robust preclinical efficacy data supports clinical development plan in IPF
- Phase 1 SAD and 50 mg BID multi dose cohorts completed
- To date* no significant adverse events observed in Phase 1 healthy volunteers and observed PK profile in line with prediction
- Plan to start a staged Phase 2 approach in 2022
- 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 2a dose-ranging study will inform Phase 2b dose
- Phase 2b will dose RXC007 over 12 months plus SoC with FVC lung function primary endpoint

*Data at 3 March 2022

FVC: Forced vital capacity; IPF: Idiopathic pulmonary fibrosis; PK: Pharmacokinetic; Rho associated protein kinase; SoC: Standard of care

Discovery Engine

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 for 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

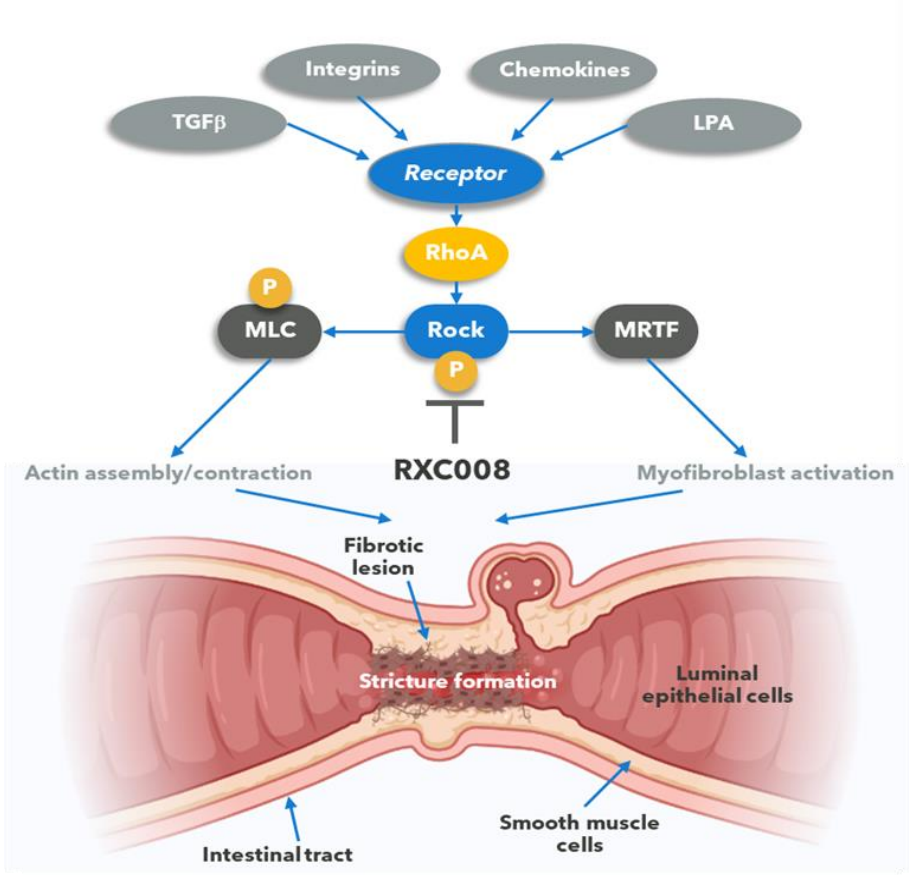
DELIVER
Redx's validated track record

- 5 compounds in clinical development - 2 remain wholly-owned
- Multiple asset deals with $48.5m in milestones earned since 2019
- Targeting 3 additional wholly-owned INDs by 2025

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

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

ROCK: nodal point for fibrotic signaling



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

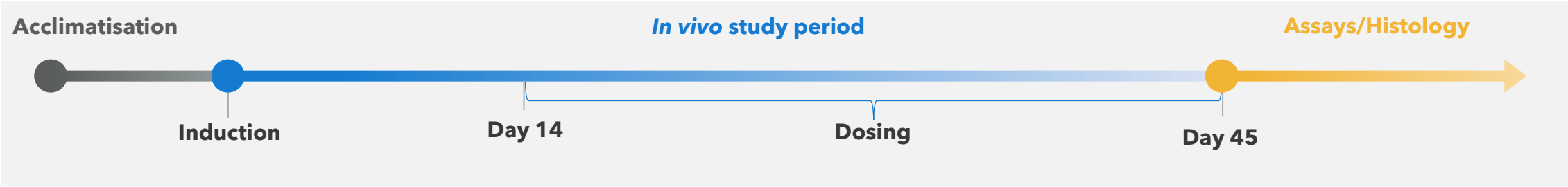
- Crohn's disease affects 1.5m[1] people globally, of which 50% will develop strictures or complications leading to fibrostenosis[2]
- No curative treatment currently available
- No approved therapies for underlying fibrosis

IND enabling work underway - Phase 1 target start end 2023

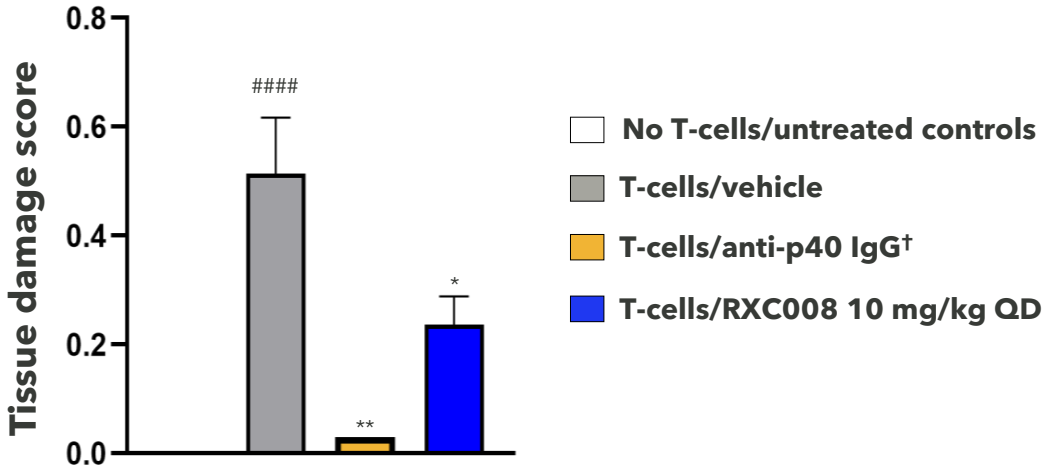
(1) GlobalData Crohn's Disease Dynamic Market Forecast to 2026 report; (2) Chan et al, 2018

IND: Investigational new drug application

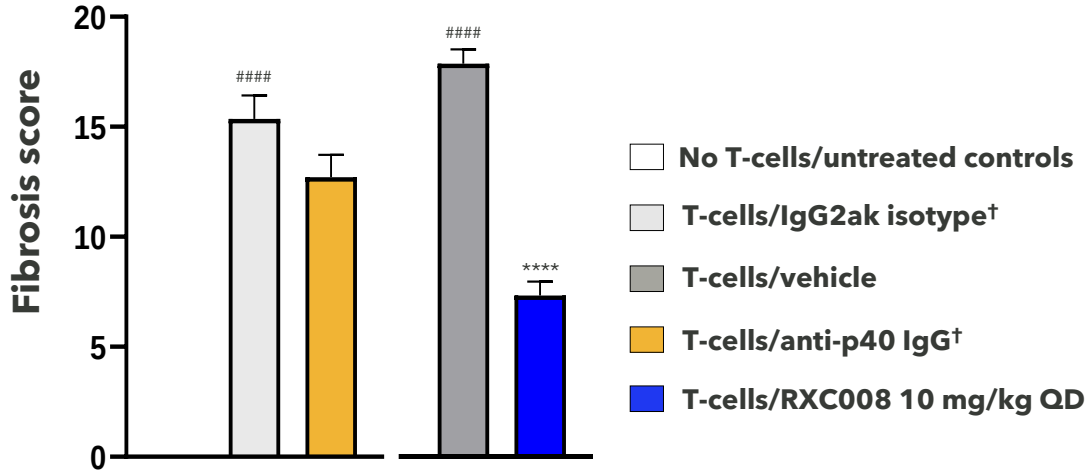
RXC008 Reduces Fibrosis in the Adoptive T-cell Transfer Model



RXC008 reduces tissue damage



RXC008 reduces fibrosis

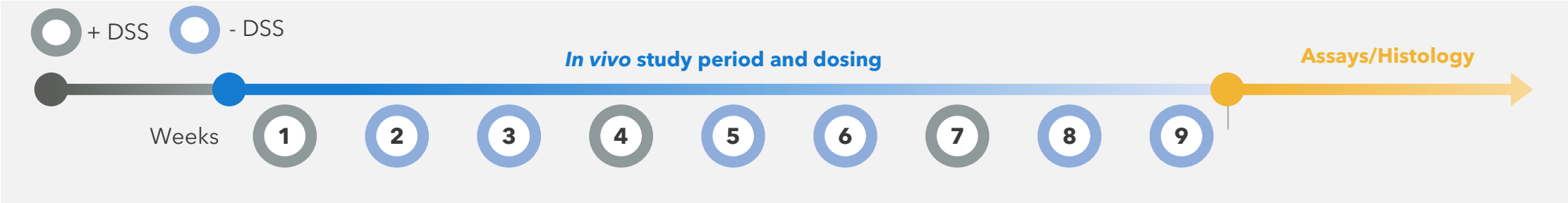


p40 data has been modified for the purpose of graphical representation
Colon damage could not be detected in the p40 treated animals.

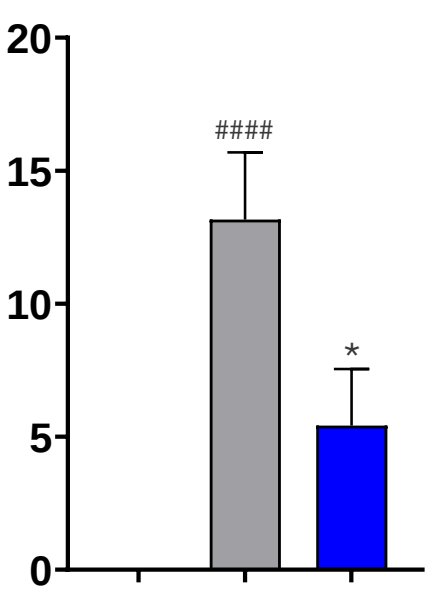
AT: Adoptive T-cell transfer; QD: Once daily

RXC008

RXC008 Reduces Fibrosis in the Chronic DSS Model



Reduction in fibrosis measured by histology



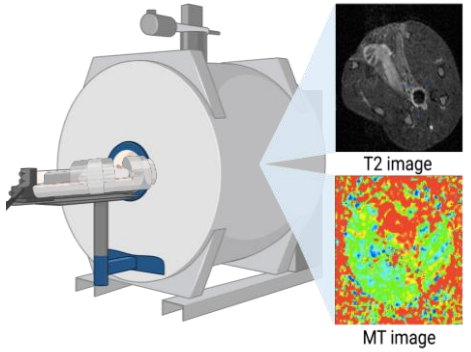
- No DSS untreated controls
- DSS/vehicle
- DSS/RXC008 10mg/kg QD

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

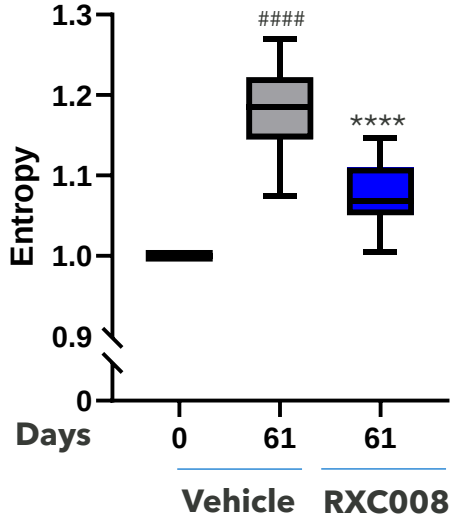
Reduction in fibrosis measured by MRI*

Analysis using MT imaging



Murine sized MRI scanner

Entropy fibrosis score

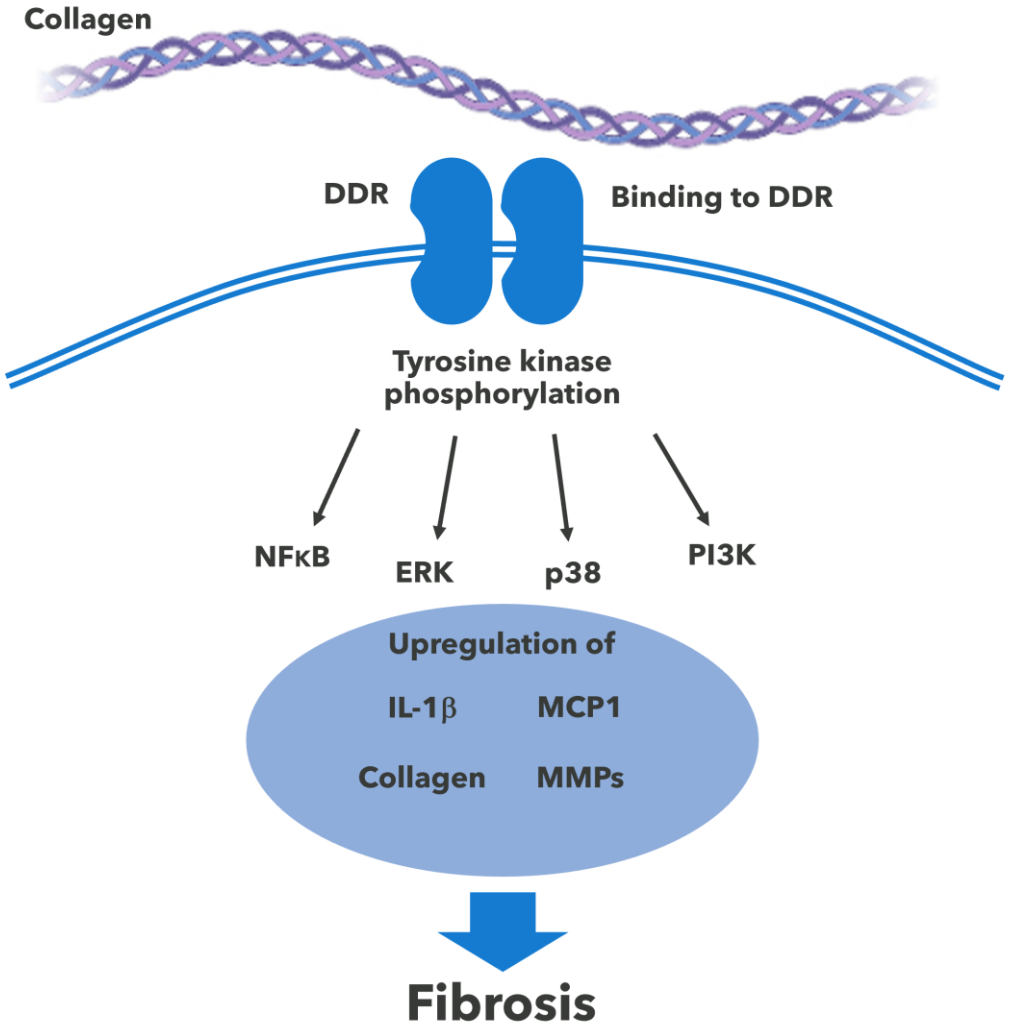


*Research in collaboration with Ghent University

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

Discovery Engine

Discoidin Domain Receptor (DDR) Inhibitors 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 ongoing

DDR: Discoidin domain receptor; PoC: Proof of concept

Funded Through 2023 to Deliver Significant Pipeline Progression

£34.3m funding
secured June 2022
- Strong support from all existing institutional investors
- New specialist investor, Invus
- Priced at market

Current cash £59.7m*

Funds through important clinical data milestones

$24m milestones triggered during FY 2022

Potential future milestones remain available

Supported by top tier Specialist Investors

Redmile Group
SOFINNOVA PARTNERS
POLAR CAPITAL
Platinum ASSET MANAGEMENT
INVUS

* 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

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

Multiple Potential Milestones During 2022 and 2023

* Calendar year	2022*	2023*
Porcupine Inhibitor RXC004	• Data from Phase 1 combination study with nivolumab (anti-PD1) ✓ Initiation of PORCUPINE2 Phase 2 study in genetically selected pancreatic and unselected biliary cancer • Initiation of PORCUPINE combination arm in genetically selected MSS mCRC	• Ph2 data - mono MSS mCRC • Ph2 data - mono biliary cancer • Ph2 interim data - mono pancreatic cancer • Ph2 data - combo MSS mCRC • Ph2 data - combo biliary
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 **DDR Inhibitor (Discoidin Domain Receptor)** **Research Targets**	✓ **H1** Select development candidate • Progress DDR inhibitor for fibrosis • Advance multiple programmes in early discovery	• Progress to target of three additional wholly-owned INDs by 2025
Porcupine Inhibitor (RXC006) **Pan-RAF Inhibitor**	✓ IND cleared triggering $5M June 2022	Next AstraZeneca milestone – Phase 2 start Next Jazz Milestone - Phase 2 start

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

Redx
Discovering Targeted Medicines

Appendix

Ambitious Leadership Team with Deep Industry Experience

Lisa Anson

Chief Executive Officer

>25 years biotech and pharma, with significant senior level commercial leadership and general manager experience

Sector profile as BIA Board member and prior President of ABPI

MBA, MA Natural Sciences

AstraZeneca abpi

Dr Richard Armer

Chief Scientific Officer

>25 years biotech and pharma with significant translational science experience bringing products from discovery to the clinic

Experience at Pfizer, Organon, Ardana, Oxagen and Lectus Therapeutics

PhD in Chemistry

Pfizer ORGANON

Dr Jane Robertson

Chief Medical Officer

>18 years in biotech and pharma, with extensive experience as former CMO at Achilles & Nucana and leading oncology clinical development programs including Lynparza

13 years in clinical practice

MD, MRCP, FRCPath

ACHILLES THERAPEUTICS NUCANA AstraZeneca

Peter Collum

Chief Financial Officer

Experienced biopharma finance and strategy executive with >24 years in biopharma as CFO, CBO and healthcare investment banking

MBA, BS in Engineering

PHARNEXT MTS Health Partners Roche Bank of America

Dr James Mead

Chief Operating Officer

>20 years in biotech and pharma with multiple finance leadership roles including CFO positions as well roles covering Investor Relations and corporate development

PhD in molecular biology, Chartered Accountant

AstraZeneca

Claire Solk

General Counsel

Experienced legal counsel with wide sector experience

Previously with AstraZeneca and Allen & Overy LLP

Admitted to practise in England & Wales and New York

AstraZeneca ALLEN & OVERY

RXC004

Significant Opportunity in Genetically Selected Wnt-ligand Driven Cancers with High Unmet Need

Approximately 74,000 patients per year in the initially targeted indications

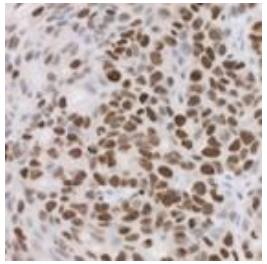
	5 Year Survival (metastatic disease)	Annual incidence of (new) metastatic cases	Prevalence of Wnt-driven tumours	Annual target market (new patients)
MSS mCRC	14%	178k	8% (3% RNF43 + 5% RSPO)	14k
Pancreatic Cancer	3%	130k	7% (RNF43)	9k
Biliary Cancer	2%	>51k	70% (>70% of all biliary cancer Wnt-driven)	>51k

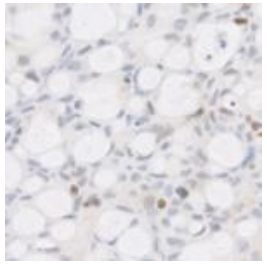
* Source: GlobalData from 7 major markets (US, EU5, Japan)

RXC004

RXC004 Has a Dual Mechanism of Action

Inhibits Tumour Cell Proliferation





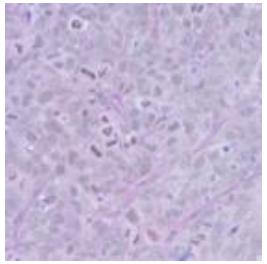
Reduces Ki67 staining in RSPO-fusion CRC xenograft model

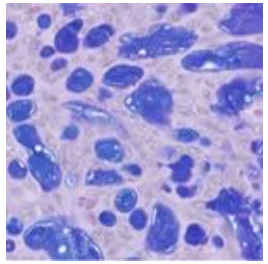
DIRECTLY TARGETS TUMOUR CELLS

RXC004

REVERSES WNT PATHWAY INDUCED IMMUNE EVASION

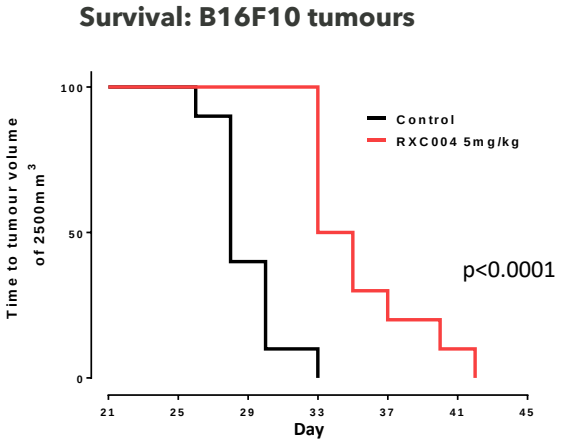
Differentiates Tumour Cells





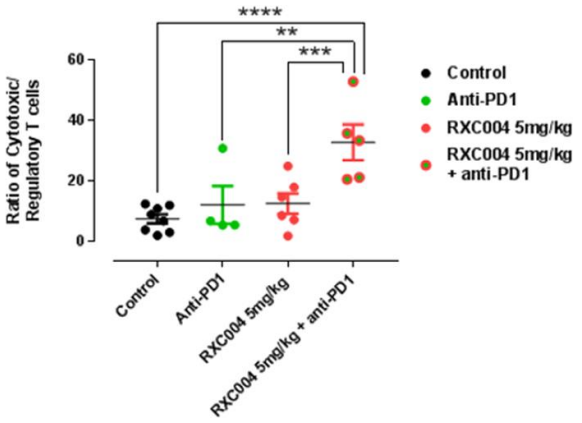
Increased size and mucin staining of tumour cells with RSPO-fusion. Cells also less metabolically active

As a Monotherapy



Increased survival rate post-RXC004 monotherapy treatment in anti-PD1-resistant mouse melanoma syngeneic model (B16F10)

In Combination with anti-PD1



Statistically relevant change in ratio of Cytotoxic T cells: Regulatory T cells with combination of RXC004 + anti-PD-1 compared to either monotherapy alone

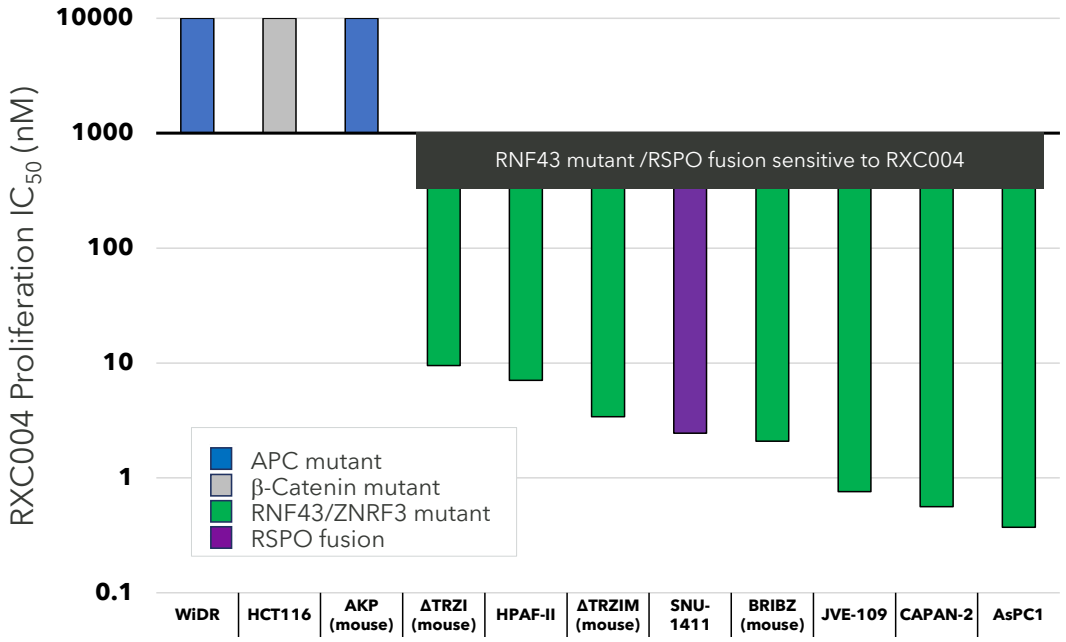
Data as of 7th June 2021

CRC: Colorectal Cancer; RSPO: R-Spondin

RXC004

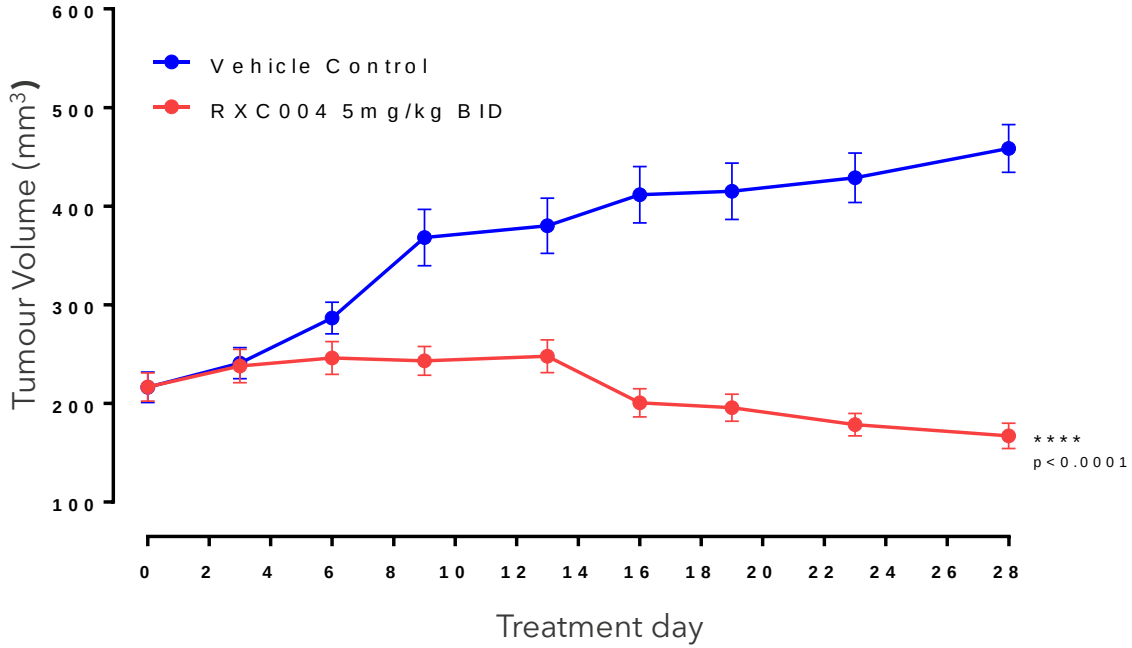
Potential for Enhanced Responses in Patients Supported by Genetically Selected Cancer Models

Cells with RNF43 mutations or RSPO fusions are sensitive to RXC004 *in vitro*



Inhibition of cell proliferation with RXC004 across 11 genetically-defined cancer cell models of Wnt pathway aberration

Efficacy translates *in vivo* in genetically defined xenograft models



RNF43 mutant human pancreatic cancer line (Capan-2) grown in a mouse xenograft model (10 mice/group)

Redx internal data

BID: Twice daily; RNF43: Ring finger protein 43; RSPO: R-spondin; ZNRF3: Zinc and ring finger 3

RXC004

Phase 1: Monotherapy Complete; Data from Dose Escalation for Anti-PD1 Combination Expected H1 2022

Phase 1 Objective: Assess safety and tolerability of RXC004 in all-comer cohorts of advanced cancer patients

Dose escalation - single ascending dose / multiple ascending dose, 3+3 design

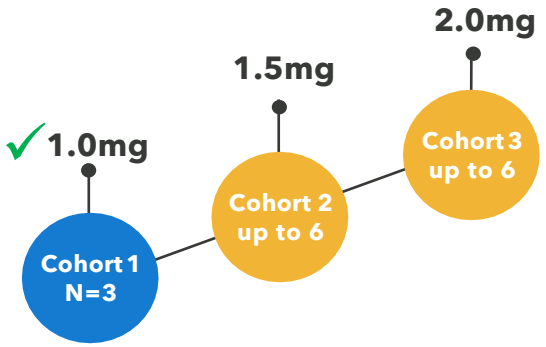
Module 1: Monotherapy, 0.5-3.0 mg, N=24

Completed - presented at ESMO 2021

- Drug well tolerated in patients up to 2 mg
  - Most common AEs: fatigue, decreased appetite, nausea, dysgeusia, vomiting
  - Dysgeusia appears dose-related; did not lead to discontinuations
- 2 mg selected as Phase 2 monotherapy dose

Module 2: Nivolumab Combination, 1.0-2.0 mg

Ongoing



- 1 mg dose was well tolerated in combination with nivolumab 480 mg every four weeks

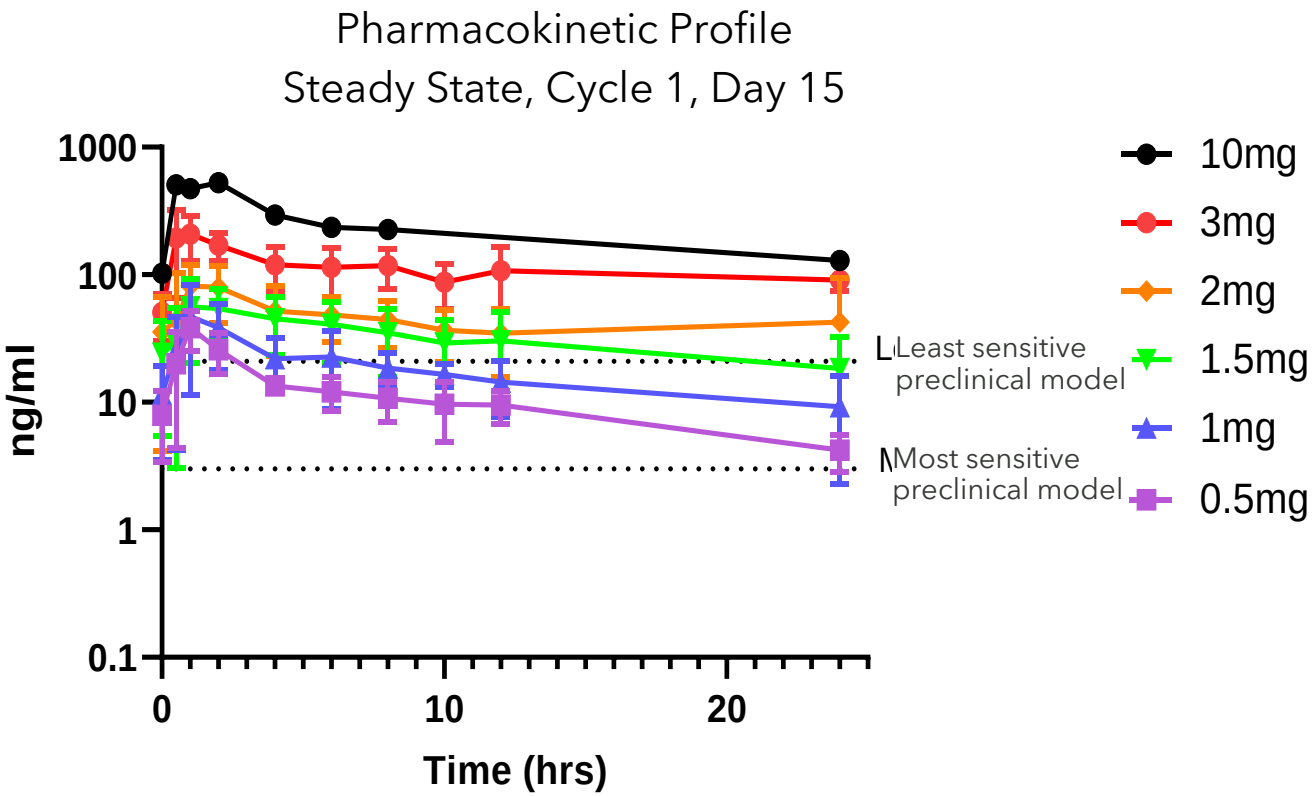
Module 3: Monotherapy Dose Scheduling, 2 mg, N=12

Initiating 2022

ESMO: European Society for Medical Oncology

RXC004

Achieving Exposures that Demonstrated Efficacy in All Preclinical Models Tested



Pharmacokinetic profile supports once daily dosing (14.5 hours half-life)

Doses ≥1.5mg achieved exposures that demonstrated efficacy in all preclinical models tested

Dotted lines represent the minimum efficacious concentration (Cmin) from preclinical oncology models. These range from Cmin cover of >1x IC50 (most sensitive model) for 24hrs to >7x IC50 (least sensitive model) for 24hrs.

Data cut-off date 30 July 2021

ECOG: Eastern Cooperative Oncology Group; ESMO: European Society for Medical Oncology; PK: Pharmacokinetic; Other tumours: Thymus cancer, High grade serous fallopian tube cancer and squamous cell anal cancer

RXC004

RXC004 Monotherapy is Safe and Well Tolerated up to 2 mg

Redx

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

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

Redx internal data

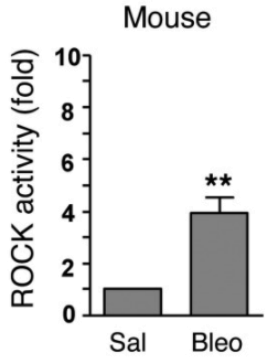
ESMO: European Society for Medical Oncology; TRAE: Treatment related adverse event; Wnt: Wingless/integrated

RXC007

Strong Literature Rationale for Targeting ROCK2 in IPF

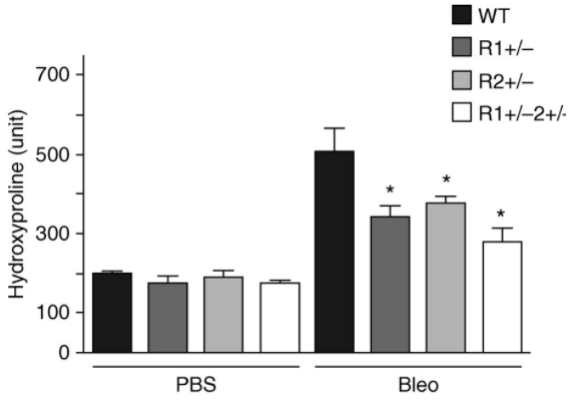
ROCK2+/- knockout mice are protected from bleomycin-induced pulmonary fibrosis

RhoA/ROCK/ROCK2 signalling pathway is enhanced in bleomycin-induced mice



Adapted from Zhou2013

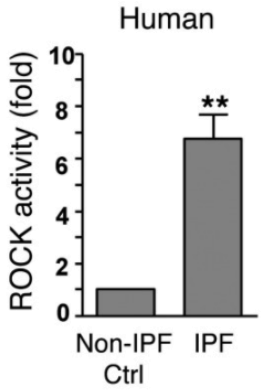
Genetic reduction in either or both ROCK isoforms affords protection from bleomycin-induced pulmonary fibrosis



Adapted from Knippe2018

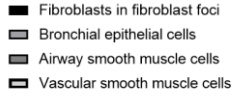
Signalling pathway is enhanced in human IPF patients

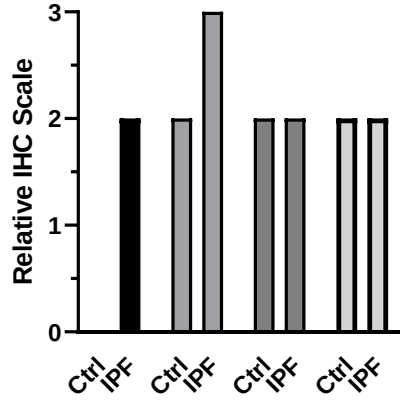
RhoA/ROCK/ROCK2 signalling pathway is enhanced in human IPF patients



Adapted from Zhou2013

Increased expression and activation of ROCK2 in IPF bronchial epithelial cells & fibroblasts





Adapted from Shimizu2014

IPF: Idiopathic pulmonary fibrosis; ROCK: Rho associated protein kinase