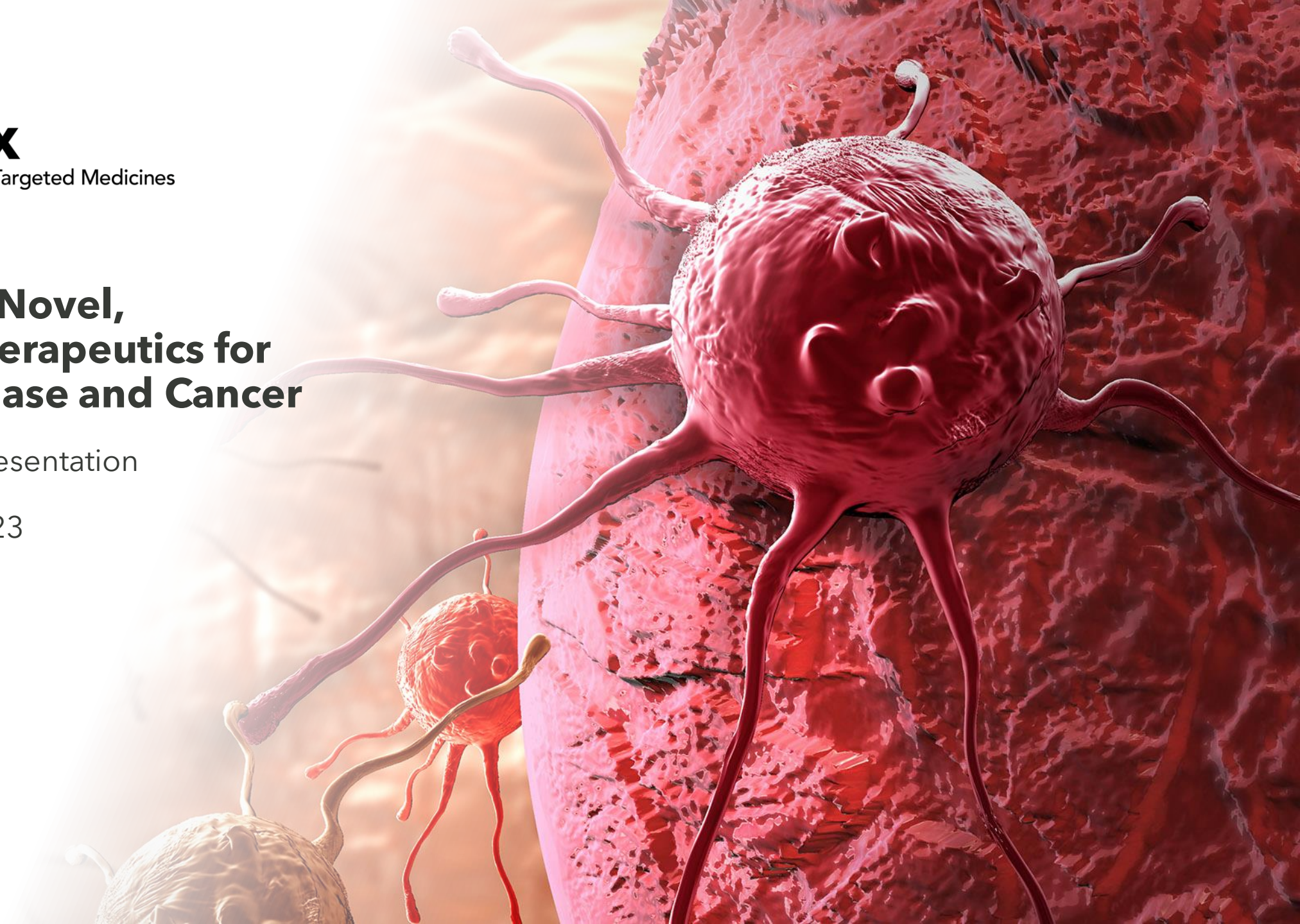
Redx
Discovering Targeted Medicines

Developing Novel, Targeted Therapeutics for Fibrotic Disease and Cancer

Annual Results Presentation

15 December 2023



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Significant Progress Lead by Differentiated ROCK Inhibitor Portfolio

Phase 2a programme ongoing

Zelasudil (RXC007)

- Phase 2a IPF trial - cohort 1 completed, cohort 2 ongoing
- Preclinical data presented from cGvHD and pancreatic cancer models
- Organ Drug Designation granted by US FDA
- Clear path forward to address FDA Partial Clinical Hold for longer dose duration

Regulatory submission completed

RXC008

- IND-enabling studies completed
- Clinical Trial Application (CTA) submitted post-period
- Phase 1 healthy volunteers expected to commence H1 2024

Refined strategy to partner

RXC004

- All Phase 2 programme modules closed for recruitment - data H1 2024
- Strategic decision to partner post-Phase 2 data readout

Extended cash runway & strengthened pipeline

Corporate

- £14.1m financing secured providing cash runway into Q3 2024
- RXC009, a selective DDR1 inhibitor nominated as novel development candidate
- Next development programme confirmed as KRAS inhibitor, targeting G12D and multi-KRAS profiles

cGVHD: Chronic Graft Versus Host Disease; FDA: Food and Drug Administration; DDR1: Discoidin Domain Receptor 1; KRAS: Kirsten rat sarcoma virus

Robust Pipeline Focused on Advancing ROCK Inhibitor Progammes

	Target/ Product	Indication(s)	Research	Preclinical	Phase 1	Phase 2	Upcoming Milestones
ROCK Portfolio	**ROCK2 Selective Inhibitor** Zelasudil (RXC007)	Idiopathic pulmonary fibrosis (IPF)					Phase 2a topline data **H1 2024**
		Pancreatic cancer*					Phase 1b commence **2024**
		cGvHD*					Phase 2a commence **2024**
	GI-targeted ROCK Inhibitor (RXC008)	Fibrostenotic Crohn's disease					Phase 1 commence **H1 2024**
Pipeline	**Porcupine Inhibitor** (RXC004)	Genetically selected MSS mCRC, biliary tract cancer and pancreatic cancer					Data report **H1 2024** Potential Partnership
	Discoidin Domain Receptor (DDR) Inhibitor (RXC009)	Fibrosis, cancer-associated fibrosis					IND / CTA Submission
	KRAS Inhibitors (G12D selective and multi)	Oncology					DC nomination
Partnered	**Porcupine Inhibitor** (RXC006/AZD5055)	Idiopathic pulmonary fibrosis (IPF)					Licensed to AstraZeneca
	Pan-RAF Inhibitor (JZP815)	Oncology					Sold to Jazz
	MAPK Pathway Target	Oncology					Licensed to Jazz

GI: Gastrointestinal; IND: Investigational new drug application; MAPK: Mitogen-activated protein kinase; MSS mCRC: Microsatellite-stable metastatic colorectal cancer; RAF: Rapidly accelerated fibrosarcoma; ROCK: Rho associated protein kinase; cGvHD: Chronic Graft Versus Host Disease; KRAS: Kirsten rat sarcoma virus
*Would require additional funding

zelasudil (RXC007)

Zelasudil (RXC007): A Selective ROCK2 Inhibitor for Fibrotic Diseases

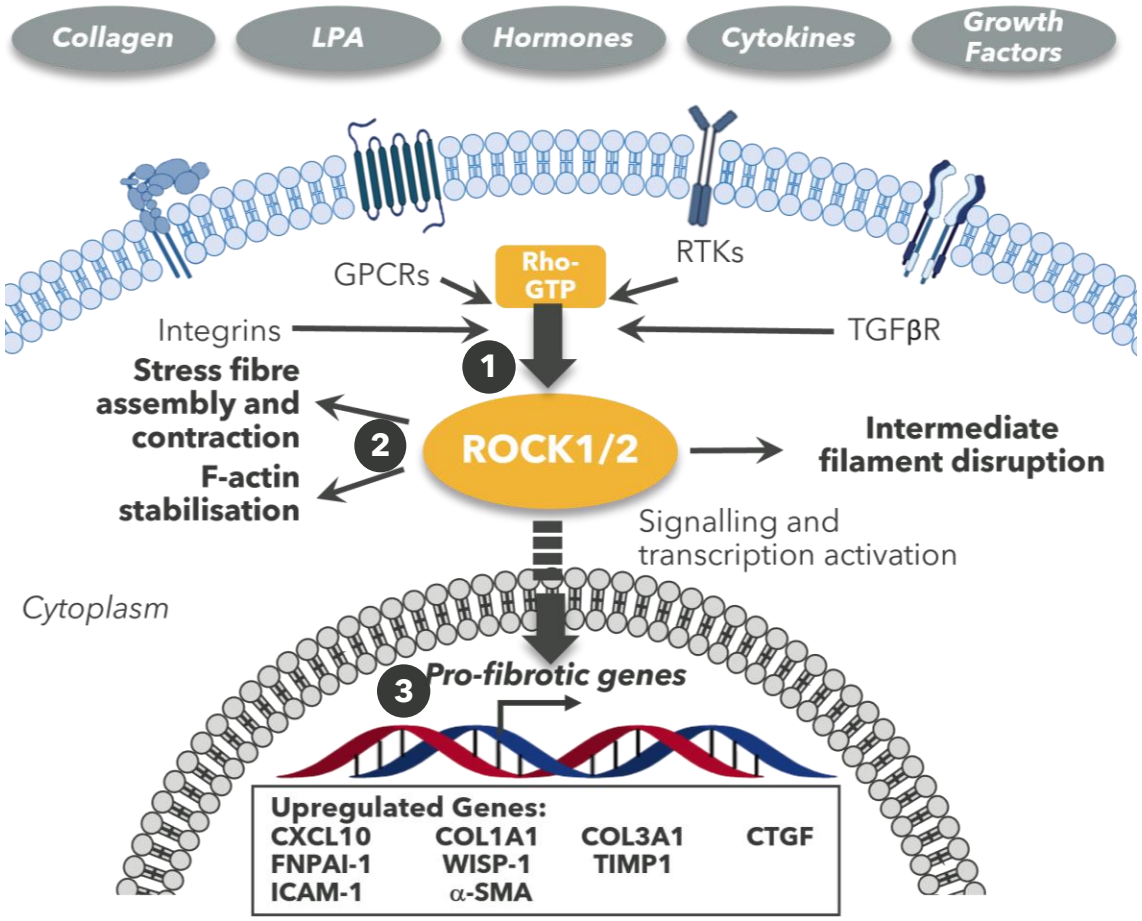
Highlights

- Zelasudil is a highly potent and orally-active selective 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, as well as potential in cancer-associated fibrosis and cGvHD
- Phase 1 healthy volunteer data in single ascending and multiple ascending dose cohorts confirms drug like profile for safety and PK
- Phase 2a in IPF recruiting - **expected to report topline data H1 2024**
  - 12-week Phase 2a dose ranging study for early efficacy readouts, safety and tolerability in IPF patients +/- SoC, in addition to target and disease biomarker engagement
  - No safety signals in review of 20 mg cohort; 50 mg cohort ongoing
- Orphan Drug Designation granted by US FDA for IPF
- FDA Type A meeting confirmed investigative dog study design is appropriate to address partial clinical hold
- Phase 2b in IPF and CF-ILD planned for zelasudil with SoC over 12 months with lung function (FVC) as primary endpoint
- Clinical development plan includes Phase 1b study of zelasudil in combination with SoC chemotherapy in first line pancreatic cancer and a Phase 2a study in cGvHD

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; GVHD:Graft Versus Host Disease

zelasudil (RXC007)

ROCK is a Compelling, Nodal Target for Fibrotic Diseases



Why Target 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 Selective?

- The role of ROCK2 in a diverse range of cellular process allows zelasudil 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

zelasudil (RXC007)

Zelasudil is a Next-Generation Selective ROCK2 Inhibitor With Potential to Improve Safety and Therapeutic Outcomes

Selectivity

Highly selective with limited off target pharmacology

Drug-drug interaction

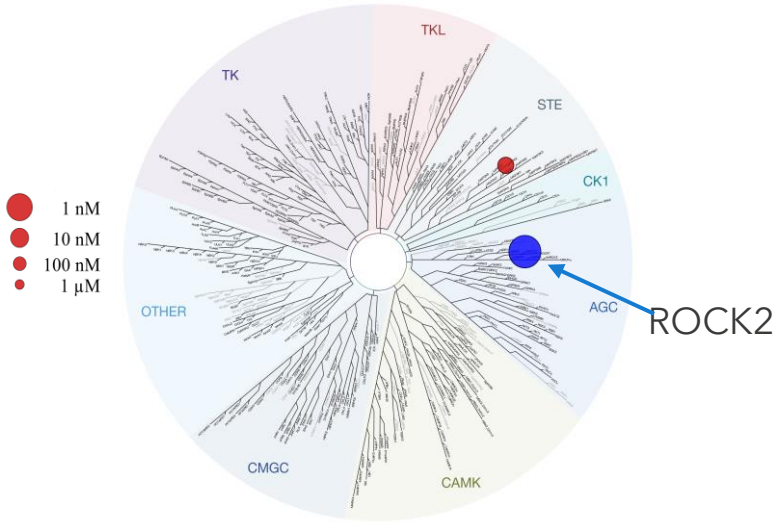
Limited cytochrome P450 interaction supports combinability

PK / Bio-distribution

Increased exposure at lower doses than previous ROCK2 inhibitors

Zelasudil
Selective ROCK2 inhibitor

Best-in-class opportunity



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

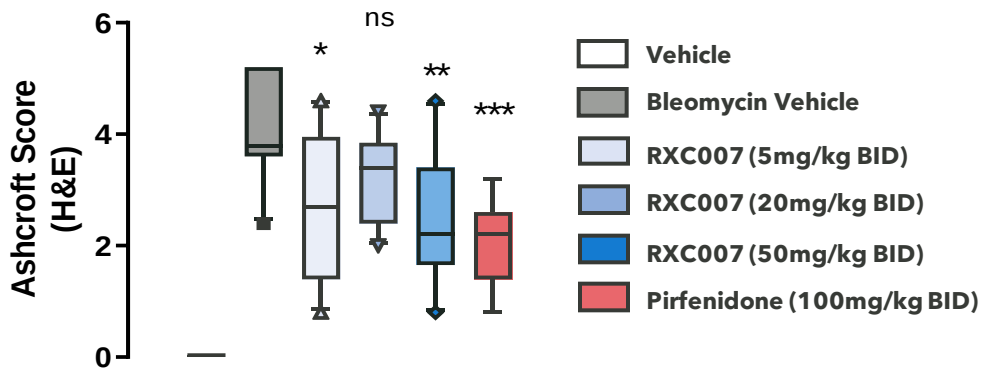
Selectivity >100-fold vs ROCK 1 and vs 468 kinases

ROCK: Rho-associated protein kinase

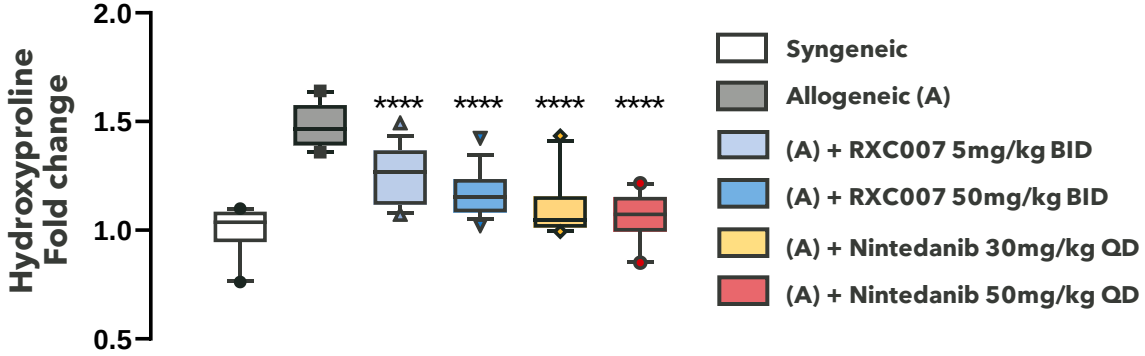
zelasudil (RXC007)

Zelasudil Activity on Patient Tissue and in Preclinical Models Supports Core Development Plan in IPF and CF-ILDs

Reduction in Collagen Deposition with zelasudil in Therapeutic Murine Bleomycin-induced Lung Fibrosis Model

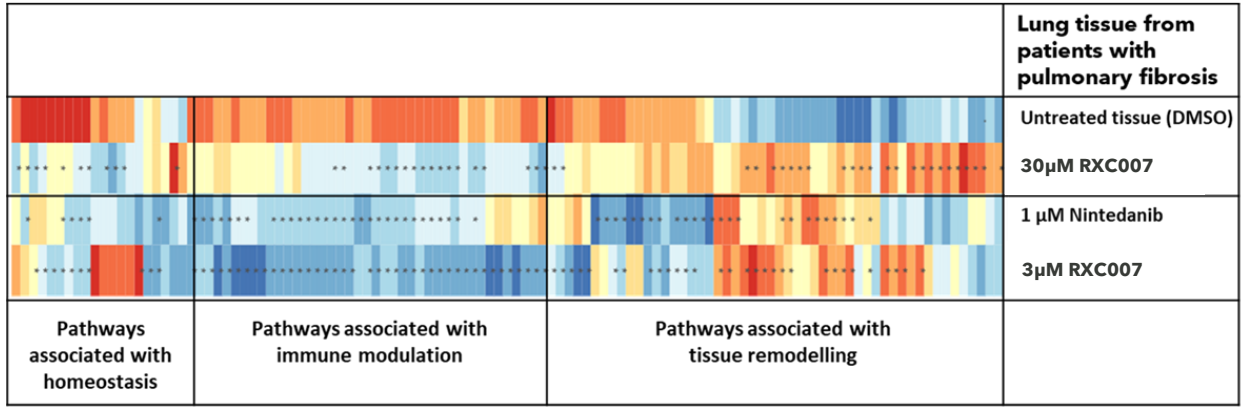


Significant Reduction of Collagen Content in Lungs in Murine Sclerodermatous chronic Graft versus Host Model



Gene Set Enrichment Analysis of human PCLS Tissues Shows ROCK2 Relevance in Disease Modulation

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

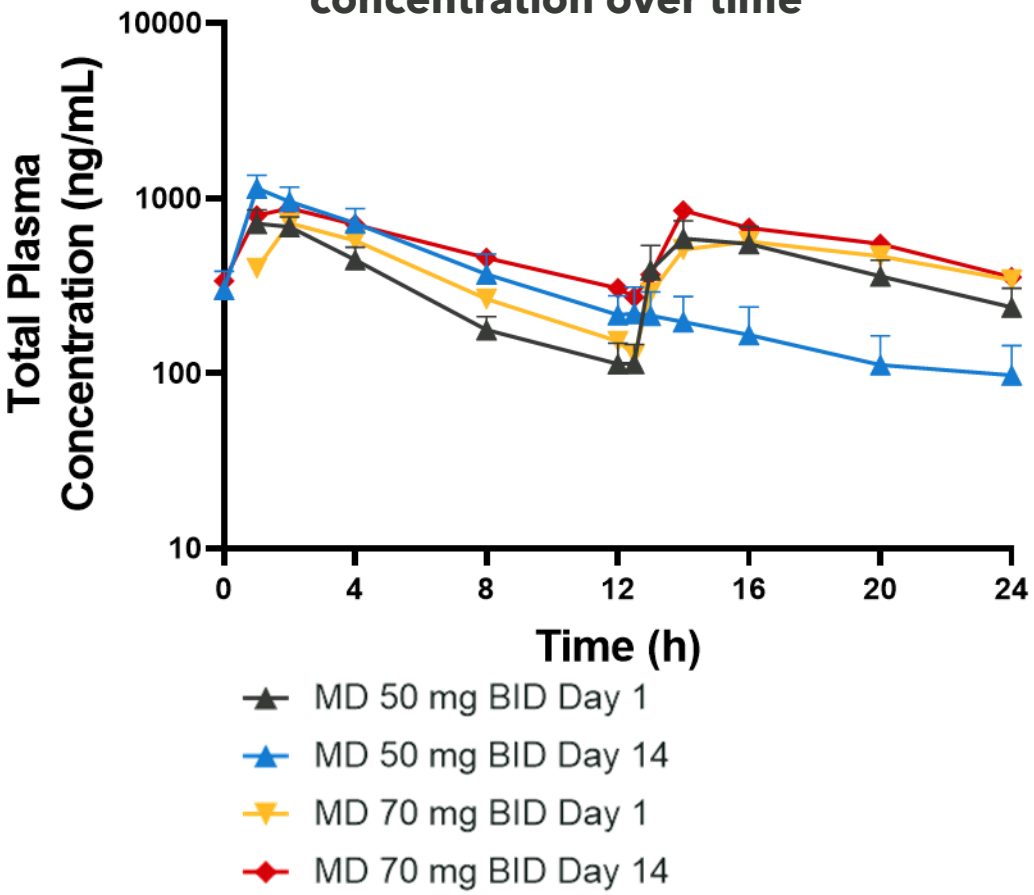


Source: Data generated by Redx

zelasudil (RXC007)

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

Multidose cohort 50mg and 70mg BID - total plasma concentration over time



PK sampling up to 72 h; only 0-24 h plotted. On day 14 only 1 dose administered
Source: Data generated by Redx

Good safety profile

- No SAEs reported in SAD or multidose cohorts
- Doses tested in SAD from 2mg-100mg QD and doses tested in MAD: 50mg BID and 70mg BID
- 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 or twice 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

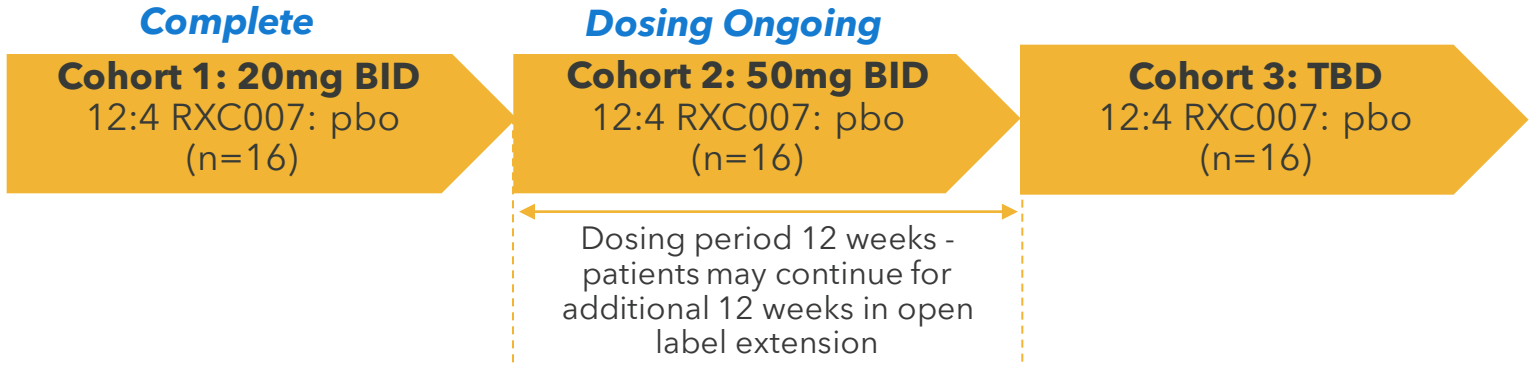
BID: Twice daily; QD: Once daily; SAD: Single ascending dose; SAE: Serious adverse event

zelasudil (RXC007)

Phase 2a Study in IPF Patients Ongoing with Data Readout Expected H1 2024

Phase 2a IPF Dose Ranging Study to Confirm Phase 2b Dose

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



Key endpoints

- Safety and tolerability
- PK profile
- Efficacy signals: changes from baseline in lung function [FVC and DLCO]; changes from baseline in Quantitative Lung Fibrosis Score, airway volume and resistance on HRCT
- Translational science: changes from baseline in blood biomarkers e.g. Pro C3, Pro C6

Status

- 9 Countries (UK + 8 EU countries) approved with 31 sites open
- US approved for 28-day dosing (sub-study)
- Plan progressing to extend preclinical package and address current US FDA partial clinical hold for dosing longer than 28 days
- Multiple patients treated up to 6 months (open label extension)
- Well tolerated with and without standard of care agents to date

Translational Science Sub-Study to provide further supportive biomarker data

Study design

- 1 or 2 cohorts
- 8 patients on zelasudil
- Dosing period of 4 weeks; patients may continue for an additional 8 weeks

Key endpoints

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

*Sub-study to follow main study
Pbo: Placebos; RP2D: Recommended Phase 2 dose

RXC008

RXC008: GI-targeted ROCK Inhibitor for Fibrostenotic Crohn's Disease

Highlights

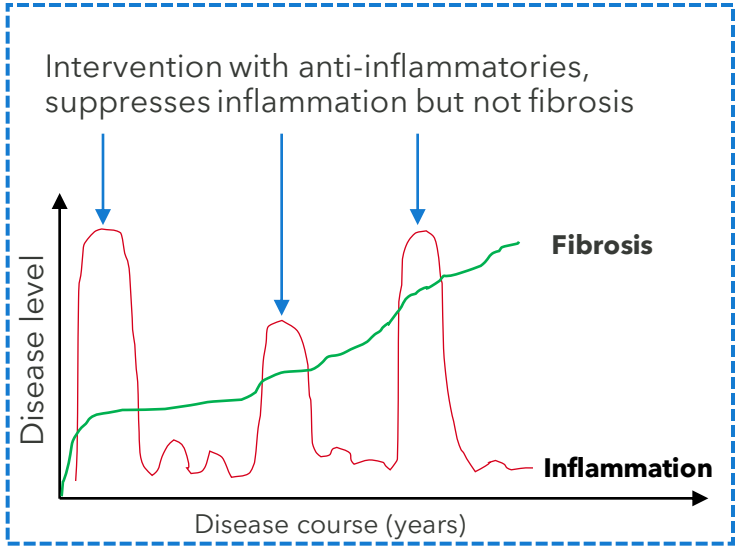
- RXC008 is a potent, oral, small molecule ROCK 1/2 inhibitor
- RXC008 is GI-targeted - designed to be selectively active in gut, avoiding the known risk of hypotension with systemic exposure with ROCK inhibitors
- Fibrostenotic Crohn's disease is a significant unmet need – only current treatment option 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 nodal target involved in fibroblast activation, and is upregulated in fibrostenotic Crohn's disease
- RXC008 has demonstrated robust preclinical efficacy, including reversal of fibrosis, in preclinical *in vivo* models
- **Phase 1 planned to commence H1 2024**
  - CMC API manufacture complete
  - Toxicology studies completed
  - Clinical Trial Application (CTA) Submitted

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

RXC008

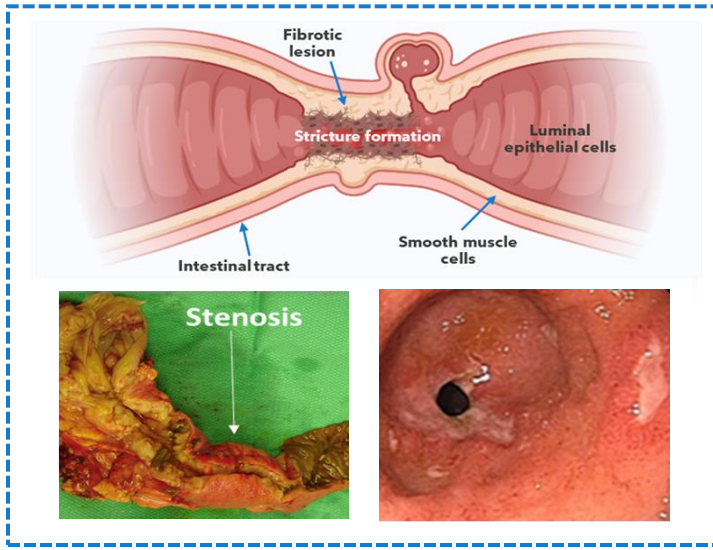
Potential First-in-Class Treatment for Fibrostenotic Crohn's Disease

Clinical progression in Crohn's



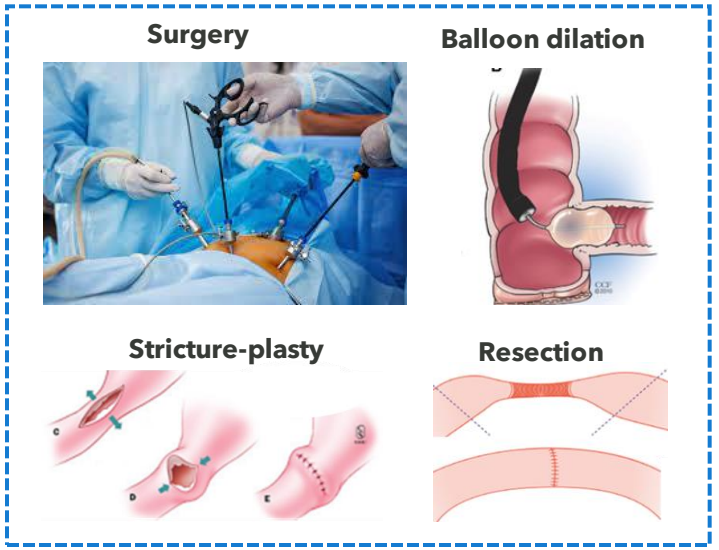
1.7 million(1) patients globally affected by Crohn's disease

Fibrotic stricture formation



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

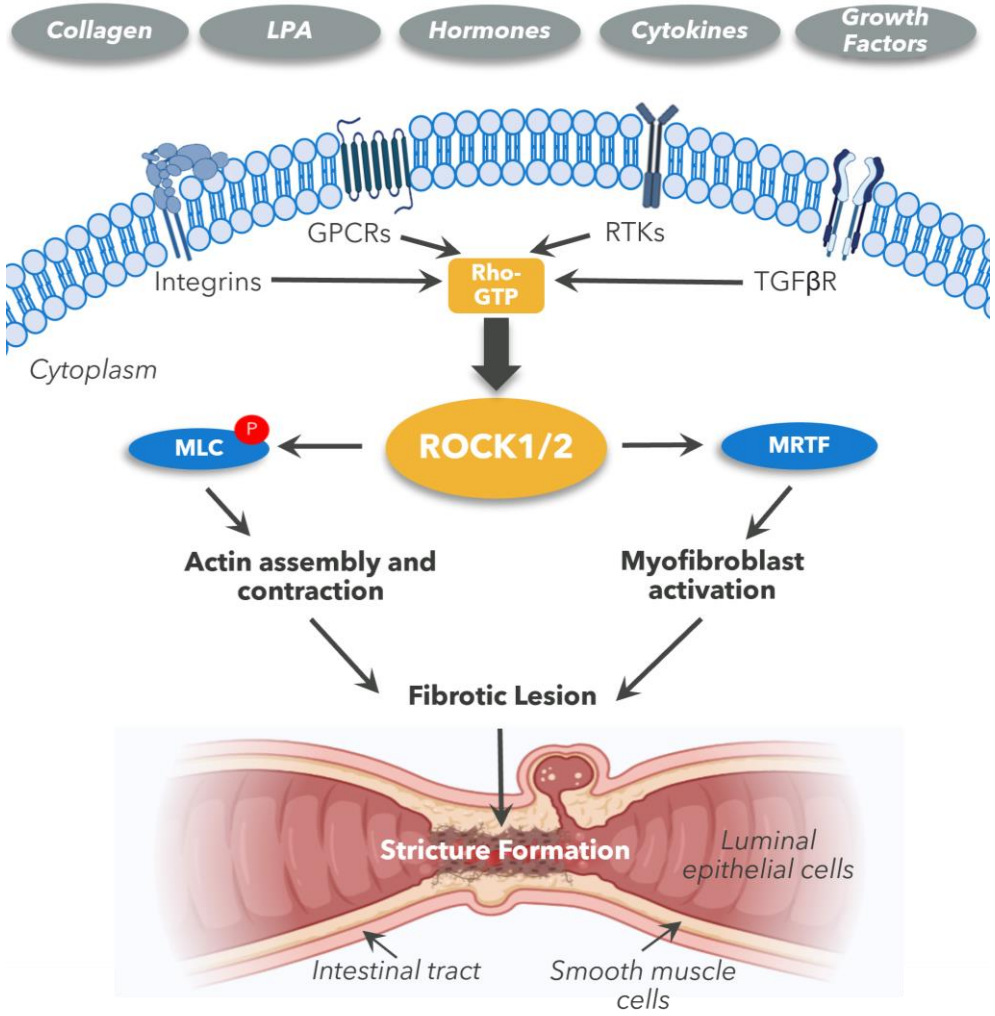
Surgical interventions



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 a Potent GI-Restricted pan-ROCK Inhibitor

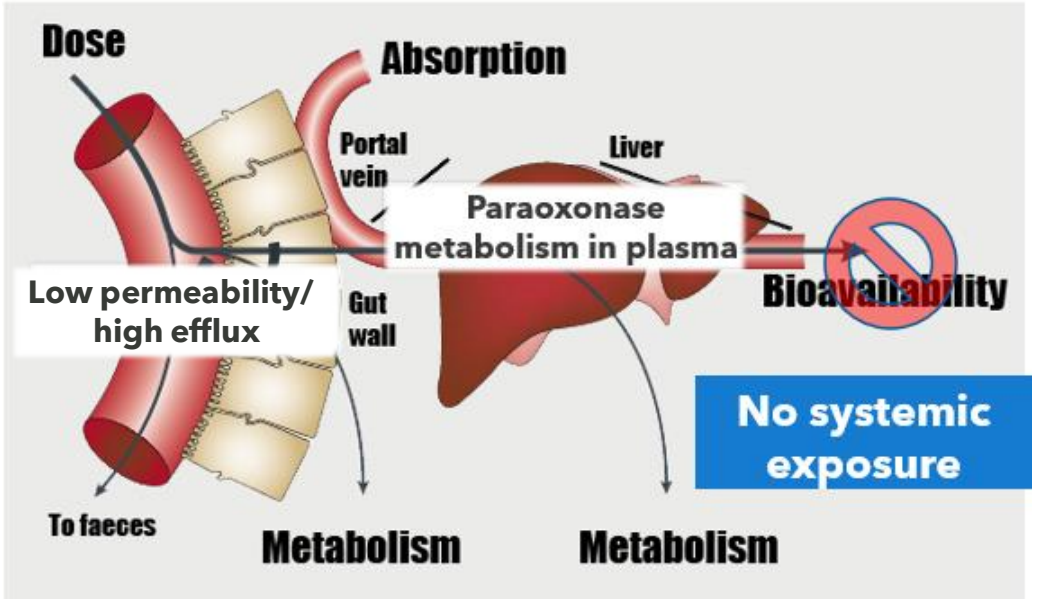
RXC008 potent ROCK inhibition, lost on metabolism by plasma paraoxonases

RXC008 & primary metabolite (REDX11246) enzyme & cell activity

	RXC008 (nM)	REDX11246 (nM)
ROCK1 IC_{50}	1.2*	13.6
ROCK2 IC_{50}	1.3*	23.5
ROCK1 pMYPT1 IC_{50}	2.0	151.4
ROCK2 pMYPT1 IC_{50}	2.3	165.8
ROCK1 + ROCK2 pMYPT1 IC_{50}	4.6	278.4

* Tight binding Limit of assay
Data generated by Redx

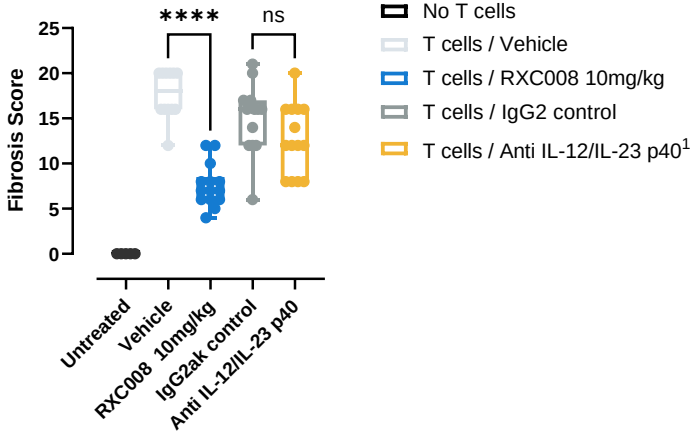
GI-restricted RXC008 activity governed by low permeability/ high efflux and rapid systemic clearance



- Plasma half-life of RXC008 is <10 minutes across species but >2h in human intestinal prep
- Metabolite (REDX11246) has poor cellular permeability and is significantly less active in cells than RXC008

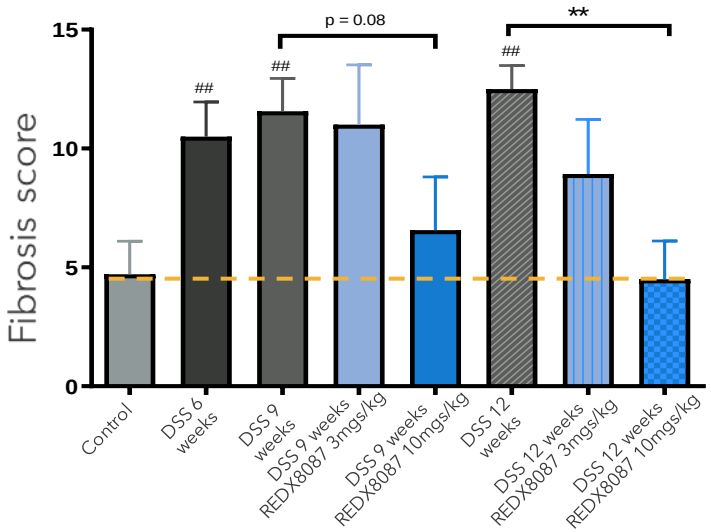
RXC008

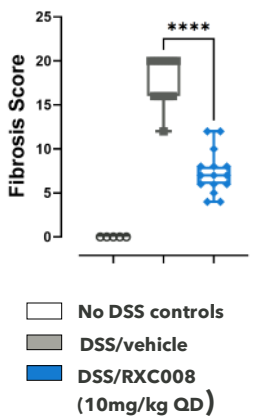
Preclinical Package Has Shown Promising Anti-fibrotic Effects in Multiple Translatable Models

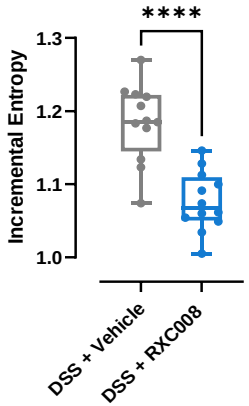


In adoptive T-cell transfer models **RXC008 reduces fibrosis and smooth muscle hyperplasia**

In a therapeutic 12-week DSS model **GI-targeted ROCK inhibition was able to reverse fibrosis**

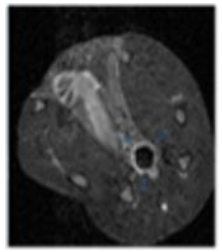






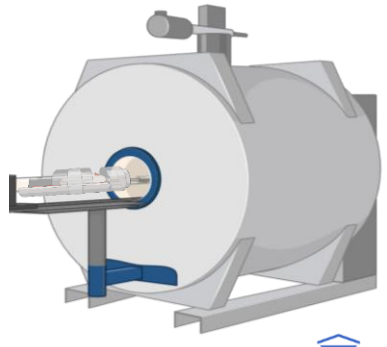
Significant reduction in fibrosis, measured by histology score **Entropy changes correlate with progression of IHC confirmed fibrosis in the DSS model**

Endpoint imaging translatable to the clinic using non-invasive MRI scans



T2 image

Murine sized MRI scanner

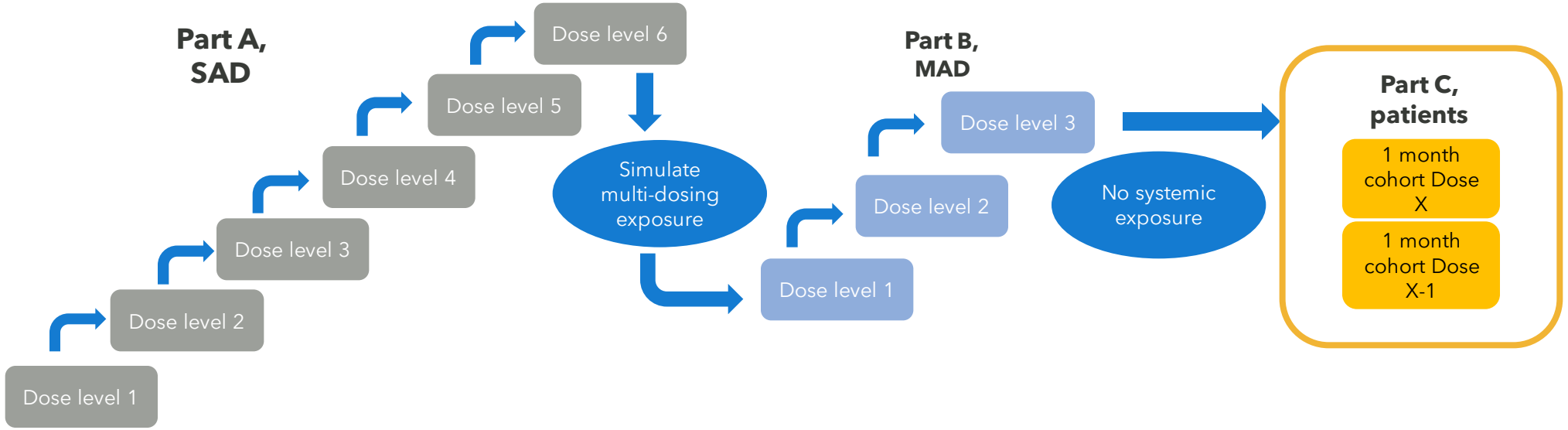


GHENT UNIVERSITY

Source: Data generated by University of Ghent on behalf of Redx. Data generated by Redx, REDX8087 is similar to RXC008 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.

RXC008

Phase 1 Study Protocol in Healthy Volunteers and Fibrostenotic Crohn's Disease Patients



Parts A and B dose escalation Healthy Volunteers

- Single Ascending Dose (SAD) and Multiple Ascending Dose (MAD) (14 days)
- Safety (no cardiovascular effects)
- PK (faeces, plasma and tissue in highest MAD cohort)

Part C : Patients with fibrostenosis due to Crohn's disease

- 1- 2 highest doses from MAD study with minimal systemic exposure
- 1 month's dosing, placebo controlled
- Safety
- PK (confirm minimal systemic exposure in patients)
- Target engagement and biomarkers
- Changes in circulating biomarkers

RXC004

RXC004: Porcupine Inhibitor for Wnt-Ligand Dependent Tumours

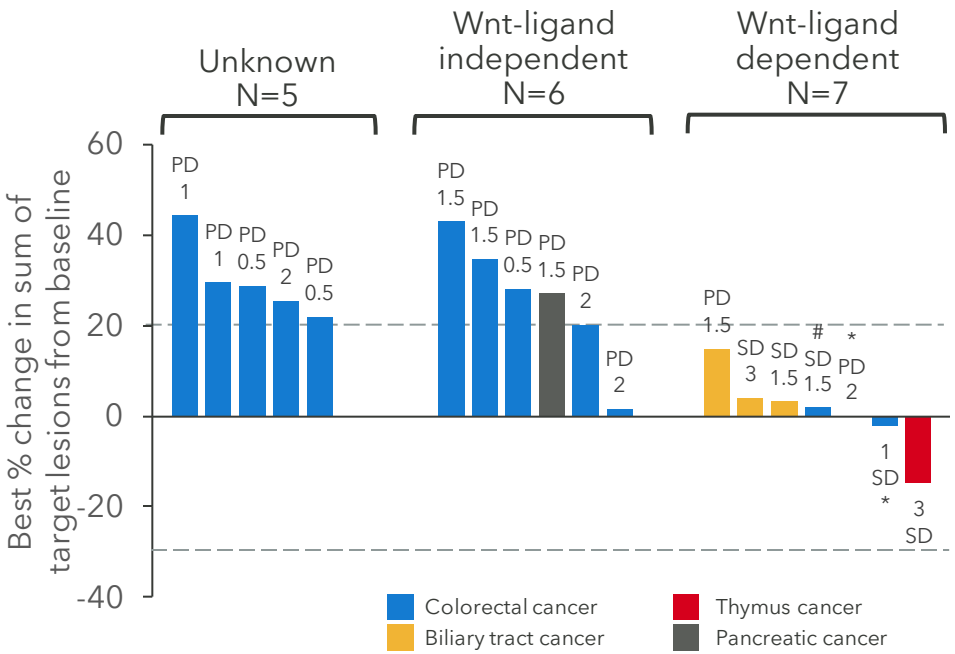
Highlights

- 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, as both monotherapy and in combination with nivolumab
- RXC004 shown to be active as a monotherapy in Phase 1, having 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-1 resistance, which could open new patient segments (SITC 2022)
- Phase 2 combination programme recruitment closed September 2023, for RXC004 with anti-PD-1 in Wnt-ligand dependent tumours – **Data readout expected H1 2024**
- Aim to seek a partner post Phase 2 data

RXC004

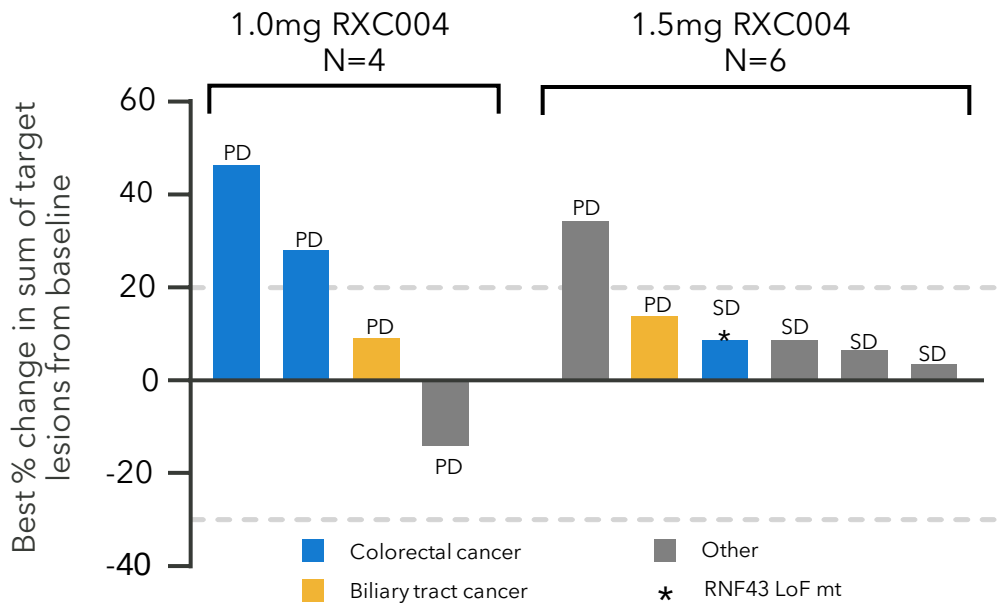
Preliminary Clinical Efficacy Data Supports Patient Selection and anti-PD-1 Combination Hypothesis

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



- 18/25 monotherapy patients had RECIST-evaluable disease
- Disease stabilisation observed in Wnt-ligand dependent tumours (5/7 patients)
- Median treatment duration higher in patients with Wnt-ligand dependent tumours (13.1 weeks vs 6.6 weeks)

Phase 1 Clinical Activity by Dose Cohort
(RXC004 with standard dose nivolumab)



- 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

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

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

RXC004

Phase 2 Combination Programme in Wnt-Ligand Dependent Tumours Expected to Deliver Topline Data H1 2024

	PORCUPINE MSS Metastatic Colorectal Cancer	PORCUPINE2 Biliary Tract Cancer
	Combination Genetically Selected RXC004 + Nivolumab	Combination Biliary Tract Cancer RXC004 + Pembrolizumab
Endpoints	**ORR** Secondary DCR, Tumour size change, DoR, PFS	**ORR** Secondary DCR, Tumour size change, DoR, PFS
Status	**Recruitment Closed**	**Recruitment Closed**
Topline data expected	**H1 2024**	**H1 2024**

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

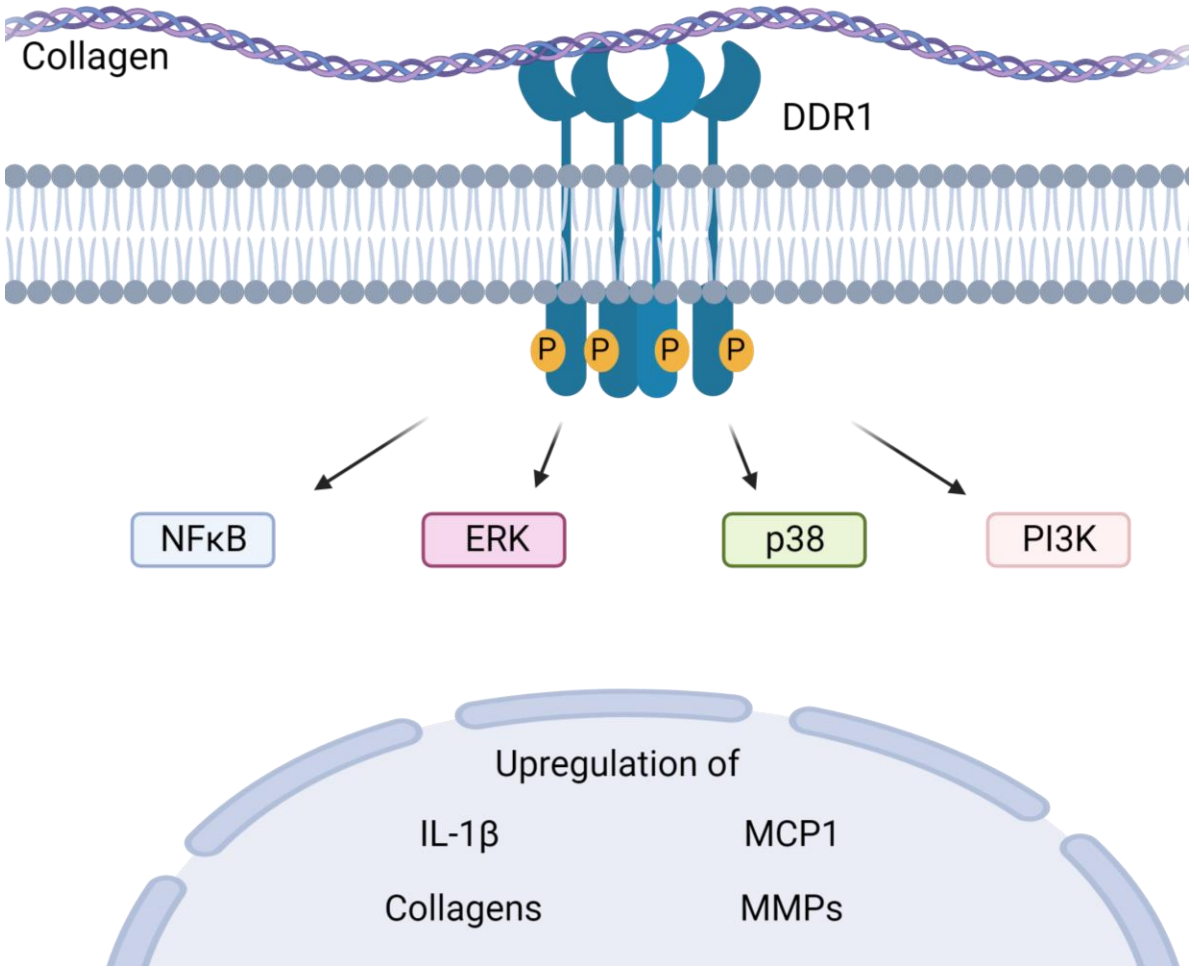
RXC009: A Highly Potent and Selective DDR1 Inhibitor With First-in-Class Potential For Chronic Kidney Disease

Highlights

- Highly potent and selective Discoidin Domain Receptor 1 (DDR1) small molecule inhibitor
- Oral route of administration
- Efficacy and target engagement demonstrated in therapeutic unilateral ureteral obstruction (UUO) model
- Suitable Absorption, Distribution, Metabolism and Excretion (ADME) profile
  - Excellent PK across species
  - Full Drug-drug interaction (DDI) assessment completed (Transporters and CYP)
- Safety Profile supporting progression to IND-enabling studies
  - Rodent toxicology study completed
  - Clean safety pharmacology (hERG, hNav1.5, and hCav1.2) and Safetyscreen profile
  - No genotoxic findings (Ames, Micronucleus)
- Scalable route

RXC009

DDR Inhibition, a Potential Novel Therapeutic Class for Fibrosis



Discoidin Domain Receptor (DDR) is a collagen target

- Two receptors of DDR: DDR1 and DDR2
- 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
- Strong literature rationale from patient samples and preclinical models support the role of DDR1 in kidney and lung indications

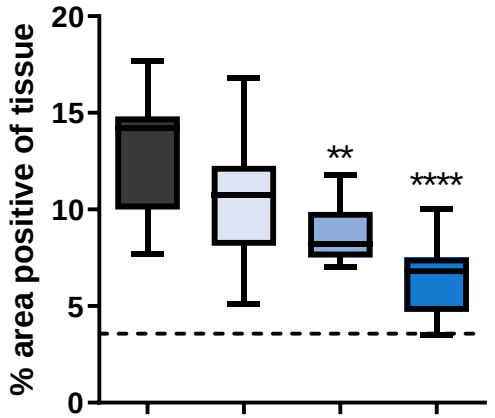
RXC009, a potent and selective DDR1 inhibitor nominated as a development candidate in October 2023

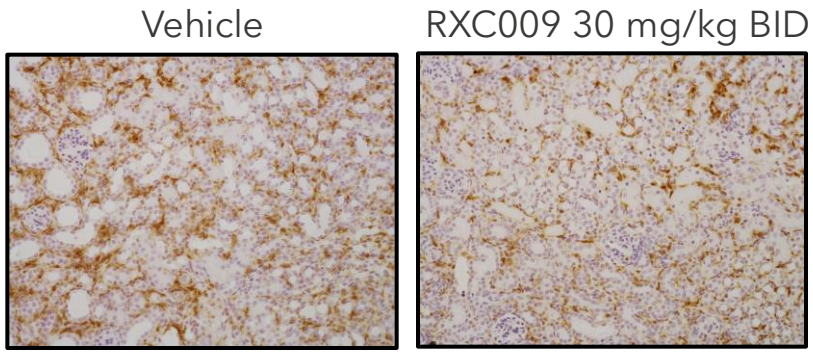
RXC009

Significantly Reduces Inflammation and Kidney Injury Associated With Chronic Kidney Disease in a Therapeutic Murine UUO Model

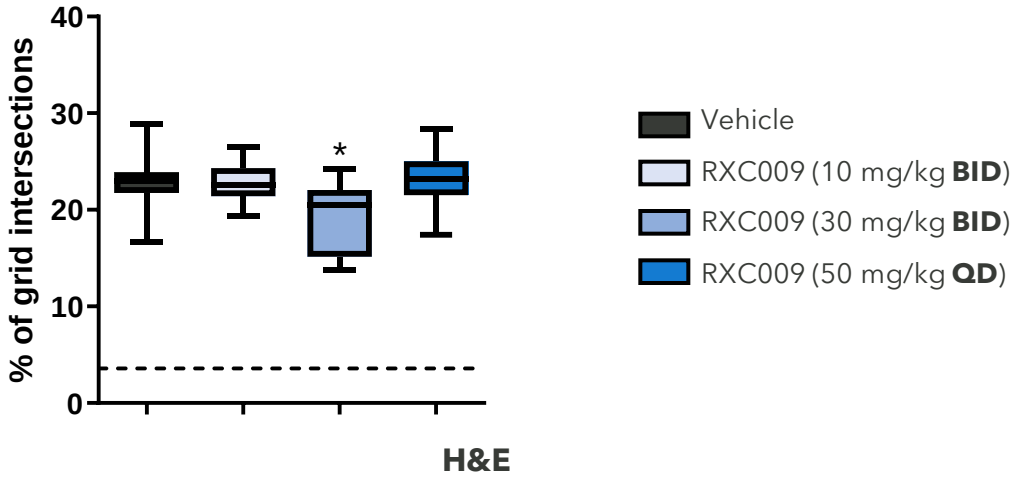
New Data

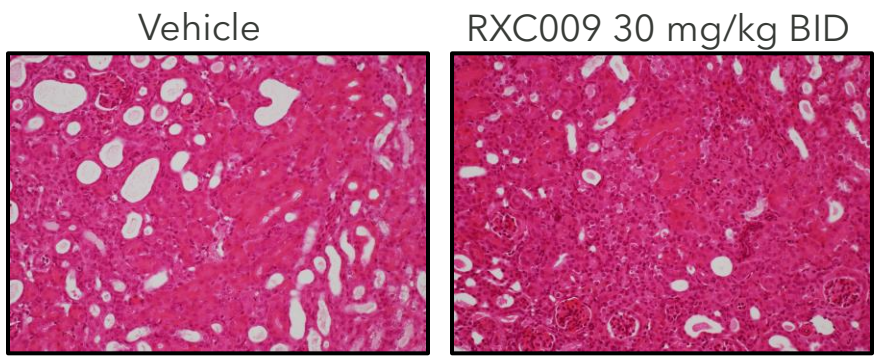
Macrophage Infiltration (F4/80)





Kidney Injury - Interstitial Expansion





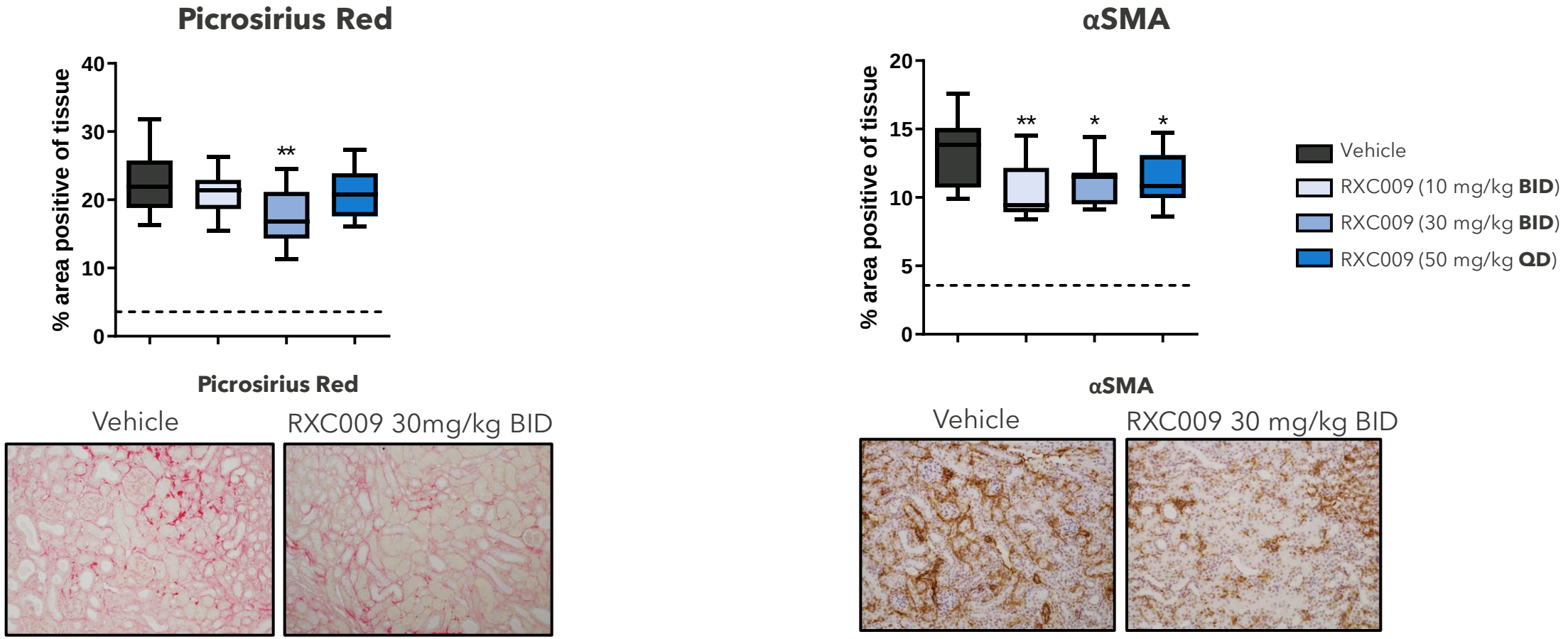
RXC009 in a 10-day therapeutic murine UUO kidney fibrosis model. Female C57BL/6J mice. Oral dosing from day 5-10 post-surgery. Terminal sampling analysis at T = 2 h. Inflammation (F4/80) and tubulointerstitial damage (H&E) as determined by immunohistochemistry.
Statistics: One-way ANOVA with Dunnett's multiple comparison test calculated relative to vehicle control.

UUO: unilateral ureteral obstruction

RXC009

Significantly Decreases Fibrosis, Collagen Deposition and Myofibroblast Transformation in a Therapeutic Murine UUO Model

New Data



RXC009 in a 10-day therapeutic murine UUO kidney fibrosis model. Female C57BL/6J mice. Oral dosing from day 5-10 post-surgery. Terminal sampling analysis at T = 2 h. Fibrosis and collagen deposition (picrosirius red), myofibroblast transformation (α-SMA) as determined by immunohistochemistry.
Statistics: One-way ANOVA with Dunnett's multiple comparison test calculated relative to vehicle control.

UUO: unilateral ureteral obstruction

Financials Reflect Continued Advancement of Pipeline with Funding to Deliver Key Milestones

Statement of Financial Position, £'000	FY'23	FY'22
Cash	18,092	53,854
Other current assets	5,210	5,524
Non-current assets	2,334	3,099
Total assets	**25,636**	**62,477**
Contract liabilities	844	4,893
Borrowings	15,731	15,731
Other current liabilities	4,432	6,581
Lease liabilities (non-current)	1,274	1,951
Total liabilities	**22,281**	**29,156**
Net assets	**3,355**	**33,321**

Statement of Comprehensive Income £'000	FY'23	FY'22
Revenue	4,202	18,690
Research & development expenses	(29,117)	(28,563)
General & administrative expenses	(8,516)	(7,932)
Reverse merger expenses	(2,393)	-
Revaluation gain on loan notes	1,609	-
Net finance costs	(577)	(1,538)
Tax credits, operating income & other items*	1,632	1,369
Total comprehensive loss for period	**(33,160)**	**(17,974)**

- **Cash** – runway into Q3 2024 following the post-period equity financing completed in November 2023 raising £14.1 million (gross)
- **Borrowings -** Convertible Loan Notes extended by one year to August 2024

- **Revenue** – all partnerships continue to progress - no milestone payments triggered during FY2023
- **Reverse merger expenses** – reflects expenses from proposed all stock merger announced with Jounce Therapeutics which did not complete due to an unsolicited all cash offer from a third-party

Significant Catalysts to Continue ROCK Portfolio Momentum With Cash Runway into Q3 2024

Cash runway to support 2024 milestones

- **RXC008** Commence Phase 1 Healthy Volunteers
- **Zelasudil** Phase 2a IPF data
- **RXC004** Phase 2 combination data
- **Zelasudil** Complete response to FDA

Multiple Value Expansion Opportunities Beyond 2024

Zelasudil
Potential in ILD and cancer-associated fibrosis

RXC008
Development in fibrostenotic Crohn's

RXC004
Explore partnership opportunities inc. other potential combinations

Discovery Engine RXC009, KRAS
Continue to advance towards IND and DC, respectively

AIM (UK) listed Ticker: REDX
Total shares in issue: 388,985,916*
Fully diluted: 543,601,142**

*As at 7 November 2023.
**As at 7 November 2023 and assuming full conversion of loan notes and exercise of employee share options.