Redx
Discovering Targeted Medicines

# Developing Novel, Targeted Therapeutics for Fibrotic Disease and Cancer

Corporate Presentation

March 2024

AIM:REDX

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# Strong Leadership Team with Extensive Industry Experience

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

## Lisa Anson
## CEO

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

## Dr Richard Armer
## CSO

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

## Dr Helen Timmis
## Interim CMO

Registered physician with >15 years' experience in industry

## Peter Collum
## CFO

Experienced finance and strategy executive with >25 years in biopharma

# Clinical Stage Biotech Discovering Targeted Medicines for Fibrotic Disease and Cancer

Progressing a pipeline of novel, differentiated **drug candidates against biologically-validated** targets in areas of high unmet medical need, including IPF and fibrostenotic Crohn's disease

Focused on clinical development of potential **best-in-class selective ROCK2** inhibitor, and **potential first-in-class** GI-targeted ROCK inhibitor

In-house medicinal chemistry and translational science expertise with successful record of drug discovery - **six** Redx discovered molecules progressed to the clinic one of which is approved, pirtobrutinib*

**Proven track record** in securing high value partnerships, with further assets in the pipeline to partner for clinical development

*the asset was subsequently sold outright to Loxo Oncology, now part of Eli Lilly, Redx has no remaining economic interest

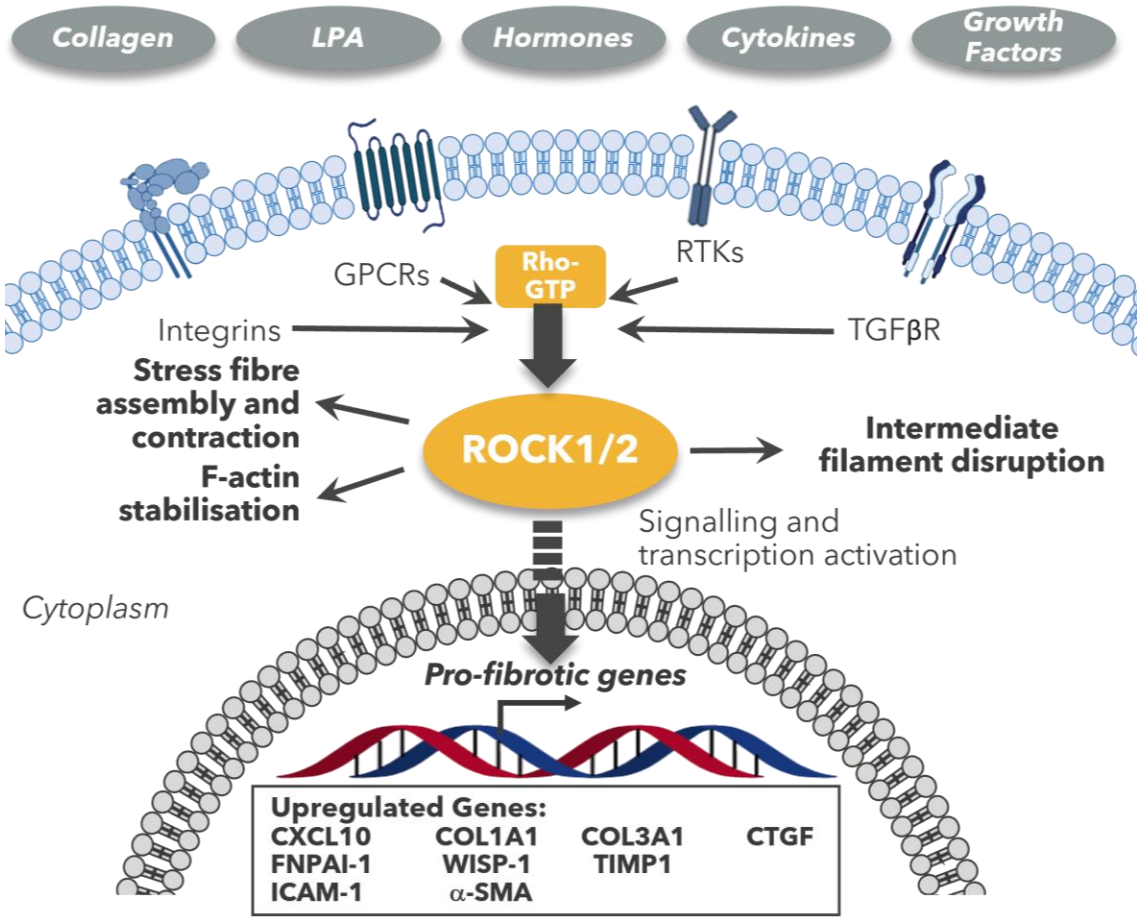
# Robust Pipeline Focused on Advancing ROCK Inhibitor Portfolio

| | 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 commencement **H2 2024** |
| | | cGvHD* | | | | | Phase 2a commencement **H2 2024** |
| | **GI-targeted pan-ROCK Inhibitor** (RXC008) | Fibrostenotic Crohn's disease | | | | | Phase 1 healthy volunteer data **H2 2024** |
| Pipeline Assets | **Porcupine Inhibitor** Zamaporvint (RXC004) | Wnt-ligand driven GI-tumours – combination | | | | | Report data **H1 2024** Potential partnership |
| | **Discoidin Domain Receptor (DDR) Inhibitor** (RXC009) | Kidney Fibrosis | | | | | IND / CTA Submission **2025** |
| Partnered | **KRAS Inhibitors** (G12D selective and pan-KRAS) | Oncology | | | | | Sold to Jazz Ongoing collaboration |
| | **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 Ongoing 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; cGvHD: Chronic Graft Versus Host Disease; KRAS: Kirsten rat sarcoma virus
*Would require additional funding

# ROCK – A Compelling Nodal Target in the Cell Signalling Pathways Central to Fibrosis




## Why Target ROCK ?

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

## Redx are Pioneers in Next-Generation ROCK Drug Discovery

- 7+ years' experience in next-generation, orally-available ROCK inhibitor design
- Two distinct approaches to overcome potential hypotensive side effects and improve on properties of first-generation ROCK inhibitors
- Broad global patents for a range of molecules including zelasudil and RXC008

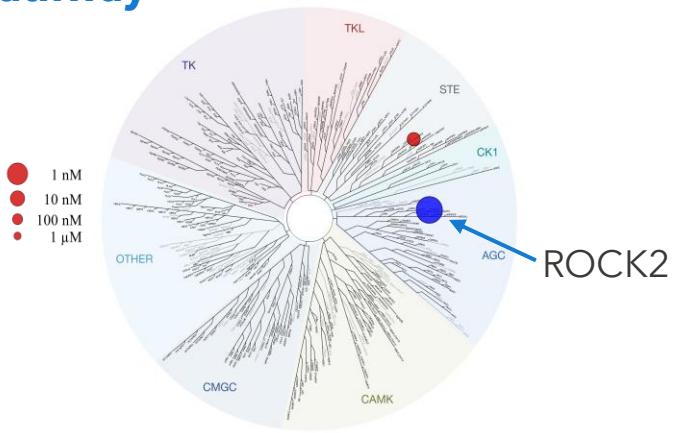
# Two Distinct Approaches to Leverage ROCK Pathway's Anti-Fibrotic Potential

## Zelasudil
### Selective ROCK2 inhibitor

**Best-in-class opportunity**

**Next-generation molecule with improved characteristics to unlock anti-fibrotic potential of the pathway**

- **Selectivity**
- **Drug-drug interaction**
- **PK / Bio-distribution**



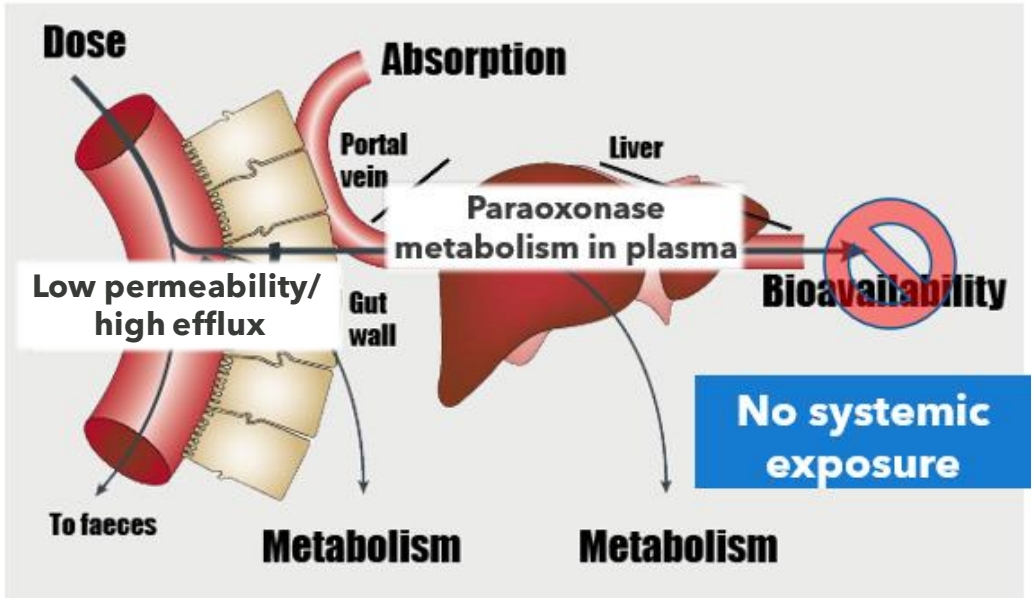

Plot of kinases inhibited by RXC007 with $IC_{50}$ < 1 µM

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

## RXC008
### GI-targeted pan-ROCK inhibitor

**First-in-class opportunity**

**Uniquely unlocks potential of pan-ROCK inhibition, whilst avoiding systemic exposure and associated risk of hypotension**



zelasudil (RXC007)

# Zelasudil (RXC007): Selective ROCK2 Inhibitor for Fibrotic Diseases, in Phase 2 Clinical Development

## Next milestone: Phase 2a IPF data readout expected H1 2024

- An orally active, highly potent and selective ROCK2 inhibitor for fibrotic diseases, initially targeting IPF and CF-ILD, with potential in pancreatic cancer, cGvHD and other indications
- Robust preclinical efficacy data across disease models supports clinical development plan
- Phase 1 healthy volunteer data in single ascending and multiple ascending dose cohorts confirms drug like profile for safety, PK and exposure
- Orphan Drug Designation granted by US FDA for IPF
- Phase 2a in IPF completing recruitment and Phase 2b in IPF/CF-ILD in planning
  - First two cohorts completed with zelasudil being well tolerated at 20mg and 50mg BID
  - Recruitment into expansion cohort ongoing
  - Expected to submit complete response to FDA partial clinical hold in Q3 2024, allowing longer dosing durations in US



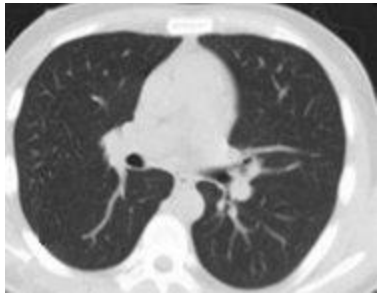
cGvHD: Chronic Graft versus Host Disease IPF: Idiopathic Pulmonary Fibrosis CF-ILD: Chronic Fibrosing Interstitial Lung Disease

zelasudil (RXC007)

# Lung Fibrosis: A Growing Clinical Need with Limited Treatment Options

## Lead indication is Idiopathic Pulmonary Fibrosis (IPF)

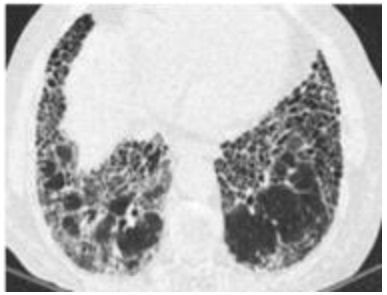
- IPF is a deadly fibrotic lung disease
- Median survival between 3 – 5 years(1)
- High unmet need: over **170,000+ patients** in the US, EU5 and Japan alone(2)
- Global IPF market projected to reach $3.6 billion by 2029(3)
- Nintedanib and pirfenidone are the only approved treatments but have significant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

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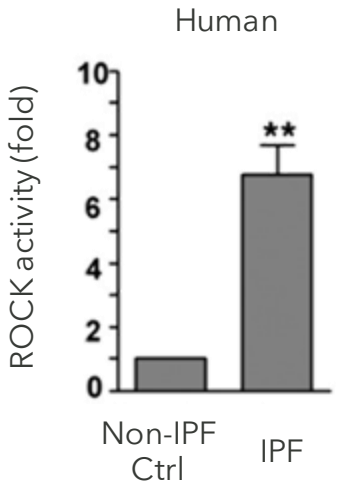
# Strong Literature Rationale on ROCK and ROCK2 Supports IPF as a Lead Indication

## ROCK as a target in IPF[1]

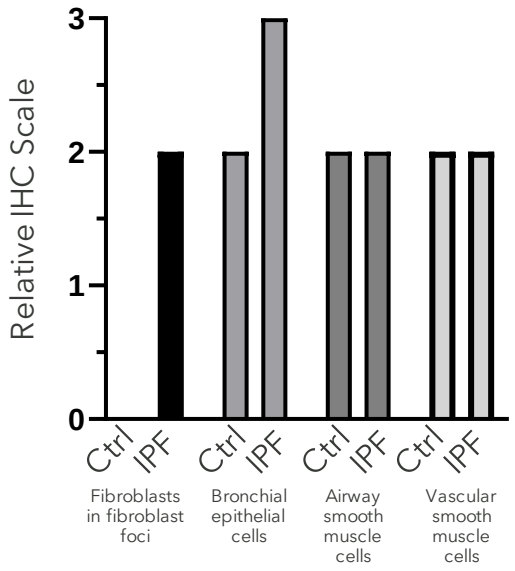
RhoA/ROCK/ROCK2 signalling pathway is upregulated in human IPF patients




(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]

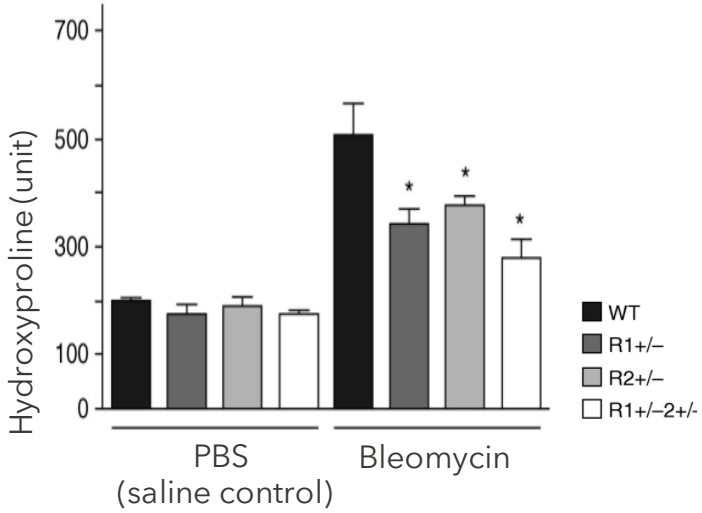
Increased ROCK2 expression in IPF bronchial epithelial cells and fibroblasts




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

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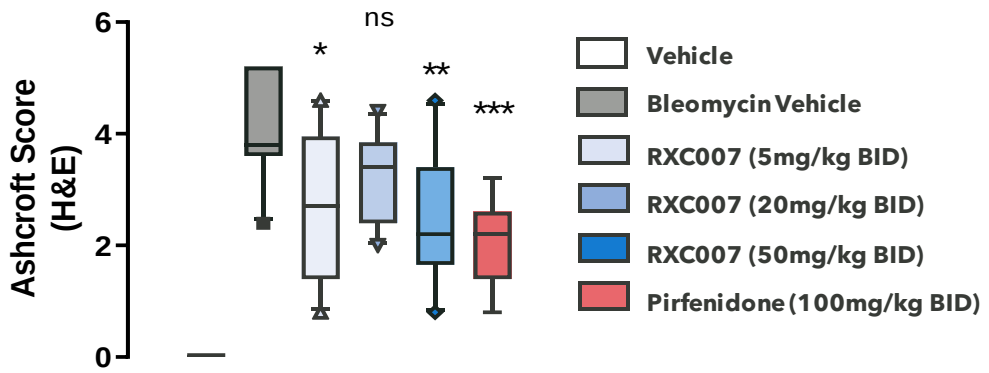
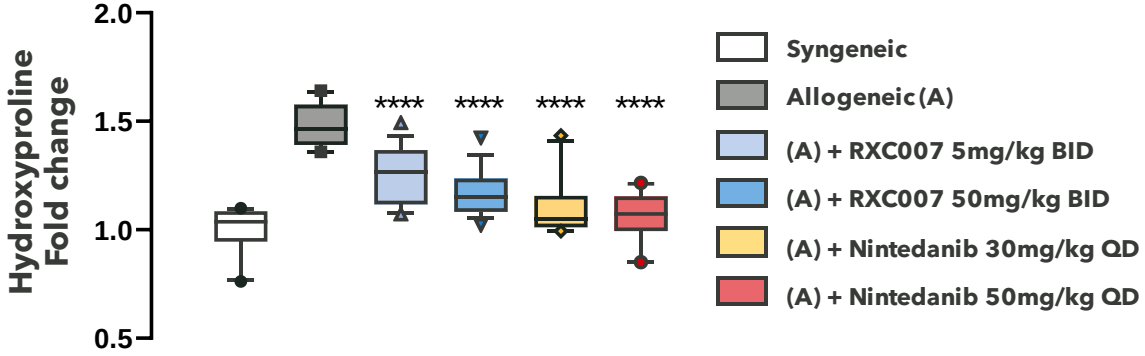
# Zelasudil Activity on Patient Tissue and in Preclinical Models Supports Core Development Plan in IPF and CF-ILD

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

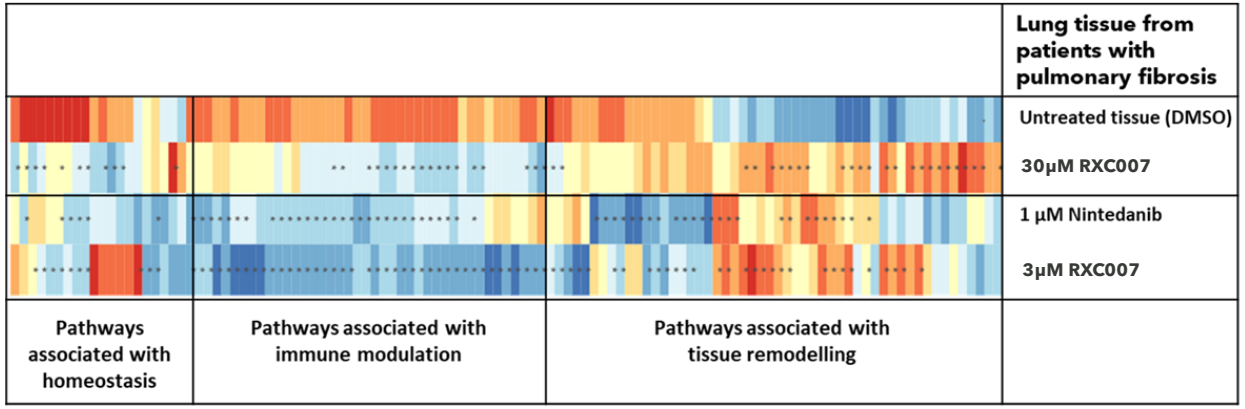



## Significant Reduction of Collagen Content in Lungs in Murine Sclerodermatous chronic Graft versus Host Model




## 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

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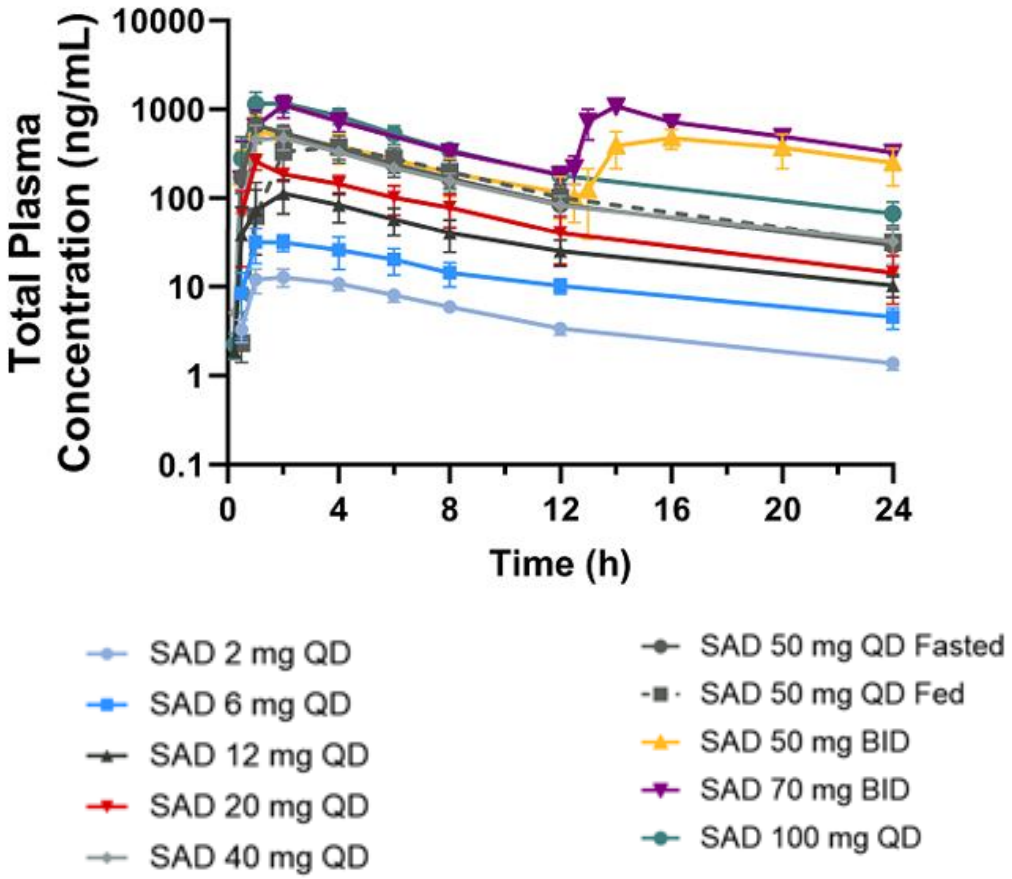
# Phase 1 Data in Healthy Volunteers Showed Good Safety and Pharmacokinetic Profile

## Human exposure demonstrates linearity




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

## 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

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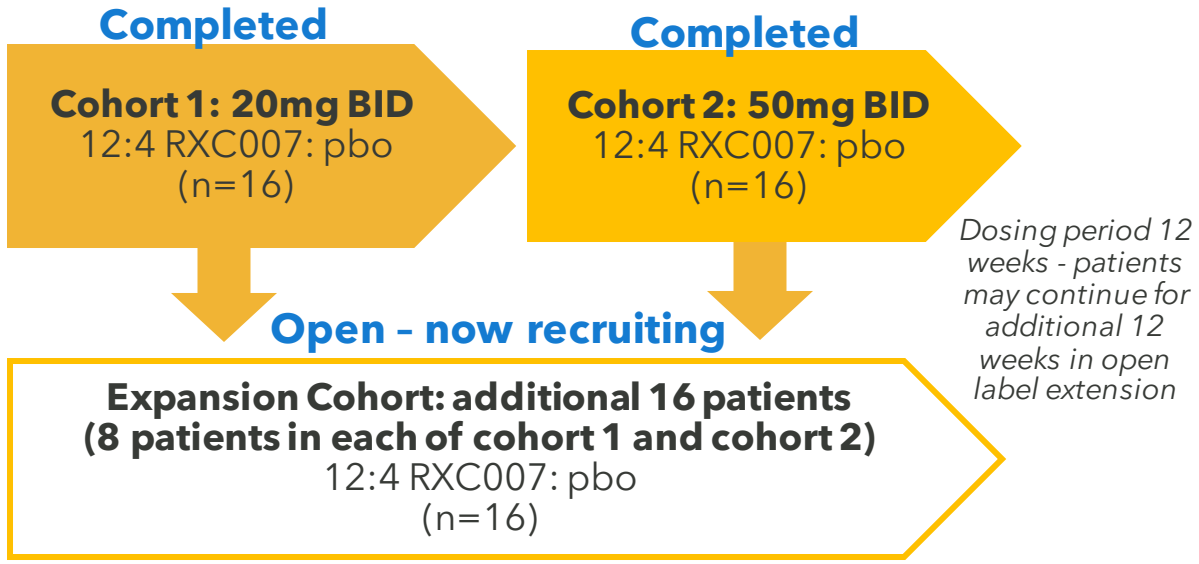
# Phase 2a Study in IPF Patients Ongoing with Data Readout Expected H1 2024

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

Total: n=48 patients, including n=12 placebo




**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
- 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



BID: Twice daily; OLE: Open Label extension; Pbo: Placebo

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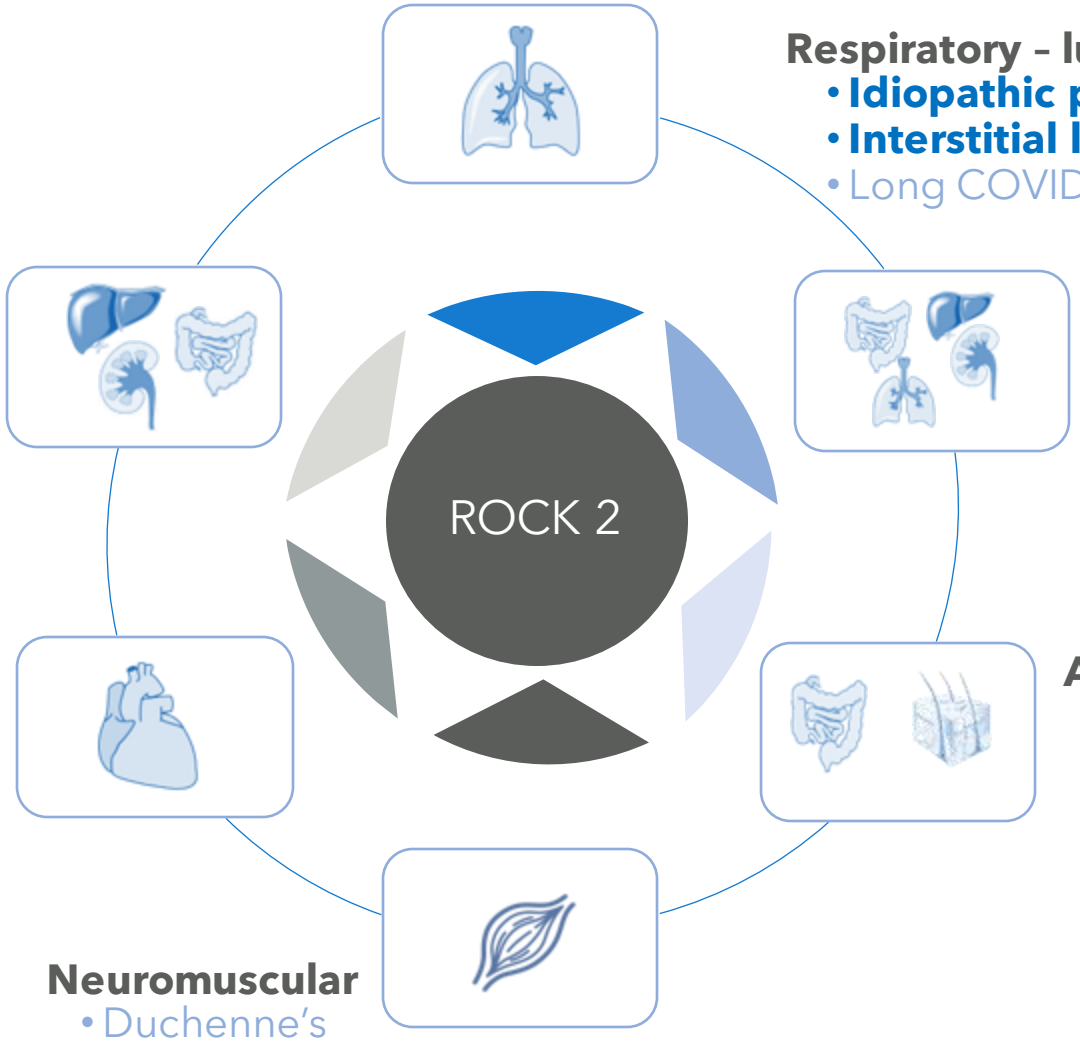
# Preclinical Data Supports ROCK2 Development in Multiple High Value Indications

**Metabolic diseases**
- Kidney fibrosis - CKD, Diabetic nephropathy
- NASH, NAFLD
- Primary sclerosing cholangitis (PSC)

**Cardiac & vascular fibrosis**
- Cardiac fibrosis
- Cerebral Cavernous Malformation (CCM)
- Pulmonary arterial hypertension (PAH)




**Neuromuscular**
- Duchenne's

**Respiratory – lung fibrosis**
- **Idiopathic pulmonary fibrosis (IPF)**
- **Interstitial lung disease (ILD)**
- Long COVID

**Oncology**
- **Pancreatic Cancer**
- Fibrotic tumour types

**Auto-immune**
- **cGvHD**
- aGvHD
- Systemic Sclerosis

**Key:**
**Redx Focus**
Supportive data in additional indications

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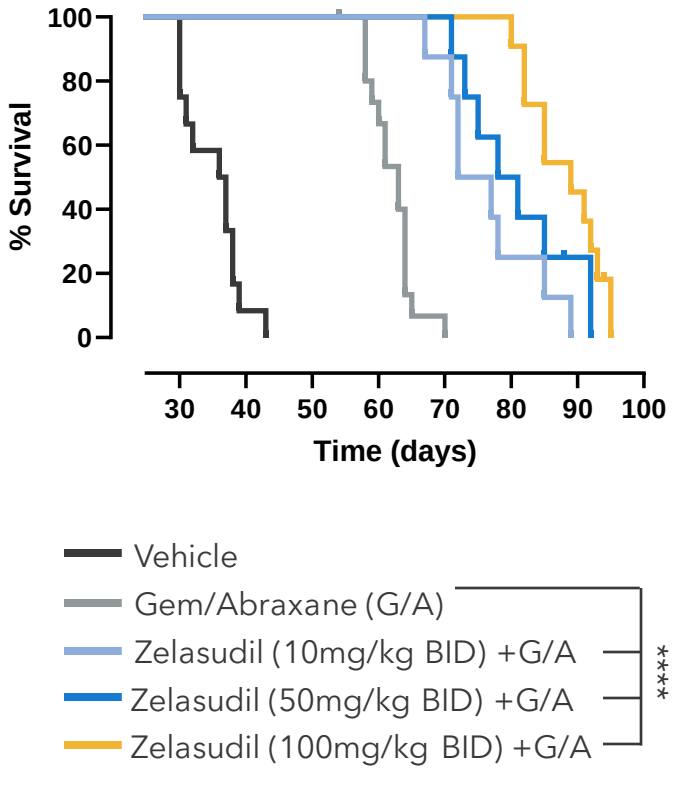
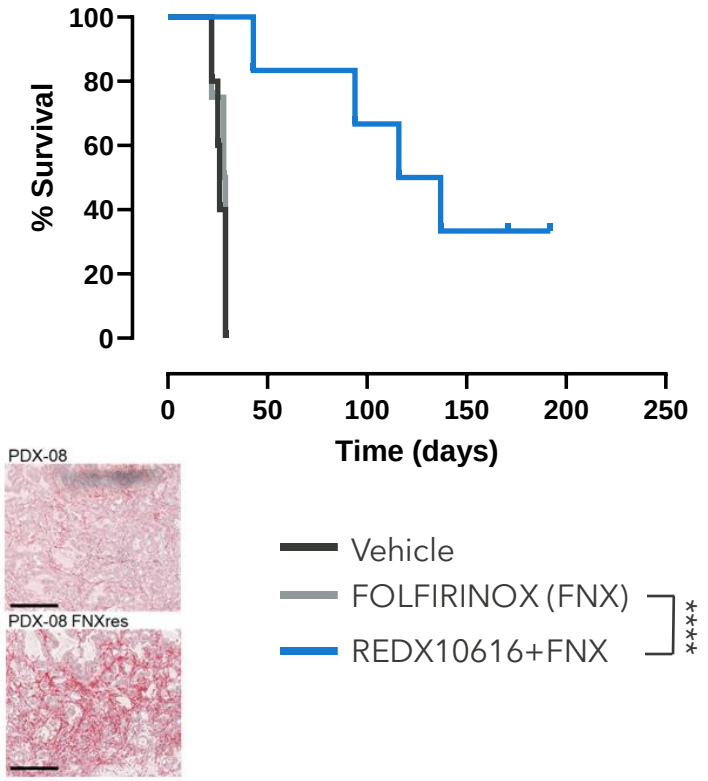
# Next-Generation ROCK2 Inhibitors Increase Survival When Combined with Chemotherapy in Pancreatic Cancer Models

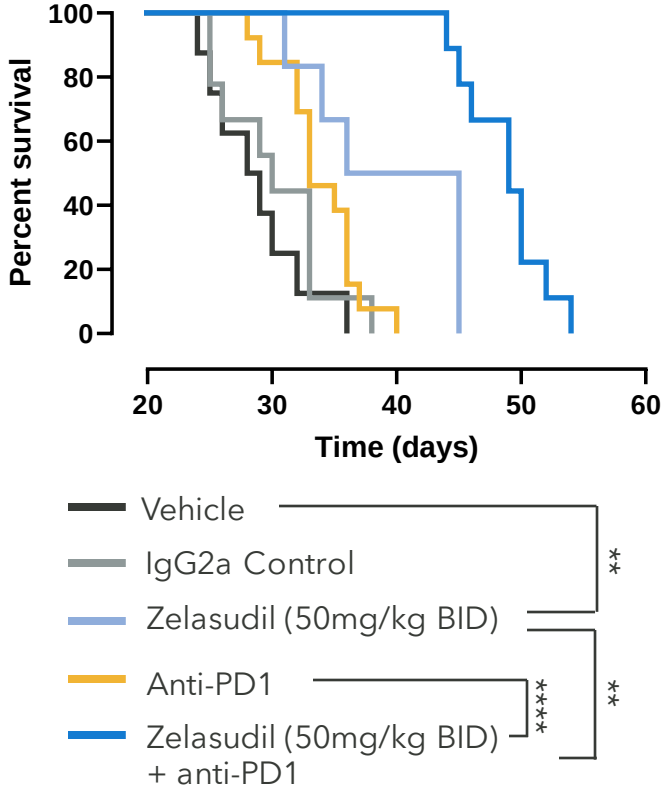
## Zelasudil plus Gem/Abraxane increases survival in metastatic PDX-PDAC xenografts




## REDX10616* plus FOLFIRINOX increases survival in FOLIFIRINOX resistant pancreatic PDX




## Zelasudil plus anti-PD1 increases survival in anti-PD1 resistant murine KPC model




Source: Data generated by the Garvan Institute *REDX10616 is a close analogue of zelasudil

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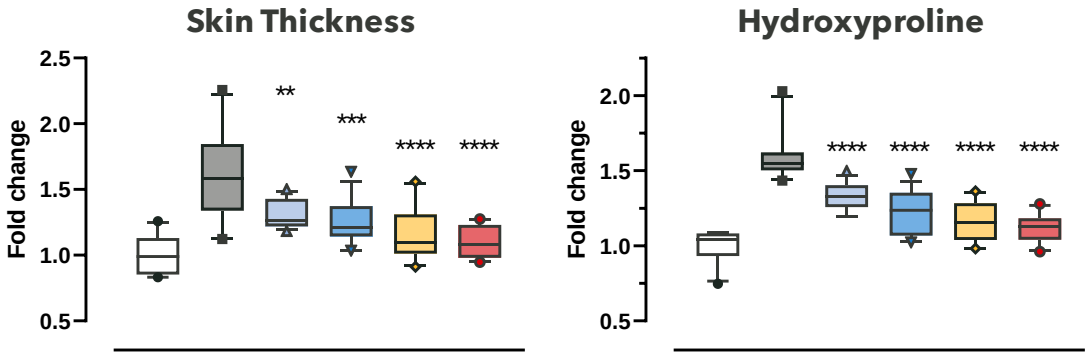
# Zelasudil Significantly Reduces Fibrotic Disease Markers Across Multiple Organs in a Murine SSc cGvHD Model

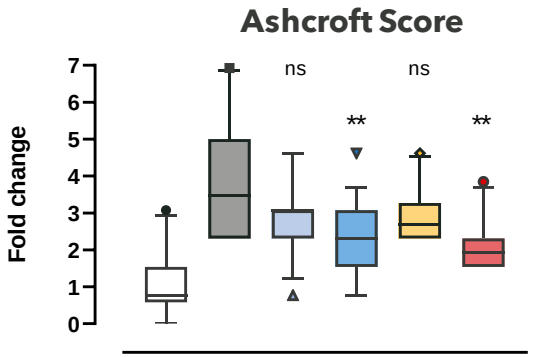
## Zelasudil Significantly Reduces Skin Fibrosis and Skin Thickness

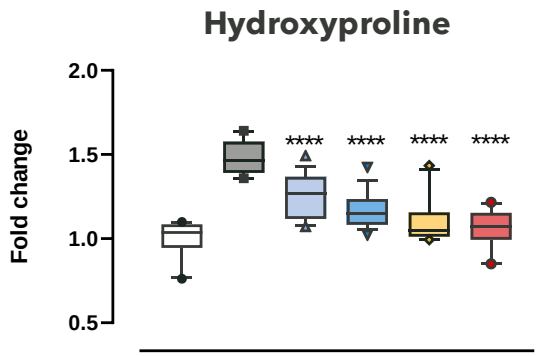




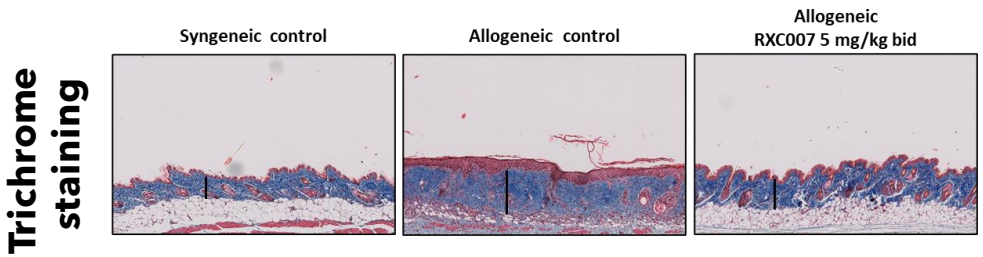


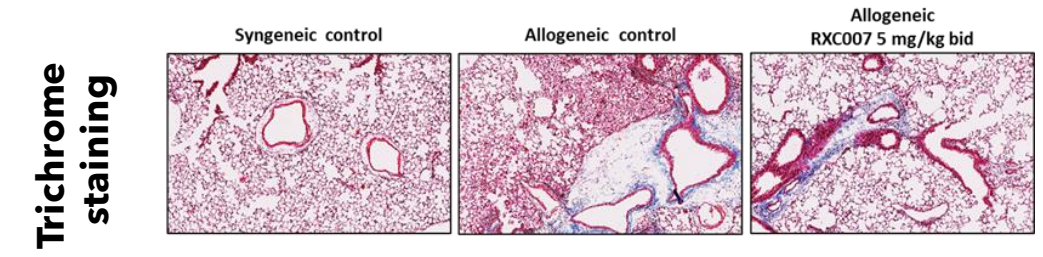
## Zelasudil Reduces Fibrosis Score and Collagen Content in Lungs




Syngeneic | Allogeneic | Allogeneic +**Zelasudil** 5mg/kg BID | Allogeneic + **Zelasudil** 50mg/kg BID | Allogeneic +Nintedanib 30mg/kg QD | Allogeneic +Nintedanib 50mg/kg QD




Significant effect of treatment determined by one-way ANOVA with Dunnett's multiple comparisons test performed versus vehicle treated group. ns non-significant, *p<0.05, **p<0.01, ***p <0.001. Note: Different vehicle used for nintedanib. 30 mg/kg dose is clinically achievable, but 60 mg/kg BID is not a clinically achievable dose and used as positive control.

Source: Data generated by Redx, Presented at AFDD2022

RXC008

# RXC008: Potential First-in-Class Pan-ROCK Inhibitor for Fibrostenotic Crohn's Disease, in Phase 1 Development

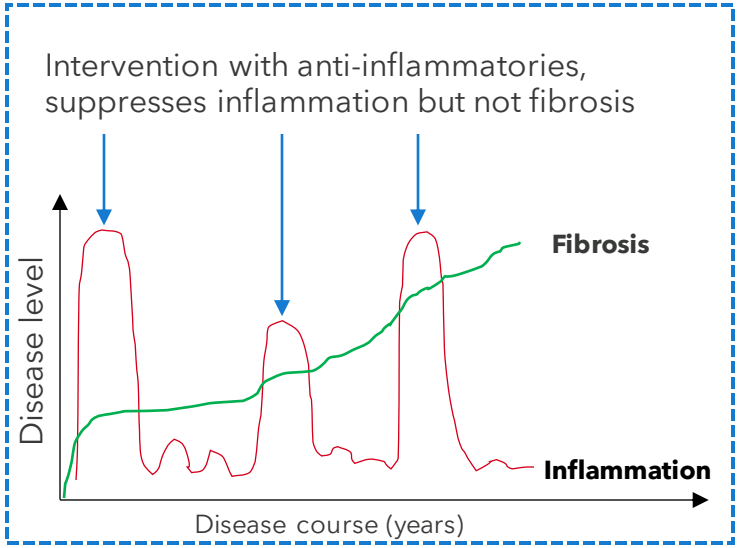
**Next milestone: Phase 1 healthy volunteers data H2 2024**

- RXC008 is an orally available, potent GI-targeted pan-ROCK Inhibitor - designed to be restricted to the gut, avoiding the known risk of hypotension resulting from systemic exposure of pan-ROCK inhibitors
- ROCK is a key nodal target involved in fibroblast activation, and is upregulated in fibrostenotic Crohn's disease
- Fibrostenotic Crohn's disease is a significant unmet need, currently treated with successive surgical intervention - RXC008 is a potential first-in class treatment
- Demonstrated robust preclinical efficacy, including reversal of fibrosis, in preclinical *in-vivo* models
- Phase 1 study in healthy volunteers commenced Q1 2024, with patient module to follow

RXC008

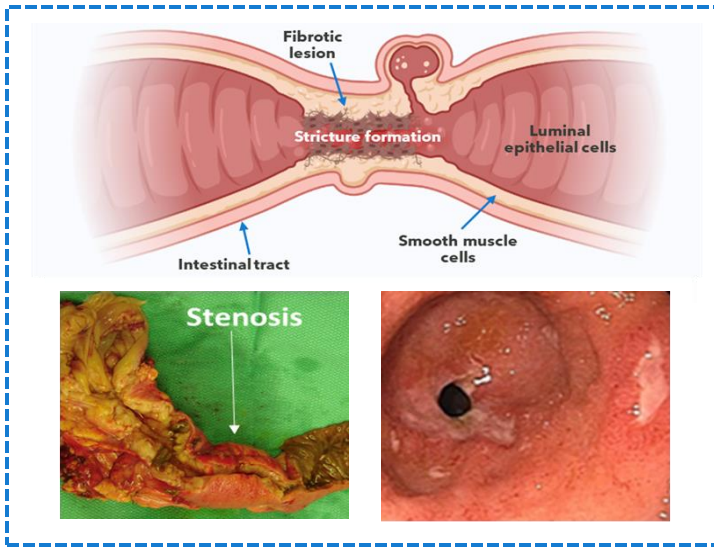
# Potential First-in-Class Treatment in Area of High Unmet Clinical Need

## Clinical progression in Crohn's



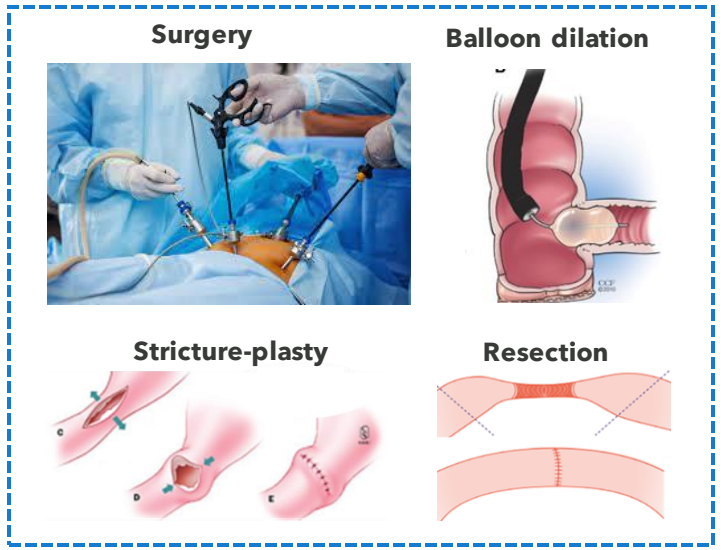

**1.7 million**(1) patients globally affected by Crohn's disease

## Fibrotic stricture formation




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

## Surgical interventions

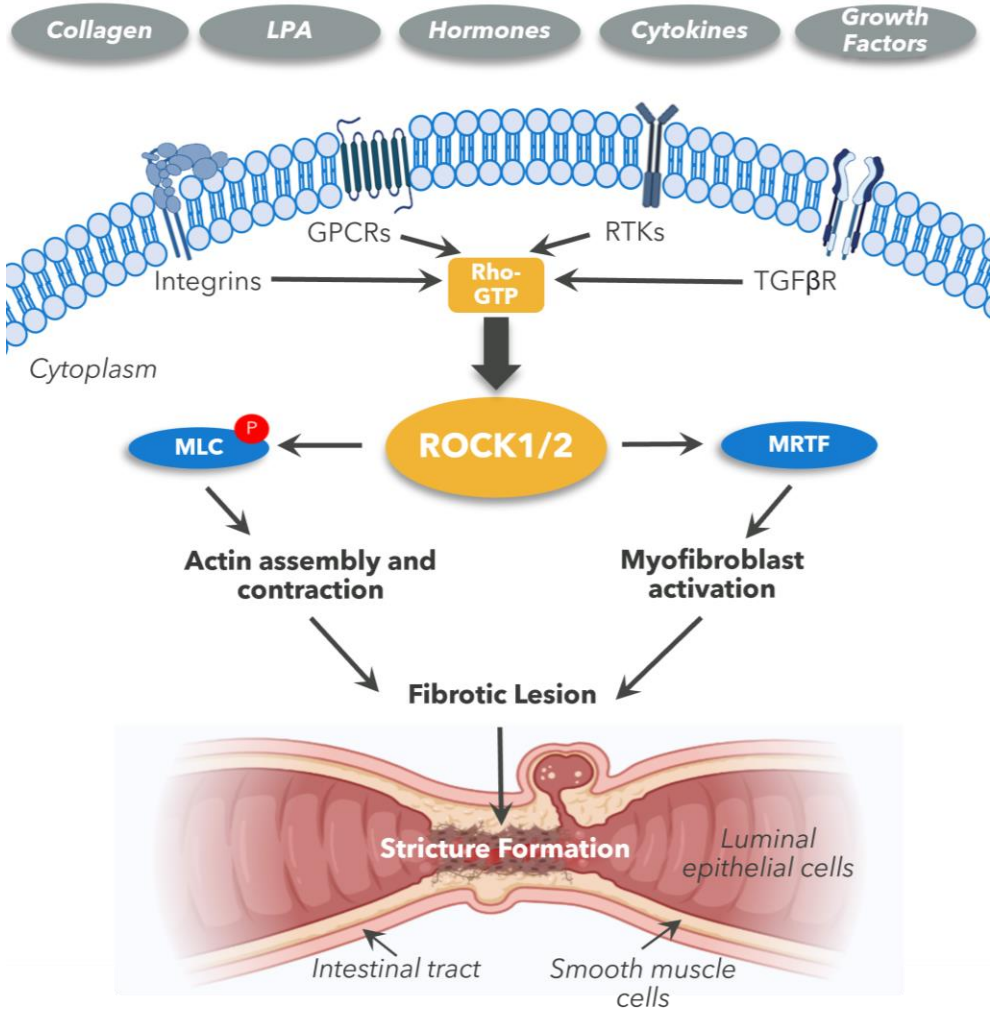



**No approved** therapies for underlying fibrosis only treatment options are debilitating surgical intervention

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

RXC008

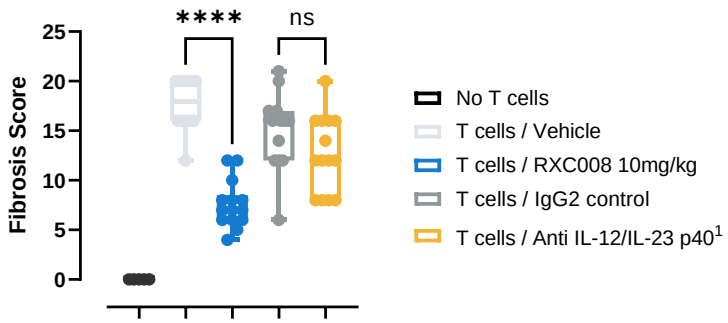
# Designed to Target ROCK Whilst Avoiding Hypotension Associated with Systemic Exposure to pan-ROCK Inhibitors




- ROCK is a nodal point in the fibrotic signalling pathway
- Inhibiting ROCK 1&2 systemically is known to result in hypotension
- GI-restriction designed to avoid hypotension from systemic pan-ROCK inhibition, enabling therapeutic potential of this approach
- 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

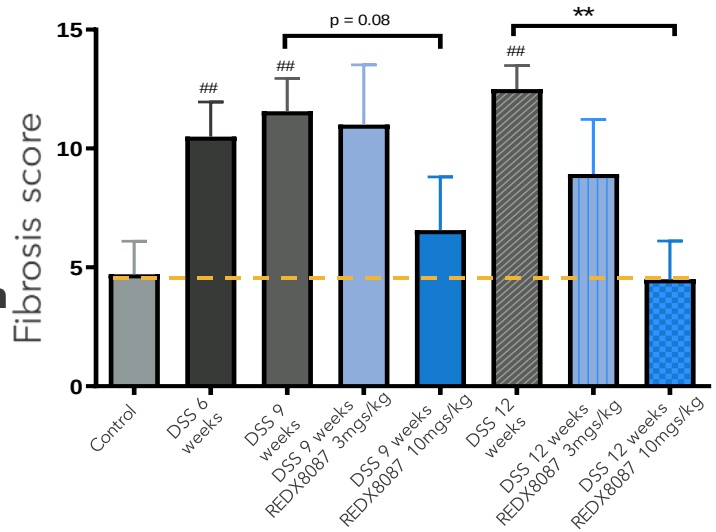
RXC008

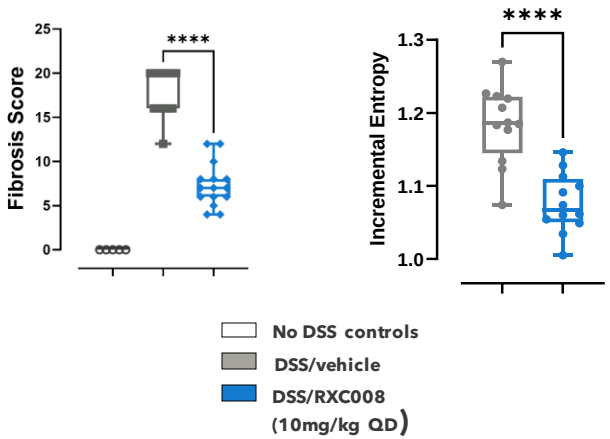
# Preclinical Package Has Shown Promising Anti-fibrotic Effects in Multiple Translatable Models




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

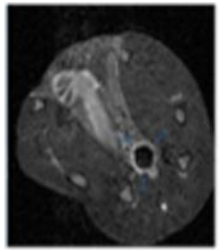
In a therapeutic 12-week DSS model **GI-targeted ROCK inhibition was able to reverse fibrosis**



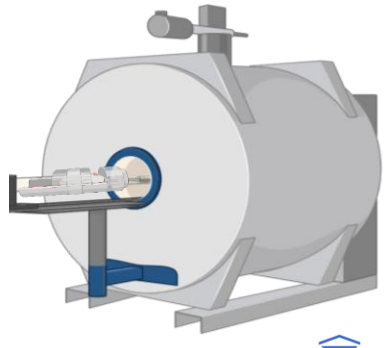

Significant reduction in fibrosis, measured by histology score **Entropy changes correlate with progression of IHC confirmed fibrosis in the DSS model**

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



T2 image

Murine sized MRI scanner



GHENT UNIVERSITY

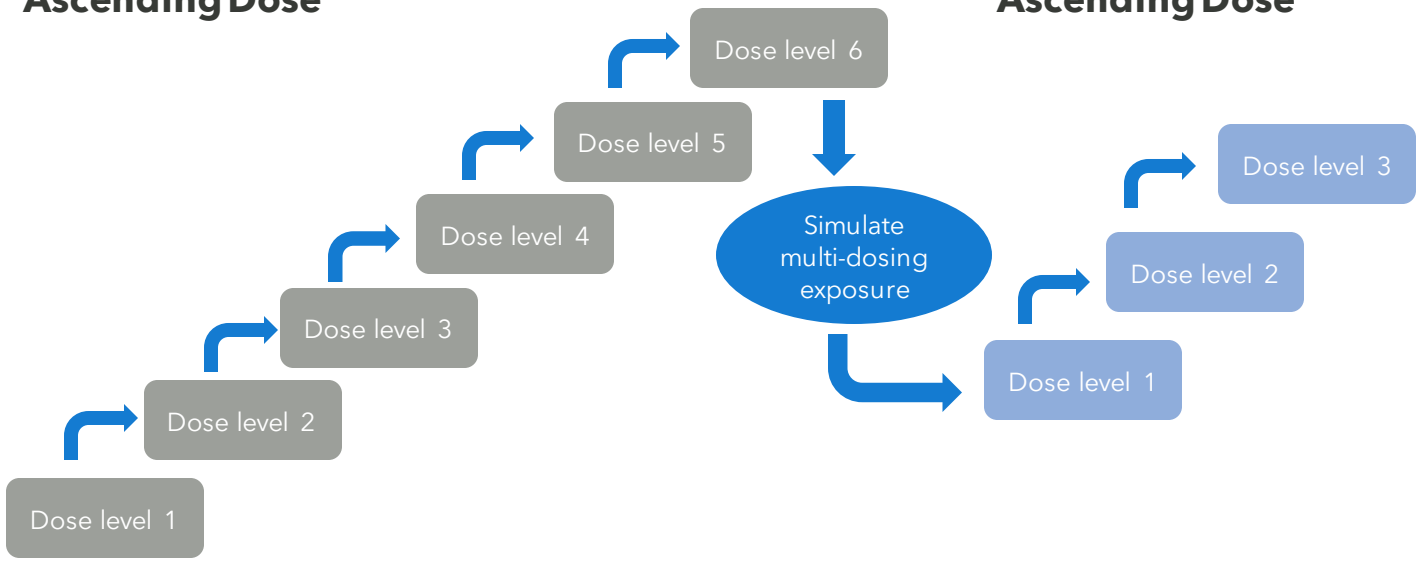
Source: Data generated by University of Ghent on behalf of Redx. Data generated by Redx, REDX8087 is similar to RXC008 1-way Anova with Dunnet's multiple comparison, # T-cells/vehicle v untreated controls, * RXC008 10mg/kg QD or anti-p40 v T-cells/vehicle.

RXC008

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

## Part A: Single Ascending Dose

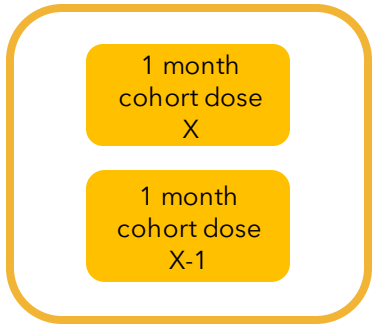
## Part B: Multiple Ascending Dose




### Parts A and B in Healthy Volunteers

- Single Ascending Dose (SAD) cohorts in Part A
- Multiple Ascending Dose (MAD) cohorts in Part B, dosed for 14-days
- Safety (no cardiovascular effects)
- PK (faeces, plasma and tissue in MAD cohorts)

## Part C: Patients with Fibrostenosis Due to Crohn's Disease




### Part C in Patients

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

zamaporvint (RXC004)

# Zamaporvint: Potent, Tolerable, Oral Porcupine Inhibitor with Clinical Activity in Wnt-ligand Dependent Cancers

Redx

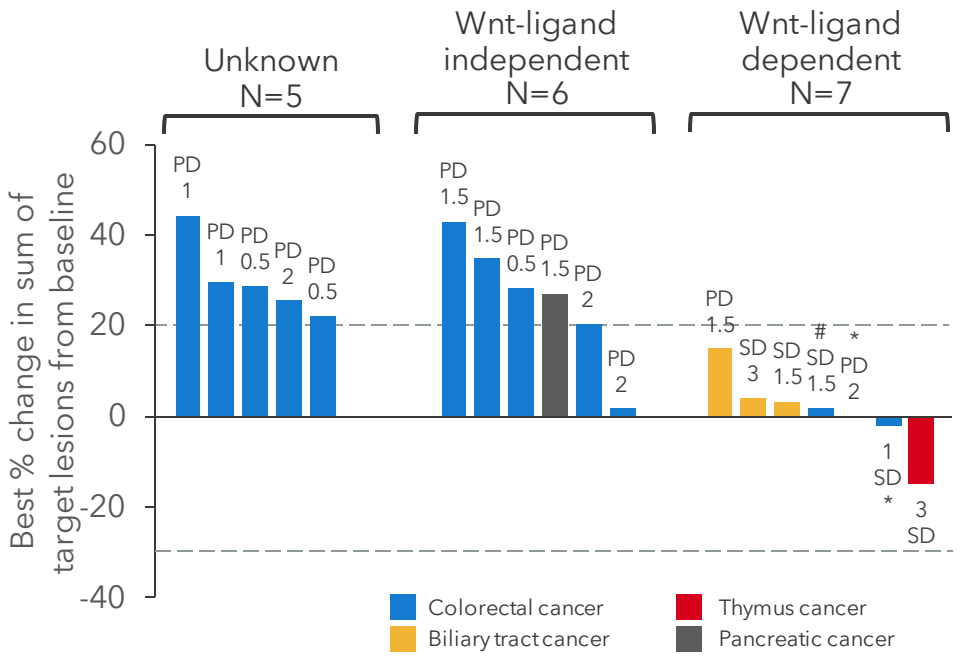
## Next Milestone: Phase 2 Combination Data Readout H1 2024

- Porcupine inhibition blocks secretion of all Wnt-ligands, preventing both tumour growth and immune evasion
- Clinical target engagement demonstrated at all doses with optimal PK profile for once daily, oral dosing
- Phase 1 trial demonstrated zamaporvint was:
  - well tolerated as both monotherapy and in combination with nivolumab
  - active as a monotherapy with differential clinical efficacy in Wnt-ligand dependent tumours (ESMO 2021)
- Primary efficacy hypothesis in hard-to-treat Wnt-ligand dependent tumors is in combination
- Recruitment into Phase 2 programme covering a range of settings closed September 2023
  - Includes testing hypothesis in combination with anti-PD-1 treatment to overcome anti-PD-1 resistance, which could open new patient segments (SITC 2022)
- Aim is to partner following Phase 2 data readout to potentially expand combination potential

zamaporvint (RXC004)

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

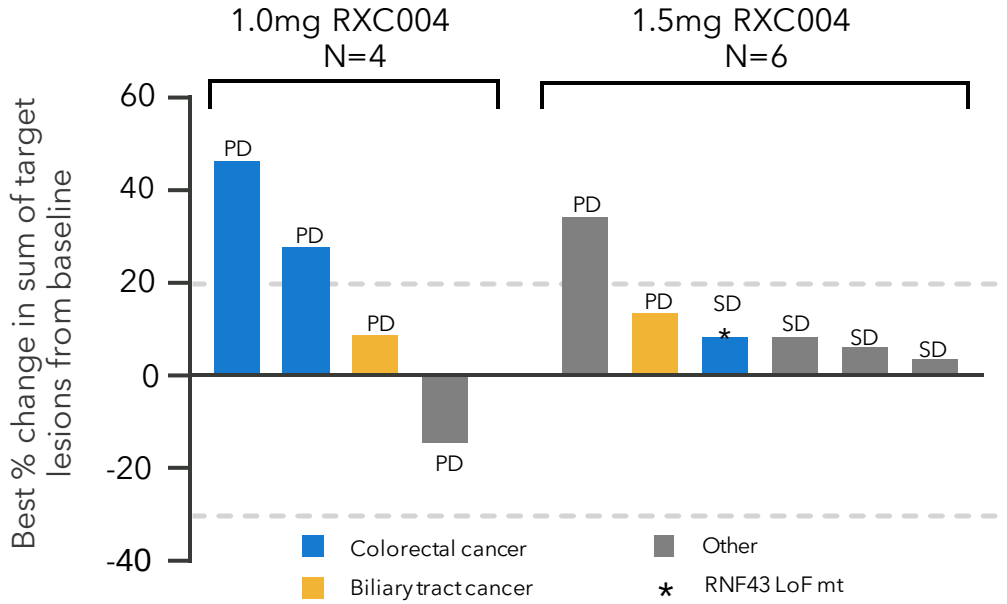
## Phase 1 Monotherapy All Comers Study Clinical Activity by Wnt-Ligand Dependence†




- 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

(Zamaporvint 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

zamaporvint (RXC004)

# Phase 2 Combination Programme in Wnt-Ligand Dependent Tumours - Data H1 2024

| | PORCUPINE<br>MSS Metastatic Colorectal Cancer | PORCUPINE2<br>Biliary Tract Cancer |
|---|---|---|
| | Combination<br>Genetically Selected<br>Zamaporvint + Nivolumab | Combination<br>Biliary Tract Cancer<br>Zamaporvint+ Pembrolizumab |
| **Endpoints** | **ORR**<br>Secondary DCR,<br>Tumour size change, DoR, PFS | **ORR**<br>Secondary DCR,<br>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 zamaporvint on tumours
- Tracking circulating tumour DNA (ctDNA)
- Baseline and on-treatment biopsies to assess changes to tumour and immune microenvironment

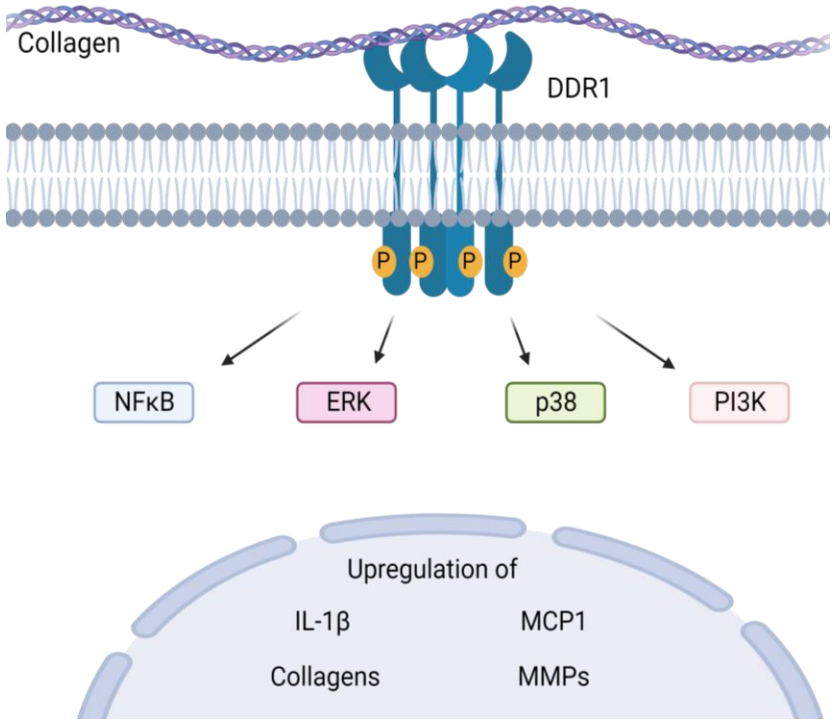


DCR: Disease control rate; DoR: Duration of response; ORR: Overall response rate; OS: Overall survival; PFS: Progression free survival

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

## Next Milestone: IND – enabling studies

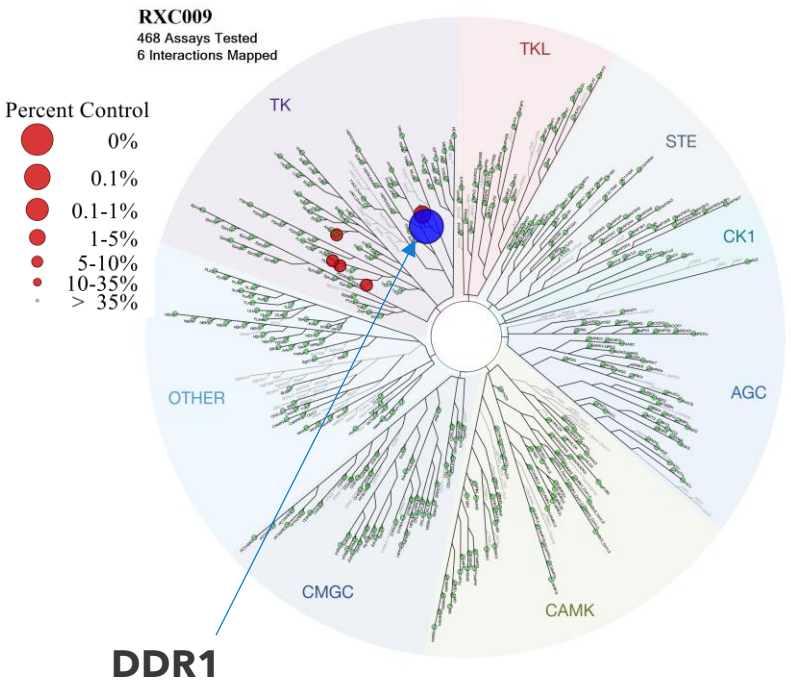
- Discoidin Domain Receptors (DDR) are non-integrin tyrosine kinase collagen receptors with expression increased in many fibrotic diseases including kidney fibrosis
- DDR inhibition is a novel druggable therapeutic target for fibrosis
- RXC009 is a DDR1 Inhibitor with potential to be a first-in-class treatment option for kidney fibrosis associated with Diabetic Kidney Diseases and Chronic Kidney Diseases such as Alport Syndrome for which there is currently no specific approved treatment
- Demonstrated efficacy and target engagement in preclinical models with excellent pharmacokinetic profile seen across species, suitable for potential use in combination
- Safety profile supports progression to IND-enabling studies



RXC009

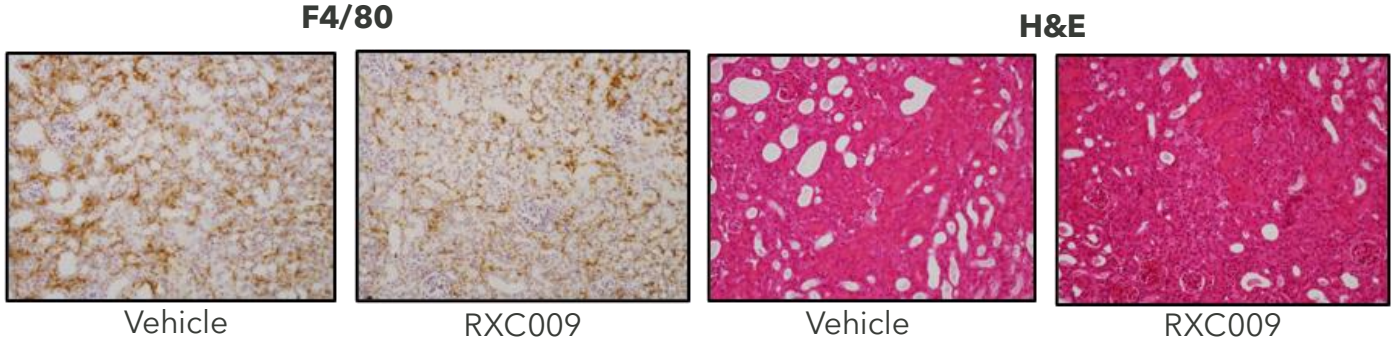
# Preclinical Data From Therapeutic Murine UUO Model, Supports Progressing RXC009 into IND-Enabling Studies

## Highly Potent and Exhibits Excellent Selectivity for DDR1

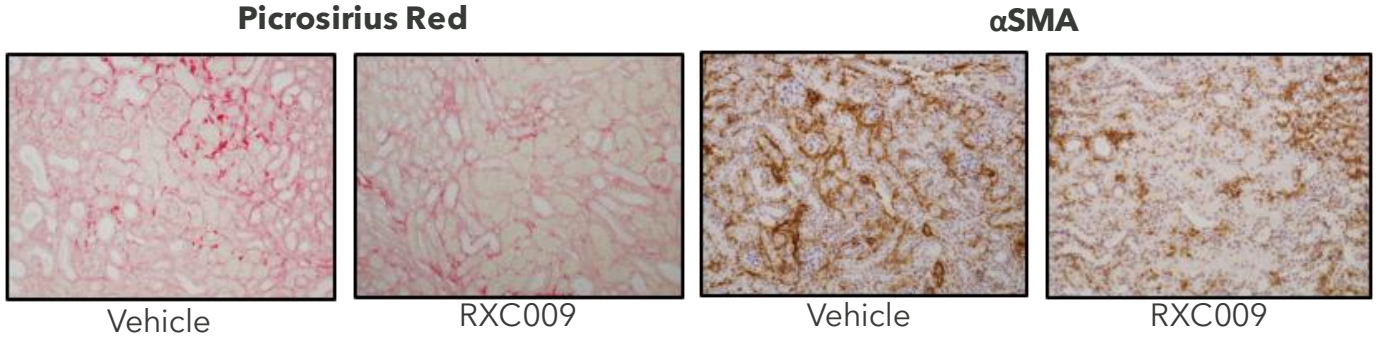



## Improves Histological Markers of Inflammation, Tubular injury and Fibrosis in Therapeutic Unilateral Ureteral Obstruction (UUO) Murine Model

### Reduction of Inflammation and kidney injury




### Reduction of fibrosis, collagen deposition, myofibroblast transformation



# Cash Runway into 2025 Funds Significant Milestones Across Portfolio

## 2024 Key Milestones

**Zamaporvint**
Phase 2 combination data

**Zelasudil**
Phase 2a IPF data

**Zelasudil**
Complete response to FDA

**RXC008**
Phase 1 healthy volunteers data

## Future Value Expansion Opportunities

**Zelasudil**
Potential in ILD and cancer-associated fibrosis

**RXC008**
Clinical proof-of-concept in fibrostenotic Crohn's

**Zamaporvint**
Explore partnership opportunities incl. 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 (at 29 February)
Fully diluted: 544,251,143 (at 29 February 2024 and assuming full conversion of loan notes and exercise of employee share options).