Redx
Discovering Targeted Medicines

# Corporate Presentation

February 2022

AIM:REDX

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# 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

## 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

## 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

## 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

## 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

## 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

# 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 preclinical pipeline

Ambitious, experienced leadership/scientific team with distinct approach and track record for consistently generating differentiated drug candidates

Pipeline financed to deliver multiple value inflection points in 2022 and backed by blue-chip specialist biotech investors

# A Clinical Stage Biotech with Three Value Drivers

## Selective Porcupine Inhibitor (RXC004)

- Ph1 monotherapy: differential activity in Wnt-ligand dependent tumours
- Ph1 combo ongoing with nivolumab
- Ph2 (PORCUPINE) initiated: genetically selected MSS mCRC
- Ph2 (PORCUPINE2) initiated H1 2022: genetically selected pancreatic/unselected biliary
- Open IND in the US

## Selective ROCK2 Inhibitor (RXC007)

- Targeting a master switch in fibrosis
- Clinically validated target, with first ROCK2 inhibitor approved by FDA in 2021
- Interim Ph1 data: no adverse events (up to 40 mg as a single dose)
- Biologically relevant exposures
- Lead indication IPF – Ph2 start in 2022

## Discovery Engine

- Strong track record:
  - Generated four molecules now in clinic incl. pirtobrutinib
  - Partnership deals with Jazz and AstraZeneca
- Partnered programmes: $26m milestones earned in 2021
- Discoidin domain receptor (DDR) inhibitors for fibrosis
- Targeting 3 wholly-owned INDs by 2025

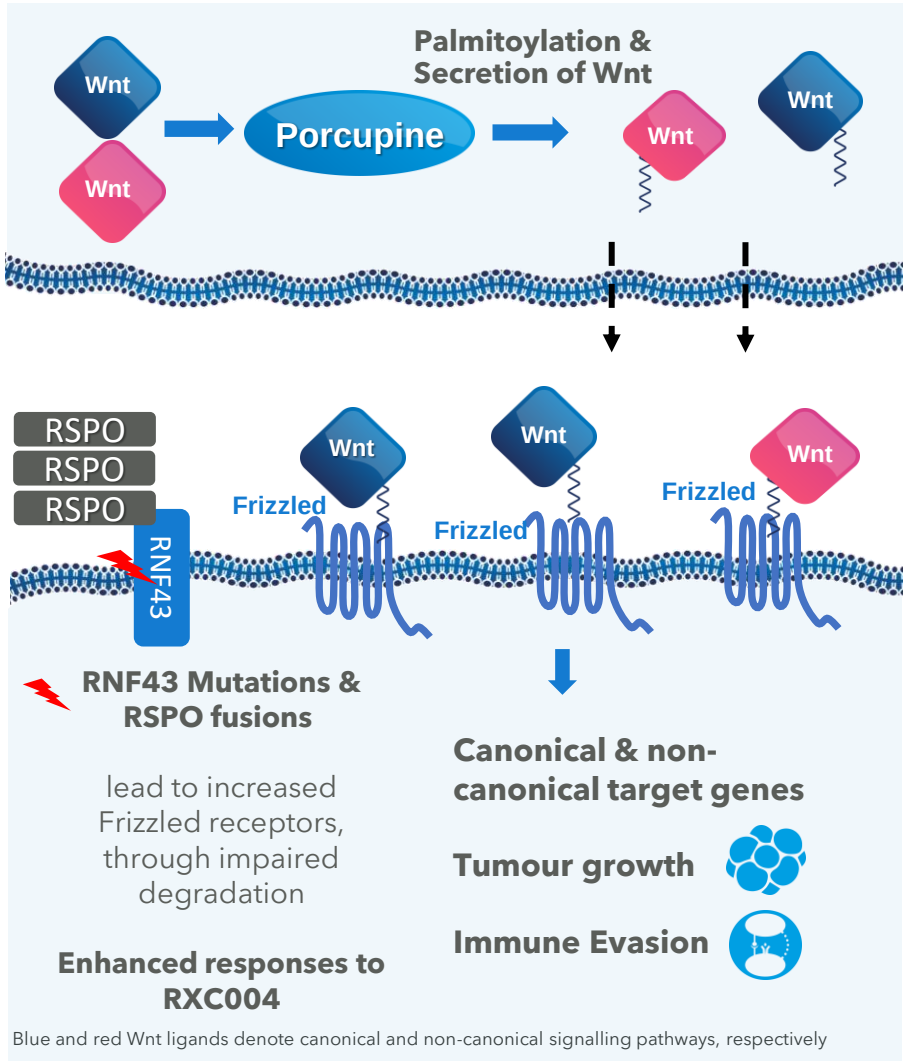
IND: Investigational New Drug application; IPF: Idiopathic Pulmonary Fibrosis; ROCK: Rho Kinase; Wnt: Wingless/integrated

# Robust Pipeline with Two Wholly-Owned Clinical Stage Assets Built from In-House R&D Engine

| | Target/Product | Research | Preclinical | Phase 1 | Phase 2 | Phase 3 | Upcoming Milestones |
|---|---|---|---|---|---|---|---|
| Oncology | **Porcupine Inhibitor** (RXC004) | Genetically selected MSS mCRC mono + nivolumab combo | | | | | Combo: Initiate Phase 2 – **2022**<br>Topline data – **H1 2023** |
| | | Genetically selected pancreatic cancer<br>Unselected biliary cancer | | | | | Initiate Phase 2 – **H1 2022**<br>Topline data – **H1 2023** |
| Fibrosis | **ROCK2 Selective Inhibitor** (RXC007) | Idiopathic pulmonary fibrosis (IPF) | | | | | Phase 1 topline results – **H1 2022**<br>Initiate Phase 2a - **2022** |
| | **GI-targeted ROCK Inhibitor** | Fibrosis in Crohn's | | | | | Preclinical development candidate – **H1 2022** |
| | **DDR Inhibitor** (Discoidin Domain Receptor) | Fibrosis | | | | | In lead optimisation |
| Partnered | **MAPK Pathway** (2 targets) | Oncology | | | | | Progress Jazz collaboration |
| | **Porcupine Inhibitor** (RXC006/AZD5055) | Idiopathic pulmonary fibrosis (IPF) | | | | | Licensed to AstraZeneca |
| | **Pan-RAF Inhibitor** (JZP815) | Oncology | | | | | Sold to Jazz Pharmaceuticals |

DDR: Discoidin Domain Receptor; RAF: Rapidly accelerated fibrosarcoma; GI: Gastrointestinal; MAPK: Mitogen-activated protein kinase; MSS mCRC: Microsatellite-Stable Metastatic Colorectal Cancer; ROCK: Rho associated protein kinase

# 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, orally active Porcupine Inhibitor

- Differentiated vs. competitors
- Encouraging Phase 1 monotherapy data reported at ESMO 2021, efficacy signal consistent with activity in Wnt-ligand selected 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 H1 2023

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

ESMO: European Society for Medical Oncology; RNF43: Ring Finger Protein 43; RSPO: R-Spondin; Wnt: Wingless/integrated

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

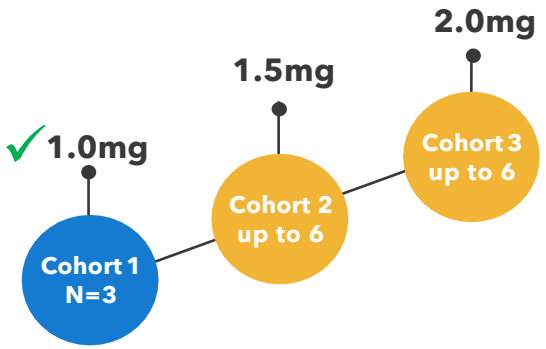
**Module 1:** Monotherapy, 0.5-3.0 mg, N=24

## Complete; presented at ESMO 2021

- Drug well tolerated in patients up to 2 mg as monotherapy
- 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

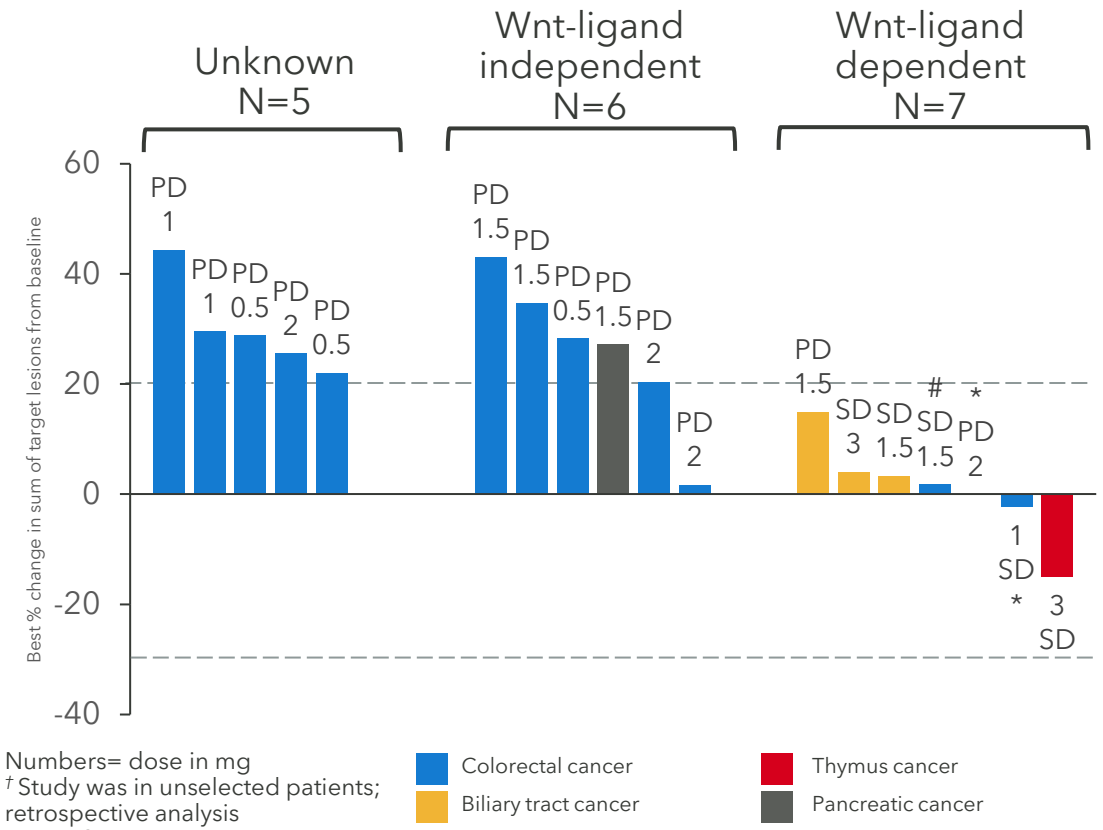
## Initiating 2022

ESMO: European Society for Medical Oncology

RXC004

# 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

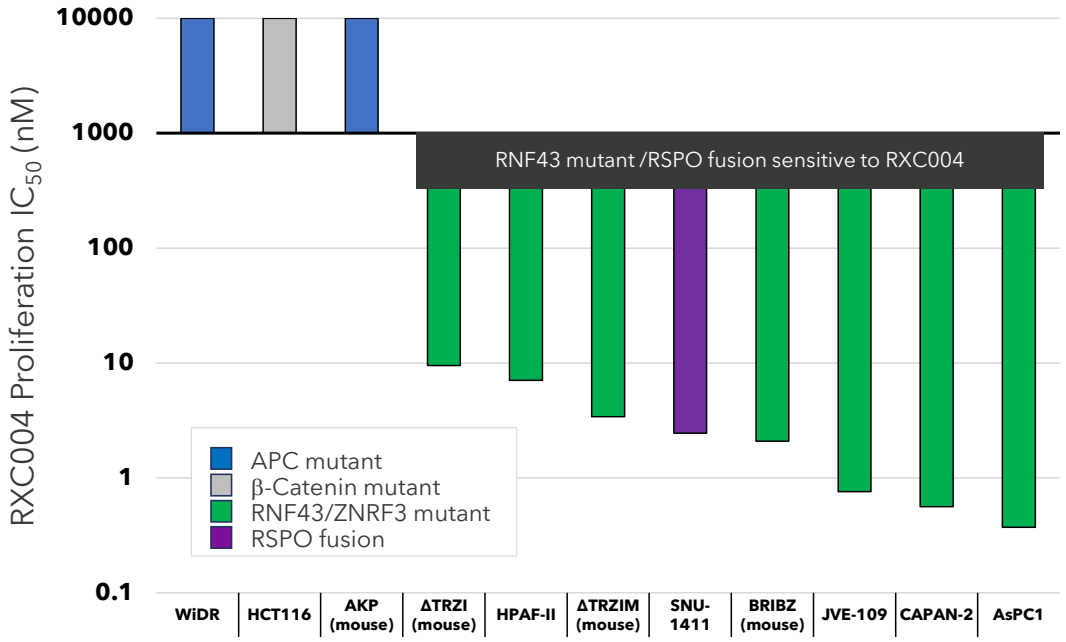
APC: Adenomatous Polyposis Coli Gene; CRC: Colorectal Cancer; LoF: Loss of Function; PD: Progressive Disease; RECIST: Response Evaluation Criteria in Solid Tumours; RNF43: Ring Finger Protein 43; RSPO: R-Spondin; SD: Stable Disease; Wnt: Wingless/integrated

Data cut-off date 30 July 2021

RXC004

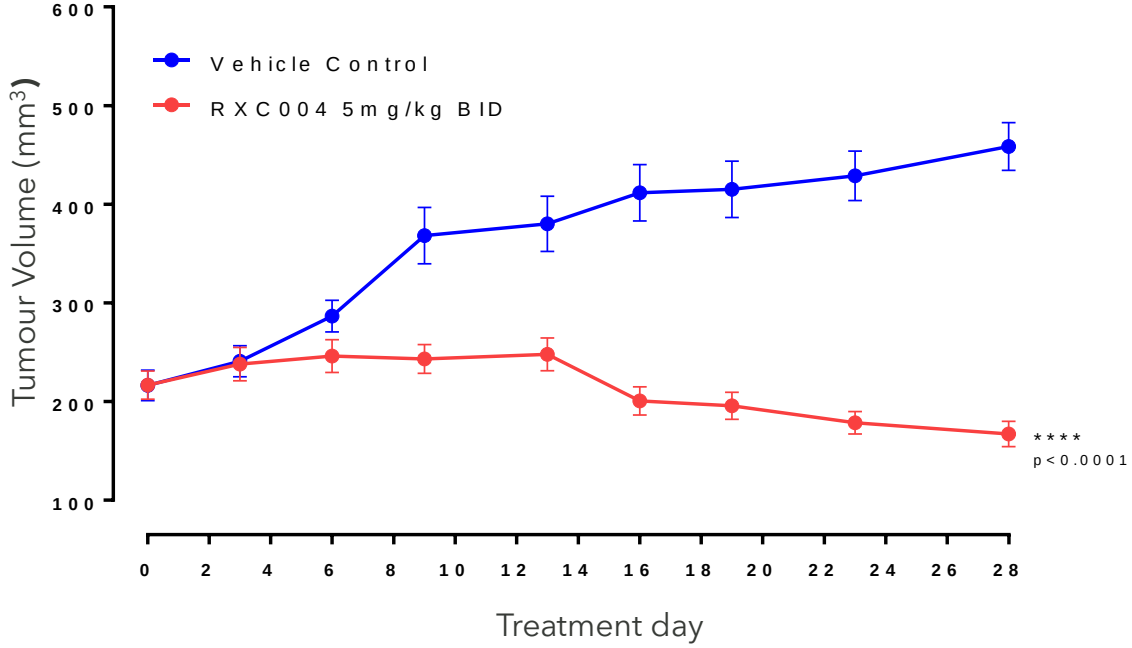
# Data in Genetically-Selected Cancer Models Supports Potential for Enhanced Responses in Selected Patients

## 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)

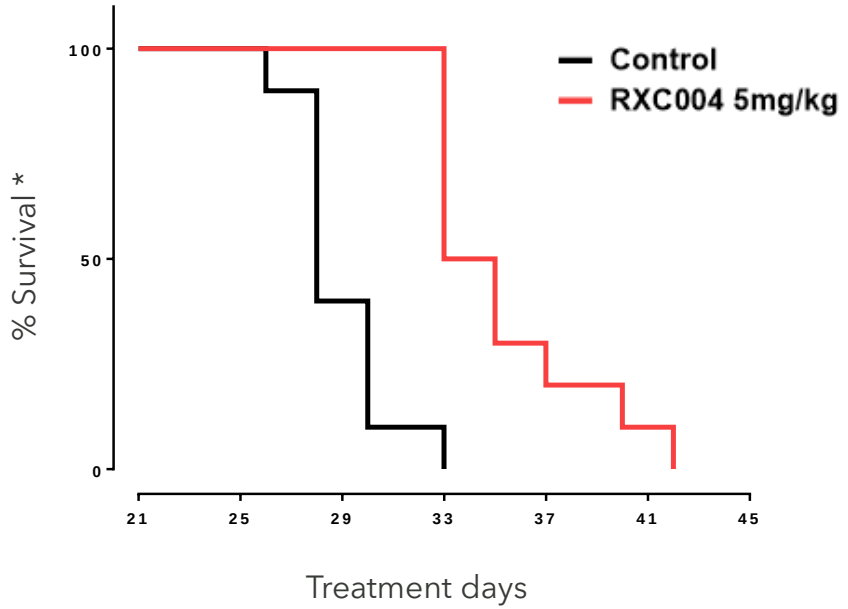
Redx internal data

BID: Twice daily; RNF43: Ring Finger Protein 43; RSPO: R-Spondin; ZNRF3: Zinc and ring finger 3

RXC004

# Preclinical Data Indicates Wnt Pathway Blockade Could Enhance Immune Related Survival – Supporting Combination Development

## 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 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) |
| **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]** | 15% | | 3% | 2% |

[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) ; [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

# 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** | 15% | 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 Showed Clinical Efficacy in Wnt-Ligand Dependent Tumours and Manageable Toxicity in Phase 1

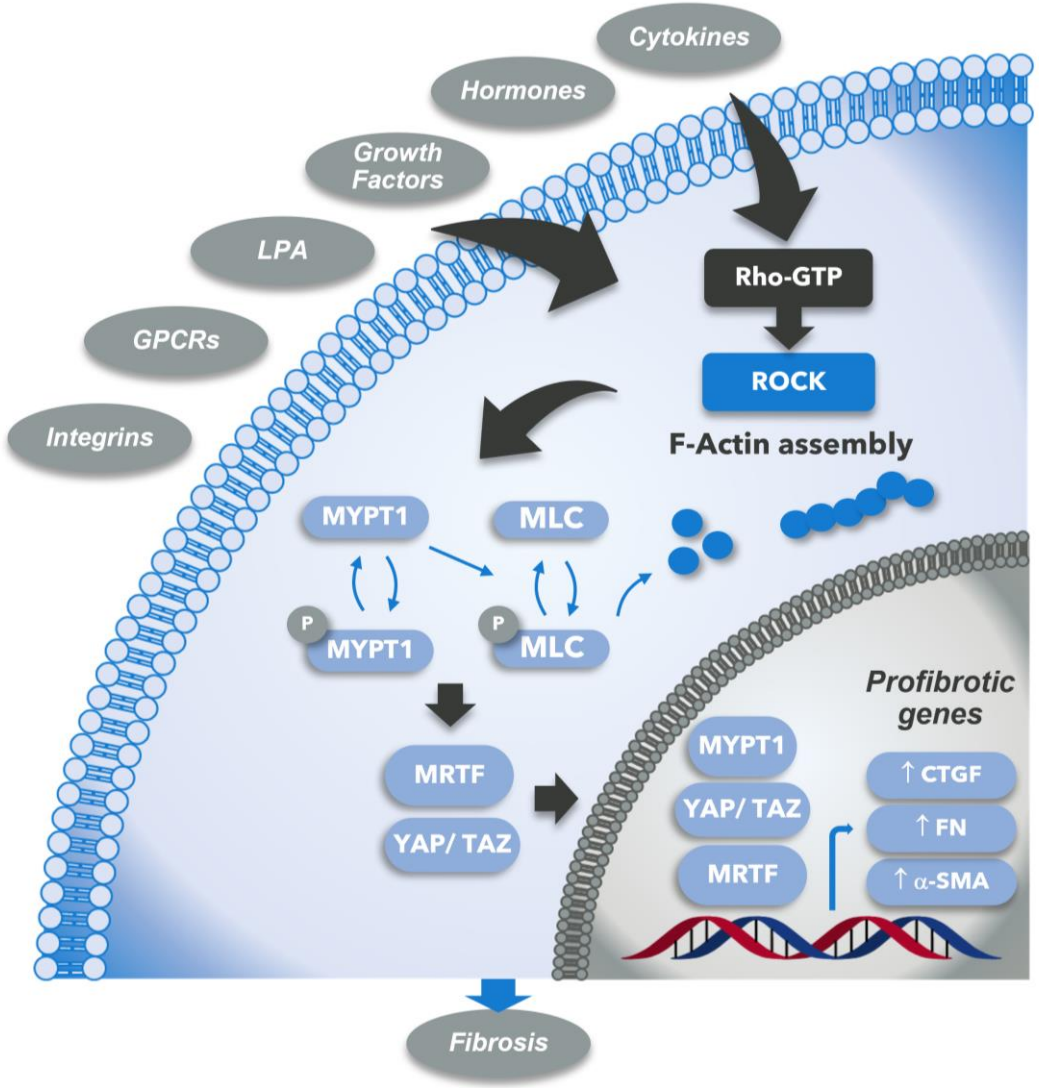
## Highlights

- Porcupine inhibition blocks all Wnt ligands, preventing tumour growth and immune evasion
- RXC004 is a highly potent, orally active, once daily Porcupine inhibitor
- Phase 1 clinical efficacy data supports development in Wnt-ligand dependent tumours
- RXC004 monotherapy was well tolerated at doses up to 2mg
- Target engagement evident at all doses, with doses ≥1.5mg achieving exposures that demonstrated efficacy in all preclinical models tested
- Selected dose for Phase 2 monotherapy studies is 2mg
- Phase 2 monotherapy programme initiated in Q4 2021; combination with nivolumab expected to commence in 2022

Wnt: Wingless/integrated

RXC007

# RXC007 Is a Selective ROCK2 Inhibitor for Fibrotic Diseases – Phase 1 Topline Data Expected H1 2022




## RXC007 is a highly selective oral ROCK2 Inhibitor

- Compelling preclinical efficacy demonstrated across fibrotic disease models
- Phase 1 topline data expected in H1 2022

## 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

## Phase 2a in IPF expected to commence 2022

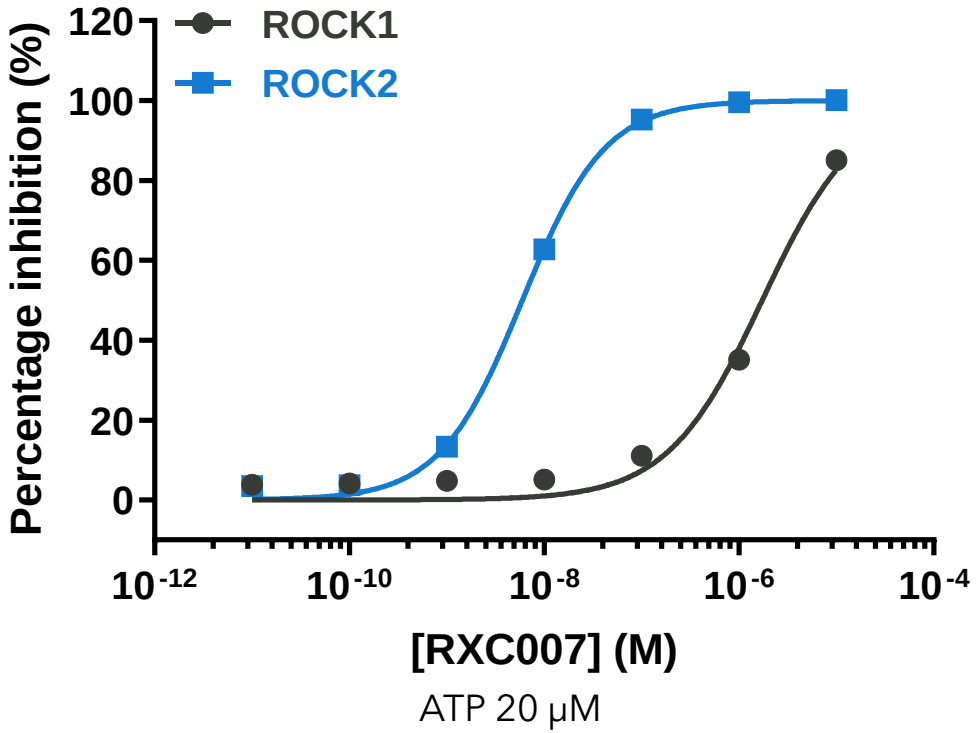
- Idiopathic Pulmonary Fibrosis (IPF) high unmet need - median survival 3-5 years
- IPF market projected to reach $3.6 bn by 2029*

** Global Data (US, EU5, Japan)*

cGvHD: Chronic graft versus host disease; ROCK: Rho associated protein kinase

RXC007

# RXC007 is a Highly Potent and Selective ROCK2 Inhibitor




- 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 highly selective, >100-fold versus ROCK1 in biochemical assays

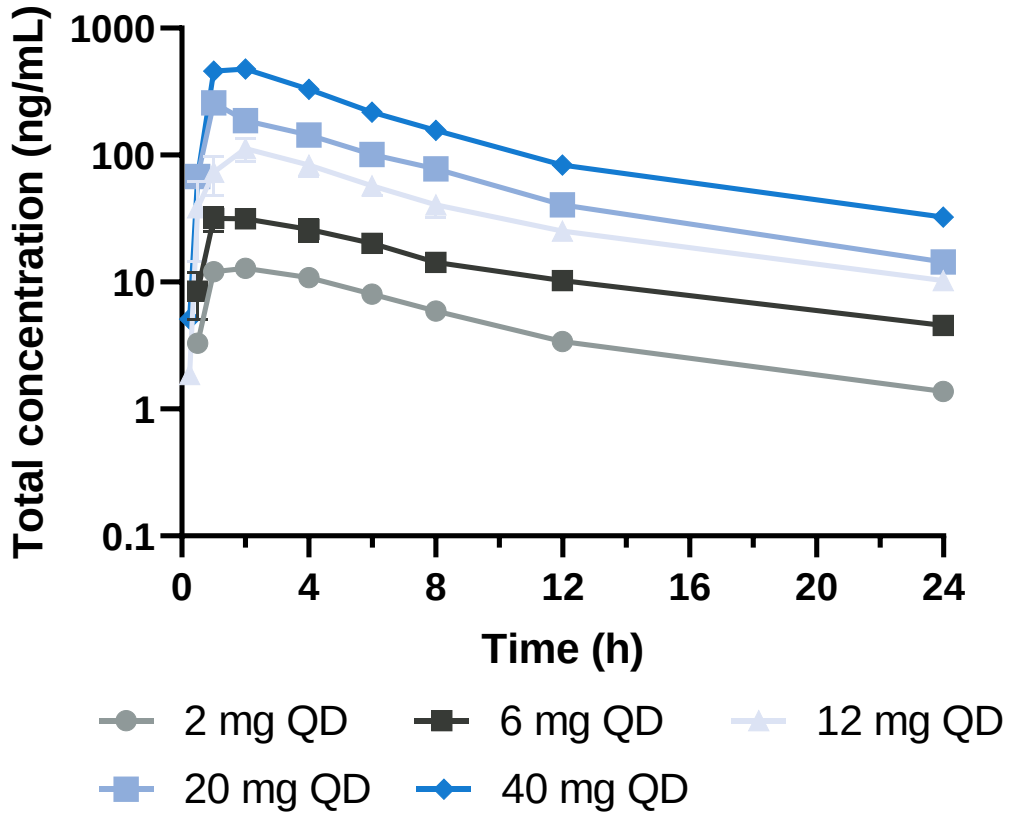
Redx internal data

ATP: Adenosine Triphosphate; ROCK: Rho Kinase

RXC007

# Strong Safety and Pharmacokinetic Profile in Phase 1 in Healthy Volunteers

**PK profile after single dose administration over 24 hours***




- No adverse events observed to date following single oral dose of 2-40 mg
- Pharmacokinetics as predicted from preclinical data
- Essentially linear exposure 2-40 mg
- Achieved biologically relevant exposures at 20mg and above
- At 40 mg, half-life ($t_{1/2}$) ~11 hours, potentially suitable for once-daily dosing
- Single ascending dose (SAD) escalations ongoing
- **Phase 1 results expected in H1 2022**

* Interim data on 14 September 2021

PK: Pharmacokinetic

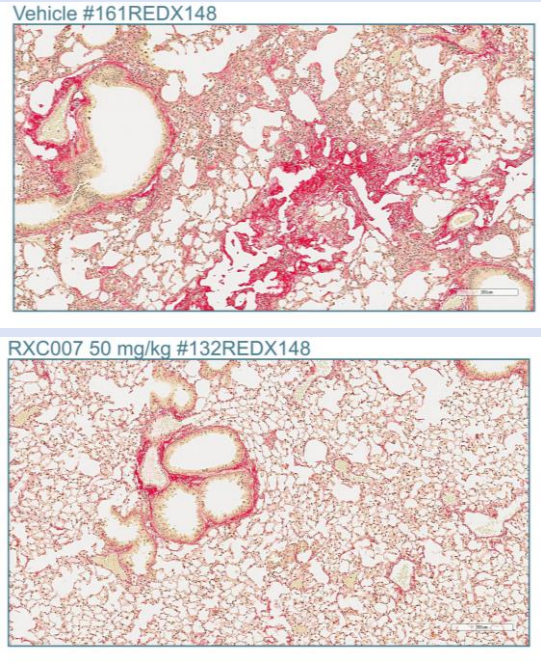
Redx internal data

RXC007

# Strong Preclinical Activity Supports Clinical Development Plan

## Good activity in industry standard IPF therapeutic model (bleomycin)

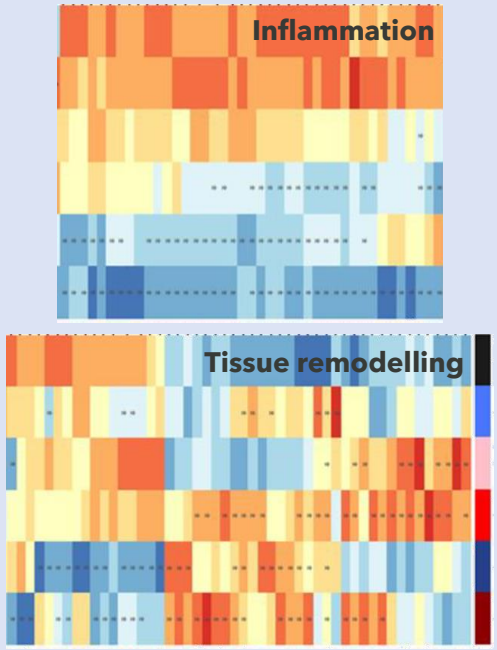
*Reduction of fibrosis and collagen deposition*




**Representative images of lung morphology**

## Strong modulation of key inflammatory and fibrotic gene signals

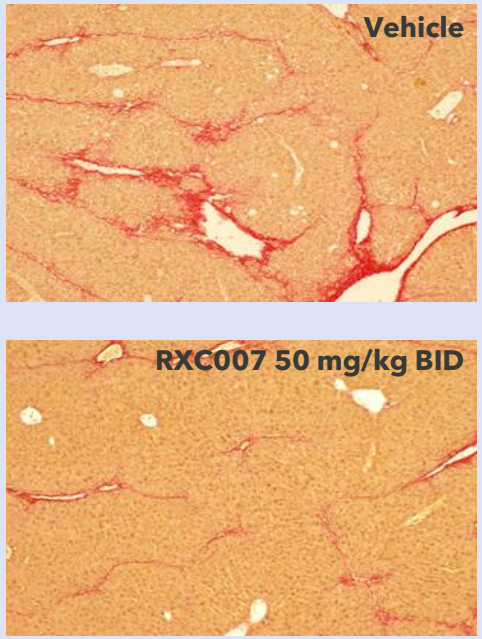
*Human post-transplant IPF tissue*




**Human precision cut lung slices (PCLS) mRNA analysis**

## Activity in Multiple Organs

*Reduction of fibrosis and collagen deposition in $CCl_4$ (carbon tetrachloride) therapeutic model of liver fibrosis*




**Representative images of liver morphology**

Redx internal data

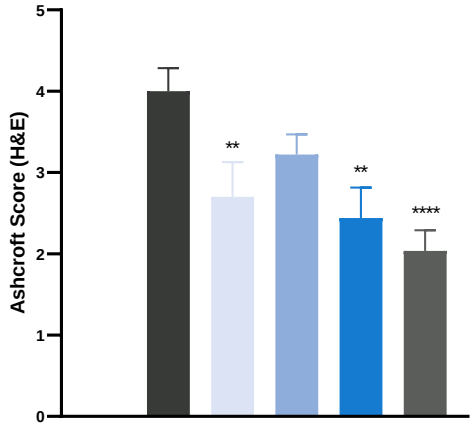
BID: Twice daily; IPF: Idiopathic Pulmonary Fibrosis

RXC007

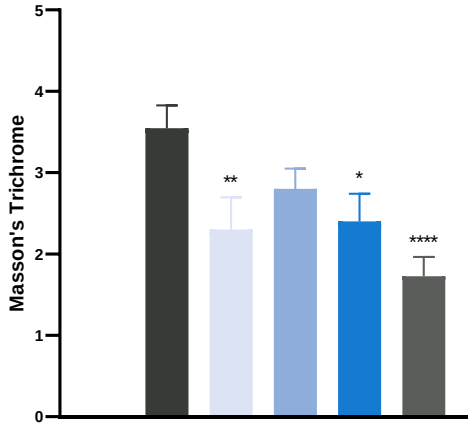
# Strong Preclinical Data Supports IPF as Lead Indication

## Efficacy in well-validated bleomycin *in vivo* model of lung fibrosis

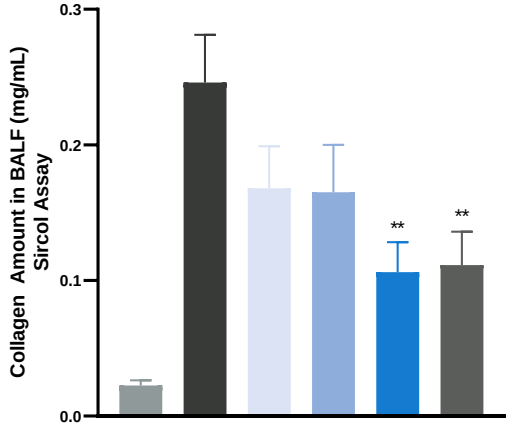
### Ashcroft Score




### Masson's Trichrome




### BALF Collagen




- Vehicle
- Bleomycin Vehicle
- RXC007 (5 mg/kg BID)
- RXC007 (20 mg/kg BID)
- RXC007 (50 mg/kg BID)
- Pirfenidone (100 mg/kg BID)†

Values expressed as mean of n = 5-11 + SEM. Uncorrected Fisher's LSD model. No differences at significance level 0.05, *: P < 0.05, **: P < 0.01, ***: P < 0.001, ****: P < 0.0001 compared to Bleomycin Vehicle † Pirfenidone dose of 100 mg/kg BID corresponds to a supra-therapeutic dose in humans

Redx internal data

IPF: Idiopathic Pulmonary Fibrosis

RXC007

# 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 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** to evaluate target and disease marker engagement; 2 cohorts of 8 patients each

**Cohort 1 b**
Dose Level 1
6:2 RXC007:pbo
- No standard IPF therapy
- Bronchoscopy at baseline and on treatment

**Cohort 3 b**
Dose Level 3
6:2 RXC007:pbo
- No standard IPF therapy
- Bronchoscopy at baseline and on treatment

**Key Endpoints**:
- Changes from baseline in blood biomarkers, and proteins and genes from broncho-alveolar lavage (BAL) fluid, BAL-fluid cells and bronchial epithelial cells



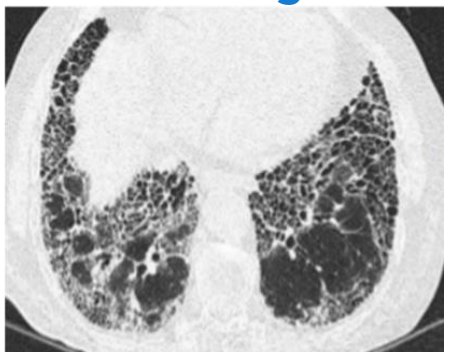
Pbo: placebo, PK: pharmacokinetics, FVC: Forced Vital Capacity, DLCO: Carbon monoxide diffusion coefficient, HRCT: High Resolution Computerized Tomography

RXC007

# Significant Market Opportunity in IPF

**Normal Lung**

**IPF Lung**



- 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

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

# RXC007 Clinical Development Planned in IPF with Staged 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
- Strong preclinical efficacy data supports clinical development plan in IPF
- To date* no adverse events observed in Phase 1 healthy volunteers and observed PK profile in line with prediction from preclinical data
- Dose escalations ongoing in Phase 1
- 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

*Interim data at 14 September 2021

FVC: Forced Vital Capacity; IPF: Idiopathic Pulmonary Fibrosis; PK: Pharmacokinetic; ROCK: Rho 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

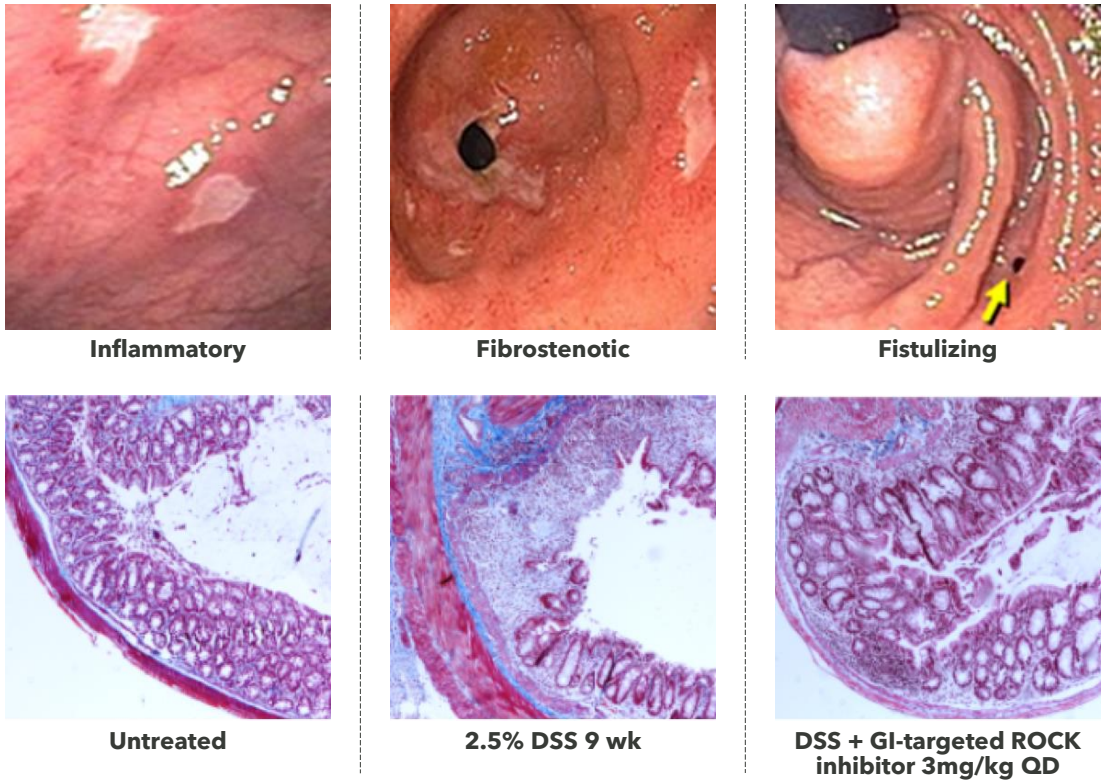
## DELIVER
**Redx's validated track record**

- 4 compounds in clinical development - 2 remain wholly-owned
- Multiple asset deals providing ~$1bn potential milestone revenue
- Targeting 3 wholly-owned INDs by 2025

ADME: Absorption, distribution, metabolism and excretion; IND: Investigational New Drug application; PoC: Proof of Concept; PK: Pharmacokinetic

Discovery Engine

# GI-targeted ROCK Inhibitor Targeting Drug Candidate in 2022




**GI-targeted ROCK inhibitor reduces collagen in mouse model of Crohn's fibrosis**

Increase of collagen staining shown in blue in the DSS treated animals.
GI-targeted ROCK inhibitor reduces production of collagen seen as a reduction in blue (trichrome) staining.

## Potent, oral small molecule 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 Crohn's disease-associated fibrosis (fibrostenosis)

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

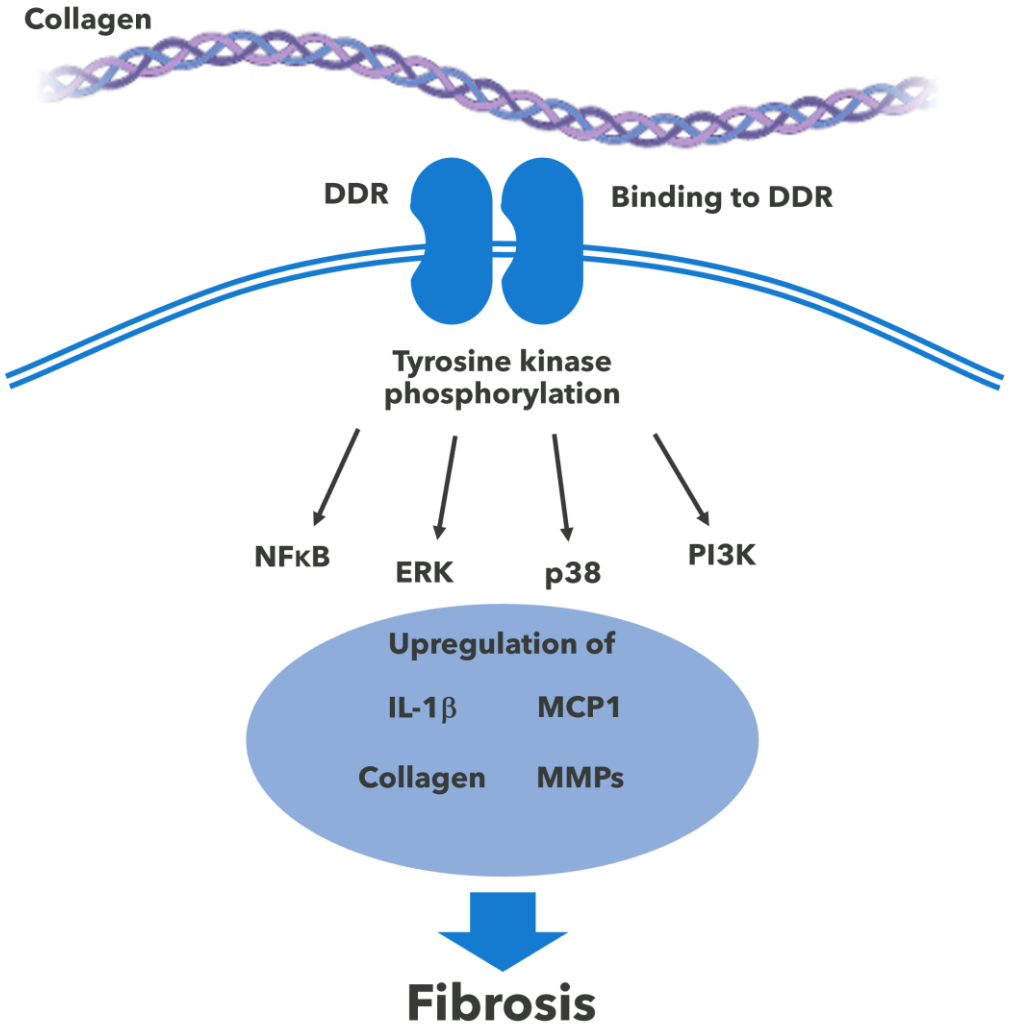
## Preclinical development candidate selection in 2022

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

Discovery Engine

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

New Programme




## 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; DS: Discoidin domain; PoC: Proof of concept

# Strong Financial Position with Support from Top Tier Specialist Investors

## Strong Financial Position

**£29.6 million cash**

as at 30 September 2021

**Cash runway through 2022***

## Productive Collaborations

**$26 million in milestones earned in 2021**

**~$1 billion in additional potential milestones**

AstraZeneca

Jazz Pharmaceuticals

## Top Tier Specialist Investors

Redmile Group

SOFINNOVA PARTNERS

POLAR CAPITAL

**AIM (UK) listed** Ticker: REDX
Total shares in issue: 275,282,205
Fully diluted: 419,148,197**

* Cash through Q4 2022 calendar year.

** assuming full conversion of loan notes and exercise of employee share options. Updated 27 September 2021

# Multiple Potential Milestones During 2022

## Selective Porcupine Inhibitor (RXC004)

- H1 2022 – Data from Phase 1 combination study with nivolumab (anti-PD1)
- H1 2022 – Initiation of PORCUPINE2 Phase 2 study in genetically selected pancreatic and unselected biliary cancer
- 2022 – Initiation of PORCUPINE combination arm in genetically selected MSS mCRC

## Selective ROCK2 Inhibitor (RXC007)

- H1 2022 – Data from Phase 1 healthy volunteer study
- 2022 - Initiation of Phase 2a study in IPF
- H2 2022 – US IND

## Discovery Engine

- 3 wholly-owned INDs by 2025
  - Targeting DC for GI-targeted ROCK inhibitor for Crohn's fibrosis
  - Progress discoidin domain receptor (DDR) inhibitor for fibrosis
  - Advance multiple programmes in early discovery
- Partnered programmes progress towards next milestones

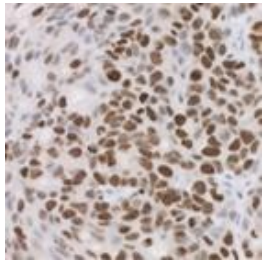
GI: Gastrointestinal; IND: Investigational New Drug application; IPF: Idiopathic Pulmonary Fibrosis; LO: Lead optimisation; MSS mCRC: Microsatellite-Stable Metastatic Colorectal Cancer; ROCK: Rho Kinase; Wnt: Wingless/integrated
All dates listed are calendar year

Redx
Discovering Targeted Medicines

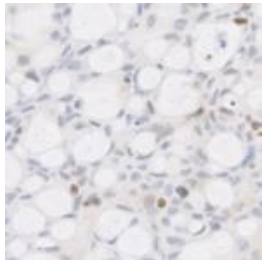
# Appendix

# RXC004 has a Dual Mechanism of Action

## Inhibits Tumour Cell Proliferation



Control



+RXC004

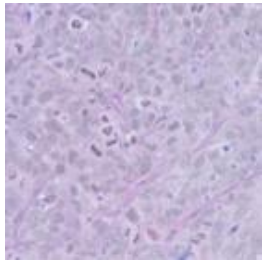
Reduces Ki67 staining in RSPO-fusion CRC xenograft model

**DIRECTLY TARGETS TUMOUR CELLS**

**RXC004**

**STIMULATES THE IMMUNE SYSTEM**

## Differentiates Tumour Cells



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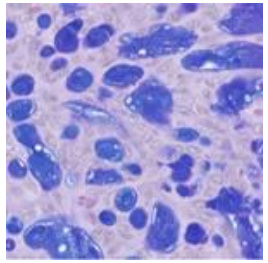
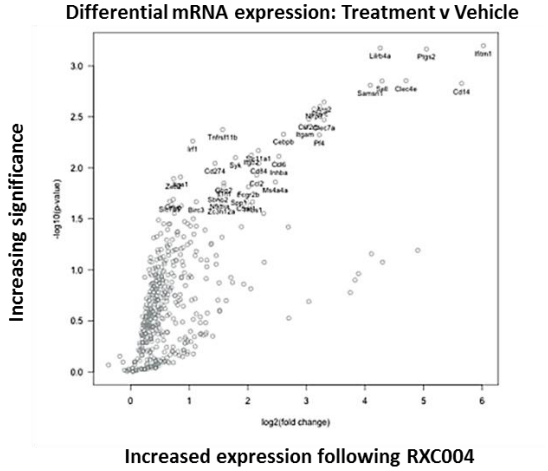


+RXC004

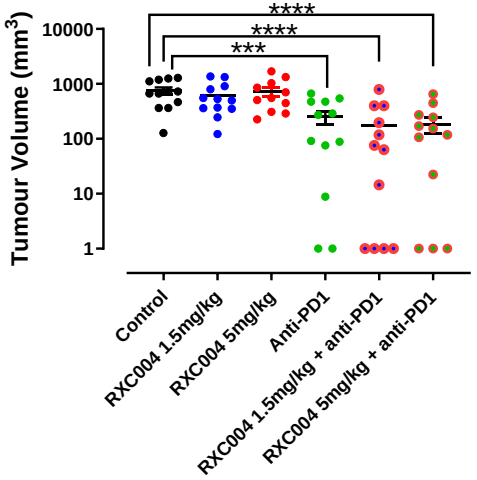
Increased size and mucin staining of tumour cells with RSPO-fusion. Cells also less metabolically active

## As a Monotherapy




Increase in immune related gene expression within tumours post-RXC004 treatment in anti-PD1-resistant mouse melanoma syngeneic model (B16F10)

## In Combination with anti-PD1



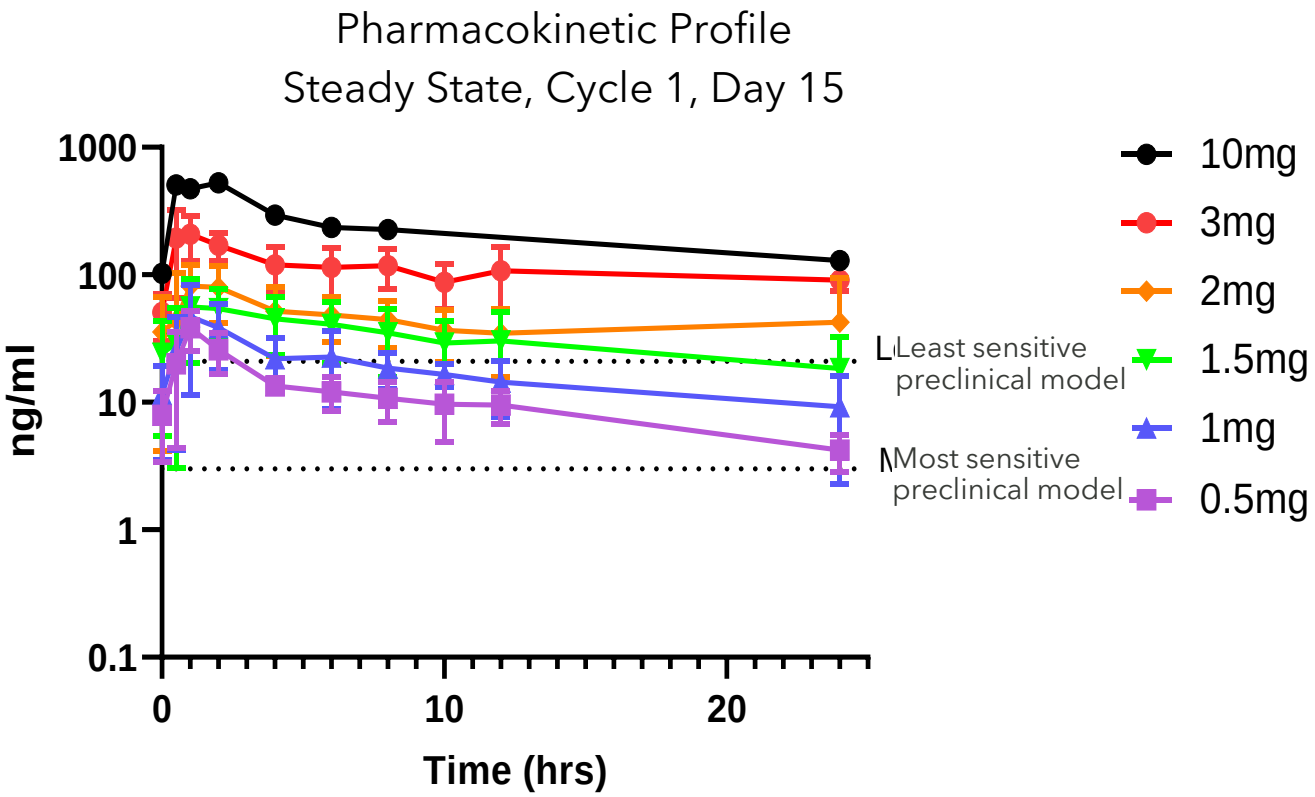

Improved responses observed when RXC004 combined with anti-PD1 in syngeneic CRC immune-mediated model (CT26)

Data as of 7th June 2021

CRC: Colorectal Cancer; RSPO: R-Spondin

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 2mg

Redx

Presented at ESMO '21

| 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 (10mg); colitis (3mg); ileitis (3mg); pancreatitis (2mg)
- 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