Redx
Discovering Targeted Medicines

Corporate Presentation

May 2021

AIM:REDX

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Redx – Discovering Targeted Medicines

Focused on novel, small molecule, targeted medicines as treatments for cancer and fibrotic disease

Distinct approach consistently generates potentially "best-in-class" drug candidates

Our approach is proven

- The invention of LOXO-305 – a motivation behind Lilly's $8 billion acquisition of Loxo Oncology; now in Phase 3
- A growing pipeline with two wholly-owned clinical assets
- Significant preclinical deals with AstraZeneca and Jazz Pharmaceuticals

Pipeline is financed to deliver multiple value inflection points in 2021/22

Ambitious, experienced leadership/ scientific team; backed by blue-chip specialist biotech investors

Ambitious and Experienced Leadership Team

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

>24 years in biopharma industry most recently as Chief Financial Officer and Chief Business Officer. Previously, spent 17 years in 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

Redx Generates "Best-in-Class" Drug Candidates

Select biologically Validated "druggable" targets

- High unmet medical need
- Significant commercial potential
- Clear path to regulatory approval
- *In vivo* PoC achieved on target / pathway
- Opportunity for best in class

Apply Redx small molecule design framework

- Select chemical start point to develop IP
- Improve on frontrunner e.g.;
  - Overcome resistance
  - Improve side-effect profile
  - Fix ADME / PK for dosing
- Leverage strength in medicinal chemistry and translational biology

Validated drug discovery engine

Successful partnering

Wholly-owned pipeline assets

Targeting 3 INDs by 2025

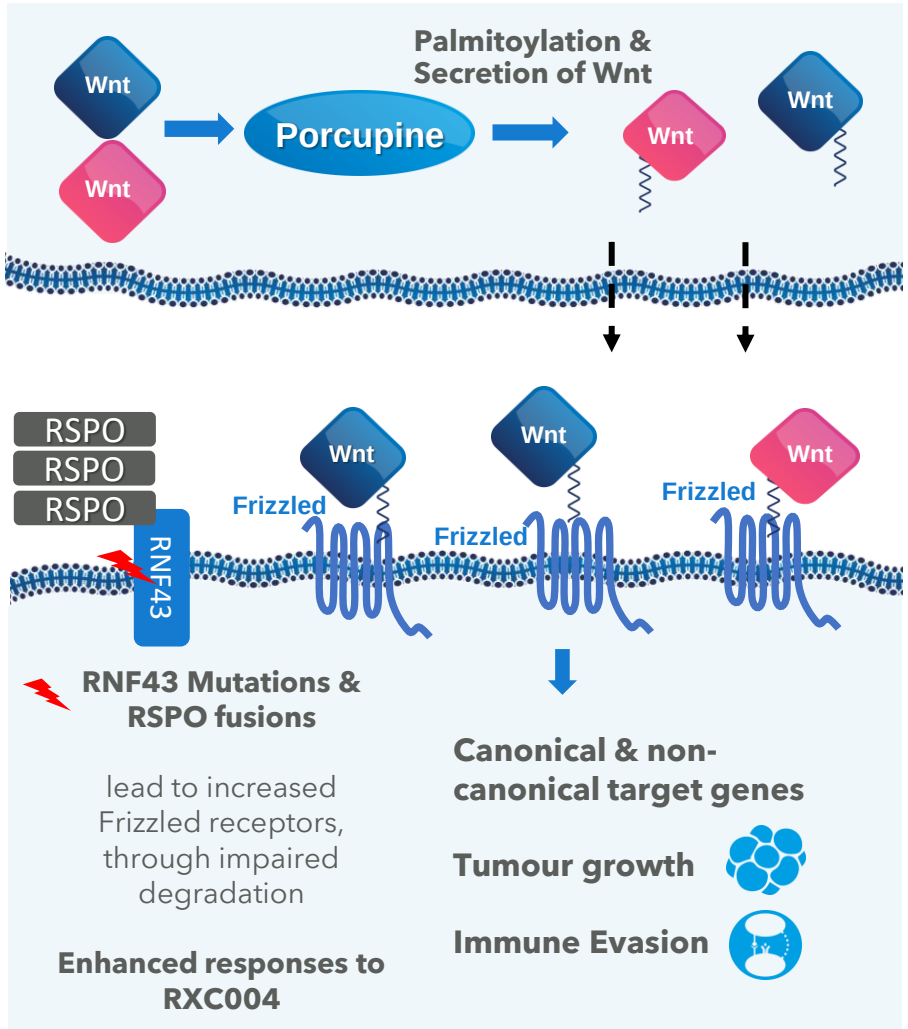
Financed to Deliver Multiple Value Inflection Points in 2021

	Target/Product	Indication(s)	Research	Preclinical Development	Clinical Phase 1/2	Upcoming Milestone
Development	**Porcupine Inhibitor** (RXC004)	Monotherapy in solid tumours (genetically selected MSS mCRC and pancreatic cancer; all comers biliary cancer) Combination with anti-PD1 (genetically selected MSS mCRC)				Phase 1 mono safety completion – **H2 2021** Phase 1 combo safety completion – **H2 2021** Phase 2 starts – **H2 2021**
Development	**ROCK2 Selective Inhibitor** (RXC007)	Lung fibrosis (IPF)				Phase 1 headline results expected – **H1 2022**
Research	**GI-targeted ROCK Inhibitor**	Fibrosis associated with Crohn's disease				Preclinical development candidate – **H2 2021**
Research	**Research Targets**	Oncology and Fibrosis				Progress wholly-owned & Jazz collaboration programmes
Partnered	**Porcupine Inhibitor** (RXC006)	Lung fibrosis (IPF)				Licensed to AstraZeneca
Partnered	**Pan-RAF Inhibitor**	Oncology				Asset sold to Jazz Pharmaceuticals

MSS mCRC = Microsatellite-Stable Metastatic Colorectal Cancer; IPF = Idiopathic Pulmonary Fibrosis

RXC004

Our Lead Asset in Oncology is RXC004, a Porcupine Inhibitor



What is RXC004?

- Highly potent, orally active porcupine inhibitor in a Phase 1 clinical trial
- Differentiated vs. competitors

Why target porcupine?

- Porcupine is a Key enzyme in the Wnt pathway, long established as a key driver of cancer
- Inhibition of Porcupine blocks the release of all Wnt ligands from cells, **preventing both tumour growth** and **tumour immune evasion**
- Targeting **genetically-selected** tumours with RNF43 mutation or RSPO fusions will lead to enhanced responses

Which lead indications?

- MSS metastatic colorectal cancer, pancreatic and biliary

RXC004

Significant Market Opportunity in Monotherapy and Combination

High unmet need in lead indications (MSS mCRC, pancreatic & biliary cancer) with combined market size of ~$10 billion[10]

Potential as

- Monotherapy in genetically-selected patients
- Monotherapy in high Wnt ligand driven tumours
- Combination with immune-checkpoint inhibitors in MSS mCRC, to overcome Wnt driven tumour immune evasion
- Lifecyle management

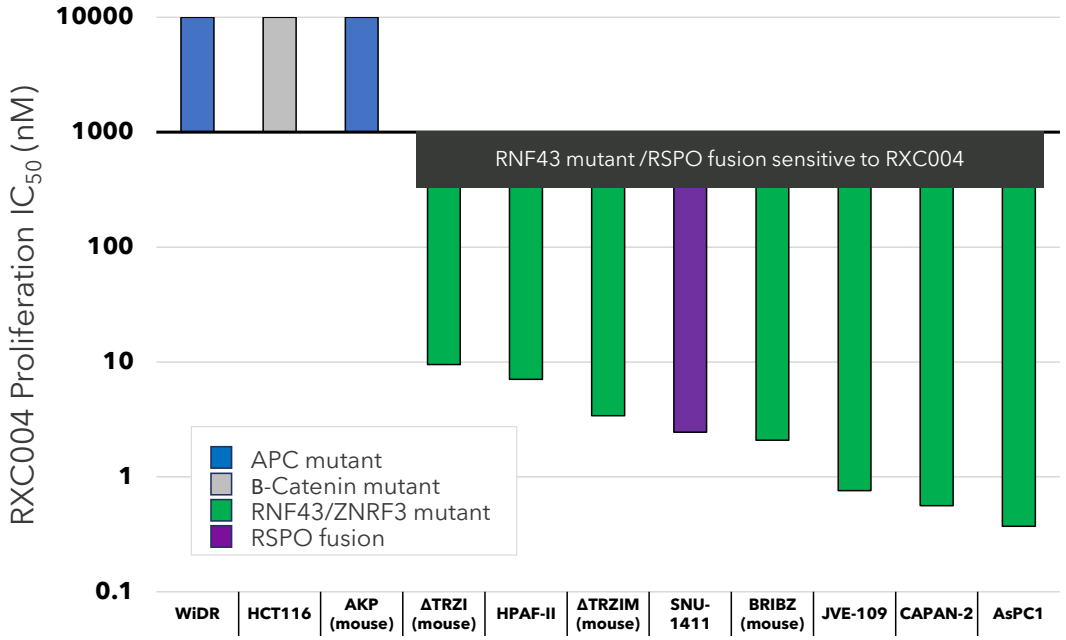
	RXC004 Addressable Indications	5-Yr Survival (Metastatic disease)[7]	Annual incidence (new) Metastatic cases (7-8MM)[8]	Prevalence of Genetic Mutation of Interest
Lead RXC004 Indications	**MSS mCRC (95% of all mCRC cases are MSS)[9]**	**14%**	**150,000+ patients**	**8% of patients** (RNF43 mutations in 3% of population[1] + RSPO fusions in 5% of population[2])
	Pancreatic Cancer	**3%**	**120,000+ patients**	**5% of patients** have RNF43 mutations[5]
	Biliary Cancer	**2%**	**60,000+ patients**	**>70% of patients** have high Wnt ligand expression[6]
LCM Opportunities	Squamous NSCLC	6%	245,000+ patients	5% of patients have RSPO fusions[3]
	CRPC	31%	90,000+ patients	6% of patients have RNF43/RSPO fusions[4]

MSS mCRC = Microsatellite-Stable Metastatic Colorectal Cancer; CRPC = Castrate-resistant Prostate Cancer; NSCLC = Non-small-cell lung carcinoma; LoF=Loss of function; GoF=Gain of Function. [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] Karhera et al. 2014; [4] Murillo-Gorzon et al 2017; [5] "Precision Panc" initiative data. RNF43 mutations in CRC patients identified by RXC004 clinical investigators; [6] Loilome et al. 2014, Boulter et al. 2015; [7] https://www.cancer.net [8] Incidence data sourced from GlobalData Epidemiology data (MM = Major Markets US, EU5, Japan, China) [9] Gong et al. March 21, 2017 (ASCO JCO) 10) GlobalData Report

RXC004

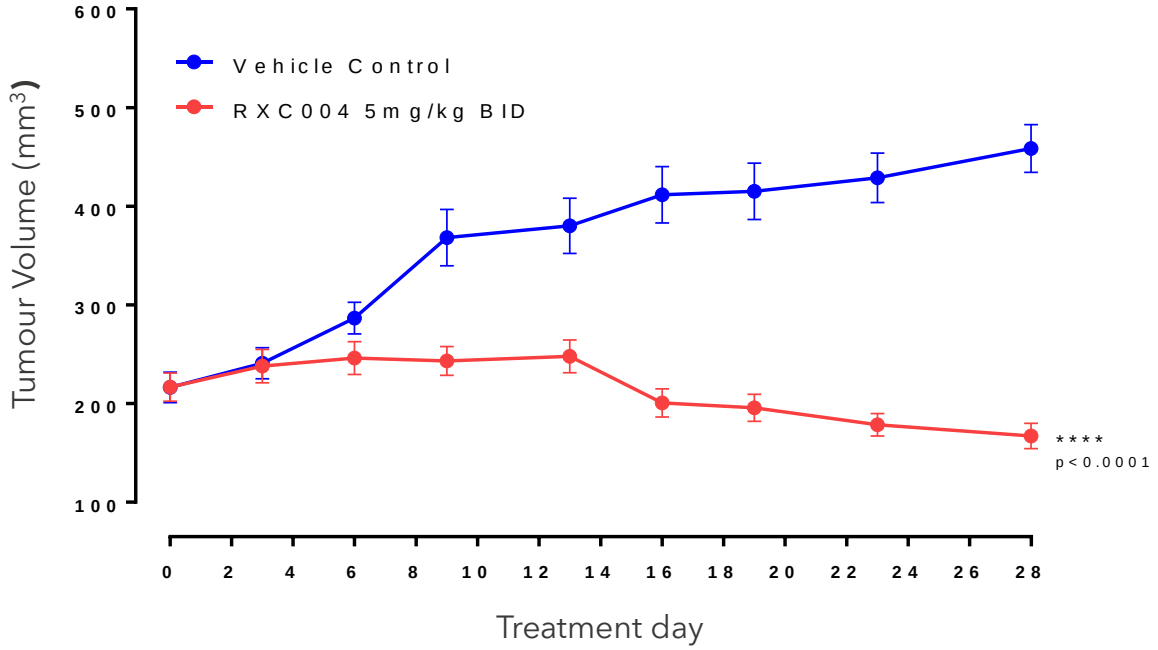
Targeting Genetically-Selected Tumours Leads to Enhanced Responses in Cancer Models

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



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

Efficacy translates *in vivo* in genetically defined xenograft models

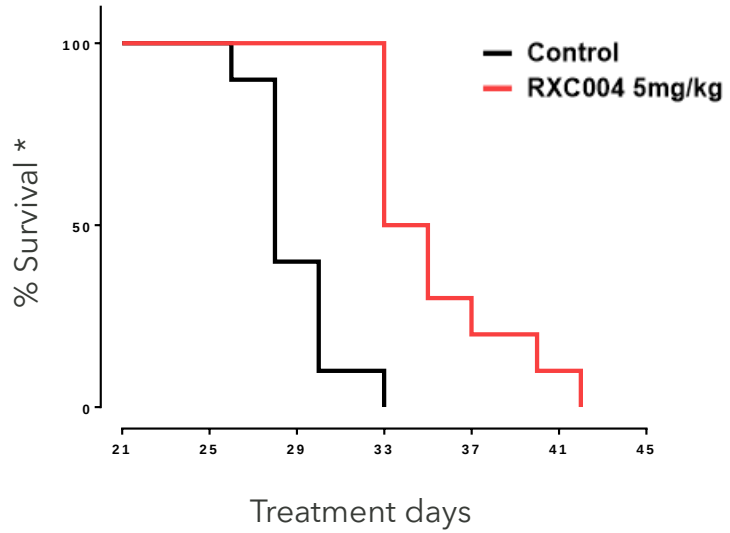


RNF43 mutant human pancreatic cancer line (Capan-2) grown in a mouse xenograft model

RXC004

Unlocking the Potential of Wnt Pathway Blockade in Immuno-Oncology

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]

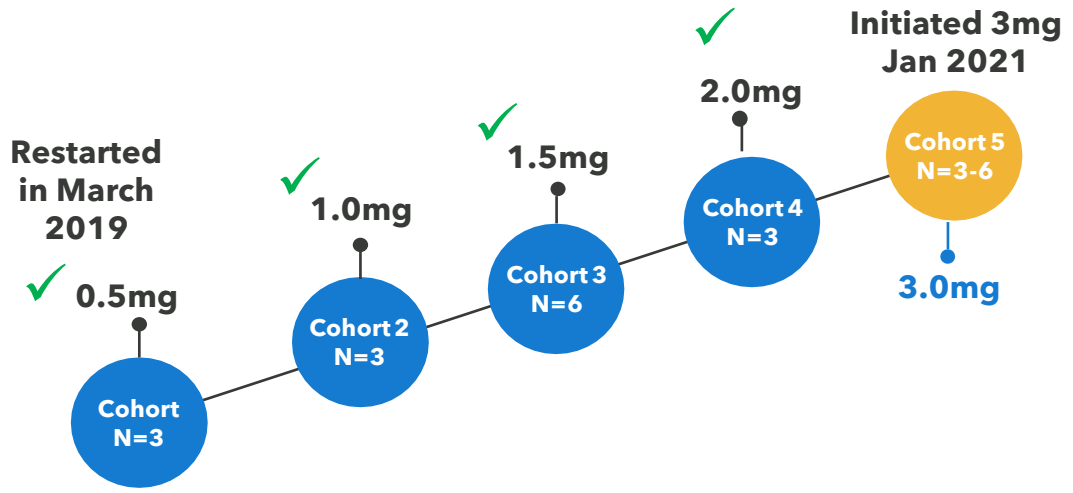
(1), Gong et al. March 21, 2017 (ASCO JCO) (2),Spranger et al., 2015; (3) Luke et al., 2019; (4) Phillips et al 2019; (5) Janku et al. (2020) AACR, CT034 - Phase I study of WNT974 + spartalizumab in patients (pts) with advanced solid tumors;
ICI = immune-checkpoint inhibitor, mCRC= metastatic colorectal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

RXC004

Phase 2 Expected to Commence 2021 Following Phase 1 data in mid-2021

RXC004 - Phase 1 - Dose Escalation

Monotherapy, Single Ascending Dose/ Multiple Ascending Dose (3+3 design)



Phase 1 objective

Assess safety and tolerability of RXC004 in all-comer cohorts of advanced cancer patients. 5 UK sites

Lead Principal Investigator

Dr Natalie Cook, Christie Hospital, UK

Phase 1: clinical summary 2021[1]

- Drug well tolerated in patients from first four cohorts
- Human PK profile confirmed
- Human exposure as predicted
- Pathway inhibition demonstrated in patient skin
- No Dose Limiting Toxicities (DLTs)
- No bone fragility fractures

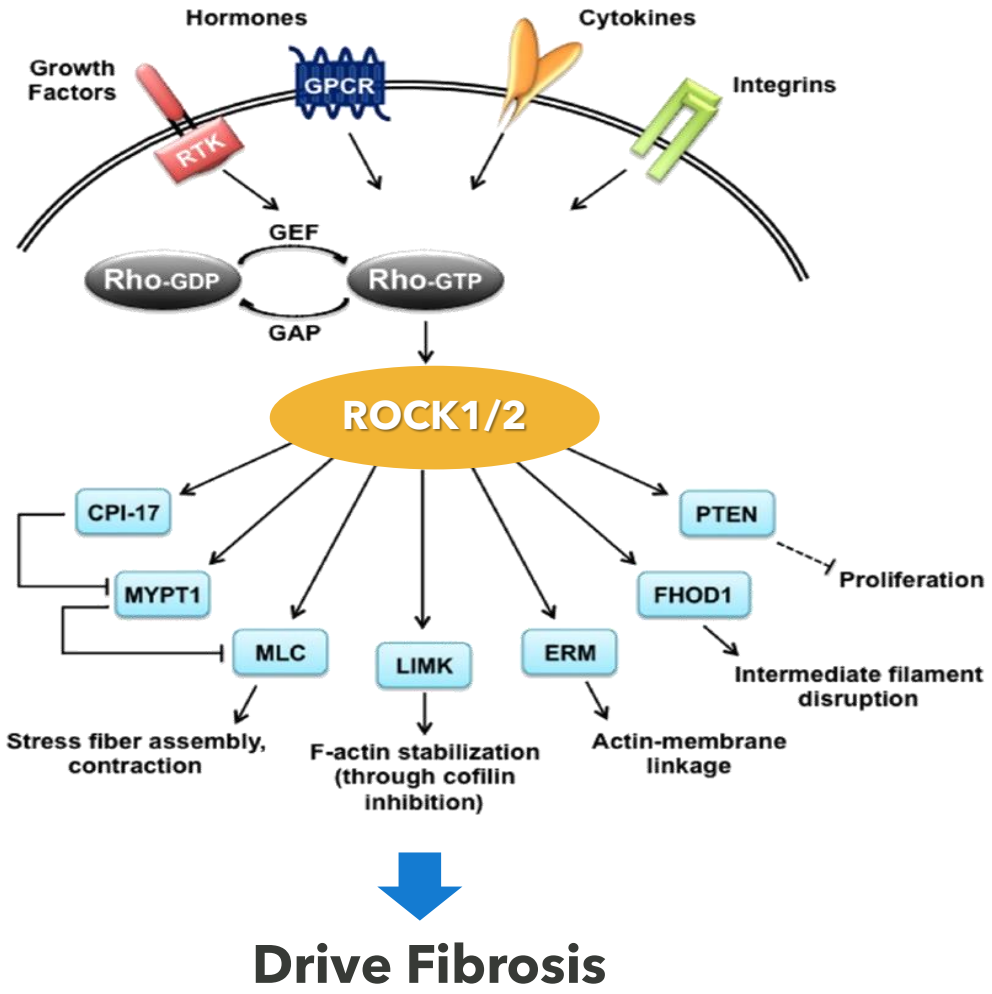
RXC004 clinical trial initiation in 2021

- **Phase 1** – Combination with anti-PD1, followed by Phase 2 in **genetically-selected** MSS mCRC
- **Phase 2** - Monotherapy in **genetically-selected** MSS mCRC
- **Phase 2** – Monotherapy in **genetically-selected** pancreatic cancer and all-comers biliary cancer

1. Redx Preliminary Results Statement, Jan 2021

RXC007

ROCK2 Selective Inhibitor for Fibrotic Diseases



What is RXC007?

- Highly selective, orally active ROCK2 inhibitor
- Compelling preclinical efficacy demonstrated across fibrotic disease models
- RXC007 first-in-human studies commenced **H1 2021**
- Differentiated vs. competitors

Why target ROCK2?

- ROCK sits at a nodal point in cell signalling pathways associated with fibrosis
- Systemic inhibition of ROCK1&2 results in hypotension, not seen with ROCK2 selective inhibition
- ROCK2 clinically validated target in inflammatory and fibrotic disease

Which lead indications?

- Potential for disease modifying efficacy across multiple fibrotic conditions including our lead indication, Idiopathic Pulmonary Fibrosis (IPF)

RXC007

Significant Market Opportunity in Idiopathic Pulmonary Fibrosis (IPF)

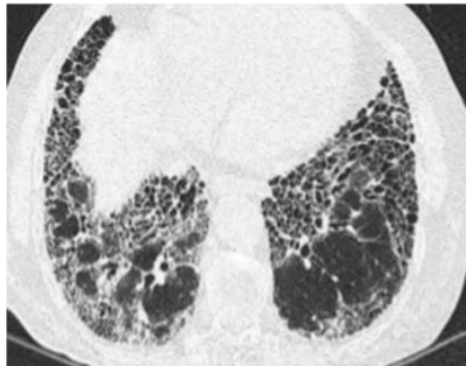
IPF market projected to reach $3.6 billion by 2029[3]

- Nintedanib and Pirfenidone are only approved treatments for IPF
  - Slow the progression of the disease
  - Side effects that limit use
  - Clear opportunity to improve on standard of care

Lead Indication

Normal Lung

IPF Lung



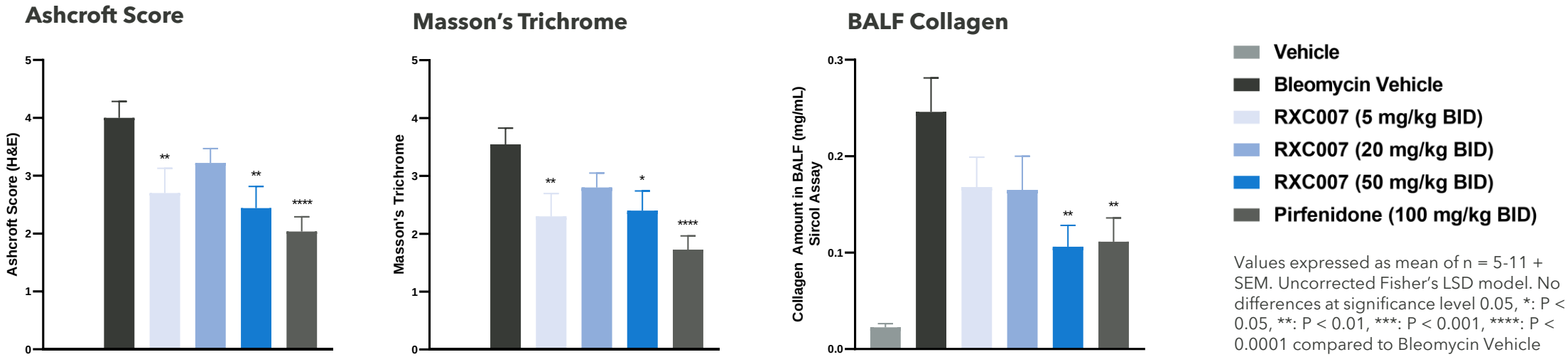
- Idiopathic pulmonary fibrosis (IPF) estimated median survival is just 2 – 5 years from diagnosis [1], resulting in >125,000 annual deaths worldwide [2]
- 170,000+patients[3]

1. Clinical Estimates from Hyun 2015, Ley 2012, Raghu 2006; 2. Globaldata (based on 16 major markets) 3. Patient numbers (diagnosed prevalence) & market size forecast data sourced from Global Data (based on 7-8 major markets/2029 estimates)

RXC007

Strong Preclinical Data Supports Clinical Development Plan

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



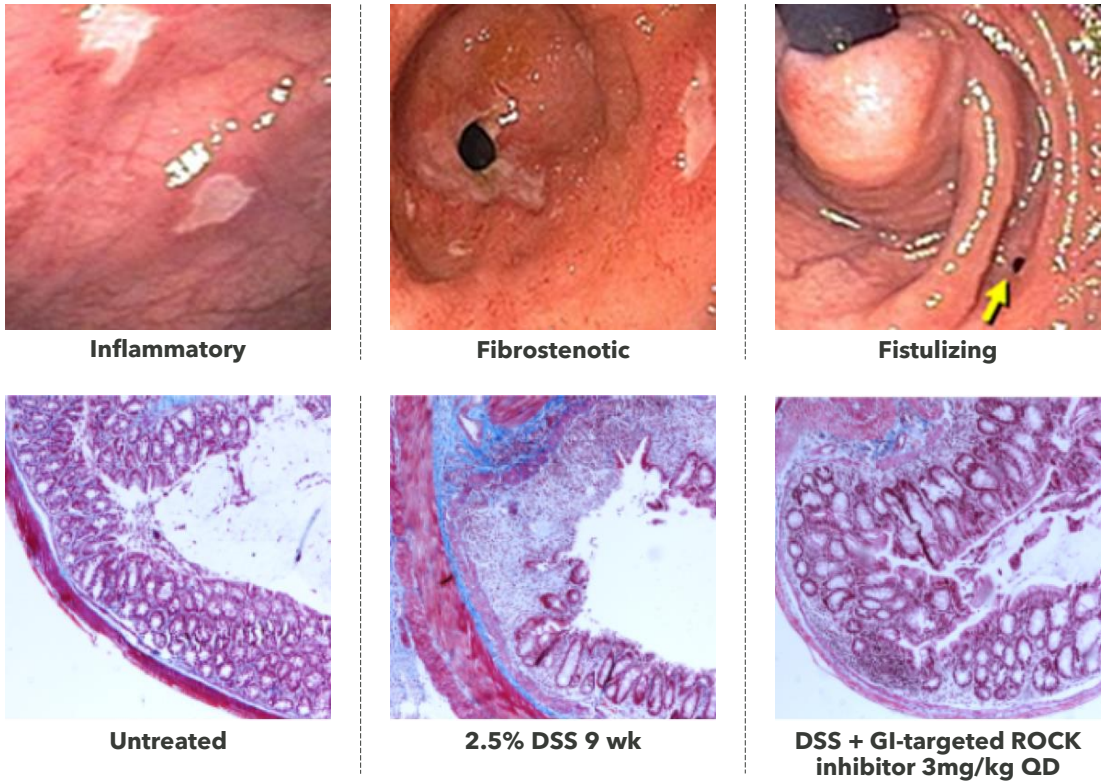
Values expressed as mean of n = 5-11 + SEM. Uncorrected Fisher's LSD model. No differences at significance level 0.05, *: P < 0.05, **: P < 0.01, ***: P < 0.001, ****: P < 0.0001 compared to Bleomycin Vehicle

- **Preclinical data support IPF lead indication**
  - RXC007 reduces fibrosis and collagen deposition in the lung and in bronchoalveolar lavage fluid (BALF) in murine bleomycin-induced IPF model with therapeutic dosing
- **Currently in preclinical development**, expected to enter Phase 1 H1 2021 with Phase 2 planned for 2022

Research

GI-targeted ROCK Inhibitor Targeting Drug Candidate in 2021

- **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 H2 2021**



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.

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

Redx - Focused on Execution and Delivery

		2021*	2022*
Development	Porcupine Inhibitor (RXC004)	✓ **H1** Ph1 start – IO combo safety **H2** Ph1 monotherapy safety completion **H2** Ph2 monotherapy (MSS mCRC, biliary, pancreatic cancer) **H2** Ph2 start – IO combo MSS mCRC	Ph2 data mono MSS mCRC Ph2 data mono biliary cancer Ph2 interim data mono pancreatic cancer and combo MSS mCRC
	ROCK2 Selective Inhibitor (RXC007)	✓ **H1** Phase 1 Start	**H1** Phase 1 safety data readout **H2** Phase 2 start
Research	GI-targeted ROCK Inhibitor	**H2** Select development candidate	Phase 1 start
	Research Targets	Progress wholly-owned & Jazz research collaborations	Progress wholly-owned & Jazz research collaborations
Partnered	Porcupine Inhibitor (RXC006)	AstraZeneca responsible for development	AstraZeneca responsible for development
	Pan-RAF Inhibitor	Progress collaboration with Jazz	Jazz responsible for clinical development

* Calendar year

Financed to Deliver Multiple Value Inflection Points with Top Tier Specialist Investors

Strong financial position

£39.9 million cash

as at 31st March 2021 (unaudited)

Cash runway until end 2022

~$1 billion in potential milestone revenues

AstraZeneca Jazz Pharmaceuticals

Supported by leading life science investors

Redmile Group

SOFINNOVA PARTNERS

POLAR CAPITAL

AIM (UK) listed. Ticker: REDX

Total shares in issue: 274,782,205
Fully diluted: 418,824,861*

*assuming full conversion of loan notes and exercise of employee share options. Updated 8 July 2021

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