



Redx Pharma

(AIM:REDX)

Compelling opportunity to invest in taking targeted oncology and fibrosis medicines into clinic

**Redx BioTech
Showcase
Presentation**

January 2019

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Executive Management Team

Ambitious new management team in place with strong scientific and commercial experience



Lisa Anson, Chief Executive Officer

20 year career at AstraZeneca plc. Significant leadership experience including President of AstraZeneca UK. Ex-President of the Association of British Pharmaceutical Industry

June
2018



Dr James Mead, Chief Financial Officer

Finance leadership roles, including CFO and Investor Relations
16 years at AstraZeneca
PhD in molecular biology

Feb
2019



Dr Andrew Saunders, Chief Medical Officer

Oncology focus since 1992 both clinical practice and pharmaceutical/ biotech industry Including senior roles at Eli-Lilly and Roche (Rituximab)

Jan
2018



Dr Richard Armer, Chief Scientific Officer

Significant experience in both small biotechnology and large pharmaceutical companies through roles in Pfizer, Organon, Ardana, Oxagen & Lectus Therapeutics
Successful in generating and progressing multiple clinical candidates

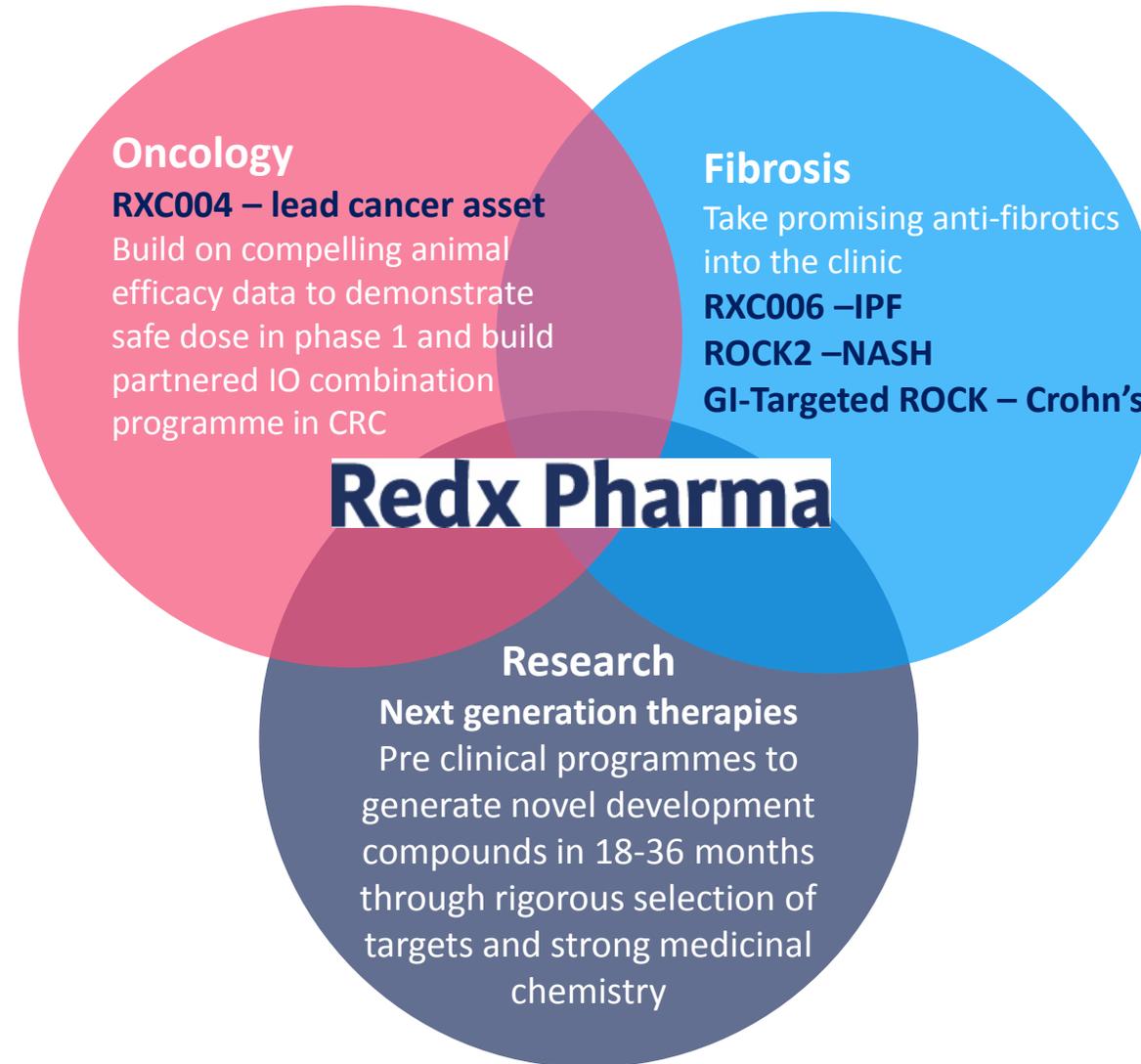
2014

Introduction

- Biotech focused on developing novel medicines in oncology and fibrosis
 - Strategy to build shareholder value by advancing selected assets into clinical development
 - Proven scientific capability – retained in house team of 50
 - 2017 sale of pre clinical BTK oncology asset for \$40m, LOXO-305 (RXC005) now moving to clinic
- Compelling opportunity to develop into clinic in commercially attractive areas
 - RXC004 unlocks the potential promise of the Wnt pathway in oncology
 - Promising pre-clinical efficacy evidence in three fibrosis programmes supports move to clinic
 - Leverage proven ability to design molecules against a validated target

A clear, focused strategy delivered by an ambitious new management team

Redx's Strategy – Three Interrelated Investment Pillars



IO = Immuno-oncology, CRC = Colorectal Cancer, IPF = Idiopathic Pulmonary Fibrosis, NASH = Non-alcoholic Steatohepatitis

Redx Pipeline

Highly selected targeted products for oncology and fibrosis

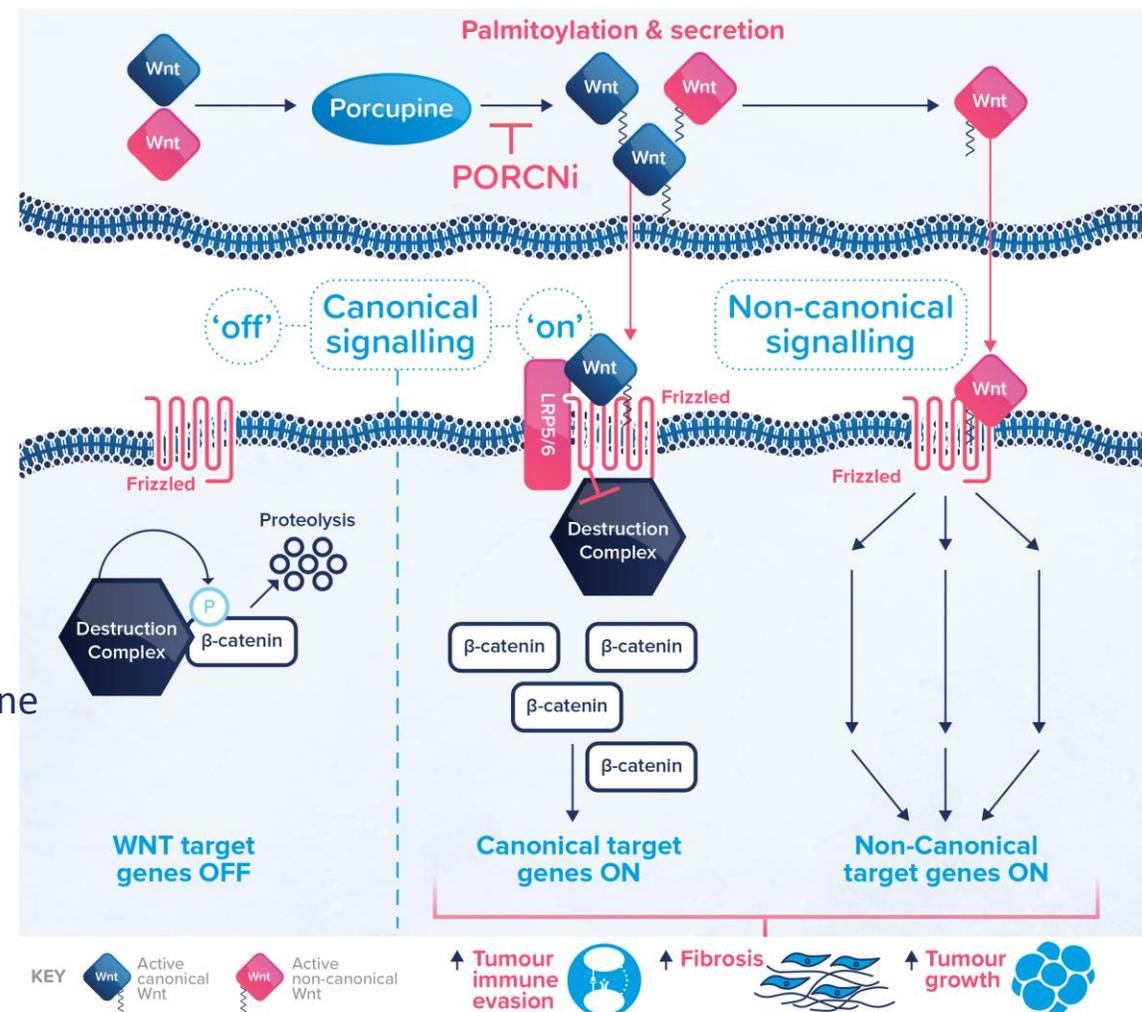
	Target/ Product	Indication	Research	Pre-clinical (CTA/IND enabling)	Clinical (Phase 1)	Milestone Date
RXC004	Porcupine	Combination with PD1 / PD-(L)1 in solid tumour (colorectal cancer)				Phase 1 safety completion – H1 20
Anti-fibrotics	Porcupine (RXC006)	Idiopathic pulmonary fibrosis (IPF)				Pre clinical 2019 Clinic ready 2020
	ROCK2 selective	Non-alcoholic Steatohepatitis (NASH)				Pre clinical development candidate H1 19 Clinic ready H2 20
	GI-targeted ROCK	Crohn's Related Fibrosis				Pre clinical development candidate H1 19 Clinic ready H2 20
Research	Validated targets (inc. SHP2 & AZ collaboration)	Oncology and Fibrosis				Lead Optimisation 2019 - 2020; Development candidates <36 months

RXC004

Potentially a best-in-class drug against a validated cancer target

- RXC004 – potent oral porcupine enzyme inhibitor (PORCNI)
 - Significant tumour growth inhibition in pre-clinical models
 - US composition of matter patent granted in 2018
- PORCN is a validated drug target
 - PORCN regulates secretion of Wnt ligands
 - Wnt pathway is key in cell proliferation
 - Wnt pathway increasingly implicated in immune tumour micro-environment
- RXC004 has dual tumour targeting and Immuno-oncology combination potential
 - Novartis PORCNI in clinical phase 1/2a in combination with an immune checkpoint inhibitor (ICI), suggesting proof of principle
 - Two others in phase 1 clinical development (A*Star and Curegenix)
- Phase 1 clinical trial to re-initiate in 1H2019 at a lower dose based on learnings about exposure and half life in first patient

The Wnt signalling pathway



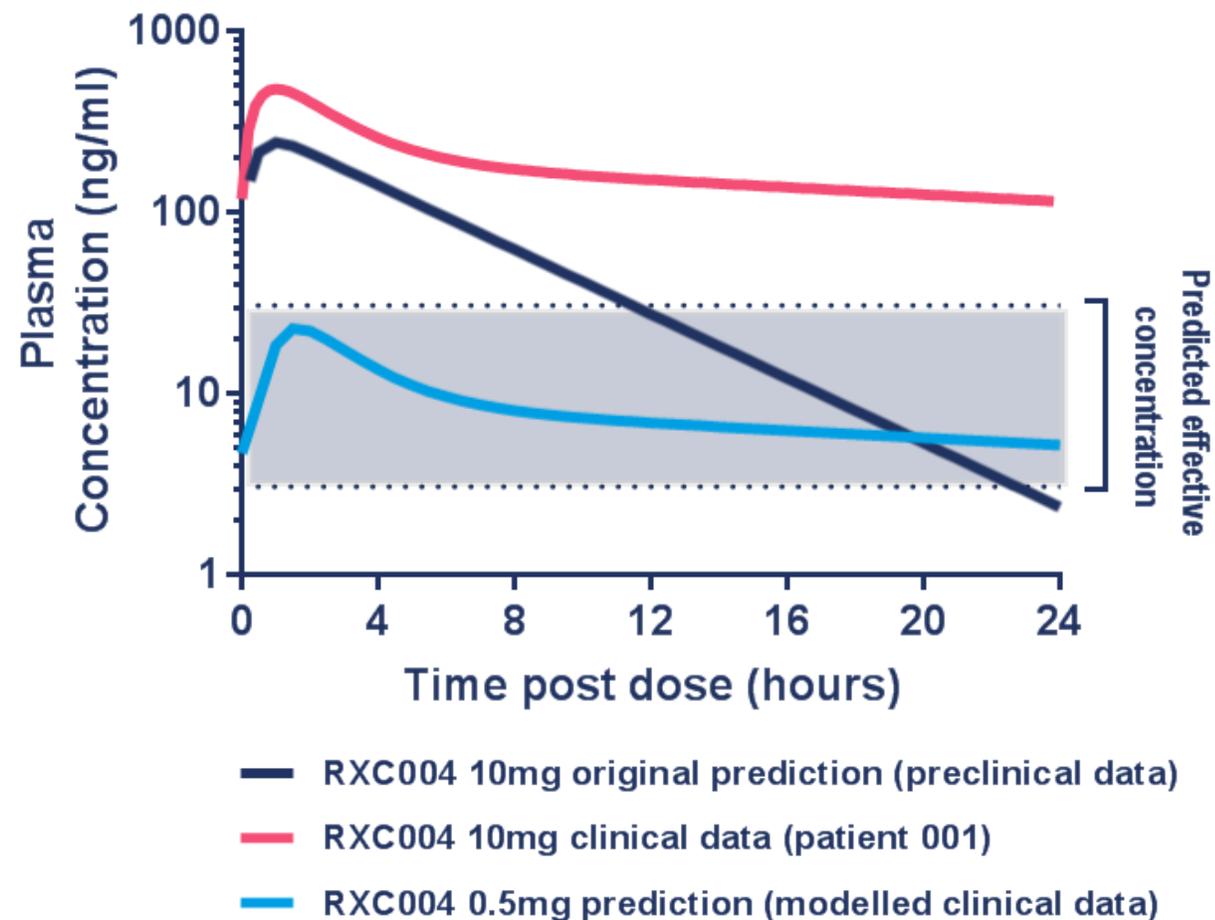
RXC004

Phase 1 Clinical trial will re-initiate in 1H2019

- Trial to be re-initiated following observed on-target side effects* at 10mg dose
 - Longer human half-life than predicted led to higher and longer exposure
 - Excellent bioavailability
 - Target engagement confirmed
 - Only expected on-target side effects noted
- Clinical pharmacokinetic data indicates a lower dose of 0.5-3mg a day should achieve efficacious exposure levels with greatly reduced risk of on-target side effects reformulation of lower dose strengths ongoing
- Revised protocol approved by MHRA in November 2018
- Plan to dose next patient in 1H2019, starting at 0.5mg

*on target side effects : diarrhoea, loss of taste, bone fragility

RXC004 Plasma Concentration

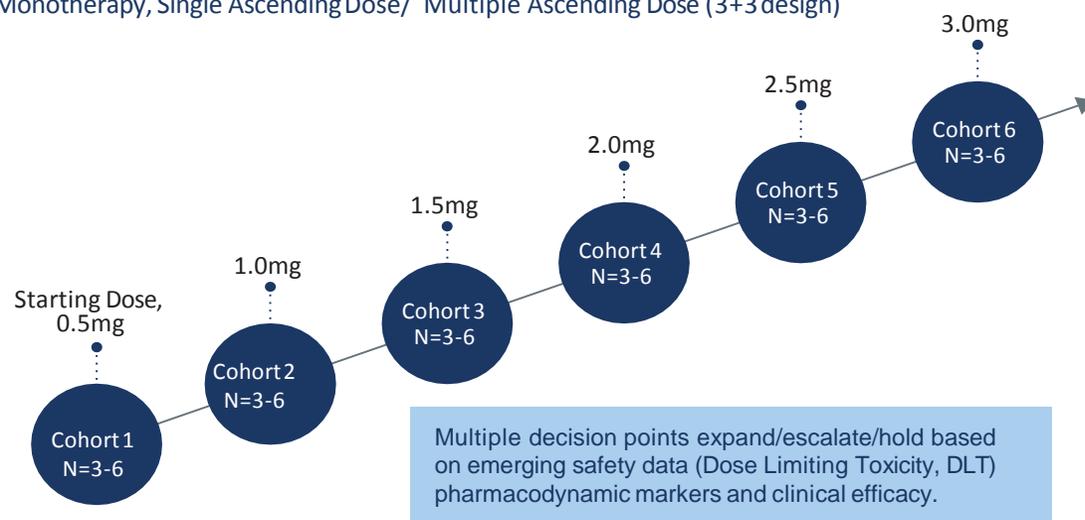


RXC004

Revised clinical trial protocol now approved by MHRA

Phase 1 - Dose Escalation

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



Phase 1 Part a	Dose escalation cohorts: To assess the safety and tolerability of RXC004 in an all-comers cohorts of advanced cancer patients. 3-5 UK sites; 12-18 months.
Phase 1 Part b	Dose expansion cohorts: To assess the efficacy of RXC004 monotherapy in biomarker selected patients (eg CRC, gastric and pancreatic cancer patient cohorts) 3-5 UK sites.
Phase 2a	To assess the safety, tolerability and efficacy of RXC004 in combination with standard of care therapies, including ICIs, in e.g. CRC.

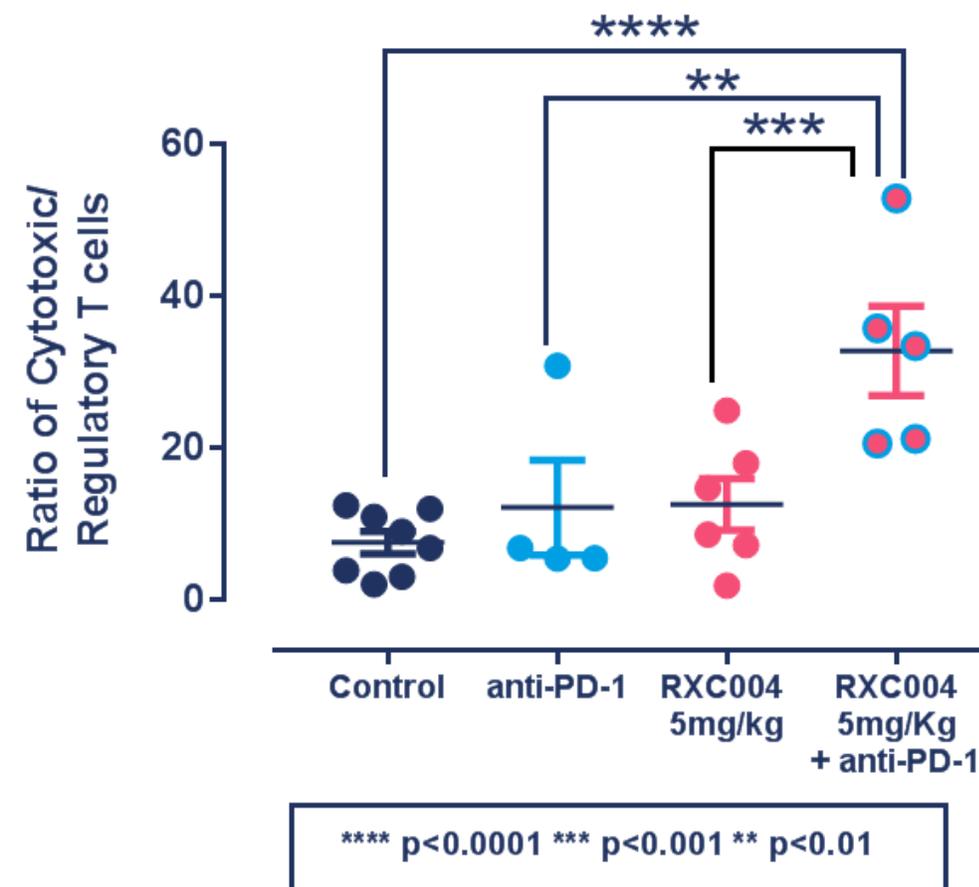
- Target starting dose 0.5mg once daily
 - 18-36 patients planned in Phase 1 dose escalation, 2-3 months per dose cohort
 - Safety, tolerability, PK and PD - Axin-2 in skin biopsy, IO markers in tumour and blood
- Lead PI - Dr Natalie Cook, Christie Hospital, Manchester, UK
 - 4 Further Centres – The Marsden, Guys (London), Oxford and Newcastle
- Once minimum biologically active dose (MBAD) achieved expansion arms can be initiated
 - monotherapy or in combination with an immune checkpoint inhibitor (anti-PD1)
- Phase 2a encompassed in trial protocol
 - allows move to a combination therapy subject to protocol amendment required

RXC004 Development Strategy

Early RXC004 evidence suggests strategy to exploit potential in immuno-oncology

- Approval of Immune Checkpoint Inhibitors* (ICIs) has revolutionised the treatment of cancer
- Colorectal Cancer (CRC) is one potential development target
- mCRC has large incidence (c.110,000 globally)** with high mortality
 - Significant commercial opportunity
- RXC004 in combination with ICIs could:
 - Increase response rate in MSI (Microsatellite Instability) segment (17%*** where 60% are non-responders and/or
 - Render some non-MSI segments (approx. 83%*** susceptible to ICI treatment
- Evidence of RXC004 safety combined with immune cell changes will command interest
 - Immuno-oncology Advisor – Prof. Aurélien Marabelle, Gustave Roussy, Paris

RXC004 in combination with anti-PD1 results in a more tumour fighting microenvironment



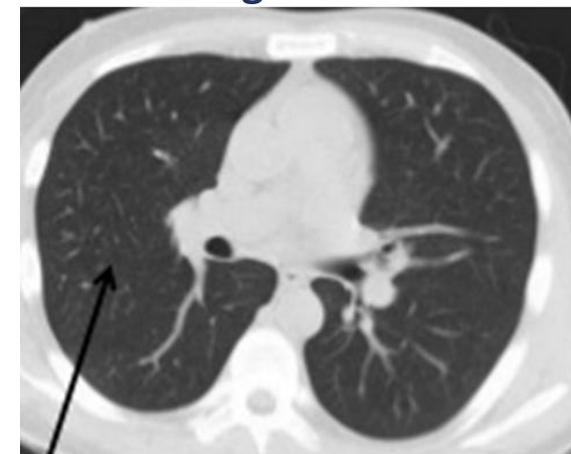
*PD1, PD-(L)1, ** Calculated from GlobalData PharmaPoint Colorectal Cancer 2015-2025), *** Ashktorab H et al Oncotarget 2016

Anti-Fibrotics: RXC006

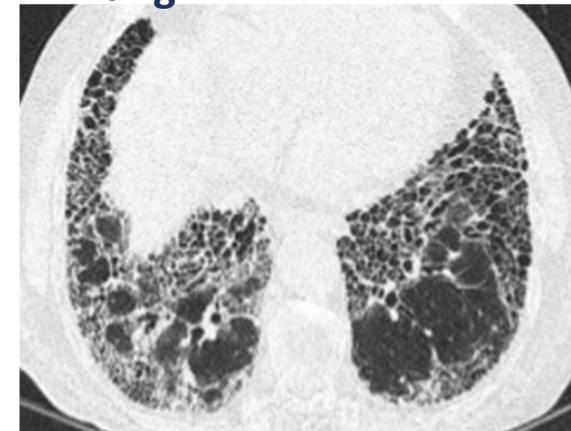
RXC006 is a PORCNI in development for Idiopathic Pulmonary Fibrosis (IPF)

- IPF is a fatal lung disease with no effective therapy
 - Median survival 2-5 years*, resulting in 25,000** annual deaths in US
 - Only Esbriet® (Roche) and Ofev® (BI) approved for mild to moderate IPF
- Scientific evidence suggests porcupine inhibition may be effective in patients with advanced fibrosis
 - Both canonical and non-canonical pathways involved in fibrosis – suggesting that universal suppression of Wnt will be effective
 - Wnt pathway involvement increases with the severity of disease
- PORCNI show robust pre clinical efficacy in murine kidney, liver and lung fibrosis models
 - RXC006 nominated as development candidate (November 2018)
 - Manufacturing and preclinical development studies during 2019 with first in man during 2020
 - Composition of matter patent (US allowance of grant), distinct from RXC004

Normal lung



IPF lung

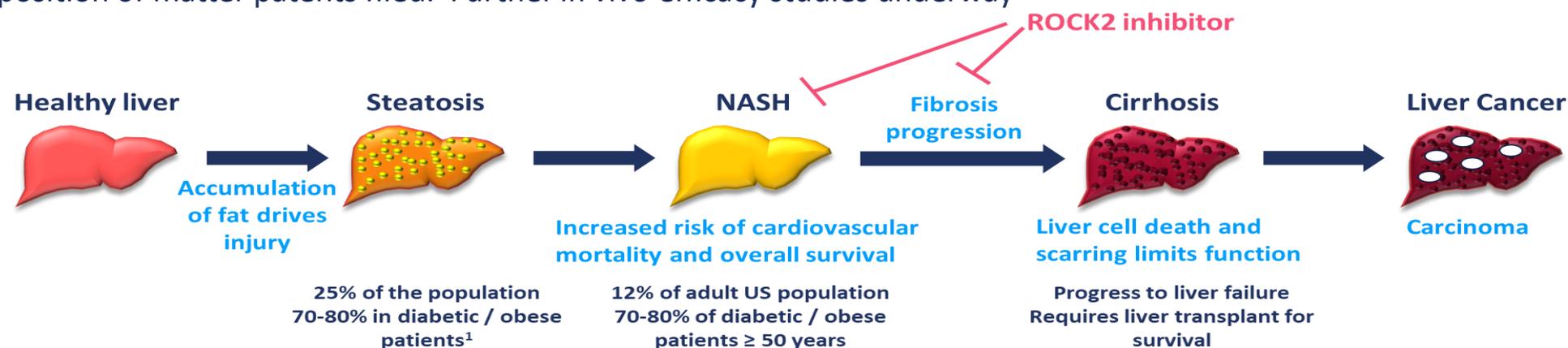


* Clinical Estimates from Hyun 2015, Ley 2012, Raghu 2006. ; ** GlobalData Opportunity Analyser IPF 2015-2025

Anti-Fibrotics: ROCK2

ROCK2 selective inhibition is an exciting approach – advancing to development candidate mid 2019

- NASH expected to become leading cause of liver cirrhosis
 - No currently approved therapies for NASH
 - Development space crowded (estimated *total* market \$25.3bn* by 2026)
 - Few targeting underlying fibrosis which is increasingly important for treatment of late stage disease - potential in NASH as anti-fibrotic treatment for late stage disease– estimated 10.5m* patients
- ROCK2 inhibition is a promising approach to a validated target
 - Decreases human hepatic stellate cell activation *in vitro* and demonstrates efficacy in acute kidney injury
- Redx series shows good pre-clinical profile with improved activity and selectivity vs. key competitor, KD025**
 - Composition of matter patents filed. Further *in vivo* efficacy studies underway

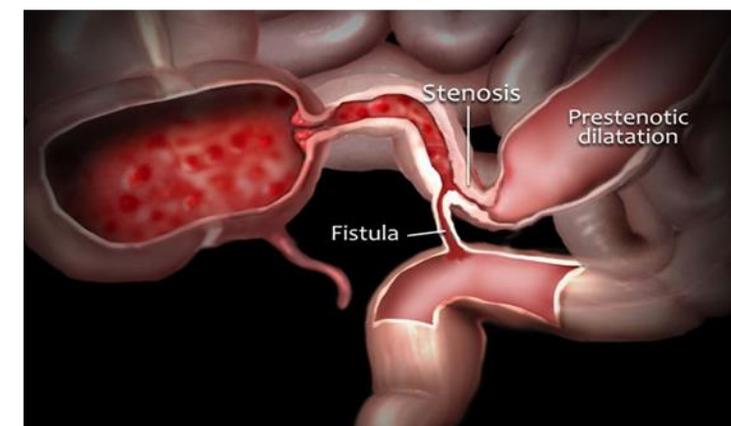


* Calculated from GlobalData Opportunity Analyser Report, Hagstrom et al (2017), *Jnl of Hepatology* based on patients at F3/F4 stage, "GlobalData: NASH – Current and Future Trends, October 2018", ** Kadmon's ROCK inhibitor in phase 2

Anti-Fibrotics: GI-targeted ROCK

GI-targeted ROCK inhibitor programme is a unique proposition in Crohn's disease

- 1.5m* people globally suffer from Crohn's disease – 50%** will develop strictures or complications
 - No treatment available or in development for underlying fibrosis
- ROCK (Rho-associated Kinase) is a biologically validated target involved in fibroblast activation
- REDX series is a potent, small molecule ROCK 1/2 inhibitor with potential to be first-in-class
 - Minimal absorption profile makes it highly selectively active in gut without risking systemic exposure
 - Blocks pro-fibrotic signals and has shown efficacy in-vivo in models and ex-vivo using tissue from Crohn's patients
 - Composition of matter patents granted
- Next Milestone is development candidate nomination H1 2019



* GlobalData: Crohn's Disease 2016, ** Chan et al, 2018

Redx Key Near-term Milestones and Value Drivers to 2020

		2018	2019	2020
Oncology	RXC004	<ul style="list-style-type: none"> ✓ 1Q First patient treated in Phase 1 study ✓ 1H Read-out on pre clinical PoC studies in fibrosis ✓ 2H MHRA approved revised protocol 	<ul style="list-style-type: none"> 1H Phase 1 re-start 1H ASCO Wnt pathway updates 2H Phase 1 initial cohort safety data 	<ul style="list-style-type: none"> 1H Phase 1 safety data readout - monotherapy - combination
Anti-Fibrotics	PORCN/ RXC006	<ul style="list-style-type: none"> ✓ Patents filed, data presented ✓ Development candidate selected 	<ul style="list-style-type: none"> 1H Manufacturing 2H GLP toxicity 	<ul style="list-style-type: none"> 1H Clinic ready (IPF)
	ROCK2 selective	<ul style="list-style-type: none"> ✓ Patents filed, data presented ✓ Series assessment ongoing 	<ul style="list-style-type: none"> 1H In vivo data completed 1H Development candidate selected for NASH 	<ul style="list-style-type: none"> 2H Clinic ready
	GI targeted ROCK	<ul style="list-style-type: none"> ✓ Patents filed ✓ Series assessment ongoing 	<ul style="list-style-type: none"> 1H Development candidate selected for Crohn's related fibrosis 	<ul style="list-style-type: none"> 2H Clinic ready

Why Redx? We are Building a Leading Biotech

- **Value generation** through advancing to clinical proof of concept for novel medicines:
 - Key value inflection point
 - Focused on rigorous selection of validated cancer and fibrosis targets
- **New management team** and strengthened Board have restructured business
- **Focused strategy** to drive existing pipeline into clinic:
 - Lead oncology asset opportunity to unlock Wnt pathway potential – Phase I completed in Q2 2020
 - Fibrosis treatments target significant commercial markets – ready to enter clinic in mid 2020
- **Leverage medicinal chemistry expertise** to supplement pipeline in house/externally
 - Excellence in drug design validated by recent sale to Loxo of preclinical oncology asset for \$40M cash
- **Strategically forge partnerships** to enable development, unlocking additional shareholder value