



# Redx Pharma

Corporate  
Presentation  
November 2017

# Forward-looking statements

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# The investment case

- Focused on novel drugs to significant commercial targets in cancer and fibrosis
- New, strengthened board and management team providing enhanced oversight and relevant industry expertise & continuity
- Strong research base has yielded a refocused development pipeline of two development programmes and five research programmes
  - Lead cancer asset, Phase 1 trial to start 1Q18; 1a results estimated 2H18
    - Best in class potential
    - Addressable market estimate for melanoma, gastric, biliary and pancreatic cancers >500,000 new cases p.a.<sup>1</sup>
  - Lead fibrosis candidate could be first drug specifically targeting Inflammatory Bowel Disease (IBD) related fibrosis
    - IBD addressable market estimated to be three million patients<sup>2</sup>
- Opening balance sheet has £13.6 million of cash, with no liabilities nor loan facilities, coupled with a reduced cost base, provides a cash runway through to early 2019<sup>3</sup>

<sup>1</sup> GlobalData 2016

<sup>2</sup> GlobalData: Crohn's Disease 2016, Ulcerative colitis 2015

<sup>3</sup> Independent working capital report prepared by Crowe Clark Whitehill

# Corporate vision and strategy

***Building significant shareholder value through advancing a differentiated pipeline of first or best in class anti-cancer and anti-fibrosis drugs to clinical proof of concept***

## **Focused commercial and corporate strategy**

- Commercially attractive areas of significant unmet medical need with no or limited competition with suboptimal product profile
- Scientifically validated targets
- Fit with Redx capability to develop differentiable 'First' or 'Best' in class candidates
- Progress drug candidates to clinical proof of concept – as significant value inflection point in developing medicines

## **Focused science strategy**

- **Cancer**
  - Targeted therapies (biomarker driven)
  - Disrupting pathways of cancer resistance
- **Fibrosis**
  - Disrupting pathways that slow or reverse fibrosis (disease modifying)
- **Leverage Redx medicinal chemistry expertise**

## Strengthened Board

### Iain Ross Executive Chairman

*Chairman, CEO and Director roles in pharma and small biotech (Sandoz, Hoffman La Roche, Celltech, e-Therapeutics, Novogen, and Anantara Lifesciences)*

### Peter Presland Non-Executive Director Chairman of Audit, Risk & Disclosure Committee

*Arthur Andersen & Co and BBDO Ltd CFO and CEO of C.E Heath plc  
Chairman of Rebus Group plc  
Director of East Kent Hospitals University Foundation NHS Trust*

### Bernd Kirschbaum Non-Executive Director Chair of Research Committee Chair of Remuneration Committee

*Board Member: Merck Serono  
Senior R&D roles: Sanofi-Aventis, Aventis, and HMR  
Chairman: Protagen Diagnostic and Omeicos Therapeutics*

### Dominic Jackson Chief Financial Officer

*Experienced CFO in numerous turnaround and restructuring situations (PwC, Deutsche Bank Frankfurt, Merrill Lynch, Dubai International Capital, and Kaupthing Bank)*

### CEO To be appointed

## Industry Experienced Management

### Nicholas Adams Chief Business Officer

*Clinical Development: Ciba-Geigy (now Novartis), Eisai, and Cephalon Business Development: Antisoma and Clavis Pharma*

### Dr. Richard Armer Chief Scientific Officer

*Senior Scientific & Management Roles in Pfizer, Organon, Ardana, Oxagen, and Lectus*

### Dr. Matilda Bingham Head of Research & Operations


*Senior Scientific & Management roles in Merck Sharpe & Dohme, Schering Plough, and Organon*

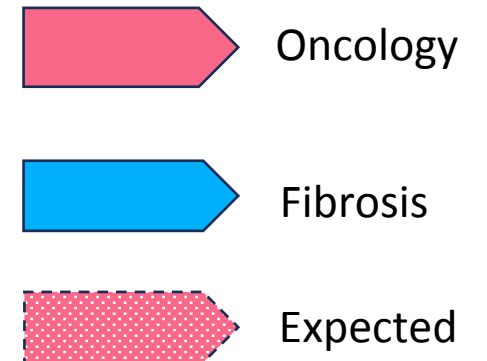
### Dominic Jackson Chief Financial Officer

### Dr. Glen Clack Clinical development Advisor

### CMO Full time CMO to be appointed

# A pipeline focused on cancer & fibrosis

Target/ Product	Indications	Lead Generation	Lead Optimisation	CTA/ IND enabling	Phase I	Partner
<b>Porcupine / RXC004</b>	Single agent: Gastric, Biliary & Pancreatic					
	Combination with PD1: Melanoma					
<b>Pan-ROCK</b>	IBD-related fibrosis					
<b>Porcupine</b>	Idiopathic pulmonary fibrosis					
<b>Pan RAF</b>	Colorectal cancer					
<b>AZ Collaboration</b>	Not disclosed					AstraZeneca 
<b>ROCK-2 Selective</b>	Diabetic nephropathy					
<b>SHP2</b>	Not disclosed					



# Porcupine inhibitor (RXC004) – Developing a best in class cancer drug

- RXC004 is a potent selective, oral once daily small molecule inhibitor of the porcupine enzyme
  - Central to the WNT pathway, a recognised oncogenic signalling pathway
  - Emerging best in class profile
    - Only 2 other porcupine inhibitors known in development (the most advanced is WNT974 (Novartis)) in phase 1/2a for colorectal cancer and in a combination study with checkpoint inhibitor (immuno-oncology)
    - Superior preclinical efficacy and pharmacokinetics in head to head studies with WNT974
  - Composition of Matter patent filed (2014)
- RXC004 - lead cancer programme expected to enter clinic in 1Q18 (MHRA approved)
  - Funded Phase 1a dose escalation trial in cancer “all-comers” (n=21); results expected 2H18 – primary objective safety. Lead centre – Christie Hospital (Manchester)
    - Subsequent phase 2a offers potential opportunity to see early signals of efficacy
- Dual strategy for further clinical development
  - As combination therapy with checkpoint inhibitors to enhance efficacy in cancer immunotherapy
  - As biomarker guided therapy in certain hard-to-treat cancers

# Porcupine inhibitor (RXC004) – Targeted therapy for challenging cancers

- Patients with gastric, biliary and pancreatic cancers currently have a very poor prognosis due to the lack of available effective therapies
  - No targeted therapy currently approved for biliary cancer
  - Gastroesophageal cancer market is forecast to grow to \$4.4 billion by 2024<sup>1</sup>
  - Pancreatic cancer market is estimated to be \$1.63 billion in 2017<sup>2</sup>
- An increased understanding of the Wnt signalling pathway has highlighted its therapeutic promise in these cancers
- Precision medicine approach targeting patients with RNF43 mutation
  - RNF43 is a marker of Wnt pathway activation in tumour cells and indicates sensitivity to porcupine inhibition
  - Improves likelihood of identifying the patients who will benefit
  - A non-invasive liquid biopsy has been developed to detect RNF43 in circulating tumour DNA
  - Published at ESMO conference (Madrid, September 2017)

<sup>1</sup>GlobalData: Pharmapoint: Gastric and gastroesophageal junction adenocarcinoma – Global drug forecast and market analysis to 2024

<sup>2</sup>GlobalData: Pancreatic cancer – Opportunity analysis and forecasts to 2017



# Porcupine inhibitor (RXC004) – Enhancing the efficacy of cancer immunotherapy

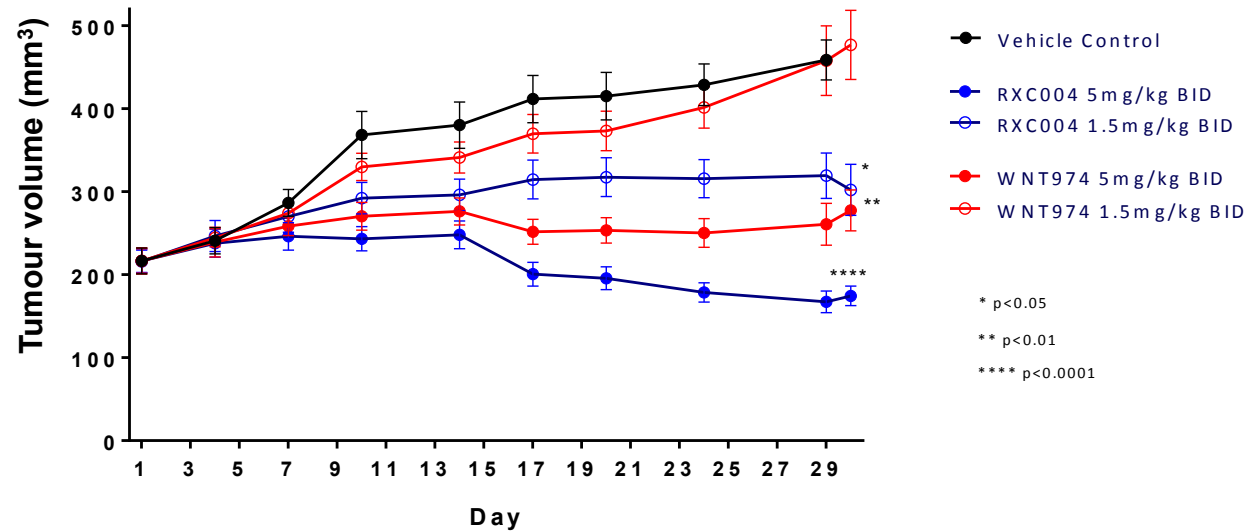
- Checkpoint inhibitors, such as anti-PD1 and anti-PDL1 antibodies, have revolutionised cancer immunotherapy
  - *But* they don't work in a significant portion of patients - the tumour-killing immune cells are not present at the 'cold' tumour site
    - Non-small cell lung cancer (10-25% responders<sup>1</sup>), Melanoma (up to 45% responders<sup>1</sup>)
  - Evidence is emerging that the Wnt signalling pathway is a relevant target in immuno-oncology
  - Inhibition of pathway makes the tumours 'hot', attracting immune cells
- Plan to test the potentially synergistic combination of a PD-1 inhibitor with RXC004
  - Preclinical data promising
  - Initiate when safety data from the Phase 1 study in hand end 2018
  - Commercial partnering interest at this stage
- Potentially a multi-billion \$ opportunity: Opdivo<sup>®</sup> sales (2016) - \$4.7 billion; Keytruda<sup>®</sup> sales (2016) - \$1.4 billion. Projected 2023 - \$12.5 billion and \$10.6 billion, respectively<sup>2</sup>

<sup>1</sup> Nature Reviews Cancer, 2017, Vol 17, 209.

<sup>2</sup>GlobalData: PharmaFocus: Visual Analysis of Immuno-Oncology Development and Opportunities (Aug 17)

# RXC004 is efficacious in animal tumour models

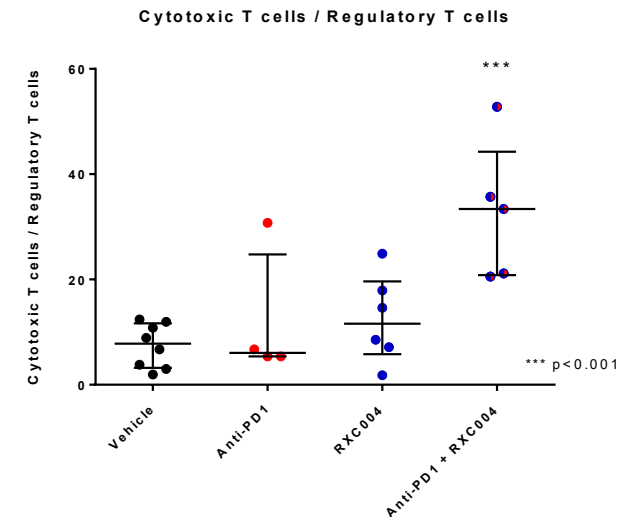
## Human pancreatic cancer model: Capan-2 Tumour Growth



RXC004 synergises with an anti-PD1 antibody to increase the ratio of ‘tumour killing’ immune cells compared with immune suppressing cells

RXC004 showed better efficacy than its closest competitor WNT974

## Mouse colon cancer model in combination with anti-PD1 antibody

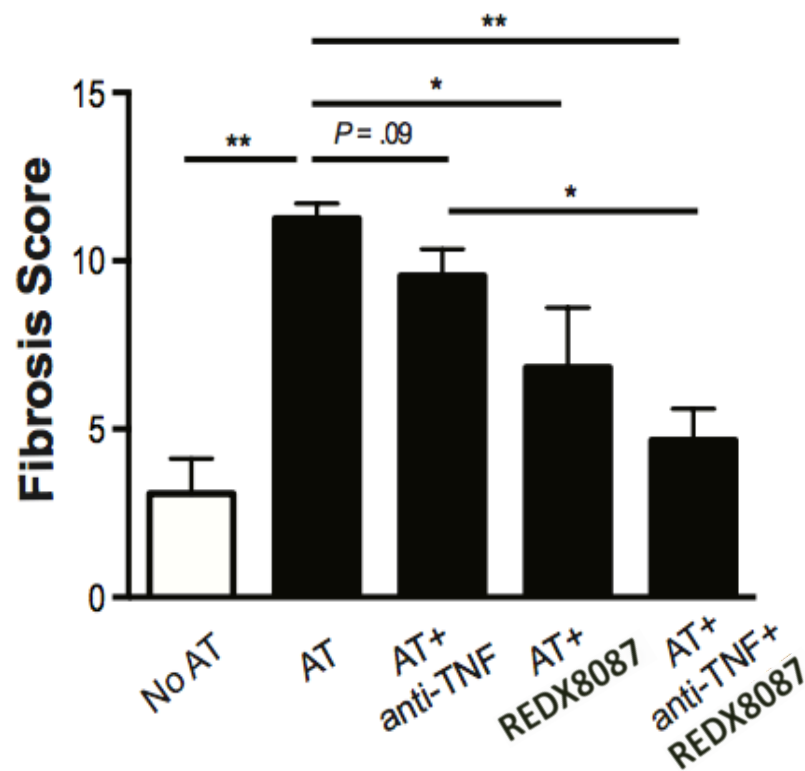


# Pan-ROCK inhibitor – Developing the first drug specifically for IBD-related fibrosis

- In the U.S. 30-40% patients have stricture formation and obstruction due to bowel wall fibrosis within ten years of diagnosis of IBD. Current therapy is bowel surgery
- Rho kinase (ROCK) enzyme inhibitor is implicated at various points in pathways leading to fibrosis
  - However, systemic ROCK 1&2 inhibition is known to induce hypotension
- Redx has identified a targeted, locally-acting small molecule ROCK inhibitor
  - Drug effectively inhibits ROCK at site of action in gastro-intestinal tract
    - Minimizes systemic exposure though rapid enzyme-mediated metabolism in blood plasma
  - Preclinical studies including those in industry-standard animal models of disease (prophylaxis and therapy) are compelling
  - Potentially disease modifying
- **First in class clinical candidate to be selected H1 2018; first in man studies planned for H2 2019**
  - Composition of matter patent filed (Granted in US and pending in other jurisdictions)
  - No competitors in development for IBD fibrosis
- IBD addressable market estimated to be three million patients<sup>1</sup>

<sup>1</sup>GlobalData: Crohn's Disease 2016, Ulcerative colitis 2015

## The central role of ROCK in fibrosis



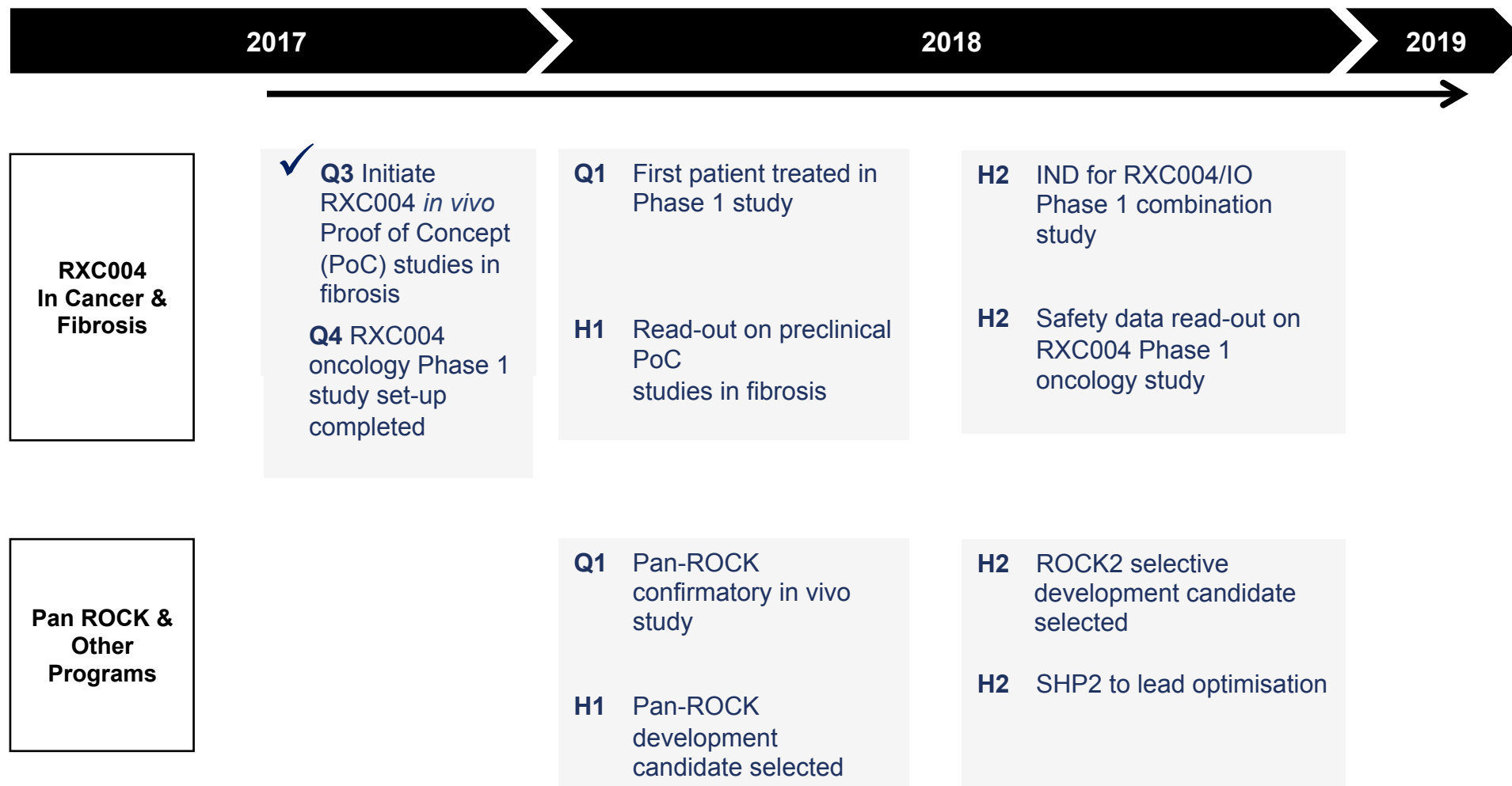
\* P < 0.05, \*\* P < 0.01

- CD4+CD25-CD62L+ naïve T-cells were injected i.p. in CB-17 SCID mice on day 0 (adoptive transfer, AT).
- Mice developed symptoms of colitis at week 2 and beyond, at which point therapy was initiated.
- Mice were treated with:
  - 25 mg/kg anti-TNF i.p. SID or with a combination of anti-TNF i.p. and 3 mg/kg REDX8087 via oral gavage SID (n=10 in each group).
  - Placebo-treated mice received 25 mg kg<sup>-1</sup>day<sup>-1</sup> IgG1 i.p. and vehicle p.o.2

<sup>1</sup>Reider, Gastroenterology 2017

<sup>2</sup>Holvoet *et al.* Gastroenterology 2017

# Financed key near-term milestones and value drivers



# The investment case

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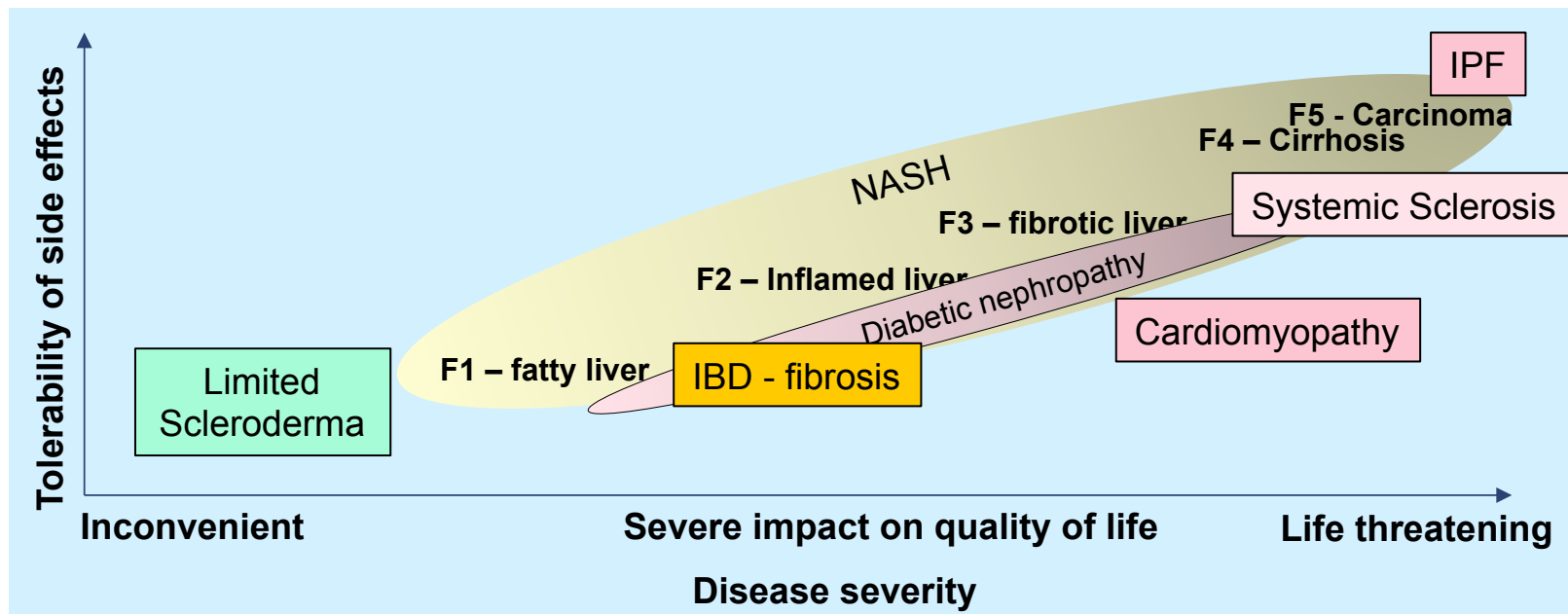
<sup>1</sup> GlobalData 2016

<sup>2</sup> GlobalData: Crohn's Disease 2016, Ulcerative colitis 2015

<sup>3</sup> Independent working capital report prepared by Crowe Clark Whitehill

# Appendix

# Key fibrotic conditions with high unmet need



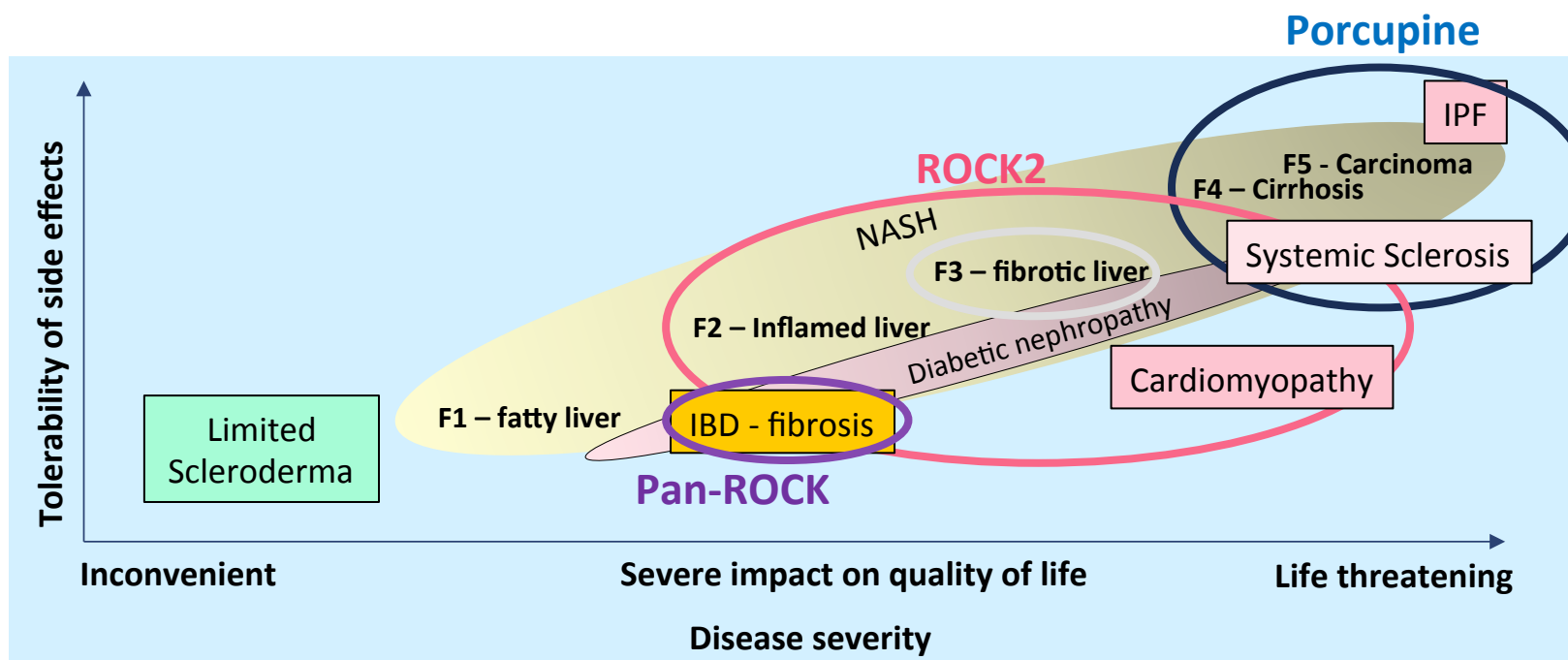
Disease	Patient Prevalence (in millions)	Disease burden & healthcare costs in USA (\$bn)
Cardiomyopathy	28	555
NASH	64	245
Type II diabetes	29	100
Inflammatory bowel disease	2	31
Idiopathic pulmonary fibrosis	0.1	3
Systemic sclerosis	0.08	1.5

## Source for statistics

<http://www.healthline.com/health/diabetes/facts-statistics-infographic#5>  
<http://www.mdedge.com/familypracticenews/article/114873/gastroenterology/nonalcoholic-fatty-liver-disease-estimated-cost>  
[http://www.ajmc.com/journals/supplement/2016/importance\\_of\\_selecting\\_appropriate\\_therapy\\_inflammatory\\_bowel\\_disease\\_managed\\_care\\_environment/importance\\_of\\_selecting\\_appropriate\\_therapy\\_inflammatory\\_bowel\\_disease\\_managed\\_care\\_environment\\_report\\_economic\\_implications\\_ibd](http://www.ajmc.com/journals/supplement/2016/importance_of_selecting_appropriate_therapy_inflammatory_bowel_disease_managed_care_environment/importance_of_selecting_appropriate_therapy_inflammatory_bowel_disease_managed_care_environment_report_economic_implications_ibd)  
[http://www.upi.com/Health\\_News/2017/02/14/Cost-of-heart-disease-in-US-to-surpass-1-trillion-by-2035-report-says/5891487126035/](http://www.upi.com/Health_News/2017/02/14/Cost-of-heart-disease-in-US-to-surpass-1-trillion-by-2035-report-says/5891487126035/)  
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[https://pharmastore.informa.com/wp-content/uploads/2016/10/idiopathicpulmonaryfibrosis\\_12770\\_10-2016.pdf](https://pharmastore.informa.com/wp-content/uploads/2016/10/idiopathicpulmonaryfibrosis_12770_10-2016.pdf)  
<https://ghr.nlm.nih.gov/condition/idiopathic-pulmonary-fibrosis>  
[http://eprints.lse.ac.uk/60809/1/\\_lse.ac.uk\\_storage\\_LIBRARY\\_Secondary\\_libfile\\_shared\\_repository\\_Content\\_Kanavos%2C%20P\\_Socio-economic%20burden\\_Kanavos\\_Socio-economic%20burden\\_2015.pdf](http://eprints.lse.ac.uk/60809/1/_lse.ac.uk_storage_LIBRARY_Secondary_libfile_shared_repository_Content_Kanavos%2C%20P_Socio-economic%20burden_Kanavos_Socio-economic%20burden_2015.pdf)



# Fibrotic diseases targeted by Redx



**Pan-ROCK:**

IBD fibrosis, F3 liver fibrosis

**Porcupine:**

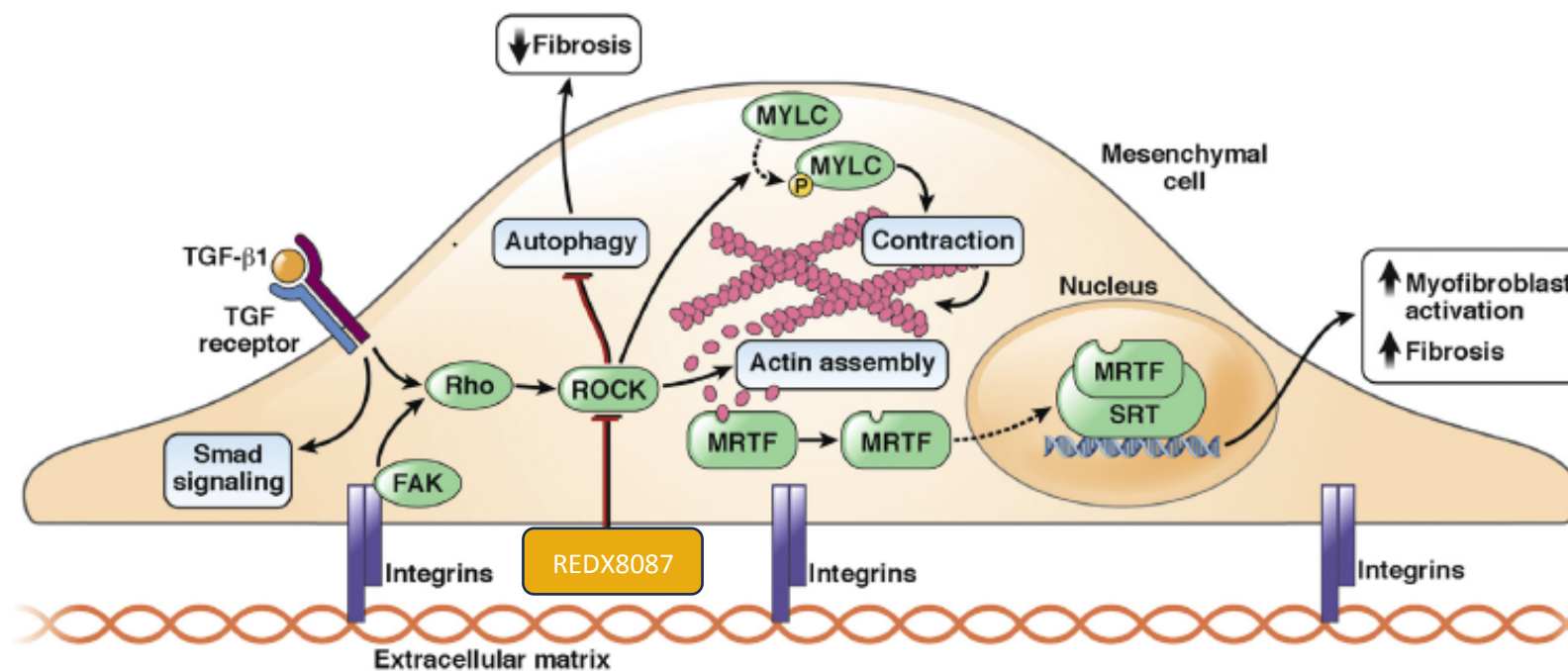
IPF, systemic sclerosis, liver cirrhosis and carcinoma

**ROCK2:**

F2/F3 liver NASH; DN, early onset systemic sclerosis

## The central role of ROCK in fibrosis

- ROCK (Rho-associated Kinase) is involved in fibroblast activation via multiple stimuli such as TGF $\beta$
- ROCK is involved in transition of GI mesenchymal cells to myofibroblasts



Model for inhibition of ROCK in intestinal fibrosis<sup>1</sup>. FAK, focal adhesion kinase; MYLC, myosin light chain; MRTF, myocardin-related transcription factor; SMAD, mothers against decapentaplegic; SRF, serum response factor; TGF, transforming growth factor

<sup>1</sup>Reider, Gastroenterology 2017