Redx
Discovering Targeted Medicines

Corporate Presentation

March 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
Distinctive Approach consistently generates potentially "best-in-class" drug candidates

Our Proven Approach has led to:

- The invention of LOXO-305 – a motivation behind Lilly's acquisition of Loxo Oncology $8 billion – now in Phase 2 clinical trials
- A growing clinical pipeline with one Phase 1 asset and second due to enter clinic in H1
- Preclinical strategic partnerships with AstraZeneca and Jazz Pharmaceuticals

Pipeline is financed to deliver multiple value inflection points in 2021/2022

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

Executive Management Team

Ambitious Experienced Leadership Team

Lisa Anson

Chief Executive Officer

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

AstraZeneca

abpi

Dr Richard Armer

Chief Scientific Officer

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

Pfizer

ORGANON

Dr Jane Robertson

Chief Medical Officer

Extensive experience of advancing oncology programmes in the clinic, through senior roles at AstraZeneca and as a Biotech CMO. Led the development of the Lynparza the first-in-class PARP inhibitor at AstraZeneca

ACHILLES THERAPEUTICS

NUCANA

AstraZeneca

Dr James Mead

Chief Financial Officer

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

AstraZeneca

Distinctive Approach Generates "Best-in-Class" Drug Candidates

Select biologically Validated "druggable" targets

- High unmet medical need
- Significant potential commercial opportunity
- 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 IND by 2025

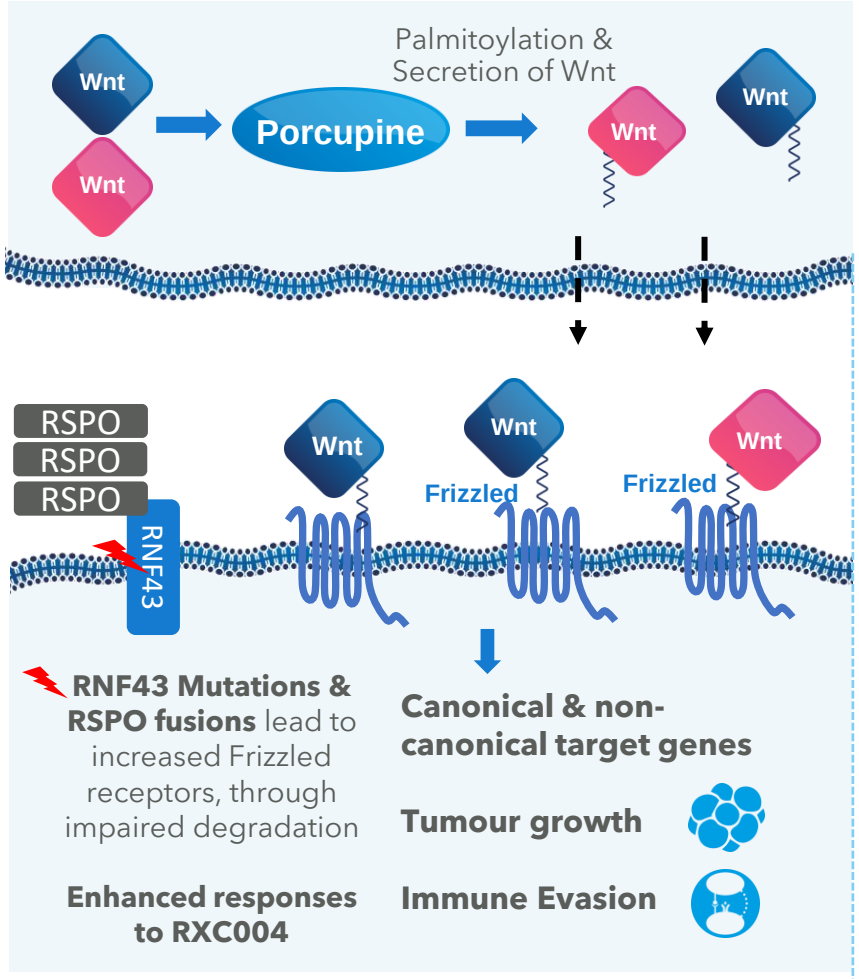
Financed to Deliver Multiple Value Inflection Points in 2021

	Target/Product	Indication(s)	Research	Preclinical Development	Clinical Phase 1/2	Upcoming Milestone
Redx 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 – **H1 2021** Phase 2 start – **2021**
Redx development	**ROCK2 Selective Inhibitor** (RXC007)	Lung fibrosis (IPF) Liver fibrosis (NASH)				Entering clinic –**H1 2021**
Research	**GI-targeted ROCK Inhibitor**	Fibrosis associated with Crohn's disease				Preclinical development candidate – **H1 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; NASH = Non-alcoholic Steatohepatitis

RXC004

RXC004: Unlocking the Potential of Wnt Pathway Blockade in Genetically Selected Cancers



Why target Porcupine?

- 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 fusion will lead to enhanced responses

Indications

- MSS metastatic colorectal cancer, pancreatic and biliary (~$10 billion whole market)

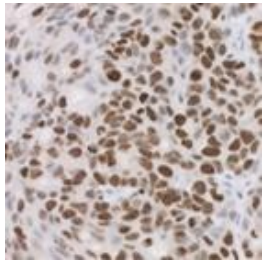
RXC004

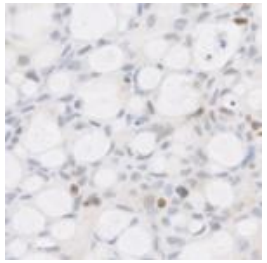
- Highly potent, orally active porcupine inhibitor in a Phase 1 clinical trial
- Differentiated with optimal PK profile

RXC004

RXC004 has a Dual Mechanism of Action

Inhibits Tumour Cell Proliferation

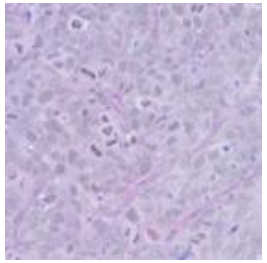


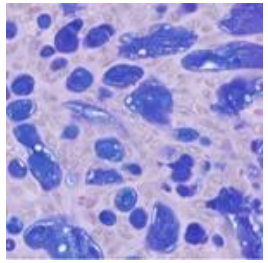


Reduces Ki67 staining in RSPO-fusion CRC xenograft model

DIRECTLY TARGETS TUMOUR CELLS

Differentiates Tumour Cells



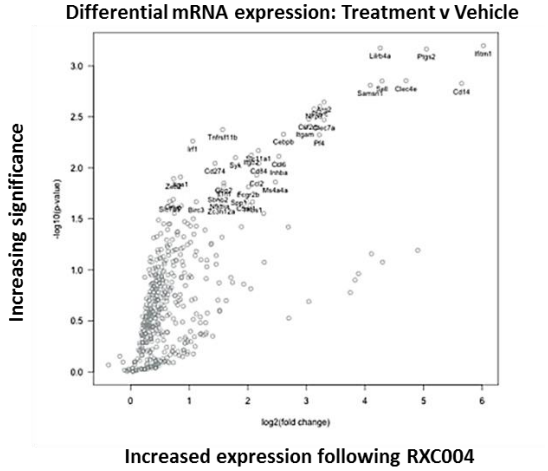


Increased size and mucin staining of tumour cells with RSPO-fusion

RXC004

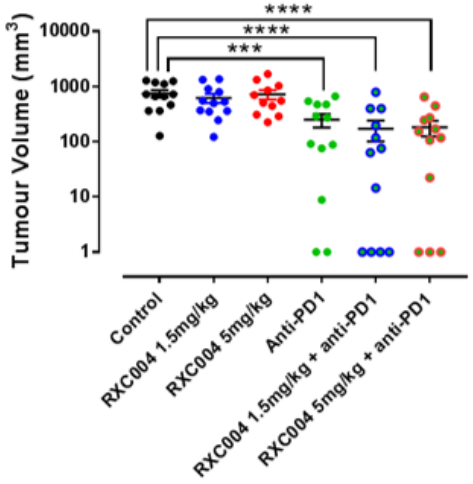
STIMULATES THE IMMUNE SYSTEM

As a Monotherapy



Increase in immune related gene expression post-RXC004 treatment in anti-PD1-resistant B16 mouse syngeneic model

In Combination with anti-PD1

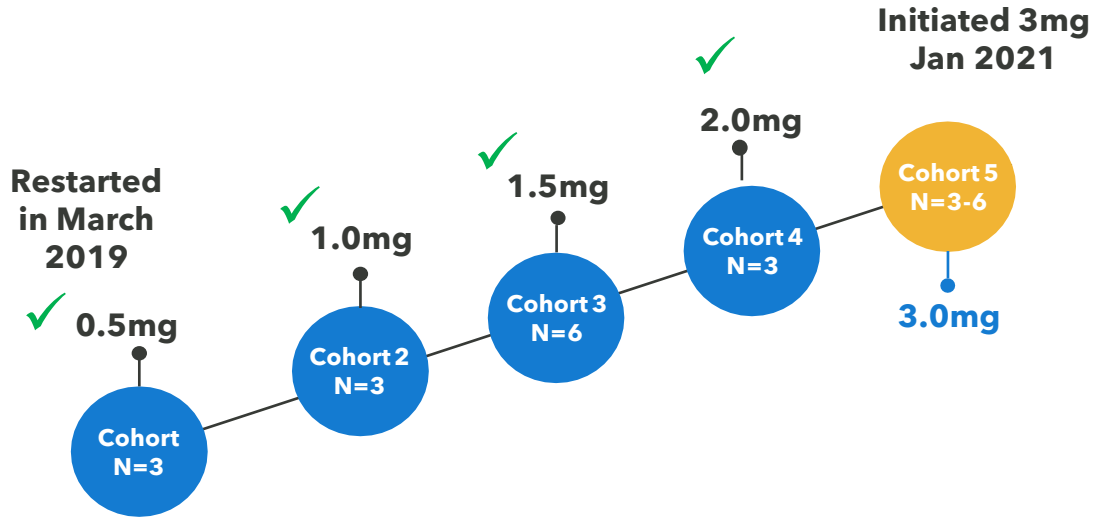


Improved responses observed when RXC004 combined with anti-PD1 in CT26 syngeneic CRC immune-mediated model

RXC004

Phase 1 Data Expected H1 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 (to January 2021)

- **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 clinic trial initiation in 2021

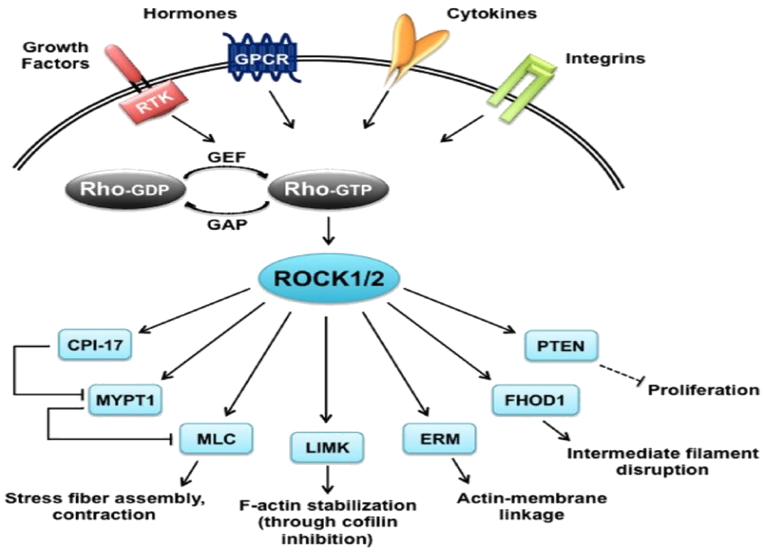
- **Phase 1**– Combination with anti-PD1
- **Phase 2** - Monotherapy in **genetically-selected** MSS mCRC
- **Phase 2** – Monotherapy in **genetically-selected** pancreatic cancer and all-comers biliary cancer

RXC007

RXC007: ROCK2 Selective Inhibitor Targeting Clinic H1 2021

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 across multiple organs



Drive Fibrosis

Indications

- Potential for disease modifying efficacy across multiple fibrotic conditions including our lead indication, Idiopathic Pulmonary Fibrosis (IPF) $3 billion market

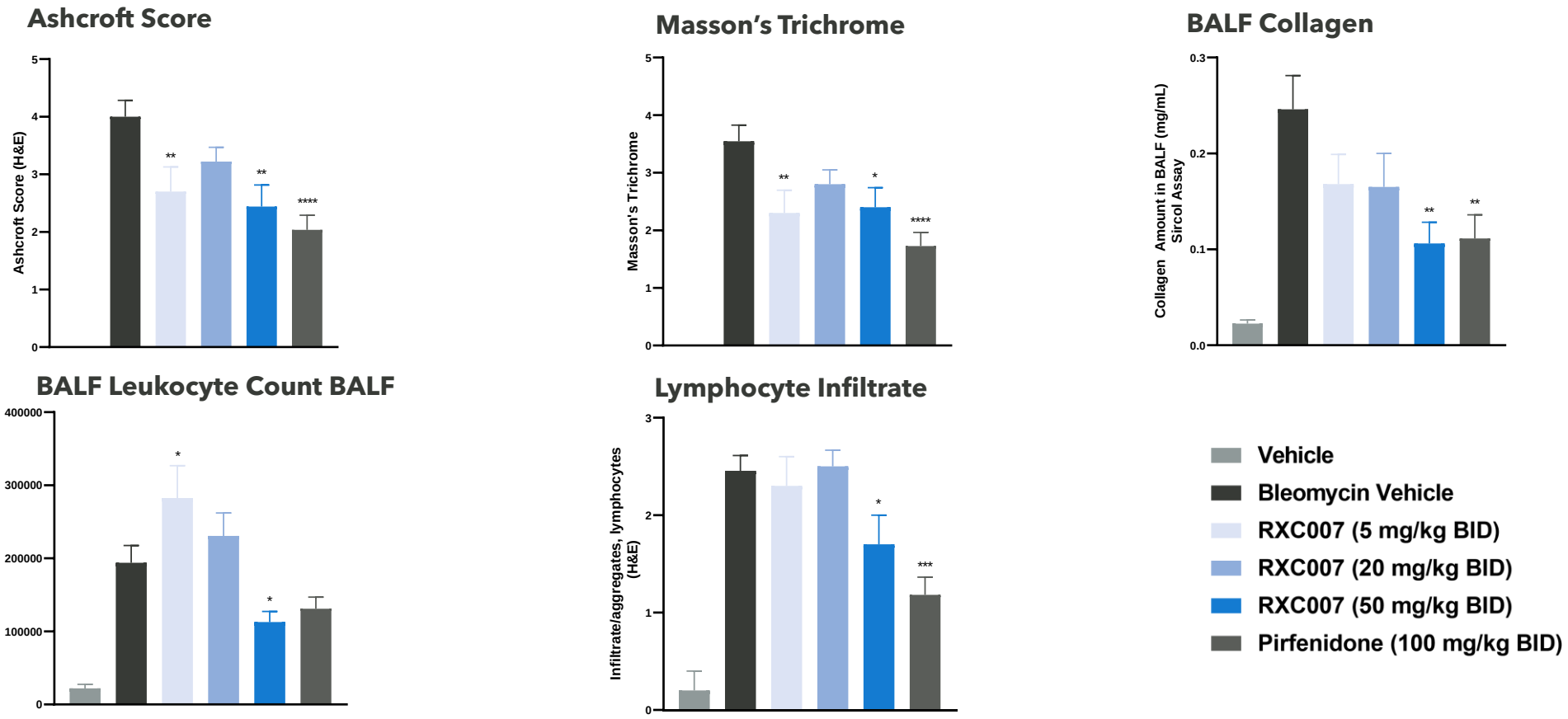
RXC007

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

RXC007

RXC007: Demonstrates Compelling Efficacy in Well-Validated Pre-clinical model of Lung Fibrosis

RXC007 reduces fibrosis and collagen deposition in the therapeutic lung and bronchoalveolar lavage fluid (BALF) in murine bleomycin-induced IPF model

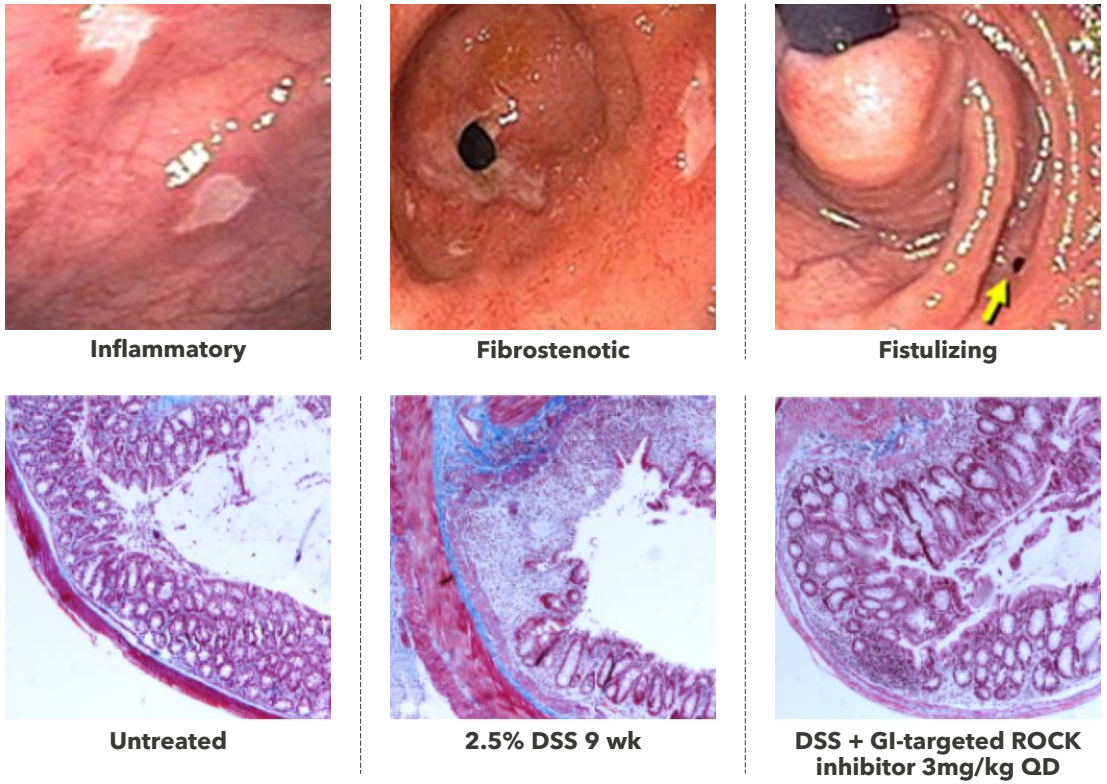


Values expressed as mean of n = 5-11 + SEM. Uncorrected Fisher's LSD model. No differences at significance level 0.05, *: P < 0.05, **: P < 0.01, ***: P < 0.001, ****: P < 0.0001 compared to Bleomycin Vehicle

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 H1 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

		2020	2021	2022
Redx development	**Porcupine Inhibitor (RXC004)**	✓ **H1** Phase 1 complete first two dose escalation cohorts ✓ **H2** Phase 1 completes two further dose escalation cohorts	**H1** Phase 1 start – IO combo safety **H1** Phase 1 monotherapy safety completion **H2** Phase 2 mono therapy (MSS mCRC, biliary, pancreatic cancer) **H2** Phase 2 start – IO combo MSS mCRC	Phase 2 data mono MSS mCRC Phase 2 data mono biliary cancer Phase 2 interim data mono pancreatic cancer and combo MSS mCRC
	ROCK2 Selective Inhibitor (RXC007)	✓ **H1** Development candidate ✓ **H2** Start GLP Toxicity study	**H1** Phase 1 Start	**H1** Phase 1 safety data readout **H2** Phase 2 start
Research	**GI-targeted ROCK Inhibitor**	✓ Ongoing research	**H1** Select development candidate	Phase 1 start
	Research Targets	✓ Progress wholly owned research programmes ✓ Two target collaboration deal Jazz Pharma	Progress wholly owned & Jazz research collaborations	Progress wholly owned & Jazz research collaborations
Partnered	**Porcupine Inhibitor (RXC006)**	✓ Out licensing agreement with AstraZeneca	AstraZeneca responsible for development	AstraZeneca responsible for development
	Pan-RAF Inhibitor	✓ Progress collaboration with Jazz	Progress collaboration with Jazz	Jazz responsible for clinical development

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