Trinity Delta

Redx Pharma

Report

Focus remains firmly on fibrosis and related diseases

10 July 2024

Redx Pharma has now delisted from AIM and re-registered as a private company. The focus remains firmly on fibrosis, and key internal programmes include two clinical ROCK inhibitors and a preclinical DDR inhibitor. Management expects top-line Phase IIa data for zelasudil in IPF (idiopathic pulmonary fibrosis) during 2024, whilst initial safety data in healthy volunteers from the Phase I trial of RXC008 for fibrostenotic Crohn's disease are expected towards end-2024. Redx also has a number of existing partnerships in place across four programmes; three with Jazz Pharmaceuticals, and one with AstraZeneca. RXC004 (zamaporvint), which recently reported Phase II data in combination with checkpoint inhibitors (CPI) for Wnt-ligand dependent cancers, has been earmarked for partnering. This note provides an overview of the current status of key programmes.

Year-end: September 30	2022	2023	2024E	2025E
Revenues (£m)	18.7	4.2	N/A	N/A
Adj. PBT (£m)	(17.3)	(28.8)	N/A	N/A
Net Income (£m)	(18.0)	(33.2)	N/A	N/A
Cash (£m)	53.9	18.1	N/A	N/A
EBITDA (£m)	(15.4)	(32.9)	N/A	N/A

Source: Redx Pharma Note: Adjusted numbers exclude share-based payments and exceptionals.

- **Zelasudil Phase IIa data expected 2024** The lead ROCK asset is zelasudil, a selective ROCK2 inhibitor in a Phase IIa trial in IPF, with topline data expected 2024. The trial is primarily to assess safety and tolerability, but will also include initial data on efficacy endpoints. Data will inform the design of a subsequent Phase IIb programme, to include broader interstitial lung diseases (ILDs).
- **RXC008 Phase I ongoing in fibrostenotic Crohn's** The second ROCK programme is RXC008, which is in a Phase I trial for fibrostenotic Crohn's disease. RXC008 is a GI-targeted pan-ROCK inhibitor which is expected to be used in combination with standard-of-care anti-inflammatories. The first part of the Phase I study includes healthy volunteers and will assess safety and PK data, with initial results expected by end-2024. A Phase II trial in fibrostenotic Crohn's patients is planned.
- **Partnering remains active** Redx has three collaborations with Jazz Pharmaceuticals and one with AstraZeneca. In addition, zamaporvint (RXC004), which is in development for Wnt-ligand dependent cancers, has been earmarked for partnering for further development following the Phase II combination data reported at the ESMO GI conference in June 2024.
- **Private company but focus remains the same** Redx Pharma's pipeline, which is focused on fibrotic disease, cancer, and cancer associated fibrosis, is based on its medicinal chemistry expertise, which has led to the discovery and development of six molecules which have entered the clinic, of which one (pirtobrutinib) is approved. In-house programmes focused on ROCK inhibition are being developed to key value-inflection points, and other certain assets are partnered, sometimes as early as preclinical, with four deals already in place. Redx delisted from AIM on 1 May 2024 and is now a private limited company. A matched bargain facility (provided by J P Jenkins) is in place to facilitate trading in ordinary shares.

Price	N/A
Market Cap	N/A
Enterprise Value	N/A
Shares in issue	N/A
12 month range	N/A
Free float	N/A
Primary exchange	N/A
Other exchanges	N/A
Sector	Healthcare
Company Code	N/A
Corporate client	Yes

Company description

Redx Pharma specialises in the discovery and development of small molecule therapeutics, with an emphasis on fibrotic diseases. It aims to progress them through proof-of-concept studies, before evaluating options for further development.

Analysts

Lala Gregorek
lgregorek@trinitydelta.org
+44 (0) 20 3637 5043

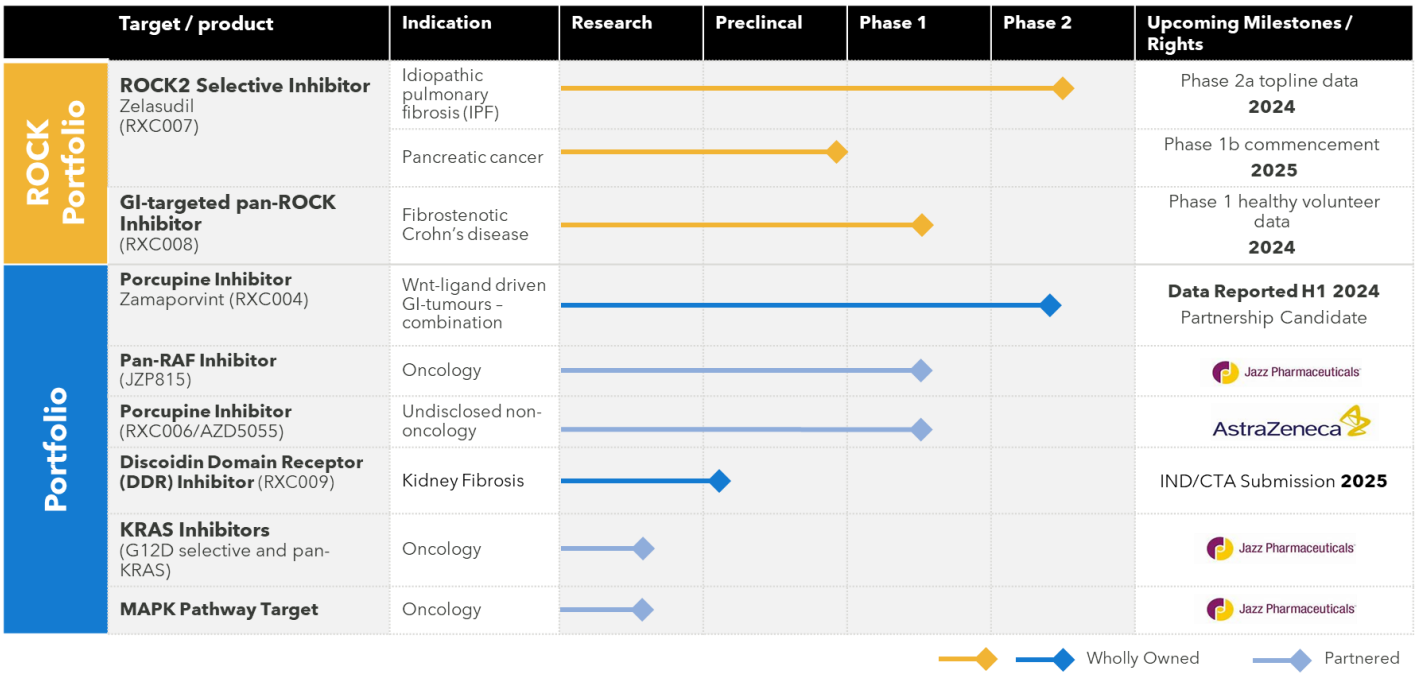
Philippa Gardner
pgardner@trinitydelta.org
+44 (0) 20 3637 5042

Redx Pharma: Focus remains fibrosis

Focus is firmly on fibrosis, with two ROCK programmes in the clinic

Redx is focused on advancing its ROCK inhibitor portfolio, with two programmes currently in the clinic: (1) zelasudil (RXC007) in IPF; and (2) RXC008 in fibrostenotic Crohn's disease. A selective DDR1 inhibitor (RXC009) is also in preclinical development for kidney fibrosis. Redx's partnering activities are also active, with three collaborations with Jazz Pharmaceuticals and one with AstraZeneca. In addition, zamaporvint (RXC004) has been earmarked for partnering. An overview of Redx's pipeline is shown in Exhibit 1.

Exhibit 1: Redx Pharma pipeline



Source: Redx Pharma Note: GI = gastrointestinal; IND = investigational new drug application; MAPK = mitogen-activated protein kinase; MSS mCRC = microsatellite stable metastatic colorectal cancer; RAF = rapidly accelerated fibrosarcoma. ROCK: Rho associated protein kinase; KRAS: Kirsten rat sarcoma virus.

Zelasudil top-line Phase IIa IPF data in 2024

Zelasudil is in a Phase IIa trial in IPF with top-line data expected in 2024

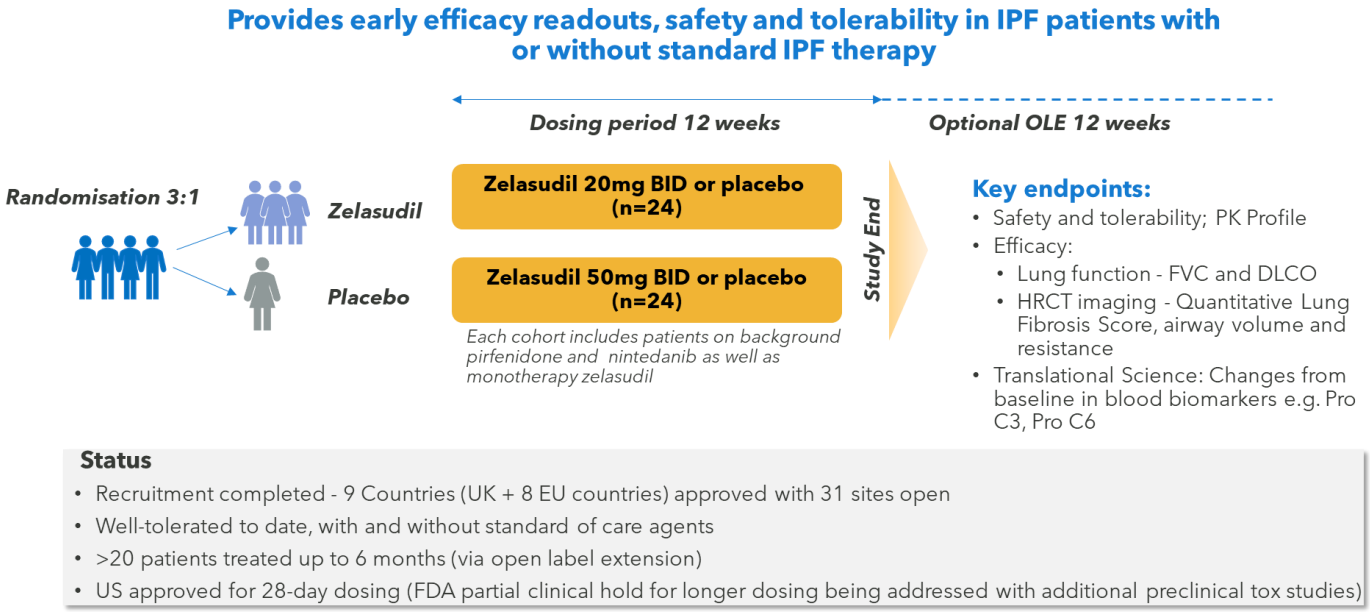
Redx's most advanced fibrosis programme is zelasudil (RXC007), a novel highly selective small molecule inhibitor of ROCK2 (Rho Associated Coiled-Coil Containing Protein Kinase 2). It is initially being developed for idiopathic pulmonary fibrosis (IPF) and management expects topline data from the ongoing Phase IIa trial in 2024. The study is a randomised, double-blind, placebo-controlled dose ranging trial, outlined in Exhibit 2, with patients in each cohort being dosed for 12-weeks, with an option to continue for a further 12-weeks in an open label extension.

Well tolerated to date

The Phase IIa study is primarily focused on the safety/tolerability profile of zelasudil in IPF patients with or without standard of care ie nintedanib or pirfenidone, and will also include initial data on efficacy endpoints. The outcome of the Phase IIa trial will define the dose that will be taken into further Phase IIb trials. On confirmation of the recommended Phase II dose, an 8-16 patient 28-day translational science sub-study will also follow, evaluating target engagement and fibrosis modification through key translational science endpoints. Recruitment

into the study, randomised 3:1 between zelasudil and placebo, has been completed, with zelasudil well tolerated to date.

Exhibit 2: Zelasudil Phase IIa study design



Source: Redx Pharma Note: IPF: idiopathic pulmonary fibrosis; BID: twice daily; OLE: open label extension; Pbo: placebo; FVC: forced vital capacity; HRCT: high-resolution computed tomography; DLCO = carbon monoxide diffusion coefficient.

Preclinical work is ongoing to address the FDA partial clinical hold

The Phase IIa study is ongoing in Europe and the UK, whilst in the US dosing of zelasudil for longer than 28-days is subject to an FDA partial hold based on skeletal muscle findings in dog toxicology studies. Preclinical work is ongoing to address this partial clinical hold. According to Redx, no similar findings have been observed in humans or other species at any dose. Redx expects to submit data from further preclinical studies to address the partial clinical hold and potentially allow for longer dosing durations in the US during 2024.

Future plans include broader lung indications and other fibrosis-related disorders

Assuming positive Phase IIa outcomes, management has outlined that the next steps for zelasudil include a larger 12-month Phase IIb study in IPF and chronic fibrosing interstitial lung disease (CF-ILD). Progressive fibrotic interstitial lung diseases (ILD) are a larger opportunity for zelasudil, with IPF representing only 20-50% of ILDs. Outside of lung fibrosis, Redx also has wider plans to expand future development of zelasudil as a fibrosis therapy, subject to funding. Opportunities that management has outlined include cancer-associated fibrosis or treatment of highly fibrotic tumours such as pancreatic cancer, with clinical development plans that include a Phase Ib study of zelasudil in combination with chemotherapy (gemcitabine/abraxane) in first line pancreatic cancer in 2025.

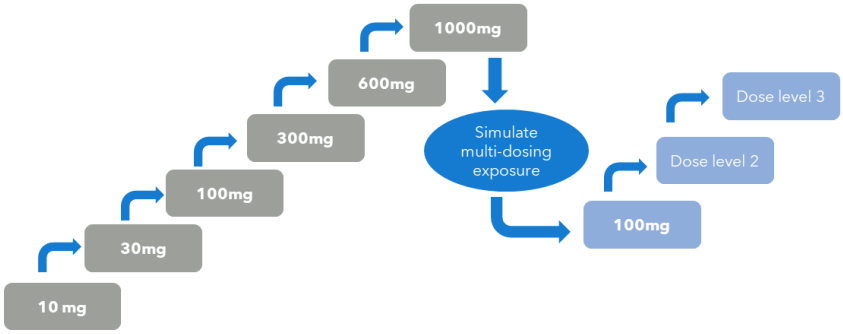
Prior preclinical data (covered in the October 2022 Update) have demonstrated marked reductions in collagen deposition and fibrosis in various relevant models. Phase I data confirmed zelasudil's safety and tolerability, with no serious adverse events and only transient, reversible, mild adverse events. The pharmacokinetics were as predicted from preclinical data, and no significant effect on exposure was seen when dosed with food. The Phase I data showed a mean half-life of approximately 9-11 hours, which suggests the potential for once or twice daily dosing.

RXC008 Phase I ongoing in fibrostenotic Crohn's

RXC008 is the second wholly-owned ROCK asset to enter clinical development

RXC008 is a GI-targeted pan-ROCK (Rho Associated Coiled-Coil Containing Protein Kinase) inhibitor in development for patients with fibrostenotic Crohn's disease (CD). Following dosing of the first participant in the Phase I study in February 2024, it is Redx's second wholly-owned ROCK asset to enter clinical development. RXC008 is a potent, oral, small molecule inhibitor of both ROCK1 and ROCK2 pathways that has been specifically designed to act only locally at sites of CD-associated fibrosis within the gastrointestinal (GI) tract. Low permeability and high efflux mean it localises to the gut, and in the event of any residual absorption it is rapidly metabolised by paraoxonase enzymes in the blood. This GI-restricted effect allows the targeting of both ROCK receptors but should avoid the cardiovascular side-effects (hypotension, tachycardia) associated with systemic pan-ROCK inhibition.

Exhibit 3: RX008 Phase I study protocol (healthy volunteers)



Parts A and B in Healthy Volunteers
- Single Ascending Dose (SAD) cohorts in Part A
- Multiple Ascending Dose (MAD) cohorts in Part B, dosed for 14-days
- Safety (no cardiovascular effects)
- PK (faeces, plasma and tissue in MAD cohorts)

Emerging Profile
- Good safety profile with no SAE's
- No clinically relevant breakthrough observed
- No hypotension observed

Phase 2 in Fibrostenotic Crohn's Patients planned to initiate in 2025
- Initial safety run in for 1 month dosing
  - One or two highest doses from Phase 1 MAD study with minimal systemic exposure
  - Safety, PK, Target engagement, biomarkers
- Followed by 24- week dosing, randomised, double-blind, placebo controlled study
  - Efficacy, safety, PK, target engagement and biomarkers

Source: Redx Pharma

Phase I trial in healthy volunteers with data expected by end-2024

The Phase I trial (Exhibit 3) is a two-part study evaluating the safety and pharmacokinetic (PK) profile of RXC008 in healthy volunteers (Part A and B). These healthy volunteer cohorts include single ascending dose (SAD) and multiple ascending dose (MAD) over 14 days, with safety as the primary endpoint and secondary endpoints evaluating PK to confirm the target profile (including data on faeces, plasma, and tissue in the MAD cohort). Management expects Phase I data by end-2024. Next steps include a planned Phase II trial in fibrostenotic CD patients, which will involve a one-month dosing safety run in to confirm minimal systemic exposure in patients (as absorption may differ from healthy volunteers), explore evidence of target engagement, and changes in circulating fibrotic biomarkers. This will be followed by a 24-week dosing study to investigate efficacy, safety, PK, target engagement and fibrotic biomarkers.

Complete fibrosis reversal in preclinical models and a synergistic effect with anti-TNFs

Preclinical data (covered in more detail in the February 2024 Update) have demonstrated the ability of a closely related GI-targeted ROCK inhibitor to completely reverse fibrosis to baseline levels, and the ability of RXC008 to reduce fibrosis and smooth muscle hyperplasia, which is a contributing factor to stricture

development. RXC008 has also been shown to have a therapeutic effect in an adoptive T-cell transfer model (where inflammation and tissue remodelling have been induced and established), demonstrating reduced fibrosis and tissue damage. Further studies with both RXC008 monotherapy and in combination with an anti-TNF demonstrated synergies in the combination.

RXC009 for kidney fibrosis in preclinical development

Preclinical RXC009 data have demonstrated efficacy in kidney fibrosis models

Redx is also developing RXC009, a selective DDR1 inhibitor. The discoidin domain receptors, DDR1 and DDR2, are non-integrin tyrosine kinase collagen receptors. DDR1 is expressed in a variety of tissues, including the brain, kidney and lung, and abnormal expression is associated with cancer progression, fibrosis and chronic inflammatory diseases. Preclinical data in kidney fibrosis models demonstrated a reduction in markers of inflammation, kidney injury and fibrosis, and target engagement in kidney tissue, supporting use in kidney fibrosis indications such as diabetic kidney diseases and chronic kidney diseases. Redx plans to progress RXC009 to IND-enabling studies, aiming for IND submission in 2025.

Four partnership agreements in place

Three agreements with Jazz and one with AstraZeneca

Redx has four partnership agreements already in place: three with Jazz Pharmaceuticals and one with AstraZeneca. Exhibit 4 summarises the respective deals. To date, upfront/milestone receipts total $58.5m.

The first Jazz deal was for JZP815; the second was focused on the MAPK pathway…

The first agreement with Jazz Pharmaceuticals covers JZP815, a precision pan-RAF inhibitor now in Phase I, which was designed to overcome the acquired resistance mechanisms associated with currently approved B-RAF selective drugs. Around one-third of cancers involve mutations that result in uncontrolled signalling in the RAS-RAF-MAPK pathway. The second Jazz collaboration addresses an undisclosed target on the MAPK pathway, which is at an earlier pre-IND stage.

…followed by a KRAS deal, including both G12D selective and pan-KRAS candidates

The most recent licensing deal between the two parties covers KRAS (Kirsten rat sarcoma virus), a well-validated oncology target that is one of the most frequently mutated oncogenes across many different cancer types. To date, targeting specific KRAS mutations, with the exception of G12C, has proved challenging. The Jazz/Redx KRAS programme includes both G12D selective and pan-KRAS candidate molecules.

AstraZeneca's AZD5055 is in Phase I for non-oncology indications

Redx's licence agreement with AstraZeneca centres on AZD5055 (formerly RXC006), a potent, highly selective small molecule of the porcupine receptor that is currently in development for non-oncology indications. AZD5055 targets the Wnt pathways that are critical elements in maintaining adult cell homeostasis, which includes wound healing and repair functions.

Exhibit 4: Redx Pharma partnerships

Partner	Asset	Deal structure	Deal terms
Jazz Pharmaceuticals	KRAS programme (preclinical, oncology)	Global licensing & commercialisation deal covering two KRAS targets (G12D selective and pan-KRAS), with separate collaboration agreement (signed February 2024)	**Licensing deal**: $10m upfront payment, plus cumulative potential development, regulatory, and commercial milestones of up to $870m, and tiered mid-single digit percentage royalties on future net sales. Jazz bears responsibility for clinical development, regulatory, manufacturing and commercialisation activities. **Collaboration deal**: Jazz to pay Redx to carry out research and preclinical development to support IND-enabling studies. **Redx milestones received**: $10m upfront. IND application clearance will trigger the first development milestone.
	Ras/Raf/MAPK programme (preclinical, oncology)	Oncology research collaboration to discover and develop drug candidiates for two targets on the RAS/RAF/MAPK pathway (signed September 2020)	**Collaboration**: Upfront of $10m and a further $10m in year two, with up to a further $400m in development, commercial, and regulatory milestones split equally between the two programmes, and tiered mid-single digit percentage royalties on net sales. Redx leads discovery and preclinical development up to IND submission, after which Jazz assumes responsibility for further development, manufacturing, regulatory activities and commercialisation. One target was discontinued in 2022 due to pipeline prioritisaton at Jazz. **Redx milestones received**: $10m upfront in September 2020; $10m milestone in December 2021. IND submission will trigger the first development milestone.
	JZP815 (Phase I, oncology)	Sale of preclinical pan-RAF inhibitor programme, with separate collaboration agreement (signed July 2019)	**Sale economics**: Upfront fee of $3.5m, plus up to $203m in cumulative potential development, regulatory, and commercial milestones, and mid-single digit percentage royalties on future net sales. Jazz funds all development, and is responsible for all post-IND development, regulatory, manufacturing, and commercial activities. **Collaboration deal**: Jazz funded Redx to carry out research and preclinical development to completion of IND-enabling studies. **Redx milestones received**: $3.5m upfront; $3m on initiation of IND-enabling studies in September 2021; $5m on IND clearance in June 2022.
AstraZeneca	AZD5055 (previously RXC006, Phase I, undisclosed non-oncology indication)	Global licensing deal for the development & commercialisation of porcupine inhibitor RXC006 (signed August 2020)	**Licensing deal:** Upfront fee and early development milestones totalling $17m between deal signing and Phase I start, plus up to $360m in development, regulatory, and commercial milestones, and mid-single digit percentage royalties on future net sales. **Redx milestones received:** Cumulative receipt of $17m to date including $4m in June 2021, and $9m in December 2021 on the initiation of Phase I studies.

Source: Trinity Delta, Redx Pharma

Zamaporvint earmarked for partnering

Targeting Wnt is not a strategic Redx priority

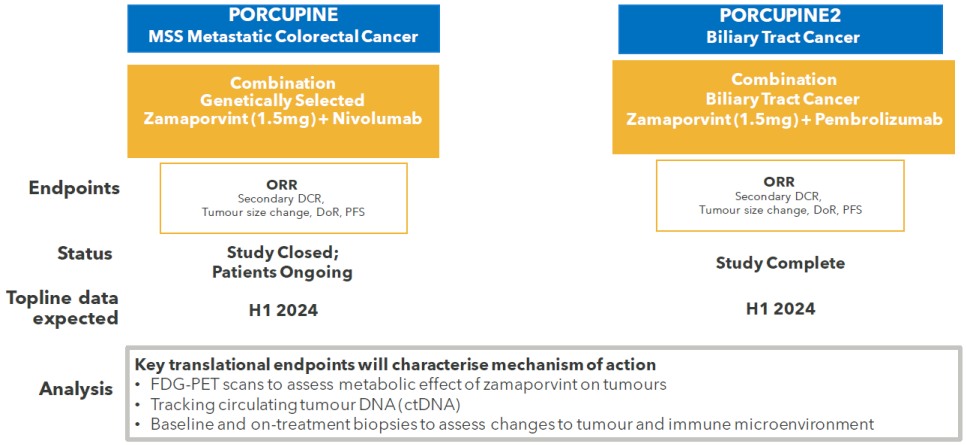
Zamaporvint (RXC004) is a highly potent and selective once-daily porcupine inhibitor in development for Wnt-ligand dependent cancers in combination with immunotherapies. This has been earmarked for partnering for further development post-Phase II.

ESMO data support combo with immunotherapies in genetically selected GI cancers

Two Phase II studies of zamaporvint in combination with a checkpoint inhibitor (CPI), shown in Exhibit 5, have completed. PORCUPINE is in genetically selected microsatellite stable metastatic colorectal cancer (MSS mCRC) in combination with nivolumab, and PORCUPINE2 is in genetically selected pancreatic cancer as monotherapy, and unselected biliary cancer in combination with pembrolizumab. Phase II data were presented at the ESMO GI conference in June 2024. In PORCUPINE, partial responses were observed in c 30% (2/7) of genetically-selected MSS mCRC patients in combination with nivolumab, a setting where anti-PD-1 therapy alone is not effective. The disease control rate at ≥16 weeks was 57% (4/7), exceeding that of zamaporvint monotherapy at 15% (2/13). In

PORCUPINE2 some durable clinical benefit was observed in biliary cancer (in an all-comers, unselected patient group) but at a lower level than in genetically-selected MSS mCRC, whilst in genetically selected pancreatic cancer one partial response was seen. These data support the principal hypothesis for use in combination with immunotherapies in genetically selected GI cancers.

Exhibit 5: Zamaporvint Phase II combination programme



Source: Redx Pharma Note: DCR = disease control rate; DoR = duration of response; ORR = overall response rate; OS = overall survival; PFS = progression free survival

Zamaporvint is being prepared for partnering

Management has outlined that preclinical data suggest there is a broader opportunity for zamaporvint in potentially synergistic combinations with other therapeutic agents, including chemotherapies and MAPK inhibitors, which is beyond the scope of Redx's resources, and outside of the priority focus.

Exhibit 6: Summary of financials

Year-end: Sept 30	£'000s	2021	2022	2023	2024E	2025E
INCOME STATEMENT						
Revenues		**10,035**	**18,690**	**4,202**	**N/A**	**N/A**
Cost of goods sold		0	0	0	N/A	N/A
Gross Profit		**10,035**	**18,690**	**4,202**	**N/A**	**N/A**
R&D expenses		(24,445)	(28,563)	(29,117)	N/A	N/A
G&A expenses		(6,492)	(10,229)	(8,069)	N/A	N/A
Underlying operating profit		**(17,117)**	**(15,737)**	**(29,790)**	**N/A**	**N/A**
Share-based payments		(3,785)	(4,365)	(3,194)	N/A	N/A
Exceptionals		0	0	(2,393)	N/A	N/A
Other revenue/expenses		1,157	3,836	1,557	N/A	N/A
EBITDA		**(19,112)**	**(15,380)**	**(32,860)**	**N/A**	**N/A**
Operating Profit		**(19,745)**	**(16,266)**	**(33,820)**	**N/A**	**N/A**
Financing costs/income		(1,698)	(1,538)	1,032	N/A	N/A
Profit Before Taxes		**(21,443)**	**(17,804)**	**(32,788)**	**N/A**	**N/A**
Adj. PBT		**(18,815)**	**(17,275)**	**(28,758)**	**N/A**	**N/A**
Current tax income		(133)	(201)	(368)	N/A	N/A
Net Income		**(21,576)**	**(18,005)**	**(33,156)**	**N/A**	**N/A**
EPS (p)		**(8.4)**	**(6.1)**	**(9.9)**	**N/A**	**N/A**
Adj. EPS		**(7.4)**	**(5.9)**	**(8.7)**	**N/A**	**N/A**
DPS (p)		**0.0**	**0.0**	**0.0**	**N/A**	**N/A**
Average no. of shares (m)		256.4	294.2	334.9	N/A	N/A
BALANCE SHEET						
Current assets		**35,815**	**59,378**	**23,302**	**N/A**	**N/A**
Cash and cash equivalents		29,552	53,854	18,092	N/A	N/A
Accounts receivable		6,231	5,498	5,210	N/A	N/A
Other current assets		32	26	0	N/A	N/A
Non-current assets		**3,730**	**3,099**	**2,334**	**N/A**	**N/A**
Property, plant & equipment		3,325	2,699	1,940	N/A	N/A
Intangible assets		405	400	394	N/A	N/A
Other non-current assets		0	0	0	N/A	N/A
Current liabilities		**(9,592)**	**(27,205)**	**(21,007)**	**N/A**	**N/A**
Short-term debt		0	(15,731)	(15,731)	N/A	N/A
Accounts payable		(4,699)	(5,958)	(3,756)	N/A	N/A
Other current liabilities		(4,893)	(5,516)	(1,520)	N/A	N/A
Non-current liabilities		**(16,821)**	**(1,951)**	**(1,274)**	**N/A**	**N/A**
Long-term debt		(14,247)	0	0	N/A	N/A
Other non-current liabilities		(2,574)	(1,951)	(1,274)	N/A	N/A
Equity		**13,132**	**33,321**	**3,355**	**N/A**	**N/A**
CASH FLOW STATEMENTS						
Operating cash flow		**(21,379)**	**(8,470)**	**(34,747)**	**N/A**	**N/A**
Profit before tax		(21,443)	(17,804)	(32,788)	N/A	N/A
Non-cash adjustments		6,116	6,776	3,122	N/A	N/A
Change in working capital		(6,065)	2,038	(7,673)	N/A	N/A
Interest paid		13	187	1,160	N/A	N/A
Taxes paid		0	333	1,432	N/A	N/A
Investing cash flow		**(754)**	**(241)**	**(195)**	**N/A**	**N/A**
CAPEX on tangible assets		(754)	(262)	(195)	N/A	N/A
Acquisitions/disposals		0	21	0	N/A	N/A
Other investing cash flows		0	0	0	N/A	N/A
Financing cash flow		**24,143**	**32,982**	**(816)**	**N/A**	**N/A**
Proceeds from equity		24,929	33,798	0	N/A	N/A
Increase in loans		0	0	0	N/A	N/A
Other financing cash flow		(786)	(816)	(816)	N/A	N/A
Net increase in cash		**2,010**	**24,271**	**(35,758)**	**N/A**	**N/A**
Cash at start of year		27,513	29,552	53,854	N/A	N/A
Cash at end of year		**29,552**	**53,854**	**18,092**	**N/A**	**N/A**
Net cash at end of year		**15,305**	**38,123**	**2,361**	**N/A**	**N/A**

Source: Redx Pharma

Philippa Gardner pgardner@trinitydelta.org +44 (0) 20 3637 5042

Lala Gregorek lgregorek@trinitydelta.org +44 (0) 20 3637 5043

Franc Gregori fgregori@trinitydelta.org +44 (0) 20 3637 5041

Disclaimer

More information is available on our website: www.trinitydelta.org