Trinity Delta

Redx Pharma

Update

Momentum and execution continue in H121

8 June 2021

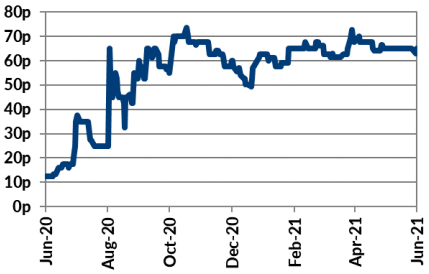
Redx Pharma's H121 results highlight continued momentum and delivery against expectations, despite COVID headwinds on clinical studies. The start of the Phase I study of RXC007, a ROCK2 inhibitor for fibrosis, means the company now has two distinctly different in-house assets in the clinic. Lead in-house programme RXC004, a porcupine inhibitor for genetically selected solid tumours, is completing Phase I studies and set to enter Phase II trials during H221. The solid cash position of £39.9m supports increased R&D investment through to end-2022, covering several important value inflection points. Our updated rNPV-based valuation is £350.7m, equivalent to 128p/share (86p fully diluted).

Year-end: September 30	2019	2020	2021E	2022E
Revenues (£m)	3.1	5.7	10.4	10.7
Adj. PBT (£m)	(7.5)	(9.5)	(19.9)	(26.2)
Net Income (£m)	(4.3)	(9.2)	(20.5)	(26.8)
Adj.EPS (p)	(4.0)	(5.6)	(7.7)	(9.4)
Cash (£m)	(3.7)	27.5	31.8	9.9
EBITDA (£m)	(6.2)	(7.5)	(20.5)	(26.7)

Source: Trinity Delta Note: Adjusted numbers exclude share-based payments and exceptionals.

- **A second in-house programme enters the clinic** Redx Pharma's acknowledged expertise in medicinal chemistry underpins its discovery platform, and its strategy to develop best- or first-in-class small molecules that address validated biological targets in oncology and fibrosis indications. Two in-house programmes are now in clinical development: RXC004, a porcupine inhibitor for genetically selected solid tumours, is completing Phase I (both monotherapy and a PD-1 inhibitor combo) and set to enter Phase II studies; while RXC007, a ROCK2 inhibitor initially in development for fibrosis, dosed the first patient in its Phase I trial earlier in June.
- **Funded through to value inflection points** Redx Pharma has a solid balance sheet with £39.9m in cash resources. Funds are earmarked to progress RXC004 and RXC007 into Phase II proof-of-concept studies. RXC004 could, COVID permitting, post Phase II monotherapy results for MSS mCRC (microsatellite stable metastatic colorectal cancer) and biliary cancer in CY22 with interim monotherapy pancreatic cancer and MSS mCRC combination data also possible. For RXC007 the Phase I safety data should be available in H122, enabling a swift start to Phase II trials during H222. Our forecasts suggest the cash runway extends to end-2022.
- **Building a track record of delivery** The value of Redx Pharma's medicinal chemistry expertise is being harnessed with a focussed, yet ambitious, strategy. The pipeline has been de-risked through preclinical outlicensing deals, with Jazz Pharmaceuticals and AstraZeneca, whilst retaining material commercial upside. However, it is the continued progress with its innovative in-house programmes that should, if successful, be transformative for the business over the medium term.
- **rNPV valuation of £350.7m (128p/share)** We value Redx Pharma using an rNPV and SOTP methodology, with conservative assumptions. Our updated model reflects recent clinical progress and generates a £350.7m valuation, or 128p/share (86p fully diluted) vs £326.4m, or 119p/share (84p, fully diluted) previously.

Price	66.0p
Market Cap	£180.8m
Enterprise Value	£140.9m
Shares in issue	273.9m
12 month range	11.7-95.0p
Free float	11.0%
Primary exchange	AIM London
Other exchanges	N/A
Sector	Healthcare
Company Code	REDX
Corporate client	Yes



Company description

Redx Pharma specialises in the discovery and early clinical development of small molecule therapeutics, with an emphasis on oncology and fibrotic disease. Typically, these are progressed through proof-of-concept studies and then partnered for further development. The strategy has been validated by several collaborations.

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Redx Pharma: delivering on all key objectives

Continued delivery against expectations

The key message from Redx Pharma's H121 results is the continued delivery of management against our, and the market's, expectations. The recently announced start of a Phase I study with RXC007, a selective ROCK2 inhibitor, means that the company now has two in-house programmes in clinical development. The lead asset, porcupine inhibitor RXC004, is completing the fifth and final cohort (3.0mg) of the Phase I dose escalation study with results expected during H221. In addition, a Phase I study of RXC004 in combination with nivolumab (Bristol Myers Squibb's PD-1 checkpoint inhibitor Opdivo), is underway with preliminary data expected in late-H221. Several RXC004 Phase II trials, in various oncology indications, are expected to start during H221.

£39.9m of cash provides runway through 2022

Redx Pharma is well funded, with ample resources to achieve multiple value inflection points. Development progress with the lead assets during H121 lifted R&D investment to £10.3m (H120: £3.2m), similarly increasing operating costs from £5.2m to £12.6m. R&D spend is set to increase further as the clinical programmes progress, with the forecast cash runway extending through 2022.

Respected specialist investors joined the register during 2020

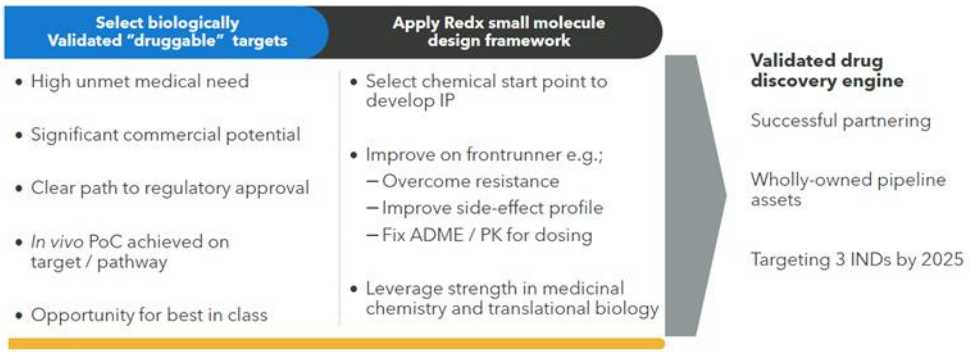
The cash balance of £39.9m at end-March 2021 was a sizeable improvement on the £1.9m figure a year earlier, reflecting the company's refinancing in summer 2020 and its most recent successful £25.7m (gross) fund raise in December 2020. During H121, £5.1m of the £22.2m outstanding loan note held by majority shareholder Redmile Group was converted into equity. The 2020 raises added specialist investors Redmile, Sofinnova Partners, and Polar Capital to the shareholder register. The involvement of these respected and supportive investors provides valuable external validation of management's clearly defined strategy.

Acknowledged medicinal chemistry expertise

Discovery and development of novel first in class/best in class small molecules

Redx Pharma is focused on developing innovative small molecule pharmaceuticals, with the aim of creating best- or first-in-class compounds. Its medicinal chemistry expertise underpins the discovery platform, which has a growing industry-wide reputation and a proven ability to generate clinically, and commercially, attractive products. Management is actively addressing complex biological pathways, for instance the Wnt/β-catenin pathway, where its insights have resulted in generating novel small molecules such as its family of porcupine inhibitors (eg RXC004 and RXC006, partnered with AstraZeneca).

Exhibit 1: Redx Pharma approach generates 'best in class' drug candidates



Source: Redx Pharma

Eli Lilly's pirtobrutinib emerged from Redx Pharma's discovery engine

Under new (current) management Redx Pharma firmly put a tempestuous period in its history (2017-2018) behind it; however, we reference its previous lead asset RXC005, a Bruton's tyrosine kinase (BTK) inhibitor, as it provides a blueprint for its discovery strategy. Somewhat ironically, RXC005 was sold for $40m (£30.2m) to Loxo Oncology in 2017 to salvage Redx Pharma out of administration (forced by Liverpool City Council to recover a £2m development loan). In 2019, RXC005 (now LOXO-305) was cited as one of the key desired programmes when Loxo was acquired by Eli Lilly for $8bn. LOXO-305 (pirtobrutinib) is currently completing an extensive Phase III trial programme, with first regulatory filings expected shortly.

Two in-house programmes now in the clinic

RXC007 joins RXC004 as the second in-house clinical asset

The recent initiation of the RXC007 Phase I trial means that Redx Pharma's two most advanced assets are now in clinical development. The company's pipeline (Exhibit 2) is well-balanced, with two in-house clinical programmes (RXC004 and RXC007), two preclinical programmes which have been successfully partnered, and earlier stage drug candidates that are showing promise. The partnership deals with AstraZeneca (porcupine inhibitor RXC006) and Jazz Pharmaceuticals (pan-RAF inhibitor, and other oncology/fibrosis research targets) were not simply financially attractive but demonstrated the active de-risking of Redx Pharma's pipeline, notably reducing the porcupine inhibitor class as a development risk.

Pipeline and discovery work focused on genetically defined cancers and fibrosis

The focus of Redx Pharma's pipeline is on genetically-defined oncology indications and fibrotic diseases, with a goal of achieving three further IND applications by 2025. The strategy is to progress selected candidates to Phase II proof of concept clinical trials with the data supporting out-licencing, with an element of downstream development and commercial economics retained; however, assets will be out-licensed earlier if the proposed returns are sufficiently attractive.

Exhibit 2: Redx Pharma pipeline

	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

Source: Redx Pharma Note: MSS mCRC = microsatellite stable metastatic colorectal cancer, IPF = idiopathic pulmonary fibrosis

RXC004 set for Phase II mono and combo studies

RXC004 Phase I monotherapy data anticipated in H221

RXC004 is a highly selective and potent porcupine (Porcn) inhibitor under evaluation as both monotherapy and in combination with checkpoint inhibitors in various solid tumours. It is completing the final stage of a 21-patient dose escalation Phase I monotherapy trial to examine its safety and tolerability. Four patient cohorts have been completed successfully, with no dose limiting toxicities (DLTs), including, importantly no bone fragility fractures, and a strong target engagement detected in markers in skin tissue. The pharmacokinetics showed good oral absorption and bioavailability and support a once daily dosing. The fifth and final patient cohort, at a 3.0mg dose, was initiated in January 2021 after a six month delay due to COVID-related restrictions on patient recruitment. The results of this monotherapy study are expected to be available during H221.

Mechanism of action and preclinical results suggest potential synergy with checkpoint inhibitors…

The porcupine enzyme is seen as an attractive target in the Wnt (Wingless type) signalling pathways, dysregulation of which is a driver of many tumour types, particularly those with a poor prognosis, as elevated activity results in drug resistance. Preclinical studies have shown that RXC004 has promising direct anti-tumour activity in cancer lines with upstream mutations in the Wnt pathway, for instance RNF43 (Ring finger protein 43) or RSPO (R-spondin) fusions. Additionally, RXC004 enhances the immune response in the tumour microenvironment and hence has a possible dual mechanism of action. This data, and the role of the Wnt pathway in both tumour growth and in tumour immune system evasion, supports evaluation of a porcupine inhibitor plus checkpoint inhibitor (CPI) combination. The hypothesis is that such a combination could result both increase the rate of response to the CPI (which typically only benefit around a third of patients when used as monotherapy due to innate or acquired resistance) and delay development of resistance in patients who do already respond.

…first patient dosed with RXC004 and nivolumab combo

In April 2021 the first patient was dosed in the Phase I study of RXC004 in combination with PD-1 checkpoint inhibitor nivolumab (Opdivo, Bristol Myers Squibb). This aim of this study is principally to examine the safety of RXC004 when used in combination although some efficacy signals may become apparent. Study completion is expected during H221, with results known shortly after.

First Phase II study in MSS mCRC on track to begin H221

Phase I results will inform plans for Phase II proof of concept studies in multiple settings with high unmet need. A 40-patient RXC004 Phase II study, both as monotherapy and in combination with nivolumab (n=20 in each arm), is set to initiate in early H221 (COVID restrictions permitting). This is an open label, multi-centre, multi-arm, study to evaluate efficacy and safety in patients with RNF43 or RSPO aberrated microsatellite stable (MSS) colorectal cancer that have progressed following current standard of care treatment. The study is likely to complete by end-2023, in our view. Additional studies in genetically selected pancreatic and all-comers biliary cancers are also being considered; biliary tract cancers are heavily Wnt-driven (>70% of patients have high Wnt ligand expression) and so will not include patient selection. We expect the availability of Phase II data would be the prelude to out-licensing discussions.

RXC007 has initiated Phase I clinical trials

RXC007 Phase I trial now up and running

RXC007, a novel and highly specific small molecule that selectively targets the ROCK2 (Rho Associated Coiled-Coil Containing Protein Kinase 2) receptor,

initiated patient enrolment in its first Phase I study in June 2021. The study, in healthy volunteers, will explore RXC007's safety profile and is expected to render results in H122. These data will guide the dosing and structure of the RXC007 Phase II programme. Future development will initially be for idiopathic pulmonary fibrosis (IPF), a progressive lung condition with a notably poor prognosis. This will likely be followed by broader fibrotic indications, potentially including liver fibrotic indications such as Non-Alcoholic Steatohepatitis (NASH).

Initially targeting IPF, but with potential in other fibrotic diseases

ROCK pathways mediate a broad range of cellular responses that involve the actin cytoskeleton and are important regulators of cellular growth, migration, metabolism, and apoptosis. ROCK2 is a biologically validated target that has been shown to sit at a nodal point in a cell signalling pathway, thought to be central to fibrosis. RXC007 has shown promising results in preclinical models of a number of fibrotic diseases. IPF has been selected as the lead indication because of the clear clinical need, limited treatment options, and sizeable market opportunity (Globaldata estimates it will be worth $3.6bn by 2029).

Belumosudil is the leading ROCK2 inhibitor, but in GVHD

RXC007 is the second ROCK2 inhibitor in clinical development. The first, belumosudil (Kadmon) has completed pivotal Phase II trials in chronic graft-versus-host disease (GVHD) and is in a Phase II study in systemic sclerosis (SSc). Belumosudil met its primary endpoint in the GVHD ROCKstar (KD025-213) study with impressive data and has been granted FDA Breakthrough Therapy designation and Orphan Drug status. It was submitted for a priority review in November 2020; however, its PDUFA date was extended to 30/08/21 following a request for additional data.

News flow expectations for 2021 and 2022

Significant news flow anticipated during 2021-22

Exhibit 3 shows expected news flow and catalysts over the next 18 months. While COVID-19 restrictions remain a sensitivity with respect to timings (impacts on patient recruitment into clinical trials is a known industry-wide consequence), we anticipate Redx Pharma will exhibit continued momentum and make significant strategic progress.

Exhibit 3: Key milestones and value drivers to 2022

		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

Source: Redx Pharma Note: *periods refer to calendar years (to end-December) not financial year (to end-September).

Valuation and Financials

Updated valuation of £350.7m, or 128p/share (86p fully diluted)

We update our valuation following H121 results with the latest cash position and increase our success probability for RXC007 from 10% to 15% to reflect its clinical progress. Our new valuation is £350.7m, equivalent to 128p/share (86p/share fully diluted), and compares to our previous valuation of £326.4m, equivalent to 119p/share (84p/share fully diluted). Exhibit 4 summarises the outputs and underlying assumptions of our valuation model, while a detailed overview of our methodology is provided in our September 2020 Initiation.

Exhibit 4: rNPV-based valuation of Redx Pharma

Programme	Total NPV ($m)	Total NPV (£m)	Likelihood of approval	rNPV ($m)	rNPV (£m)	rNPV/ share (p)	Notes
RXC004 (porcupine inhibitor: oncology)	738.5	568.1	18%	86.5	66.5	24.3	Peak sales: $2.55bn (£1.96bn) Launch year: 2027
RXC007 (ROCK2 inhibitor: IPF/NASH)	1,036.9	797.6	15%	106.9	82.2	30.0	Peak sales: $3.13bn (£2.41bn) Launch year: 2028
RXC006 (AstraZeneca: porcupine inhibitor: IPF)	288.4	221.9	7%	38.3	29.5	10.8	Peak sales: $1.66bn (£1.28bn) Launch year: 2028
Pan-RAF (Jazz Pharma: oncology)	147.1	113.1	7%	27.6	21.3	7.8	Peak sales: $707m (£544m) Launch year: 2029
GI-targeted ROCK (ROCK1/2: Crohn's disease)	144.7	111.3	5%	34.3	26.4	9.6	Peak sales: $1.61bn (£1.24bn) Launch year: 2029
Discovery engine				160.0	123.1	44.9	
Operating costs	(33.3)	(25.6)		(33.3)	(25.6)	(9.4)	
Net cash	35.5	27.3		35.5	27.3	10.0	At H121
Total	**2,357.9**	**1,813.8**		**455.9**	**350.7**	**128.1**	
Total (fully diluted)				**465.0**	**357.7**	**86.3**	Based on all options and CLNs

Source: Trinity Delta Note: The rNPV of RXC004 and RXC007 includes a deal success factor of 80%, and of 75% for GI-targeted ROCK; other valuation assumptions include a 12.5% discount factor, £/$ FX rate of 1.30, and 10% taxation from 2028 (UK patent box).

Higher investment in R&D increased H121 net loss...

Redx Pharma H121 revenues of £2.1m (H120: £1.17m) were derived from collaboration partners, demonstrating progress under these deals. Higher operating expenses of £12.6m (H120: £5.2m) were driven by increased R&D investment (£10.3m vs £3.2m in H120) as pipeline assets advanced through preclinical and clinical development. Consequently, the H121 net loss grew from £4.0m in H120 to £12.7m.

...and is set to remain high as RXC004 and RXC007 are taken through to Phase II proof of concept studies

R&D investment is expected to further increase as RXC004 and RXC007 proceed to their next clinical value-inflection points, earlier stage assets approach IND filing, and discovery engine research activities ramp up. For FY21 we forecast R&D spend of £28.0m and £34.6m for FY22, with G&A rising more modestly due to inflation and an expanding organisation. On our forecasts Redx Pharma's £39.9m in cash provides a runway through 2022. Importantly, this will fund completion of RXC004 Phase I monotherapy and immunotherapy combination trials and planned Phase II studies, initiation of planned Phase I and Phase II trials for RXC007, as well as expansion of oncology and fibrosis research and identification of suitable next wave development candidates.

Exhibit 5: Summary of financials

Year-end: Sept 30	£'000s	2018	2019	2020	2021E	2022E
INCOME STATEMENT						
Revenues		**129**	**3,131**	**5,685**	**10,361**	**10,722**
Cost of goods sold		0	(350)	0	0	0
Gross Profit		**129**	**2,781**	**5,685**	**10,361**	**10,722**
R&D expenses		(7,424)	(8,339)	(12,215)	(28,094)	(34,555)
G&A expenses		(3,182)	(1,831)	(1,988)	(1,934)	(2,259)
Underlying operating profit		**(10,477)**	**(7,389)**	**(8,518)**	**(19,667)**	**(26,092)**
Share-based payments		(282)	(45)	(568)	(1,780)	(1,815)
Exceptionals		(596)	948	73	0	0
Other revenue/expenses		1,186	241	812	828	845
EBITDA		**(10,005)**	**(6,154)**	**(7,536)**	**(20,534)**	**(26,744)**
Operating Profit		**(10,169)**	**(6,245)**	**(8,201)**	**(20,618)**	**(27,062)**
Financing costs/income		23	(90)	(967)	(186)	(83)
Profit Before Taxes		**(10,146)**	**(6,335)**	**(9,168)**	**(20,803)**	**(27,145)**
Adj. PBT		**(10,454)**	**(7,479)**	**(9,485)**	**(19,852)**	**(26,174)**
Current tax income		1,301	2,017	(45)	281	346
Net Income		**(8,845)**	**(4,318)**	**(9,213)**	**(20,523)**	**(26,799)**
EPS (p)		**(7.0)**	**(3.4)**	**(5.4)**	**(8.1)**	**(9.8)**
Adj. EPS		**(7.2)**	**(4.0)**	**(5.6)**	**(7.7)**	**(9.4)**
DPS (p)		**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Average no. of shares (m)		126.4	126.4	170.1	254.2	273.9
BALANCE SHEET						
Current assets		**9,705**	**5,807**	**29,468**	**34,020**	**12,154**
Cash and cash equivalents		6,471	3,704	27,513	31,784	9,854
Accounts receivable		2,023	1,232	1,923	1,923	1,923
Other current assets		1,211	871	32	313	378
Non-current assets		**614**	**551**	**4,120**	**4,341**	**3,960**
Property, plant & equipment		191	134	136	627	428
Intangible assets		423	417	411	409	405
Other non-current assets		0	0	3,573	3,305	3,127
Current liabilities		**(3,950)**	**(4,867)**	**(10,934)**	**(10,697)**	**(25,476)**
Short-term debt		0	(468)	0	0	(11,864)
Accounts payable		(3,803)	(3,445)	(3,362)	(6,742)	(7,602)
Other current liabilities		(147)	(954)	(7,572)	(3,955)	(6,010)
Non-current liabilities		**(605)**	**0**	**(19,967)**	**(14,019)**	**(1,977)**
Long-term debt		0	0	(16,758)	(11,864)	0
Other non-current liabilities		(605)	0	(3,209)	(2,155)	(1,977)
Equity		**5,764**	**1,491**	**2,687**	**13,645**	**(11,339)**
CASH FLOW STATEMENTS						
Operating cash flow		**(17,177)**	**(4,668)**	**395**	**(18,986)**	**(21,816)**
Profit before tax		(10,146)	(6,335)	(9,168)	(20,803)	(27,145)
Non-cash adjustments		656	(782)	2,123	2,049	2,215
Change in working capital		(8,391)	(265)	6,425	(269)	2,915
Interest paid		(23)	13	7	83	(83)
Taxes paid		727	2,701	1,008	(45)	281
Investing cash flow		**(109)**	**32**	**(55)**	**(573)**	**(115)**
CAPEX on tangible assets		(132)	(28)	(59)	(573)	(115)
Acquisitions/disposals		23	60	4	0	0
Other investing cash flows		0	0	0	0	0
Financing cash flow		**(49)**	**1,869**	**23,469**	**23,830**	**0**
Proceeds from equity		0	0	1,876	24,616	0
Increase in loans		0	1,000	22,563	0	0
Other financing cash flow		(49)	869	(970)	(786)	0
Net increase in cash		**(17,335)**	**(2,767)**	**23,809**	**4,271**	**(21,931)**
Cash at start of year		23,806	6,471	3,704	27,513	31,784
Cash at end of year		**6,471**	**3,704**	**27,513**	**31,784**	**9,854**
Net cash at end of year		**6,471**	**3,236**	**10,755**	**19,920**	**(2,011)**

Source: Company, Trinity Delta Note: Redmile/Sofinnova Convertible Loan Note has August 2023 conversion date, with a 15.5p conversion price, equating to a potential 96m of new shares.

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Disclaimer

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