

**REDX PHARMA PLC**  
**("Redx" or the "Company")**

**Redx Presents Encouraging Phase 1 Data for its Porcupine Inhibitor RXC004 in Patients with Advanced Solid Tumours**

*Clinical activity differentiated in tumours with Wnt-ligand dependence*

*Data presented at ESMO supports monotherapy Phase 2 start in H2 2021*

*Company to host R&D event on 11 October 2021*

**Alderley Park, UK, 20 September 2021** - Redx Pharma (AIM: REDX), the drug discovery and development company focused on cancer and fibrosis, today announces data from the monotherapy module of its Phase 1 clinical study of RXC004 for the first time. The data was presented at the European Society for Medical Oncology (ESMO) Congress 2021 by the study's lead investigator, Dr Natalie Cook, from the University of Manchester and Christie NHS Foundation Trust.

The Phase 1 trial ([clinicaltrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT03447470) NCT03447470) is evaluating RXC004, a wholly owned small-molecule Porcupine inhibitor as a monotherapy (Module 1) and in combination with nivolumab (Module 2) in unselected patients with advanced solid tumours for whom no standard therapy is available. The primary objective of the open label, '3+3' dose escalation Phase 1 study is to assess the safety and tolerability of RXC004 with secondary endpoints including pharmacokinetics (PK) and anti-tumour activity, as measured by Response Evaluation Criteria in Solid Tumours (RECIST 1.1). The data presented are from 25 patients in the completed monotherapy module of the trial and informed the selection of 2mg as the dose for the planned Phase 2 monotherapy trials testing RXC004 in three different Wnt-ligand dependent cancers.

**Dr Natalie Cook, Lead Investigator of the Study, from the University of Manchester and Christie NHS Trust, commented:** *"This Phase 1 study provides encouraging evidence of the potential of Porcupine inhibition as a targeted treatment approach and supports the progression of RXC004 into Phase 2 development in selected patients with Wnt-ligand driven cancers."*

**Lisa Anson, Chief Executive Officer of Redx Pharma, added:** *"The first clinical data on our Porcupine inhibitor, presented at the prestigious ESMO Congress, illustrate RXC004's potential to improve outcomes in patients with Wnt-ligand driven advanced solid tumours who have limited treatment options. RXC004 demonstrated a well-tolerated profile at the selected dose and showed differentiated signs of efficacy in Wnt-ligand dependent tumours. We are excited to move to Phase 2 later this year, with a larger number of patients with Wnt-ligand driven cancers, who represent those most likely to benefit from treatment with RXC004."*

**Key results presented at ESMO highlighted:**

- **RXC004 was safe and well tolerated as a single agent at doses up to 2mg** No grade 4 or 5 adverse events (AEs) were reported at these dose levels and the most common treatment-related AEs across all patients were fatigue (52% of patients), nausea (44%), decreased appetite (40%), dysgeusia ('altered taste') (40%) and vomiting (24%). RXC004, given at doses up to 2mg alongside denosumab prophylaxis, averted the bone toxicity traditionally associated with Wnt-pathway inhibition, as evidenced by the absence of both increases in the bone turnover marker  $\beta$ CTX and spontaneous fractures.
- **An oral dose of 2mg once daily is selected as the Phase 2 dose of RXC004 in monotherapy** The 2mg once-daily dose demonstrated high plasma exposure levels, while minimising adverse events. RXC004 exposures were dose proportional and median half-life was 14.5 hours. In addition, the pharmacodynamic marker of Axin-2 levels in skin showed active target engagement.
- **Efficacy data supports further investigation of RXC004 use in Wnt-ligand dependent tumours.** Although the study was not designed to assess efficacy as a primary endpoint, 18 patients had RECIST-evaluable disease. Of these patients:
  - o 7 patients had Wnt-ligand dependent tumours, defined as those having detectable ring-finger protein 43 (RNF43) Loss of Function or R-spondin (RSPO) fusion, biliary-tract cancers or thymus cancers; 6 patients had Wnt-ligand independent tumours, defined as those having no detectable RNF43 Loss of Function or RSPO fusion, or colorectal tumours with detectable downstream adenomatous polyposis coli (APC) mutations; 5 patients were of unknown Wnt-ligand status.
  - o At the data cut-off date on 30 July 2021, 5 of 7 patients (71%) with Wnt-ligand dependent tumours had durable RECIST stable disease (SD) versus 0 of 11 (0%) patients with independent or unknown Wnt-ligand status.
  - o Median treatment duration was 13.1 weeks (6.4 - 25.4 weeks) for patients with Wnt-ligand dependent tumours versus 6.6 weeks (5.4 - 7.3 weeks) for patients with either Wnt-ligand independent tumours or tumours of unknown Wnt-ligand status.

The results from the second module in the Phase 1 study testing RXC004 in combination with nivolumab (OPDIVO® - Bristol Myers Squibb, an anti-PD-1 antibody) are expected in H2 2021 and will be used to define a dose of RXC004 to be used in combination with standard dose nivolumab in a Phase 2 study in patients with genetically selected MSS mCRC.

A link to the presentation can be found here: <https://www.redxpharma.com/wp-content/uploads/2021/09/ESMO-Presentation-on-Redx-Website-1.pdf>

**Redx to host R&D Event**

Today's data will be discussed by Medical Experts during Redx's online R&D Event to be held on Monday 11 October 2021 at 1:00pm BST / 8.00am EDT. The event will also cover the Company's pipeline beyond RXC004.

To register for the event, please email [redxpharma@fticonsulting.com](mailto:redxpharma@fticonsulting.com)

**About the Phase 2 programme for RXC004**

Redx plans to commence a global Phase 2 monotherapy programme in three tumour types to assess RXC004 efficacy in patients with Wnt-ligand driven cancers. For patients with microsatellite stable metastatic colorectal cancer (MSS mCRC) only those with RNF43 mutations or RSPO fusions will be enrolled. For pancreatic cancer patients only those with RNF43 mutations will be enrolled. The third tumour type to be studied will be biliary-tract cancer, a tumour known to have high Wnt-ligand dependency which will enrol unselected patients. All three of these cancer types have high unmet need with limited treatment options and poor 5-year survival rates of less than 3% for biliary and pancreatic cancer and 14% for MSS mCRC. All three studies are planned to commence in H2 2021 and initial results are expected in 2022.

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**About RXC004**

RXC004 is a wholly owned, potent, selective, oral, small-molecule inhibitor of the Porcupine enzyme, a key activator of Wnt ligands in the Wnt-signalling pathway. The Wnt pathway is well established as a driver of both tumour growth and immune evasion. Aberrant Wnt signalling contributes directly to tumour growth and plays an important role in immune evasion, which has also been linked to resistance to immune-checkpoint inhibitors (ICIs) such as nivolumab. By selecting patients with tumours that have high Wnt-ligand dependency, such as tumours with mutations in the RNF43 gene and fusions in the RSPO gene family, RXC004 has an opportunity to both directly inhibit the tumour growth and have an immune-enhancing effect to allow the patient's immune system to better recognise and attack the tumour.

ICIs such as anti-PD-1 antibodies have revolutionised the treatment of cancer, but do not work in all patients. Wnt-pathway activation can enhance the ability of the tumour to evade destruction by the immune system and has been linked to lack of response to ICIs in these tumours. Redx scientists have demonstrated preclinically that RXC004 can block activation of the Wnt pathway and restore the ability of the immune system to fight the tumour. Thus, RXC004 offers potential as a monotherapy or combination therapy with ICIs.

**About Redx Pharma Plc**

Redx Pharma (AIM: REDX) is focused on the discovery and development of novel targeted medicines for the treatment of cancer and fibrotic diseases, aiming initially to progress them to clinical proof of concept, before evaluating options for further development and potential value creation. Redx's lead oncology asset, the Porcupine inhibitor RXC004, is expected to commence a Phase 2 programme in H2 2021. The Company's selective ROCK2 inhibitor, RXC007, is in development for idiopathic pulmonary fibrosis and commenced a Phase 1 clinical study in June 2021 for which results are expected in 2022.

The Company has a strong track record of discovering new drug candidates through its core capability of converting medicinal chemistry insights into differentiated and commercially attractive drug candidates, with five proprietary or partnered assets in late pre-clinical or clinical development. One of those assets, a BTK inhibitor - pirtobrutinib/LOXO 305 - was sold to Loxo Oncology (now Eli Lilly) and is currently in Phase 3 clinical studies in chronic lymphocytic leukaemia. In addition, Redx has forged pre-clinical asset partnerships with other blue chip companies including AstraZeneca and Jazz Pharmaceuticals.

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