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

Redx Announces RXC004 Phase 2 Studies Will Open Patient Enrolment for Combination Arms with Immune Checkpoint Inhibitors

Phase 1 data from the study of the porcupine inhibitor in combination with an anti-PD-1 antibody presented at Society for Immunotherapy of Cancer Conference

Alderley Park, UK, 10 November 2022 Redx (AIM:REDX), the clinical-stage biotechnology company focused on discovering and developing novel, small molecule, highly targeted therapeutics for the treatment of cancer and fibrotic disease, today announces that the ongoing Phase 2 clinical studies of RXC004 will open enrolment into the combination arms, where RXC004 will be combined with immune checkpoint inhibitors (ICIs). The PORCUPINE study of RXC004 in genetically selected patients with microsatellite stable metastatic colorectal cancer (MSS mCRC) will open a combination arm with nivolumab (OPDIVO® - Bristol Myers Squibb, an anti-PD-1 antibody) and PORCUPINE 2 in patients with biliary tract cancer will open a combination arm with pembrolizumab (KEYTRUDA® - MSD International Business GmbH, an anti-PD-1 antibody). The recommended RXC004 dose for both combination arms is 1.5mg once daily. Results from these open label Phase 2 studies are expected from H1 2023.

The poster, presented today, at the Society for Immunotherapy of Cancer (SITC) Conference (8- 12 Nov Boston, MA, USA) provided encouraging data from the combination module ("Module 2") of the Phase 1 clinical study of RXC004 with nivolumab. Results from the monotherapy module ("Module 1") of the study were previously presented at the European Society of Medical Oncology (ESMO) Congress in September 2021[1].

Tumour-derived Wnt-ligand signalling is implicated in reduced intrinsic and adaptive resistance to ICI therapy in multiple cancers[2][3][4]. Inhibition of Wnt-ligand signalling can enhance ICI efficacy by reversing dendritic cell tolerisation, decreasing Treg cells, and reducing the recruitment of myeloid-derived suppressor cells[5]. RXC004 can reverse immune evasion in mouse tumour models and has potential for clinical synergy with anti-PD-1 therapies[6].

Lisa Anson, Chief Executive Officer of Redx Pharma, said: *"The poster presented today shows RXC004 to have a manageable tolerability profile in combination with nivolumab for Wnt-ligand dependent tumours, and a PK profile supporting once daily dosing. We are pleased that the data support our decision to open the combination arms of the Phase 2 proof-of-concept studies to understand the potential efficacy of RXC004 in combination with PD-1 inhibitors., This is an exciting development, which may open up new treatment options for patients with a very poor prognosis. We look forward to reporting initial headline data from our Phase 2 programme from H1 2023."*

Dr Natalie Cook, Lead Investigator of the Study, from the University of Manchester and Christie NHS Trust, commented: *"The Phase 1 study results from RXC004 in combination with a standard dose of the PD-1 inhibitor, nivolumab, presented today at SITC are consistent with the previously presented Phase 1 results of RXC004 as monotherapy. Together, these data support the continued clinical development of RXC004 - both as monotherapy and in combination with checkpoint inhibitors - as a potential targeted treatment in selected patients with Wnt-ligand dependent cancers."*
The Phase 1 trial (clinicaltrials.gov NCT03447470) evaluated RXC004, a highly potent, selective and orally active Porcupine inhibitor as a monotherapy (Module 1), and in combination with the approved dose of 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 was to assess the safety and tolerability of RXC004 with additional endpoints including pharmacokinetics (PK), pharmacodynamic effects on peripheral immune cells and preliminary anti-tumour activity, as measured by Response Evaluation Criteria in Solid Tumours (RECIST 1.1). The data presented at the SITC conference were from 13 patients who completed Module 2, up to 18 October 2022. Previously 25 patients completed Module 1 and the

results, which were reported at ESMO 2021, supported commencement of the ongoing monotherapy arms of the Phase 2 Programme.

Key results presented at the SITC conference highlighted:

RXC004 at doses of 1mg and 1.5mg once daily in combination with standard dose nivolumab had a manageable tolerability profile, with a pharmacokinetic profile supporting once daily dosing. The treatment related adverse event profile reported for Module 2 was similar to that previously reported from Module 1, with fatigue, nausea, dysgeusia ('altered taste') and decreased appetite being reported most frequently. While the per-protocol Phase 2 dose for RXC004 monotherapy is 2mg, RXC004 doses higher than 1.5mg were not explored in Module 2 because of the potential for overlapping toxicity of colitis, which was reported in Module 1, and is a known adverse effect of immune checkpoint inhibitors. As in Module 1, the treatment combination was administered alongside denosumab prophylaxis which, together with the low dose of this potent molecule, averted the bone toxicity traditionally associated with Wnt pathway inhibition.

Preliminary efficacy data from Module 2 supports continued investigation of combination of RXC004 at 1.5mg dose once daily with checkpoint inhibitors. At the cut-off date, 10 out of the 13 unselected patients in Module 2 had RECIST-evaluable disease. Of these, 4/6 patients[7] in the 1.5mg RXC004 cohort had RECIST stable disease as best response. Analysis of blood samples from some patients on treatment indicated changes in peripheral immune cell compartments consistent with those seen in preclinical models and were suggestive of an anti-tumour immune response. Of note, CD8+ T-cell proliferation increased in some patients and was more pronounced in patients with stable disease. This observation is reported to correlate with improved response to immune checkpoint inhibitors[8]. This effect will be further investigated in the Phase 2 programme in recurrent MSS mCRC and biliary tract cancers, where immune checkpoint inhibitors alone are ineffective.

About the Phase 2 programme for RXC004

RXC004 entered Phase 2 clinical trials in November 2021. The first study in the Phase 2 programme, PORCUPINE, (clinicaltrials.gov NCT04907539) is focused on patients with advanced MSS mCRC who have progressed following treatment with standard of care and is evaluating preliminary efficacy and safety of RXC004 in genetically selected patients with Ring finger protein 43 (RNF43) or R-spondin (RSPO) aberrated, advanced MSS mCRC. Given the dual mechanism of action of RXC004, which preclinically was shown to inhibit tumour growth and immune evasion, there is a strong rationale for immune therapy combination in the MSS mCRC setting, and the second module of the trial will evaluate RXC004 in combination with nivolumab, a PD-1 inhibitor. This combination module is now approved by the FDA, which will allow patient recruitment to commence in US trial centres. A second Phase 2 study of RXC004, PORCUPINE2, (clinicaltrials.gov NCT04907851), as a monotherapy for genetically selected pancreatic cancer and unselected biliary cancer, a highly Wnt-ligand dependent cancer, commenced in January 2022, and a second arm of the biliary cancer module will evaluate RXC004 in combination with pembrolizumab, a PD-1 inhibitor. Redx expects to report topline data readouts from the Phase 2 programme starting in the first half of 2023.

Additional data presented at SITC by the Garvan Institute of Medical Research

In addition, a second poster on RXC004 was presented at SITC by Redx's collaboration partner, Associate Professor Marina Pajic of the Garvan Institute of Medical Research in New South Wales, Australia. The poster was titled, *"Effective Co-targeting of Fibrotic and Immune Microenvironments to Improve the Overall Anti-tumour Response in Models of Advanced Pancreatic Cancer"* and demonstrated the therapeutic potential of RXC004 (PORCUPINE inhibitor) and a ROCK2 selective inhibitor, in targeting fibrosis associated with pancreatic cancer. The data showed an increased survival in mouse models and highlights the potential of RXC004 to modulate the tumour immune environment of pancreatic cancers.

A copy of both posters will be made available on the Company's website at: https://www.redxpharma.com/scientific-publications/

For further information, please contact:

Redx Pharma Plc T: +44 (0)1625 469 918
UK Headquarters
Caitlin Pearson, Head of Communications

ir@redxpharma.com

Lisa Anson, Chief Executive Officer

US Office
Peter Collum, Chief Financial Officer

SPARK Advisory Partners (Nominated Adviser) T: +44 (0)203 368 3550
Matt Davis/ Adam Dawes

WG Partners LLP (Joint Broker) T: +44 (0)203 705 9330
Claes Spång/ Satheesh Nadarajah/ David Wilson

Panmure Gordon (UK) Limited (Joint Broker) T: +44 (0)207 886 2500
Rupert Dearden/ Freddy Crossley/ Emma Earl

FTI Consulting T: +44 (0)203 727 1000
Simon Conway/ Ciara Martin

About Redx Pharma Plc

Redx Pharma (AIM: REDX) is a clinical-stage biotechnology company focused on the discovery and development of novel, small molecule, highly targeted therapeutics 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 product candidate, the Porcupine inhibitor RXC004, being developed as a targeted treatment for Wnt-dependent cancers, commenced a Phase 2 programme in November 2021. The Company's lead fibrosis product candidate, the selective ROCK2 inhibitor RXC007, is in development for interstitial lung disease and commenced a Phase 2a trial for idiopathic pulmonary fibrosis in October 2022. Redx's third drug candidate, RXC008, a GI-targeted ROCK inhibitor for the treatment of fibrostenotic Crohn's disease, is currently in pre-IND stage, with Phase 1 clinical studies expected to commence in 2023.

The Company has a strong track record of discovering new drug candidates through its core strengths in medicinal chemistry and translational science, enabling the Company to discover and develop differentiated therapeutics against biologically or clinically validated targets. The Company's accomplishments are evidenced not only by its two wholly-owned clinical-stage product candidates and rapidly expanding pipeline, but also by its strategic transactions, including the sale of pirtobrutinib (RXC005, LOXO-305), a BTK inhibitor now in Phase 3 clinical development by Eli Lilly following its acquisition of Loxo Oncology and AZD5055/RXC006, a Porcupine inhibitor targeting fibrotic diseases including idiopathic pulmonary fibrosis (IPF), which AstraZeneca is progressing in a Phase 1 clinical study. In addition, Redx has forged collaborations with Jazz Pharmaceuticals, which includes JZP815, a pan-RAF inhibitor developed by Redx which Jazz is now progressing through Phase 1 clinical studies and an early stage oncology research collaboration.

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[1] Cook et al, 2021, ESMO Annual Congress

[2] Spranger and Gajewski 2018 Nat Rev Cancer. 18(3): 139-147

[3] Rodriguez et al 2018 Rodriguez-Pascual et al . Cancer Drug Resist 2019;2:980-93

[4] Luke et al 2019, Clin. Cancer Res. 25(10):3074-3083

[5] Devito et al, 2021 Cell Reports 35, 109071, May 4, 2021

[6] Phillips et al, 2022, Cancer Res Commun. 2(9):914-928.

[7] One patient each with: signet cell rectal cancer (loss of function mutation; ring finger protein 43), pleural epithelioid mesothelioma, malignant pulmonary cylindroma, recurrent solitary fibrous tumour of pleura

[8] Huang et al. 2017, Nature, 545; 60-65.

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