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

Redx Signs Clinical Trial Collaboration and Supply Agreement with MSD to evaluate RXC004 in combination with KEYTRUDA® (pembrolizumab) in PORCUPINE2 Study in Biliary Cancer

Alderley Park, UK, 16 December 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, announces that the Company has entered into a clinical trial collaboration and supply agreement with MSD (Merck & Co., Inc., Rahway, NJ, USA), for the supply of KEYTRUDA® (pembrolizumab), MSD's anti-PD-1 therapy, to be used in the combination arm of Redx's ongoing PORCUPINE2 Phase 2 clinical study evaluating RXC004 as a potential treatment for patients with biliary cancer.

RXC004, Redx's lead oncology asset, is being developed as a targeted treatment for Wnt-ligand dependent tumours. It is a potent, selective, oral, small-molecule inhibitor of the Porcupine enzyme, a key activator of Wnt-ligands in the Wnt signalling pathway. RXC004 is being investigated both as a monotherapy treatment and in combination, where RXC004 will be combined with immune checkpoint inhibitors (ICIs).

Biliary cancer is known to be heavily reliant upon Wnt signalling, with over 70%[1] of biliary cancer patients showing high Wnt-ligand expression, potentially making this indication highly sensitive to the benefits of Porcupine inhibition. 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]. It has been shown that RXC004 can reverse immune evasion in mouse tumour models and therefore there may be an additive benefit when given in combination with ICI therapies[6] such as pembrolizumab.

Professor Juan Valle, Professor and Honorary Consultant in Medical Oncology, University of Manchester & The Christie NHS Foundation Trust and RXC004 PORCUPINE2 Chief Investigator commented: *"Currently, advanced biliary cancer has only a 2% 5-year survival rate, with a critical unmet need for additional treatment options. It is important to study agents such as the Porcupine inhibitor RXC004, which may sensitise some types of tumours to ICI therapies, in an effort to find effective treatment combinations that may improve outcomes for these patients, who have a particularly poor prognosis."*

Dr Jane Robertson, Chief Medical Officer, Redx Pharma commented: *"We are delighted to enter into a collaboration agreement with MSD for our ongoing PORCUPINE2 study to evaluate RXC004 in combination with their anti-PD-1 therapy, pembrolizumab. Biliary cancer is a devastating disease that is heavily reliant on Wnt signalling, so we are keen to explore the potential of combining RXC004 with ICIs. Our hypothesis, based on the preclinical data we have generated, is that when combined, there may be a greater chance of the patients showing an immune response, which we hope will lead to improved outcomes."*

About the RXC004 Phase 2 Clinical Trial Programme

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 microsatellite stable metastatic colorectal cancer (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. A second Phase 2 study of RXC004, PORCUPINE2, (clinicaltrials.gov NCT04907851), as a monotherapy for genetically selected pancreatic cancer and biliary cancer, a highly Wnt-ligand dependent cancer, commenced in January 2022.

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 November 2022, Phase 1 clinical data evaluating the safety and tolerability of RXC004 in combination with nivolumab, in patients with advanced malignancies was presented as a poster at the Society of Immunotherapy of Cancer (SITC) Conference. The data was suggestive of an anti-tumour immune response, which is reported to correlate with an improved response to PD-1 immune checkpoint inhibitors. The results of the study supported a dose selection of 1.5mg once daily to be used in combination modules of both PORCUPINE and PORCUPINE2.

The combination module of the PORCUPINE trial will evaluate RXC004 in combination with nivolumab, (OPDIVO® - Bristol Myers Squibb, a PD-1 inhibitor) and this module is now approved by the FDA, which will allow patient recruitment to commence in US trial centres. The second module of the PORCUPINE2 study, (clinicaltrials.gov NCT04907851), will evaluate RXC004 in combination with pembrolizumab (KEYTRUDA® - MSD's anti-PD-1 therapy) in biliary cancer. Redx expects to report topline data readouts from the Phase 2 programme starting in the first half of 2023.

KEYTRUDA® is a registered trademark of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, U.S.A.

[1] Loilome et al. 2014, Boulter et al. 2015

[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.

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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 (IPF) 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 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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