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REDX PHARMA LIMITED

("Redx" or the "Company")

Redx Reports Encouraging Zamaporvint (RXC004) Phase 2 Combination Data in MSS mCRC at ESMO GI Congress Supporting Genetic Selection Hypothesis in Hard-to-Treat GI Cancers

Zamaporvint in combination with anti-PD-1, in genetically-selected MSS mCRC patients led to partial responses being observed in ~30% patients, potentially higher than current SOC and in a setting where anti-PD-1 therapy alone is not effective

Data supports genetic selection of patients in hard-to-treat GI cancers

Alderley Park, UK, 28 June 2024 Redx Pharma (JPJ:REDX), the clinical-stage, small molecule biotechnology company, announced data from all Phase 2 clinical trial modules of zamaporvint (RXC004), a potent, selective, orally-active Porcupine inhibitor in development for Wnt-ligand dependent, hard-to-treat GI cancers at the European Society for Medical Oncology Gastrointestinal Cancers (ESMO GI) Congress.

These data were from small, signal searching patient cohorts in the PORCUPINE study, investigating genetically-selected patients (RNF43_mutant/RSPO-fusion subgroup) with microsatellite stable metastatic colorectal cancer (MSS mCRC) as monotherapy and in combination with anti-PD-1 (NCT04907539); and the PORCUPINE2 study investigating all-comers biliary tract cancer (BTC) as monotherapy and anti-PD-1 combination, as well as genetically-selected pancreatic cancer as monotherapy (NCT04907851).

Natalie Cook, Chief Investigator for the zamaporvint Study Programme commented: "It is very encouraging to see the data returned from this signal-searching study. The indications targeted are in populations with a particularly poor prognosis and limited treatment options. Wnt inhibition has long held promise for this genetically-selected patient group and a tolerable, clinically active Porcupine inhibitor in combination with anti-PD-1 could potentially offer a new treatment option for patients with these particularly hard to treat cancers."

Dr. Helen Timmis, Interim Chief Medical Officer, Redx Pharma commented: "We are delighted to report the Phase 2 data from our zamaporvint study programme which shows a disease control rate of 57% including partial responses in ~30% of the patients treated with zamaporvint in combination with nivolumab in MSS mCRC. Real world evidence shows that the prognosis for the RNF43/RSPO mutant subgroup of MSS mCRC is significantly worse than in MSS mCRC patients without these Wnt aberrations, where outcomes are already poor. This early signal indicates that, in the right patient groups, the combination of Porcupine and immune checkpoint inhibition has the potential to provide a much-needed improvement on the current standard of care."

Zamaporvint has been shown to have a tolerable safety profile and is the first Porcupine inhibitor to demonstrate efficacy across this hard-to-treat RNF43/RSPO patient subgroup. Partial responses observed in ~30% (2/7) of genetically-selected patients when combined with nivolumab in the PORCUPINE MSS mCRC module is encouraging in a late-line patient population who have previously undertaken a median of two prior lines of therapy, and where anti-PD-1 alone is not effective[1]. This suggests activity levels potentially better than late-line standard of care in this setting[2]. Furthermore, a disease control rate ≥16 weeks of 57% (4/7), higher than zamaporvint monotherapy at 15% (2/13), indicates the potential for zamaporvint in combination with immune checkpoint inhibition to drive durable efficacy outcomes. Consistent with this,

robust metabolic (FDG-PET) and molecular (ctDNA) responses were observed in all patients that achieved disease control (partial response or stable disease) following zamaporvint treatment with or without nivolumab.

The results from the PORCUPINE2 study also showed some durable clinical benefit in the BTC module in an all-comers (unselected) patient group, albeit at a lower level than that observed in genetically-selected MSS mCRC. In the RNF43 mutated pancreatic ductal adenocarcinoma (PDAC) cohort, although one partial response was observed in the monotherapy module, participant numbers in the present study are too low to support any conclusion on efficacy. However, further investigator sponsored studies in this indication are being planned.

In both the PORCUPINE and PORCUPINE2 studies all patients received prophylactic denosumab that successfully prevented any treatment related bone effects, a known effect of Wnt inhibition.

Overall, the data from these signal searching studies show enhanced activity of zamaporvint within the RNF43/RSPO MSS subgroup of GI cancers. Furthermore, they support clinical development in this subgroup in combination with anti-PD-1 where we see an exciting opportunity for Wnt pathway inhibition by zamaporvint to reverse innate anti-PD-1 resistance.

Other rational zamaporvint combination opportunities to enhance patient benefit, such as with early line chemotherapies or with EGFR/MAPK pathway inhibitors, also exist in wider GI cancer patient populations. Redx is seeking a partner to support ongoing clinical development.

A copy of both posters is available on the Company website at: https://www.redxpharma.com/scientific-publications/

About zamaporvint

Zamaporvint (RXC004), is a potent, selective, oral small molecule inhibitor of the enzyme, Porcupine, a key activator of Wnt-ligands in the Wnt signalling pathway. Aberrant Wnt signalling contributes directly to tumour growth and plays an important role in immune resistance to treatment with immuno-oncology agents such as anti-PD-1 checkpoint inhibitors.

Wnt-ligand activation is common in GI cancers and by selecting patients with tumours that have high Wnt-ligand dependency, such as tumours with mutations in the RNF43 gene or fusions in the RSPO gene family, zamaporvint has an opportunity to directly target tumours in addition to potentially reversing or delaying resistance to multiple conventional and targeted cancer therapies.

About the PORCUPINE Clinical Study

PORCUPINE, (clinicaltrials.gov NCT04907539) is focused on genetically-selected patients with aberrated, advanced MSS mCRC with a histologically confirmed Ring finger protein 43 (RNF43) or R-spondin (RSPO) mutations who have progressed on more than one prior standard of care treatment. RNF43/RSPO mutations account for a particularly complex and difficult to treat patient population with an especially poor prognosis and limited treatment options. Given the dual mechanism of action of zamaporvint, which preclinically was shown to inhibit both tumour growth and immune evasion, there is a strong rationale for immune therapy combination in the MSS mCRC setting and zamaporvint was evaluated in combination with nivolumab, a PD-1 inhibitor, as well as a single agent monotherapy.

25 patients were enrolled with a median of two prior lines of therapy, with 13/17 being efficacy evaluable from Arm A (zamaporvint monotherapy; 2mg QD) and 7/8 patients being efficacy evaluable from Arm B (zamaporvint (1.5mg QD) in combination with nivolumab).

About the PORCUPINE2 Clinical Study

PORCUPINE2, (clinicaltrials.gov NCT04907851), evaluated zamaporvint as a monotherapy in patients that had histologically-confirmed RNF43 mutated pancreatic ductal adenocarcinoma (PDAC), or evaluated zamaporvint in patients

that had molecularly-unselected biliary tract cancer (BTC; a highly Wnt-ligand expressing cancer) that had progressed after 1st line treatment, as either monotherapy and in combination with pembrolizumab, a PD-1 inhibitor.

45 patients were enrolled, with Module 1 being PDAC patients with a confirmed RNF43_LoF mutation (M1: N=6), and Modules 2 and 3 being BTC (M2: N=20, M3: N=19). Patients received zamaporvint monotherapy in M1 and M2 (2mg QD) or in combination with pembrolizumab for M3 (1.5mg QD). Of the 45 patients enrolled, 37 were efficacy evaluable.

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About Redx Pharma Limited

Redx Pharma (JPJ: REDX) is a clinical-stage biotechnology company focused on the discovery and development of novel, small molecule, targeted therapeutics for the treatment of fibrotic disease, cancer and the emerging area of cancer-associated fibrosis. Redx aims to progress its programmes to clinical proof of concept before evaluating options for further development and potential value creation. The Company is currently progressing an industry leading ROCK inhibitor portfolio through the clinic, including zelasudil, a selective ROCK2 inhibitor for the treatment of interstitial lung diseases including idiopathic pulmonary fibrosis and RXC008, a GI-targeted pan-ROCK inhibitor for the treatment of fibrostenotic Crohns disease. Additionally, the Company has a Phase 2 precision oncology programme, zamaporvint, which it intends to partner for further development.

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. To date, six Redx discovered molecules have been progressed into the clinic with the Company's accomplishments evidenced not only by its wholly-owned clinical-stage product candidates and discovery pipeline, but also by its strategic transactions, which includes the sale of pirtobrutinib (RXC005, LOXO-305), the only non-covalent or reversible BTK inhibitor now approved by the US FDA, and transactions with both AstraZeneca and Jazz Pharmaceuticals.

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[1] Le et al (2015)

[2] (Fruquintinib ORR 1.5% [FRESCO]; trifluridine/tipiracil + bevacizumab ORR 6.1% [SUNLIGHT]).

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