Redx Pharma Announces Way Forward For RXC004

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Redx (AIM: REDX), the drug development company focused on cancer and fibrosis, announces that having presented an amended study protocol to the Medicines and Healthcare products Regulatory Agency (MHRA, "the Agency"), the Agency has agreed, in principle, with the proposed re-start of the Company's phase 1/2a clinical study for the Porcupine inhibitor, RXC004. Redx will now work with the investigators to finalise this protocol, with the intention of restarting dosing of patients in the first half of 2019.

Based on a thorough analysis of the data from the only patient in the currently suspended trial, Redx, together with the study investigators, believe that the desired systemic exposure, with the potential for clinical benefit[1], can now be achieved using a significantly lower starting dose, with subsequent dose-escalation. Following a positive meeting with the Company, the MHRA has agreed, in principle, with this newly proposed starting dose and revised protocol, including enhanced safety monitoring.

Porcupine is a recognized drug target on the Wnt cell signaling pathway. There is now strong evidence that this pathway plays a key role in how tumours avoid detection by the patient's own tumour fighting immune cells, tumours of this type have been termed "cold" tumours. Scientists at Redx have demonstrated the ability of RXC004 to enhance the host's immune system response to cancer in preclinical models, turning these cold tumours into "hot" tumours. The Company confirms it aims to position RXC004 as a potentially attractive combination partner for immune-oncology agents e.g. anti-PD1 (immune checkpoint inhibitors) in cancers where they currently have clinical benefit in only a small percentage of patients e.g. colorectal cancer.

Lisa Anson, Chief Executive Officer commented: "I am pleased to announce that Redx has held a positive meeting with the MHRA in which the Agency agreed, in principle, with a revised protocol for restarting our previously suspended RXC004 phase 1/2a trial. Importantly this new protocol includes a significantly lower starting dose followed by carefully monitored dose-escalation. We look forward to submitting our final protocol amendments, with the aim of initiating the next patient in the first half of 2019. I would like to thank my colleagues at Redx and our clinical

investigators for all their hard work that has resulted in our Phase 1/2a proposal being positively received by the MHRA.

“I would also like to confirm that our aim at the next stage of clinical testing will be to focus on RXC004 in combination with immune-oncology agents in solid tumours e.g. colorectal cancer patients.”

Natalie Cook, Consultant Oncologist and Principal Investigator from the Christie Hospital in Manchester commented: “We have learnt a significant amount from the data of the first patient, and this provides the basis for an optimised RXC004 development plan and confidence to evaluate the clinical potential of RXC004 in cancer patients.”

RXC004 and the Clinical Programme

RXC004 is a novel, oral, potent small molecule Porcupine inhibitor, which targets the Wnt pathway. The Wnt pathway is an embryonic signalling pathway that is implicated in the maintenance of cancer stem cells in multiple cancer types. This pathway is associated with tumorigenesis, metastasis, recurrence and resistance in cancer.

The first-in-man clinical trial for this drug is a modular, multi-arm, multi-part, Phase 1/2a, adaptive design study whose primary objective is to evaluate the safety and tolerability of the drug in patients with advanced malignancies. It is anticipated that a total c.50 patients will be enrolled. (ClinicalTrials.gov Identifier: NCT03447470). In the first part of the study patients are allocated to a dose and followed for a period of time for potential dose limiting toxicities. Under the proposed amended protocol patient dosing will be recommenced at 0.5mg as opposed to the original starting dose of 10mg. Once this period is complete the protocol dictates that the next arm of the study will be at a higher dose until a maximum tolerated dose is reached.

As previously announced, Redx Pharma suspended recruitment of patients to its phase 1/2a clinical study for RXC004 in March 2018 following dosing of the first patient. This was due to the observation of clinically significant adverse events, which were believed to be related to the on-target effects of RXC004 on the inhibition of the Wnt pathway. Further analysis of clinical data from this first patient indicates that their systemic RXC004 exposure was significantly higher than that predicted from pre-clinical animal studies. While the maximum plasma concentration of the drug (C_{max}) was in line with expectations, the terminal half-life of the drug ($t_{1/2}$) was significantly longer than that predicted from such animal models, due to the actual rate of elimination being lower. The Company believes that higher drug exposure in humans compared to pre-clinical studies is not uncommon in the field of drug

development. It typically arises from differences between the metabolism observed in the animals used in pre-clinical models on translating potential medicines into humans for the first time.

On successful completion of this initial phase 1 monotherapy study, RXC004 has the potential to be developed in two distinct cancer treatment settings with major unmet medical need based on two distinct mechanisms of action, as well as having pre-clinical data suggesting an anti-fibrosis action.

Emerging data shows that Wnt is critical to the immune environment and targeting the Wnt pathway is a recognised and important mechanism to activate the immune system and may convert immune “cold” tumours into immune “hot” tumours facilitating response to immune-oncology agents. This may make RXC004 an attractive combination partner for immune-oncology agents e.g. anti-PD1 (immune checkpoint inhibitors) in cancers where they currently have modest clinical benefit e.g. colorectal cancer.

Additionally, and separately, targeting tumours with specific Wnt pathway alterations may offer clinical benefit on exploiting RXC004 as both monotherapy, and in combination with standard of care treatments, in tumours where such genetic alterations occur most commonly e.g. Pancreatic, colorectal, gastric and castrate-resistant prostate cancer.

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About Redx Pharma Plc

Redx is a UK biotechnology company whose shares are traded on AIM (AIM:REDX). Redx's vision is to become a leading biotech focused on the development of novel precision medicines that have the potential to transform treatment in oncology and fibrotic diseases.

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[1] The primary objective of the study remains the safety and tolerability of the drug