Preclinical data evaluating RXC004 presented at the NCRI cancer conference

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

Alderley Park, 5 November 2018. Redx (AIM: REDX), the drug development company focused on cancer and fibrosis, is pleased to announce the presentation of positive data from preclinical studies evaluating RXC004 during a poster session, entitled 'Efficacy of the Porcupine inhibitor RXC004 in genetically-defined tumour types' today at the National Cancer Research Institute (NCRI) 2018 Cancer Conference in Glasgow. RXC004 is a novel, oral, potent small molecule Porcupine inhibitor, which targets the Wnt/β-catenin pathway. It is expected to re-enter the clinic in H1 2019 in a Phase 1/2a study in patients with advanced malignancies.

The full abstract of the presentation can be found below:

Richard Armer, Chief Scientific Officer commented: "*We are delighted to showcase some of the fantastic science happening at Redx. We are encouraged by the preclinical data presented at the NCRI, which demonstrates the exquisite sensitivity of specific genetically defined cancer models to our Porcupine inhibitor, RXC004. The strength of these data highlight some of the broad and multiple options available for the future development of this programme as we look to re-enter the clinic in the first half of 2019.*"

NCRI 2018 Abstract

Background

Potent and selective porcupine (PORCN) inhibitor RXC004 is being investigated in a Phase 1 clinical trial (NCT03447470). PORCN is a membrane bound O-acyltransferase responsible for post-translational modification of Wnt ligands, essential for Wnt secretion and activity. Wnt pathway alterations, including RNF43 loss-of-function mutations and RSPO fusions, result in increased levels of surface Fzd receptors, increasing Wnt-ligand dependent signalling. These alterations are implicated in colorectal, gastric, pancreatic and biliary cancer. This work assesses the direct tumour targeting effects of RXC004 in genetically selected cancer lines in vitro and in vivo.

Method

RXC004 was evaluated in 2D and/or 3D in vitro proliferation assays across a panel of colorectal and pancreatic cancer cell lines. In parallel, cell cycle analysis was assessed using flow cytometry. Downstream markers of target engagement for the Wnt pathway, Axin2 and c-Myc, were analysed for mRNA expression using qPCR. RXC004 was orally dosed for efficacy, PK and PD studies in RNF43 mutant and RSPO fusion xenograft models.

Results

RXC004 potently inhibited proliferation in vitro in several genetically selected cell lines. Mechanistically RXC004 arrested the cell cycle at the G1/S and G2/M cell cycle checkpoints. Axin2 mRNA expression was potently inhibited by RXC004 (sub-nM) across all RNF43 mutant and RSPO fusion cell lines tested. Furthermore, inhibition of c-Myc expression correlated with the anti-proliferative effects of RXC004. In contrast, RXC004 had no anti-proliferative effects on APC mutant colorectal cancer cells, and Axin2 and c-MYC expression was not inhibited. In vivo, RXC004 demonstrated significant efficacy and PD responses in multiple RNF43 mutant and RSPO fusion xenograft models.

Conclusion

Cancer cells carrying RNF43 mutations or RSPO fusions are sensitive to RXC004 both *in vitro* and *in vivo*. This data suggest RXC004 monotherapy would benefit patients with tumours baring RNF43 mutations or RSPO fusions and support a genetically-defined patient selection strategy for ongoing RXC004 clinical studies.

The poster, entitled ‘Efficacy of the Porcupine inhibitor RXC004 in genetically-defined tumour types’ presented at the National Cancer Research Institute (NCRI) 2018 Cancer Conference in Glasgow, UK, can be accessed here from **noon GMT on 5th November 2018**:

Efficacy of the Porcupine inhibitor RXC004 in genetically-defined tumour types

To learn more about our RXC004 inhibitor programme you can visit: https://www.redxpharma.com/programmes/rxc004-porcupine-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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