**INTRODUCTION**

ROCK2 is a nodal point in cell signalling pathways associated with fibrotic diseases

- ROCK inhibitor PoC in human IPF trial
- Clinical response in lung scars in cLiILD
- ROCK2-protected lung fibrosis
- ROCK2 inhibitor = efficacy across multiple organs in GSD8 animal model
- ROCK2 inhibitors = efficacy in skin (dfs) model
- ROCK2 conditional KO = ↓ hypertension, hypertrophy & atherosclerosis

**RESULTS**

**ROCK2 selective inhibitors for the treatment of fibrosis**

Nicolas E.S. Guisot; Peter Bunyard; Phillip MacFaul; Emily P. Offer; Katie Anderson; Stuart A. Best; Matthew R. Box; Sara Ceccarelli; Amy Cooke; Charles Crossland; Gayle E. Douglas; Camille Gignoux; Neil Hawkins; Rebecca Holland; Alison Hunter; Paula Jackson; Clifford D. Jones; Rosie Knowles; Jean-Francois Margathe; Sam M. Smith; Richard Armer.

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**REDX10843 reverse the myofibroblast phenotype of activated human hepatic stellate cell myofibroblasts**

**REDX10843 reduces kidney tubular damage and fibrosis in UUO model**

**REDX10843 suppresses fibrosis in murine bleomycin-induced IPF model**

**REDX10843 suppresses fibrosis in murine STAM NASH liver model**

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**SUMMARY**

- Redx developed a series of compounds that are potent ROCK2 inhibitors in biochemical & cellular in vitro assays and highly selective against ROCK1 and a panel of kinases and other receptor targets.
- Demonstration that physiologically relevant ROCK2 inhibitors fibrotic pathways can be modulated in vivo in disease relevant phenotypic assays.
- No safety concerns highlighted from early in vitro assessment (HERG, CERP, AMEL, micromuscle, CYP inhibition, CYP 450, reaction phenotyping).

- Reduced pretclinal efficacy demonstrated with REDX10843, a lead from the series, in murine liver, kidney and lung fibrosis models.

- Reticular fibroblasts produce and deposit collagen III in the liver, positive cells determined by automated quantification
- Significant reduction of pro-fibrotic fibroblasts in the liver when REDX10843 dosed QD or BID
- Significant reductions in both liver collagen quantity and bridging fibrosis with QD and BID dosing.