RXCO07, a Potent, Highly Selective ROCK2 Inhibitor, Demonstrates Preclinical Efficacy Across Fibrosis Models and Good Phase 1 Safety Profile, Supporting Development in IPF and ILD

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ROCK and ROCK2 Pathway

- ROCK is a kinase that links numerous fibrotic signalling pathways to pro-fibrotic gene expression
- ROCK is involved in diverse cellular processes
- Upregulation of these genes leads to actin cytoskeleton organisation, cell adhesion and motility, proliferation, and extracellular matrix remodelling

Preclinical Murine Validation of ROCK2 Inhibition

- Haploinsufficient ROCK1, ROCK2 and ROCK1/ROCK2 mice show reduced hydroxyproline expression in bleomycin induced lung fibrosis at day 14
- Similar reduction in SMA expression in fibroblasts is observed in the 3 haploinsufficient phenotypes

RXCO007 reduces fibrosis and collagen deposition in a therapeutic murine bleomycin-induced lung fibrosis model

- Significant reduction in collagen content and collagen deposition in the skin following administration of RXCO007
- Similar effect on the cutaneous cGVHD score between nintedanib and RXCO007
- Significant reduction of fibrosis score and collagen content in the lungs around the bronchioles following administration of RXCO007

Summary

- RXCO007 is a highly potent, selective and orally-active ROCK2 inhibitor
- ROCK2 is a validated, compelling target at a key junction in cell signalling pathways central to fibrosis
- Robust preclinical efficacy data across disease model supports clinical development plan in lung fibrosis - IPF and cILD
- Phase 1 data in SAD and multi-dose cohorts confirms drug-like profile for safety and PK
- No significant adverse events observed in healthy volunteers and predictable PK profile
- Phase 2a in IPF expected to commence H2 2022, is a dose-ranging study to inform Phase 2b dose
  - Initial 12-week Phase 2a study for early efficacy readouts, safety and tolerability in IPF patients ± 5C, in addition to target and disease biomarker engagement
- Phase 2b planned for RXCO007 plus SoC over 12 months with lung function (FVC) as primary endpoint

References

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