246 OCR7602, New Modality for the treatment of ADPKD

Asset Overview

Product Type	Protein
Indication	Autosomal Dominant Polycystic Kidney Disease (ADPKD)
Current Stage	Preclinical
Target(MoA)	Inhibition of Ireα-Xbp1 pathway
Brief Description	• Identified the Ireα-Xbp1 pathway as a modulator of cyst growth • Inhibition of this pathway at the genetic level slows down disease progression in orthologous animal models through specific apoptosis of mutant cells • Generated a pre-clinical efficacy package around a novel use for an Ireα inhibitor previously tested in human trials
Organization	Yale University

Differentiation

□ **Autosomal Dominant Polycystic Kidney Disease (ADPKD)**

- >600,000 in US population; 12.5 M worldwide
- ~4% of prevalent End-Stage Renal Disease (ESRD)
- Orphan condition designation (2012) with estimated prevalence in US 1:2000
- One approved therapy: Tolvaptan (Jinarc) – approved April, 2018
- Targets low level proliferation and secretion in cysts originating from collecting duct; unknown long term efficacy and significant side effects including liver toxicity (Hy's law)
- Pipelines for polycytic kidney disease: 3 in phase III, 4 in phase II, 3 in phase I

□ **Reasonable repositioning of the clinical drug, Ireα-Xbp1 inhibitor for ADPKD**

- The HSP40 cochaperone SEC63 is associated with the SEC61 translocon complex in the ER.
- In mice, loss of SEC63 induces cyst formation both in liver and kidney as the result of reduced polycystin-1 (PC1).
- Loss of Sec63 selectively activates the IRE1α-XBP1 UPR branch. Activation of IRE1α/XBP1 is a compensatory mechanism in SEC63-deficient cells.

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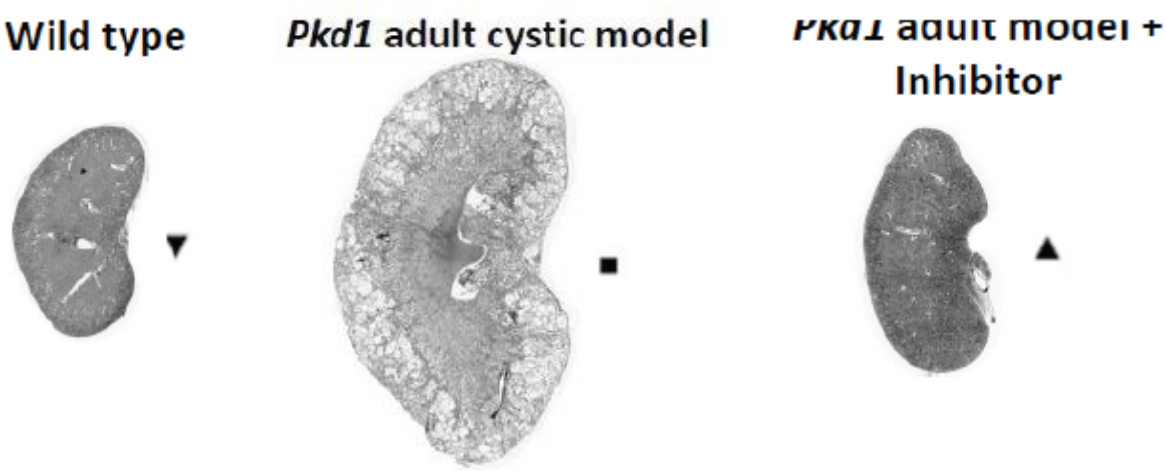
Key Data

Efficacy in cystic model



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Intellectual Property

Patent No.	
Application Date	
Status	
Country	

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