Welireg® (belzutifan) – New indication

- On December 14, 2023, Merck announced the FDA approval of Welireg (belzutifan), for the treatment of adult patients with advanced renal cell carcinoma (RCC) following a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor and a vascular endothelial growth factor tyrosine kinase inhibitor (VEGF-TKI).

- Welireg is also approved for the treatment of adult patients with von Hippel-Lindau (VHL) disease who require therapy for associated RCC, central nervous system (CNS) hemangioblastomas, or pancreatic neuroendocrine tumors (pNET), not requiring immediate surgery.

- The approval of Welireg for the new indication was based on a LITESPARK-005, an open-label, randomized, active-controlled study in 746 patients with unresectable, locally advanced or metastatic clear cell RCC that progressed following PD-1 or PD-L1 checkpoint inhibitor and VEGF receptor targeted therapies either in sequence or in combination. Patients were randomized to receive Welireg or everolimus. The major efficacy endpoints were progression free survival (PFS) and overall survival (OS). An additional endpoint was objective response rate (ORR).

    - Median PFS was 5.6 months (95% CI: 3.9, 7.0) with Welireg and 5.6 months (95% CI: 4.8, 5.8) with everolimus (hazard ratio 0.75, 95% CI: 0.63, 0.90; p = 0.0008).
    - OS results were immature.
    - The ORR was 22% (95% CI: 18, 27) with Welireg vs. 4% (95% CI: 2, 6) with everolimus (p < 0.0001).

- Welireg carries a boxed warning for embryo-fetal toxicity.

- The most common adverse reactions (≥ 25%), including laboratory abnormalities, with Welireg use were decreased hemoglobin, fatigue, musculoskeletal pain, increased creatinine, decreased lymphocytes, increased alanine aminotransferase, decreased sodium, increased potassium, and increased aspartate aminotransferase.

- The recommended dosage of Welireg for both of its indications is 120 mg administered orally once daily until disease progression or unacceptable toxicity.