Welireg™ (belzutifan) – New drug approval

- On August 13, 2021, the FDA announced the approval of Merck's Welireg (belzutifan), for treatment of adult patients with von Hippel-Lindau (VHL) disease who require therapy for associated renal cell carcinoma (RCC), central nervous system (CNS) hemangioblastomas, or pancreatic neuroendocrine tumors (pNET), not requiring immediate surgery.

- VHL is a rare genetic disease with an estimated incidence of 10,000 people in the U.S. Patients with VHL disease are at risk for benign blood vessel tumors as well as some cancerous ones, including RCC.

- Welireg is the first FDA approved hypoxia-inducible factor-2 alpha (HIF-2α) inhibitor. As an inhibitor of HIF-2α, Welireg reduces transcription and expression of HIF-2α target genes associated with cellular proliferation, angiogenesis, and tumor growth.

- The efficacy of Welireg was established in an open-label study in 61 patients with VHL-associated RCC. Patients received Welireg until progression of disease or unacceptable toxicity. The major endpoint was overall response rate (ORR). An Additional efficacy endpoint was duration of response (DOR).

    - The ORR was 49% (95% CI: 36, 62).
    - The median DOR was not reached (range: 2.8+, 22+).

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

- Additional warnings and precautions for Welireg include anemia and hypoxia.

- The most common adverse reactions (≥ 25%) with Welireg use were decreased hemoglobin, anemia, fatigue, increased creatinine, headache, dizziness, increased glucose, and nausea.

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

- Merck's launch plans for Welireg are pending. Welireg will be available as a 40 mg tablet.