2023 Areas of Interest for Belzutifan

Clinical:

Belzutifan as a single agent or in combination with SOC therapies in the following the areas.

- VHL-disease related disease/neoplasm that has not been studied (Germline mutations)
- Disease or neoplasm that have VHL somatic mutations
- Tumor with mutations to HIF2a pathway ie FH, SDHx, EPAS1/HIF2, ELOC/TCEB1, ENGL1.
- Tumor in which HiF2a pathway could be related to resistance.
- Perioperative or in advanced setting in solid and liquid tumors, where there is a strong rationale supported by preclinical and/or clinical data.

Preclinical:

- Understand the mechanistic basis of response to belzutifan and potential resistance mechanisms in the context of von Hippel-Lindau disease
- Identify indications outside of VHL diseases that would benefit from belzutifan treatment
    - Understand biomarkers that would predict response outside of VHL disease
- Identify additive and or antagonistic mechanisms of action between belzutifan and novel combination partners in the context of VHL disease and other tumor indications
- Development of tractable *in vitro* models for sensitivity and resistance to belzutifan

Special Note: Diversity & Inclusion

We seek to foster diverse and inclusive representation within the individual Areas of Interest for each tumor type, and so encourage study concept submissions across our program which:

- Specifically focus on the outcome disparities in underrepresented populations
- Are led by non-academic programs/institutions
- Are conducted in under-represented regions or countries