



Figure S1. Proposed Mechanism of Action. Dual inhibition of glutamine and glucose metabolism by telaglenastat plus everolimus or cabozantinib results in depletion of key nutrients that fuel cancer cell proliferation and survival. Telaglenastat inhibits glutaminase, a key enzyme that converts glutamine to glutamate, while signal transduction inhibitors, everolimus and cabozantinib, have known roles in inhibiting glucose metabolic pathways. Preclinical studies have demonstrated dual inhibition of the two pathways, as well as enhanced or synergistic anti-proliferative effects of RCC cell lines and xenografts when combining telaglenastat with everolimus or cabozantinib.