Phase 1/1B Study of Sitravatinib + Nivolumab + Ipilimumab in Patients With Advanced Clear Cell Renal Cell Carcinoma (accRCC) and Potentially Solid Other Malignancies

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Background

- Sitravatinib is a spectrum-selective TKI targeting TAM receptors (Tyro3/Axl/Mer) and Vascular Endothelial Growth Factor (VEGF) receptors. It may augment antitumor immune responses by reversing an immunosuppressive TME through a reduction in regulatory suppressor cells and cytokile and an increase in the ratio of M1/M2 macrophage phenotypes.

- In a Phase 1B study of single-agent sitravatinib in patients with accRCC who had progressed after an antihuman cancer treatment, the objective response rate (ORR) was 25.3% (95% CI: 14.5%–39.5%) and sitravatinib demonstrated a manageable safety profile (Figure 1).

- In a Phase 1/2 study of sitravatinib + nivolumab in patients with accRCC who had progressed after an antihuman cancer therapy, the objective response rate (ORR) was 30.0% (95% CI: 20.2%–42.7%) (Figure 2). The combination of sitravatinib and nivolumab demonstrated an acceptable safety profile and manageable adverse events.

- Both TAM and Split RTKs cooperate to drive tumors thus potentially augmenting immune responses.

- The most common grade 3 treatment-related adverse events (TRAEs) included lipase increase, proteinuria, amylase increase, diarrhea, and fatigue.

- 10% of patients discontinued treatment due to AEs.

- Both regulatory of non-trial evaluation, PD-1 and CTLA-4 play important, nonredundant roles in the immune regulatory mechanisms of immune responses.

- The combination of nivolumab + ipilimumab is approved for patients with intermediate- or poor-risk metastatic ccRCC.