Phase 3 study of tislelizumab (TIS) with sitravatinib versus chemotherapy (chemo) in patients with locally advanced/metastatic non-small cell lung cancer (NSCLC) previously treated with chemo and an anti-programmed cell death protein 1/ligand 1 (PD-[L]1) antibody

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Background: Most patients (pts) with advanced NSCLC do not respond to PD-(L)1 inhibitor monotherapy. Sitravatinib is an oral spectrum-selective tyrosine kinase inhibitor, which can reduce the number of myeloid-derived suppressor cells and regulatory T cells, and increase the ratio of M1/M2 polarized macrophages, promoting an antitumor microenvironment. TIS is an anti-PD-1 antibody engineered to minimize binding to FcγR on macrophages to abrogate antibody-dependent phagocytosis, a potential mechanism of resistance to PD-1 therapy. In a Phase 1 study (NCT03666143), sitravatinib plus TIS demonstrated clinical efficacy and had a manageable safety profile.

Trial Design: This is a Phase 3, global, randomized, open-label study (NCT04921358) designed to evaluate the efficacy and safety of sitravatinib plus TIS vs chemo, for the treatment of pts with locally advanced or metastatic NSCLC. A total of 420 pts will be randomized (1:1) to take TIS 200 mg intravenously (IV) once every three weeks (Q3W) plus sitravatinib 100 mg orally once a day, or docetaxel monotherapy 75 mg/m^2 IV Q3W, until disease progression, intolerable toxicity, or death. Adult pts with disease progression on or after ≤ 2 lines of prior systemic chemo and PD-(L)1 therapy with an ECOG performance status of ≤ 1 and ≥ 1 measurable lesion are eligible. Stratification factors are histology (squamous vs non-squamous), PD-L1 expression (< 1% tumor cell [TC] vs ≥ 1% TC assessed by the VENTANA SP263 assay), and race (Asian vs non-Asian). Co-primary endpoints are overall survival and independent review committee (IRC) assessed progression-free survival (PFS [RECIST v1.1]) in the intent-to-treat population. Secondary endpoints include investigator-assessed (INV) PFS, IRC-assessed objective response rate (ORR), duration of response (DoR), disease control rate (DCR), quality of life, safety, and pharmacokinetics (PK) of

sitravatinib. Exploratory endpoints include INV-assessed ORR, DoR, DCR, PK of the active metabolite of sitravatinib, predictive and prognostic value of PD-L1 expression, and biomarker analysis.