AdvanTIG-301: Anti-TIGIT monoclonal antibody (mAb) ociperlimab (OCI) + tislelizumab (TIS) + concurrent chemoradiotherapy (cCRT) followed by OCI + TIS or TIS + cCRT followed by TIS vs cCRT followed by durvalumab (DUR) in previously untreated, locally advanced, unresectable NSCLC

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Background:

Around one third of patients (pts) with NSCLC present with Stage III, locally advanced disease at initial diagnosis. Programmed death-ligand 1 (PD-L1) inhibitor, DUR, is the current standard of care for pts whose disease had not progressed following cCRT. Anti-T cell immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domain (TIGIT) is a co-inhibitory immune checkpoint receptor upregulated on T cells and natural killer cells in multiple solid tumors. OCI is a humanized mAb that binds TIGIT with high specificity and affinity, blocking interaction with its ligands on tumor cells. TIS is an anti-PD-1 antibody engineered to minimize binding to FcγR on macrophages to abrogate antibody-dependent phagocytosis. Dual targeting with OCI and TIS produced synergistic immune cell activation and enhanced antitumor activity in preclinical models.

Trial Design:

AdvanTIG-301 is a Phase 3, multicenter, international, randomized, open-label study (NCT04866017) in adult pts with newly diagnosed, histologically confirmed, locally advanced, Stage III unresectable NSCLC. Approximately 900 pts will be randomized 1:1:1 to receive: two cycles of OCI 900 mg IV + TIS 200 mg IV Q3W + cCRT followed by OCI 900 mg IV + TIS 200 mg IV Q3W up to 1 year after cCRT (Arm A), two cycles of TIS 200 mg IV Q3W + cCRT followed by TIS 200 mg IV Q3W up to 1 year after cCRT (Arm B), two cycles of cCRT followed by DUR 10 mg/kg IV Q2W (or 1500 mg IV Q4W) up to 1 year after cCRT (Arm C). Key eligibility criteria include ECOG PS ≤1 and no *EGFR* and *ALK* mutation. Primary endpoints, all by Independent Review Committee (IRC; RECIST v1.1), are progression-free survival (PFS) between Arm A and C, complete response rate between Arm A and C, and PFS between Arm B and C. Secondary

endpoints include overall survival, IRC-assessed PFS between Arm A and C in the PD-L1-positive population, and investigator-assessed PFS, IRC- and investigator-assessed overall response rate and duration of response (all between Arm A and B, Arm A and C and Arm B and C), and safety and tolerability.