High levels of PD-1 and VEGF expression in and around tumor tissue potentially drives anti-tumor activity in combination with chemotherapy for first line treatment of advanced or metastatic non-small cell lung cancer (NSCLC) without observed genomic alterations (AGA) in EGFR/ALK

**Methods**

An open-label, multi-center phase I study evaluating the efficacy and safety of Ivonescimab (AK112/SMT112) in combination with chemotherapy for first line treatment of advanced or metastatic NSCLC. The study design was open-label, non-randomized, dose-escalation study. The starting dose was 5 mg/kg with drug escalation every 2 weeks. Primary endpoint was ORR in RECIST 1.1. Safety was assessed by AE, DLT, and toxicity profiles. All subjects with measurable disease and available baseline and post-baseline imaging were included in the analysis. The study included 3 cohorts: Cohort 1: N=19; Cohort 2: N=13; Cohort 3: N=7. Median follow up was 13.3 months. Side effect profile of Ivonescimab was manageable and the combination was well tolerated. The median ORR was 41% (95% CI: 22-59) and the median DOR was 9 months (95% CI: 8-19). Table 2 shows the ORR and DOR across all cohorts.

**Results**

The median OS for Cohort 1 was 10.8 months (95% CI: 7.5-15.3), median DOR was 12.3 months (95% CI: 4.6-15.4). There were no treatment-related deaths. The most common adverse events (AE) across all cohorts were: neutropenia, anemia, decreased appetite, constipation and abdominal pain. The median duration of treatment beyond progression was 6.9 months. The most frequent grade ≥3 adverse events were neutropenia (15%), anemia (9%), and thrombocytopenia (3%). Table 3 shows the grade ≥3 adverse events across all cohorts.

**Conclusion**

Ivonescimab is currently being evaluated in Phase III studies in advanced NSCLC in combination with chemotherapy and targeted agents. The combination of Ivonescimab and chemotherapy has demonstrated promising ORR and DOR, with an acceptable safety profile. Further studies are needed to confirm these findings and explore the potential role of Ivonescimab in earlier lines of therapy.