Phase 2 Results of Ivonescimab, a Novel PD-1/VEGF Bispecific in Combination with Chemotherapy for First Line treatment of Patients with Advanced/Metastatic Squamous Non-small cell Lung Cancer (NSCLC)

**Background**

Since the initial approval of bevacizumab, BRAF/VEGFR/FGFR tyrosine kinase (TKI) inhibitors, and PD-L1/PD-L2 antibodies, there has been an increase in the development of targeted therapies for advanced metabolic diseases. Among these, non-selective anti-VEGF agents show promising results in patients with squamous non-small cell lung cancer (NSCLC) (non-Sq) and small cell lung cancer (SCLC) (non-Sq). However, the potential of anti-VEGF agents in combination with chemotherapy has been focused on patients with non-Sq histology. In this context, the Squamous NSCLC phase 2 of Ivonescimab (Eltrombopag) combined with chemotherapy for first line advanced or metastatic NSCLC in patients with squamous or non-squamous histology was conducted to evaluate safety, efficacy, and quality of life (QoL) in patients with advanced NSCLC.

**Methods**

Ivonescimab is a novel anti-VEGF molecule that binds to VEGF-A and VEGF-B with high affinity. The bispecific molecule is designed to bring two validated oncologic mechanisms into one novel tetravalent molecule. It binds to VEGF-A and VEGF-B, blocking their interaction with VEGF receptors. This binding increases affinity to VEGF by >4X, decreases VEGF-induced signaling, and enhances activity of T cells. It also significantly improves anti-tumor activity and safety. The primary objective of the study was to evaluate the safety and efficacy of Ivonescimab combined with chemotherapy for first line advanced or metastatic NSCLC in patients with squamous or non-squamous histology.

**Results**

As of data cut from the study (Table 4, results from Cohorts 2 and 3), the overall confirmed objective response rate (ORR) was 57% (90.5% CI 51.2, 75.9) in patients with advanced or metastatic NSCLC. The disease control rate (DCR) was 80.4% (95% CI 75.9, 84.8). The median progression-free survival (PFS) was 10.6 months (95% CI 7.9, 13.3). The median overall survival (OS) was 17.0 months (95% CI 14.7, 23.4).

**Conclusions**

Ivonescimab combined with chemotherapy significantly improved anti-tumor activity and safety in patients with advanced/metastatic NSCLC. This study provides a promising therapeutic approach for the management of advanced NSCLC.