GEMSTONE-302: a Phase III Study of Platinum-Based Chemotherapy with or without CS1001, an Anti-PD-L1 Antibody in Chemo-Naïve Advanced Non–Small Cell Lung Carcinoma (NSCLC)

Caicun Zhou[1], Ziping Wang[2], Jianhua Chang[3], Wu Zhuang[4], Yan Yu[5], Xueqin Chen[6], Zhiyong Ma[7], Hong Shen[8], Mengzhao Wang[9], Jianying Zhou[10], You Lu[11], Yongqian Shu[12], Yiping Zhang[13], Benquan Sun[14], Jingru Wang[14], Didi Jin[14], Dongmei Lu[14]

1. Shanghai Pulmonary Hospital, Tongji University, Shanghai.
2. Beijing Cancer Hospital, Beijing.
3. Fudan University Shanghai Cancer Center, Shanghai.
4. Fujian Provincial Cancer Hospital, Fujian Medical University, Fuzhou.
5. Harbin Medical University Cancer Hospital, Harbin.
6. Affiliated Hangzhou First People's Hospital, Zhejiang University, Hangzhou.
7. The Affiliated Cancer Hospital of Zhengzhou University, Henan Cancer Hospital, Zhengzhou.
8. The Second Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou.
9. Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing.
10. The First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou.
11. West China Hospital, West China School of Clinical Medicine, Sichuan University, Chengdu.
12. Jiangsu Province Hospital, The First Affiliated Hospital of Nanjing Medical University, Nanjing.
13. Zhejiang Cancer Hospital, Hangzhou.
14. CStone Pharmaceuticals (Su Zhou) Co., Ltd., Suzhou.

Background: Platinum-based chemotherapy is the current standard-of-care (SOC) for patients with newly diagnosed advanced NSCLC in China. However, the survival benefit conferred by this therapy leaves considerable space for improvement. Recent studies have shown the synergy effect of immune checkpoint inhibitors with platinum-based chemotherapy in patients with advanced NSCLC. CS1001 is the first full-length, fully human PD-L1 targeted immunoglobin G4 (IgG4, s228p) monoclonal antibody developed by the OMT transgenic rat platform. The Phase Ia/Ib study (GEMSTONE-101, NCT03312842) demonstrated that CS1001 was well tolerated and had promising anti-tumor activities across a range of tumors including NSCLC. GEMSTONE-302 (NCT03789604) is a randomized, double-blind, Phase III study to compare the efficacy and safety of platinum-doublet chemotherapy with or without CS1001 as first-line treatment in NSCLC.

Methods: Patients with Stage IV NSCLC, who have ECOG PS of 0-1 and no prior systemic chemotherapy are eligible. Approximately 480 patients will be randomized 2:1 to two arms. Randomization will be stratified by histology (squamous *vs.* non-

squamous), PD-L1 expression status (PD-L1≥1% *vs.* PD-L1 < 1%), and ECOG PS (PS 0 *vs.* PS 1). Patients with squamous NSCLC will receive four 21-day cycles of CS1001 (1200 mg, IV) or placebo in combination with carboplatin (AUC = 5 mg/mL/min, IV) and paclitaxel (175 mg/m^2, IV), followed by maintenance therapy with CS1001 or placebo; patients with non-squamous NSCLC will receive four 21-day cycles of CS1001 (1200 mg, IV) or placebo in combination with carboplatin (AUC = 5 mg/mL/min, IV) and pemetrexed (500 mg/m^2, IV), followed by maintenance therapy with CS1001 plus pemetrexed or placebo plus pemetrexed. Study treatment will be given for up to 2 years or until disease progression, intolerable toxicity, or investigator or patient decision to withdraw. AEs will be monitored throughout the study and graded per NCI CTCAE v4.03. Tumor response will be assessed by RECIST v1.1 at week 6 and 12, then every 9 weeks until week 48 and every 12 weeks thereafter. The primary endpoints are investigator-assessed PFS in patients with PD-L1 expression level ≥ 1% and PFS in all patients. Secondary endpoints include blinded independent center review (BICR)-assessed PFS, OS, investigator-assessed ORR, safety, and PK profile. The trial is currently enrolling patients in China in over 30 sites.

Clinical trial identification: NCT03789604