Gemstone-301: A Phase III Clinical Trial of CS1001 As Consolidation Therapy in Subjects with Locally Advanced/Unresectable (Stage III) Non-Small Cell Lung Cancer (NSCLC) Who Have Not Progressed after Prior Concurrent/Sequential Chemoradiotherapy (CRT)

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Background: In China, the standard of care for patients with unresectable Stage III NSCLC is platinum-based doublet chemotherapy given concurrently or sequentially with radiotherapy. However, the median progression-free survival (PFS) of those patients is poor (approximately 8-10 months) and 5-year overall survival (OS) rate is only 15%. Recently, treatment with durvalumab resulted in significantly longer PFS and OS than placebo for patients with locally advanced/unresectable NSCLC whose disease did not progress after definitive concurrent chemoradiotherapy (cCRT) in PACIFIC trial. CS1001 is the first full-length, fully human programmed death ligand-1 (PD-L1) targeted immunoglobin G4 (IgG4, s228p) monoclonal antibody (mAb) 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-301 (NCT03728556) is a randomized, double-blind, Phase III study to compare the efficacy and safety of CS1001 versus placebo as consolidation therapy in Stage III unresectable NSCLC patients. This is the first Phase III trial on an anti-PD-(L)1 mAb initiated in China for this indication.

Methods: In this trial, eligible patients with locally advanced/unresectable (Stage III) NSCLC who have not progressed after prior concurrent/sequential CRT are 2:1

randomized to receive CS1001 1200 mg, every 3 weeks or placebo, every 3 weeks. Stratification factors for randomization include ECOG status (0 versus 1), chemoradiotherapy (concurrent versus sequential) and total radiotherapy dose (< 60 Gy versus ≥ 60 Gy). Study treatment will be given for up to 24 months or until disease progression, intolerable toxicity, consent withdrawal, or discontinuation for other reason. Tumor assessments will be performed every 9 weeks in the first year and every 12 weeks thereafter by RECIST v1.1. AEs will be monitored throughout the study and graded according to NCI-CTCAE v4.03. Primary endpoint is PFS evaluated by investigators according to RECIST v1.1. Secondary endpoints are PFS evaluated by Blinded Independent Center Review (BICR), objective response rate, OS, time to death/distant metastasis (TTDM), safety and pharmacokinetics (PK) profile. Enrollment is ongoing across sites in China and will continue until 402 patients are randomized.

Clinical trial identification: NCT03728556