A Phase 2 Trial in Progress to Evaluate the Efficacy and Safety of Tislelizumab in Chinese Patients With Previously Treated Locally Advanced Unresectable or Metastatic Solid Tumors With Microsatellite Instability-High or Mismatch Repair Deficiency

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Background: Microsatellite instability (MSI) is a molecular tumor phenotype resulting from genomic hypermutability. Impairments of the DNA mismatch repair (MMR) system leads to MSI, which is defined by changes of microsatellite length. The PD-1/PD-L1 axis plays a central role in suppressing antitumor immunity; dysregulation of this axis may be exploited by cancer cells in order to help evade the immune system. Tumors with DNA mismatch repair deficiency (dMMR) and high MSI (MSI-H) are sensitive to PD-1 blockade as they have a significant upregulation of immune checkpoint proteins (including PD-1 and PD-L1) and increased mutation-associated neoantigen load. Tislelizumab, an investigational humanized IgG4 monoclonal antibody with high affinity and specificity for PD-1, was engineered to minimize binding to FcγR on macrophages in order to abrogate antibody-dependent phagocytosis, a mechanism of T-cell clearance and potential resistance to anti-PD-1 therapy. Previous reports showed single-agent tislelizumab was generally well tolerated and had antitumor activity in patients (pts) with advanced solid tumors, including tumors with MSI-H/dMMR.

Methods: This single-arm, open-label, phase 2 study (NCT03736889) is designed to evaluate the efficacy and safety of tislelizumab in pts with previously treated locally advanced unresectable or metastatic MSI-H or dMMR solid tumors. Approximately 60 adult pts (≥18 yr) with MSI-H/dMMR confirmed by central laboratory, who have progressed on their most recent anticancer regimen, and have ≥1 measurable lesion per RECIST v1.1, will be enrolled from approximately 25 sites in China. Enrolled pts will receive tislelizumab 200 mg IV Q3W until disease progression, intolerable toxicity, or withdrawal. The primary endpoint is objective response rate (RECIST v1.1) assessed by Independent Review Committee (IRC). Secondary endpoints include IRC-assessed duration of response, time to response, disease control rate, progression-free and overall survival, and the monitoring of adverse events to assess the tislelizumab safety/tolerability profile.