Preliminary Safety, Efficacy, and PK/PD Characterization of GARNET, a Phase 1 Clinical Trial of the Anti-PD-1 Monoclonal Antibody, TSR-042, in Patients with Recurrent or Advanced MSI-H Endometrial Cancer

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**BACKGROUND**

- TSR-042 is an investigational humanized anti-programmed death-1 (PD-1) monoclonal antibody, currently being evaluated in the US for the treatment of endometrial cancer. It binds with high affinity to PD-L1 and PD-L2.
- Blocking PD-1 has been shown to increase antitumor immune response (progression) and to increase survival of patients with multiple kidney types.
- The ongoing GARNET trial (NCT02715284) is evaluating TSR-042 in patients with advanced solid tumors.
- The study is now enrolling patients with specific tumor types into fixed-dose safety cohorts (all comers).

**OBJECTIVES**

- To evaluate the clinical activity of TSR-042 at the RP2D in patients with previously treated recurrent or advanced MSI-H EC.
- To evaluate the safety and tolerability of TSR-042 at the RP2D in patients with advanced solid tumors.
- To further characterize the PK profile of TSR-042.
- To further characterize the pharmacodynamic profile of TSR-042.

**METHODS**

**Patients**

- Patients with MSI-H EC who had progressed on or after at least one line of treatment with an approved therapy, and for whom there was no standard of care, were eligible.
- Key exclusion criteria included: prior therapy with agents targeting PD-1, PD-L1, or PD-L2.
- The study did not include patients with prior PD-1/PD-L1/PD-L2 therapy.

**RESULTS**

- **Dosing Schedule**: The recommended phase 2 dose (RP2D) was 1000 mg Q6W for the first 4 cycles then 1000 mg Q3W thereafter.
- **Safety**: Of 59 patients, 12 enrolled in the Part 2A cohort (all comers) and 100 patients were enrolled in the Part 2B: Expansion Cohorts at RP2D. Overall, 28 patients (45.7%) had treatment-related adverse events (AEs) that were grade ≥ 3 in intensity. The most frequently reported grade ≥ 3 treatment-related AEs were leukopenia (4.5%) and anemia (3.5%).

**Conclusion**

- Preliminary safety data indicates robust anti-tumor activity of TSR-042 in MSI-H EC patients with previously treated advanced disease. TSR-042 was well tolerated, with a profile characteristic of approved PD-1/PD-L1 inhibitors.

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