A Phase 2 Study of Vudalimab (XmAb® 20717), an Anti-PD-1/CTLA-4 Bispecific Antibody, in Patients With Selected Gynecological Malignancies and High-Risk Metastatic Castration-Resistant Prostate Cancer

Vudalimab (XmAb® 20717) is a humanized bispecific monoclonal antibody (Figure 1) that simultaneously targets programmed death-ligand 2 (PD-L2) and cytotoxic T lymphocyte-associated protein 4 (CTLA-4) and binds preferentially to PD-1/CTLA-4 dual positive cells.

In a Phase 1 study of vudalimab, the recommended Phase 2 dose was 10 mg/kg intravenously every 2 weeks, which was generally well tolerated, with rash, pruritus, and increased transaminases being the most frequently reported immune-related adverse events. The overall response rate (ORR) for patients receiving 10 mg/kg (n = 78; efficacy analyses) was 35.9% and responses seen in several solid tumor types are currently being checked in inhibitor-experienced patients. Responses were also seen in metastatic castration-resistant prostate cancer (mCRPC; 2 partial responses) and ovarian (1 complete response) patients.

Background and Study Schema

**Objectives**

**Primary Objective**
- To assess the preliminary antitumor activity of vudalimab using ORR per Response Evaluation Criteria in Solid Tumors (RECIST) v 1.1 and Prostate Cancer Working Group 3 for the mCRPC cohort

**Secondary Objectives**
- To assess antitumor activity based on best observed response, duration of response (DOR), progression-free survival, and overall survival, as well as checkpoint-related response in the mCRPC cohort
- To characterize the pharmacokinetics of vudalimab
- To evaluate the safety and tolerability of vudalimab

**Exploratory Objectives**
- To establish potential biomarkers associated with clinical response
- To explore pharmacodynamic effects in peripheral blood and tumor tissue and their association with clinical response

**Background and Study Schema**

**Figure 1. Vudalimab-PD-1 & CTLA-4 Bispecific monoclonal antibody**

- Pharmacokinetic modeling of Phase 1 study data was used to establish a flat-dose regimen of vudalimab that extends dosing to 3-week intervals.

**Figure 2. Study schema**

- **Dosing** 200 mg (body weight ≥ 80 kg) or 100 mg (body weight < 80 kg) every 3 weeks (Q3W; optional on treatment) through cycle 8; every 3 cycles thereafter.

**Study Status and Sites**

- Approximately 13 sites in the United States will participate.

**Study Details**

**This Phase 2, multicenter, 2-stage, parallel-group, open-label study (NCT03521248) is designed to evaluate the safety and antitumor activity of vudalimab in selected gynecologic tumor types and high-risk mCRPC.**

**Stage 1**
- **Stage 1 (1/15) Expansion**
  - Patients currently receiving immunotherapy therapy are excluded.
  - Endpoints include ORR (≥20%) at Week 12.

**Stage 2**
- **Stage 2 (2/26) Expansion**
  - Patients currently receiving immunotherapy therapy are excluded.
  - Endpoints include ORR (≥20%) at Week 12.

**Table 1. Key Inclusion and Exclusion Criteria**

**Inclusion Criteria**
- Histologically confirmed diagnosis of one of the following tumor types:
  - Endometrial, or
  - Serous ovarian cancer

**Exclusion Criteria**
- Active known or suspected autoimmune disease
- Failure to recover from any toxicity related to prior immunotherapy
- Failure to recover from any immunotherapy-related toxicity related to prior immunotherapy
- Failure to recover from any toxicity related to prior immunotherapy
- Failure to recover from any toxicity related to prior immunotherapy

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