Pamiparib, a Novel PARP 1/2 Inhibitor, Monotherapy for gBRCAm Patients with Recurrent Ovarian, Fallopian, and Primary Peritoneal Cancer: an Open-label, Multicenter, Phase 2 trial in China

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Background: Poly(ADP-ribose) polymerase inhibitors (PARPis) represent a class of antitumor agents that exert their cytotoxic effects by inhibiting PARP activity. PARPis are also capable of trapping PARP proteins complexes on damaged DNA, further augmenting cell death. Pamiparib is a selective PARP1/2 inhibitor with potent PARP trapping ability that can cross the blood-brain barrier and has demonstrated antitumor activity in both *in vitro* and *in vivo* nonclinical tumor models harboring *BRCA* gene mutations (*BRCA*^{mut}) and other homologous recombination deficiencies. In Phase 1 studies (NCT02361723; NCT03333915), single-agent pamiparib was generally well tolerated and showed antitumor activity, notably in patients with high-grade non-mucinous ovarian cancer (HGOC). Antitumor activity was observed in patients with *BRCA* mutant and *BRCA* wild type ovarian cancers, whose tumors were either sensitive or had platinum-resistant disease. Data from these Phase 1 studies support the recommended Phase 2 pamiparib monotherapy dose of 60 mg PO BID.

Trial Design: In this ongoing study of pamiparib in China (NCT03333915), patients with HGOC harboring germline *BRCA*^{mut} who have received ≥2 prior lines of therapy are being enrolled in the Phase 2 part of the study. Patients with either platinum-sensitive (progression occurring ≥6 months after last dose of platinum) or platinum-resistant (progression occurring <6 months after last dose of platinum) HGOC are eligible. Germline *BRCA*^{mut} status is identified or confirmed by central testing before enrollment. Approximately 100 patients with HGOC (platinum-sensitive, n=80; platinum-resistant, n=20) will receive pamiparib 60 mg PO BID until disease progression. The primary objective is to assess overall response rate according to RECIST v1.1; secondary objectives include assessment of pamiparib's safety, tolerability, and pharmacokinetic profile. Evaluation of antitumor activity will include an estimation of overall and progression-free survival, as well as duration of clinical response.