Pamiparib, a Novel PARP 1/2 Inhibitor Monotherapy for Patients With Recurrent Ovarian, Fallopian, and Primary Peritoneal Cancer With Germline *BRCA* Mutations: an Open-label, Multicenter, Phase 2 Trial in China

Xiaohua Wu[1], Jing Wang[2], Qi Zhou[3], Beihua Kong[4], Tingting Gu[5], Kathy Zhang[6], Juan Liang[5], Song Mu[7], Ruimin Ge[5], Haiyuan Yang[8], Xiaofang Liang[5], Yaqing Li[5], Vivian Huang[5], Lai Wang[5], Miao Li[5]

[1]Fudan University Shanghai Cancer Center, Shanghai, China; [2]Hunan Cancer Hospital, Changsha, China; [3]Chongqing Cancer Hospital, Chongqing, China, [4]Qilu Hospital of Shandong University, Shandong, China; [5]BeiGene (Beijing) Co. Ltd., Beijing, China; [6]BeiGene USA, Inc., Emeryville, CA; [7]BeiGene USA, Inc., Fort Lee, NJ; [8]BeiGene (Shanghai) Co., Ltd., Shanghai, China

Objective 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 protein complexes on damaged DNA, further augmenting cell death. Pamiparib is a selective PARP 1/2 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 early phase clinical studies in Caucasian and Chinese patients (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*^{mut} and *BRCA* wild type ovarian cancers whose tumors were either sensitive or resistant to platinum-based chemotherapy. These studies also established 60 mg orally twice daily (PO BID) as the recommended phase 2 dose.

Methods 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 the overall response rate according to RECIST v1.1; secondary objectives include assessment of the safety, tolerability, overall survival, progression-free survival, duration of clinical response, and pharmacokinetic profile of pamiparib.