A Phase 2 Trial in Progress: Pamiparib, an Investigational PARP Inhibitor, in Patients with Metastatic Castration-Resistant Prostate Cancer and a Circulating Tumor Cell Homologous Recombination Deficiency (HRD) Phenotype or *BRCA* Defects.

Simon Chowdhury, Joaquin Mateo, Mitchell Gross, Andrew J. Armstrong, Marcia Cruz-Correa, Josep M. Piulats, Jean-Yves Blay, Delcia Rivas, Luis Quintero, Henry Castro, Andong Nkobena, Mitch Raponi, Robert Pelham, Mark Andrew Landers, Robert B. Montgomery; Guy's and St Thomas' Hospital, London, United Kingdom; Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; USC Westside Cancer Center, University of Southern California, Beverly Hills, CA; Duke Cancer Institute, Duke University, Durham, NC; The University of Puerto Rico and MD Anderson Cancer Center, San Juan, PR; Institut Català d'Oncologia-IDIBELL-CIBERONC, Barcelona, Spain; Centre Léon Bérard, Lyon, France; BeiGene USA, Inc., San Mateo, CA; Epic Sciences, Inc., San Diego, CA; University of Washington, Seattle, WA

Background: Men with metastatic castration-resistant prostate cancer (mCRPC) who have a *BRCA1/2* mutation (*BRCA1/2*^{mut}) or mutations in other HRD genes have a poor prognosis. The EPIC liquid biopsy test is a novel assay that can identify circulating tumor cells (CTC) with HRD associated phenotypes. Preliminary studies have shown that these men may respond to treatment with a PARP inhibitor. Pamiparib is an investigational PARP1/2 inhibitor that has shown brain penetration and potent PARP–DNA complex trapping in nonclinical studies. In early phase clinical studies (NCT02361723; NCT03333915), pamiparib was generally well tolerated and showed preliminary antitumor activity; 60 mg orally twice daily (BID) was established as the recommended investigational dose. **Methods:** This open-label, global, phase 2 study (NCT03712930) will evaluate antitumor activity and safety of pamiparib in mCRPC pts with CTC-HRD, assessed by the EPIC CTC-HRD assay, or deleterious germline/somatic *BRCA1/2*^{mut} status. Patients must have progressed on/after ≥1 androgen receptor-targeted therapy, have received ≥1 taxane-based therapy, and have prostate-specific antigen (PSA) progression per PCWG3 criteria. Four cohorts of patients will receive pamiparib 60 mg BID in 28-day cycles. Cohort 1 will include ~50 pts with CTC-HRD^{+} +/- *BRCA1/2*^{mut} mCRPC with measurable metastatic disease; Cohort 2 will include ~30 pts with CTC-HRD^{+} +/- *BRCA1/2*^{mut} mCRPC with bone-only disease; Cohorts 3 & 4 will include ~20 pts with CTC-HRD$^{-/unknown}$ + *BRCA1/2*^{mut} mCRPC with measurable metastatic disease (Cohort 3), or bone-only disease (Cohort 4). Disease status will be assessed every 8 wks for 24 wks, then every 12 wks; PSA levels will be tested every 4 wks. Co-primary endpoints are radiographic ORR assessed by IRC (pts with measurable disease) and confirmed PSA response rate per PCWG3 criteria (pts +/- measurable disease). Secondary endpoints include ORR, time to PSA response/progression, duration of PSA response, time to symptomatic skeletal event, radiographic progression-free survival, overall survival, and safety.