



News Release

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Janssen Presents New Data Demonstrating the Combination of Niraparib and Abiraterone Acetate Plus Prednisone Significantly Improved Radiographic Progression-Free Survival as a First-Line Therapy in Patients with HRR Gene-Mutated Metastatic Castration-Resistant Prostate Cancer

Initial results from Phase 3 MAGNITUDE study, to be featured in a late-breaking oral presentation at ASCO GU, highlight subset of patients with mCRPC most likely to benefit from treatment

SAN FRANCISCO, Feb. 14, 2022 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced initial results from the Phase 3 MAGNITUDE study evaluating the investigational use of niraparib, a selective poly-ADP ribose polymerase (PARP) inhibitor, in combination with abiraterone acetate plus prednisone in patients with metastatic castration-resistant prostate cancer (mCRPC) with or without specific homologous recombination repair (HRR) gene alterations. At the final analysis for radiographic progression-free survival (rPFS), the treatment combination of niraparib and abiraterone acetate plus prednisone demonstrated a statistically significant improvement in patients with HRR gene alterations. Results will be featured in a late-breaking oral presentation (Abstract #12; Oral Abstract Session A) at the American Society of Clinical Oncology’s Genitourinary (ASCO GU) Cancers Symposium, taking place in San Francisco and virtually from February 17-19, 2022.

MAGNITUDE ([NCT03748641](https://clinicaltrials.gov/ct2/show/study/NCT03748641)) is a Phase 3, randomized, double-blind, placebo-controlled,

multicenter study evaluating the safety and efficacy of the combination of niraparib and abiraterone acetate plus prednisone as a first-line therapy in patients with mCRPC. The MAGNITUDE study was intentionally designed with two independent cohorts to assess treatment effect in patients with and without HRR gene alterations (including ATM, BRCA1, BRCA2, BRIP1, CDK12, CHEK2, FANCA, HDAC2, PALB2 alterations) versus standard of care. The cohort of patients with prospectively-identified HRR gene alterations enrolled 423 patients, with patients randomized to receive the combination of niraparib and abiraterone acetate plus prednisone (combination arm [n=212]) or placebo and abiraterone acetate plus prednisone (control arm [n=211]). At 18.6-month median follow-up, patients in the combination arm of the cohort with HRR gene alterations showed a significant improvement in rPFS, with a reduction in the risk of progression or death of 27 percent (hazard ratio [HR] 0.73; p=0.022). This improvement was most pronounced in patients with BRCA1/2 gene alterations, where a 47 percent risk reduction was observed for rPFS (HR 0.53; p=0.001), as analyzed by blinded independent central review (BICR). A consistent but greater improvement was observed in investigator-assessed rPFS, which showed an overall 36 percent risk reduction in patients with HRR gene alterations (HR: 0.64; p=0.002), and a 50 percent risk reduction in patients with BRCA1/2 gene alterations (HR: 0.50; p=0.0006).¹

The cohort without HRR gene alterations (n=233) met the predefined futility criteria in August 2020, showing no benefit from the treatment combination (HR>1) in the HRR biomarker negative population.¹ Enrollment into this cohort was stopped at the time of futility at the recommendation of the Independent Data Monitoring Committee. Investigators and patients were unblinded and given the opportunity to continue treatment with niraparib and abiraterone acetate plus prednisone or receive only abiraterone acetate plus prednisone at the discretion of the study investigator.

“When choosing a treatment plan for patients with prostate cancer, physicians must consider individual needs, particularly for patients with mCRPC with HRR gene alterations who face a poor prognosis,” said Dr. Kim Chi, Medical Oncologist at BC Cancer - Vancouver and principal investigator of the MAGNITUDE study.* “The MAGNITUDE data provide important context about the subgroup of patients with prostate cancer who may benefit from treatment with niraparib in combination with abiraterone acetate plus prednisone in the first-line setting, as well as those who may be better served by other treatment options.”

In patients with HRR gene alterations, clinically relevant improvements in outcomes were also seen at this first interim analysis for secondary endpoints including time to initiation of cytotoxic chemotherapy, time to symptomatic progression and time to PSA progression. Additionally, objective response rate was improved by the combination of niraparib and abiraterone acetate plus prednisone. Overall survival data were immature at this interim analysis and follow-up will continue for all secondary endpoints.¹

“These data suggest clinically meaningful improvements in outcomes in patients with prostate with HRR gene alterations who may derive benefit from this combination regimen, highlighting the importance of biomarkers to guide the patient selection process,” said Mary Guckert, RN, MSN, Vice President, Development Leader, Prostate Cancer, Janssen Research & Development, LLC. “The design of this trial aligns with the real-world setting as it includes patients with prostate cancer who were able to start first-line standard of care treatment, while awaiting HRR biomarker results, and shows the need to prospectively test for and identify patients most likely to benefit from the combination of niraparib and abiraterone acetate with prednisone.”

The observed safety profile of the combination of niraparib and abiraterone acetate plus prednisone was consistent with the known safety profile of each agent. Of the patients with HRR gene alterations, 67 percent experienced Grade 3 adverse events (AEs) and 46.4 percent experienced Grade 4 AEs, largely driven by anemia and fatigue. Discontinuation rates for the combination arm and control arm were 10.8 percent and 4.7 percent respectively. The combination of niraparib and abiraterone acetate plus prednisone also maintained overall quality of life in comparison with placebo and abiraterone acetate plus prednisone as measured on the Functional Assessment of Cancer Therapy–Prostate (FACT-P) scale.¹

Patients with HRR gene alterations, such as BRCA1/2, are at an increased risk of developing prostate cancer, and BRCA-related prostate cancer is usually aggressive.² Long-term survival is low for patients with mCRPC and those who have HRR gene alterations face a worse prognosis, driving a significant unmet medical need for novel therapies in this disease.^{3,4}

About MAGNITUDE

[MAGNITUDE](#) is a Phase 3 randomized, double-blind, placebo-controlled, multicenter clinical study evaluating the safety and efficacy of the combination of niraparib and abiraterone acetate plus prednisone as a first-line therapy for patients with mCRPC, with or without certain HRR gene alterations. The study includes two cohorts in which patients were randomized to receive either niraparib and abiraterone acetate plus prednisone or abiraterone acetate (placebo) plus prednisone cohorts: one cohort of patients with predefined HRR gene alterations (including ATM, BRCA1, BRCA2, BRIP1, CDK12, CHEK2, FANCA, HDAC2, PALB2 alterations) and one cohort of patients without HRR gene alterations. In a third, open-label cohort, all patients received a combination tablet of niraparib and abiraterone and a separate tablet of prednisone. The primary endpoint of the MAGNITUDE trial is rPFS. Secondary endpoints include time-to-initiation of cytotoxic chemotherapy, time to symptomatic progression, and overall survival.

About Niraparib

Niraparib is an orally administered, selective poly-ADP ribose polymerase (PARP) inhibitor, that is currently being studied by Janssen for the treatment of patients with prostate cancer. Additional ongoing studies include the Phase 3 [AMPLITUDE](#) study evaluating the combination of niraparib and abiraterone acetate plus prednisone in a biomarker-selected patient population with metastatic castration-sensitive prostate cancer and [QUEST](#), a Phase 1b/2 study of niraparib combination therapies for the treatment of mCRPC.

In April 2016, Janssen Biotech, Inc. entered a worldwide (except Japan) collaboration and license agreement with TESARO, Inc. (acquired by GSK in 2018), for exclusive rights to niraparib in prostate cancer. In the U.S., niraparib is indicated for the maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube or primary peritoneal cancer who are in a complete or partial response to first-line platinum-based chemotherapy; for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy; for the treatment of adult patients with advanced ovarian, fallopian tube or primary peritoneal cancer who have been treated with three or more prior chemotherapy regimens and whose cancer is associated with homologous recombination deficiency (HRD) positive status defined by either: a deleterious or suspected deleterious BRCA mutation, or genomic instability and who have progressed

more than six months after response to the last platinum-based chemotherapy. Niraparib is currently marketed by GSK as ZEJULA[®].⁵

About Metastatic Castration-Resistant Prostate Cancer

Metastatic castration-resistant prostate cancer (mCRPC) characterizes cancer that no longer responds to androgen deprivation therapy and has spread to other parts of the body. The most common metastatic sites are bones, followed by lymph nodes, lungs and liver.⁶ Prostate cancer is the second most common cancer in men worldwide, behind lung cancer.² More than one million men around the world are diagnosed with prostate cancer each year.⁷ Patients with mCRPC and HRR gene alterations have a worse prognosis than those without HRR alterations.⁸

About the Janssen Pharmaceutical Companies of Johnson & Johnson

At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity and healing hopelessness with heart. We focus on areas of medicine where we can make the biggest difference: Cardiovascular & Metabolism, Immunology, Infectious Diseases & Vaccines, Neuroscience, Oncology and Pulmonary Hypertension.

Learn more at www.janssen.com. Follow us at [@JanssenGlobal](https://twitter.com/JanssenGlobal) and [@JanssenUS](https://twitter.com/JanssenUS). Janssen Research & Development, LLC and Janssen Biotech, Inc. are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

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*Dr. Chi has served as a consultant to Janssen; he has not been paid for any media work.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding product development and the potential benefits and treatment impact of niraparib. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of Janssen Research & Development, LLC, Janssen Biotech, Inc., or any of the other Janssen

Pharmaceutical Companies and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behavior and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended January 2, 2022, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in Johnson & Johnson's subsequent Quarterly Reports on Form 10-Q and other filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of the Janssen Pharmaceutical Companies nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

¹ Chi et al. Phase 3 MAGNITUDE study: First results of niraparib (NIRA) with abiraterone acetate and prednisone (AAP) as first-line therapy in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) with and without homologous recombination repair (HRR) gene alterations. ASCO GU 2022.

² Castro, E., Eeles, R. (2012). The role of BRCA1 and BRCA2 in prostate cancer. *Asian journal of andrology*, 14(3), 409–414. <https://doi.org/10.1038/aja.2011.150>

³ Castro E, Romero-Laorden N, Del Pozo A, et al. PROREPAIR-B: A Prospective Cohort Study of the Impact of Germline DNA Repair Mutations on the Outcomes of Patients With Metastatic Castration-Resistant Prostate Cancer. *J Clin Oncol*. 2019;37(6):490-503. doi:10.1200/JCO.18.00358

⁴ Mehtälä J, Zong J, Vassilev Z, Brobert G, et al. (2020) Overall survival and second primary malignancies in men with metastatic prostate cancer. *PLOS ONE* 15(2): e0227552. <https://doi.org/10.1371/journal.pone.0227552>

⁵ ZEJULA® U.S. Prescribing Information, May 2021.

⁶ Cancer.org. Understanding advanced cancer, metastatic cancer, and bone metastasis. <https://www.cancer.org/treatment/understanding-your-diagnosis/advanced-cancer/what-is.html>. Accessed October 2021.

⁷ World Health Organization. "Globocan 2012: Prostate Cancer: Incidence, Mortality and Prevalence Worldwide, 2012." <http://gco.iarc.fr/today/data/pdf/fact-sheets/cancers/cancer-fact-sheets-19.pdf>. Accessed October 2021.

⁸ Castro E, Romero-Laorden N, Del Pozo A, et al. PROREPAIR-B: A Prospective Cohort Study of the Impact of Germline DNA Repair Mutations on the Outcomes of Patients With Metastatic Castration-Resistant Prostate Cancer. *J Clin Oncol*. 2019;37(6):490-503. doi:10.1200/JCO.18.00358