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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 in a first line setting

February 15, 2022 (BEERSE, BELGIUM) – The Janssen Pharmaceutical Companies of Johnson & Johnson 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 (AAP) as a first line therapy 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 AAP demonstrated a statistically significant improvement in patients with HRR gene alterations as compared to placebo and abiraterone acetate plus prednisone.[1] 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.

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"Despite treatment advances for metastatic castration-resistant prostate cancer, long-term survival is often severely shortened, and this is especially the case for prostate cancer harbouring (or containing) HRR gene alterations that we now know behave more aggressively," commented Professor Gerhardt Attard**, Primary Study Investigator and Clinician Scientist and Team Leader at University College London Cancer Institute. "It is therefore encouraging to see the results from the MAGNITUDE study, that confirms a very real benefit for treatment with niraparib in combination with abiraterone acetate plus prednisone in selected groups of patients."

MAGNITUDE (NCT03748641) is a Phase 3, randomised, double-blind, placebo-controlled, multicentre study evaluating the safety and efficacy of niraparib combined with AAP as a first-line therapy in patients with mCRPC. The MAGNITUDE study was intentionally designed and powered with two independent cohorts based on patient biomarker status to evaluate the efficacy of the combination of niraparib and AAP relative to placebo and AAP in subjects with and without HRR gene alterations (including ATM, BRCA1, BRCA2, BRIP1, CDK12, CHEK2, FANCA, HDAC2, PALB2 alterations*). In a third, open-label cohort, all patients received a fixed dose combination tablet of niraparib and abiraterone and a separate tablet of prednisone. The cohort of patients with prospectively-identified HRR gene alterations enrolled 423 patients, with patients randomised to receive the combination of niraparib and AAP (combination arm [n=212]) or placebo and AAP (control arm [n=211]). [1]

At 18.6-month median follow-up, patients in the combination arm of the cohort with HRR gene alterations showed a significant clinical 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 analysed 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=0.0022), 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

* HRR gene alterations include ataxiatelangiectasia (ATM), breast cancer gene 1 and 2 (BRCA1/BRCA2), BRCA1 interacting protein 1 (BRIP1), cyclin-dependent kinase 12 (CDK12), CHEK2, fanconi anaemia (FANCA), histone deacetylase (HDAC2) and partner and localiser of BRCA 2 (PALB2).

biomarker negative population.[1] Enrolment 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 patients were given the opportunity to continue treatment with niraparib and AAP or receive only AAP at the discretion of the study investigator.

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 AAP. Overall survival data were immature at this interim analysis and follow-up will continue for all secondary endpoints.[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]

"The MAGNITUDE study demonstrates that in people with metastatic castration-resistant prostate cancer with HRR gene mutations, the treatment combination of niraparib and abiraterone acetate plus prednisone significantly improves radiographic progression free survival with a reduction in the risk of progression or death. These data reinforce the importance of biomarkers in helping to provide an individualised treatment plan for these patients," said Martin Vogel, MD, EMEA Therapeutic Area Lead Oncology, Janssen-Cilag GmbH.

The observed safety profile of the combination of niraparib and AAP was in line with the known safety profile of the two individual drugs, and manageable, with no new safety signals identified. Of the patients with HRR gene alterations, 67 percent and 46.4 percent experienced Grade 3/4 adverse events (combination of niraparib and AAP, and placebo and AAP respectively), largely driven by anaemia 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 AAP also maintained overall quality of life in comparison with

placebo and AAP as measured on the Functional Assessment of Cancer Therapy–Prostate (FACT-P) scale.[1]

About MAGNITUDE

MAGNITUDE (NCT03748641) is a Phase 3 randomised, double-blind, placebo-controlled, multicentre clinical study evaluating the safety and efficacy of the combiniation of niraparib and abiraterone acetate plus prednisone (AAP) 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 randomised to receive either niraparib and AAP or placebo and AAP 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 fixed dose 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.[1]

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 AAP in a biomarker-selected patient population with metastatic hormone-sensitive prostate cancer (mHSPC) and QUEST, a Phase 1b/2 study of niraparib combination therapies for the treatment of mCRPC.[5,6]

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 European Union, 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. Niraparib is currently marketed by GSK as ZEJULA®.[7]

About abiraterone acetate

Abiraterone acetate is an orally-administered androgen biosynthesis inhibitor. In the European Union, abiraterone acetate is indicated with prednisone or prednisolone for the treatment of newly diagnosed high risk metastatic hormone-sensitive prostate cancer in adult men in combination with ADT; the treatment of mCRPC in adult men who are asymptomatic or mildly symptomatic after failure of ADT in whom chemotherapy is not yet clinically indicated; and the treatment of mCRPC in adult men whose disease has progressed on or after a docetaxel based chemotherapy regimen (ZYTIGA SmPC 2020).
Abiraterone acetate is currently marketed by Janssen BV as ZYTIGA®.[8]

About Metastatic Castration-Resistant Prostate Cancer

Metastatic castration-resistant prostate cancer (mCRPC) characterises cancer that no longer responds to ADT and has spread to other parts of the body. The most common metastatic sites are bones, followed by lymph nodes, lungs and liver.[9] Prostate cancer is the most common cancer in men in Europe.[10] More than one million men around the world are diagnosed with prostate cancer each year.[11] Patients with mCRPC and HRR gene alterations have a worse prognosis than those without HRR alterations.[3]

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/emea/. Follow us at www.twitter.com/JanssenEMEA for our latest news. Janssen Research & Development, LLC; Janssen-Cilag, S.A. and Janssen Biotech, Inc. are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

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

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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 materialise, 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 3, 2021, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's most recently filed Quarterly Reports on Form 10-Q and the company's subsequent 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. Neither 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.

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[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.

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