News Release

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Final Multivariate Analysis from the Phase 3 MAGNITUDE Study Shows Trend Toward Improvement in Overall Survival in Patients with Metastatic Castration-Resistant Prostate Cancer with *BRCA* Alterations Treated with Niraparib and Abiraterone Acetate Plus Prednisone

Niraparib and abiraterone acetate plus prednisone combination therapy also showed clinically relevant improvement versus standard of care in time to symptomatic progression and time to cytotoxic chemotherapy

MADRID, October 22, 2023 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced results from the final analysis (FA) of the Phase 3 MAGNITUDE study, in which a pre-planned multivariate analysis [MVA] showed niraparib, a highly selective poly (ADP-ribose) polymerase (PARP) inhibitor, combined with abiraterone acetate and given with prednisone, improved overall survival (OS) and time to symptomatic progression (TSP) and showed a favorable trend in time to cytotoxic chemotherapy (TCC) in patients with metastatic castration-resistant prostate cancer (mCRPC) with *BRCA* alterations. These data were featured today in a Late-Breaking Mini Oral Presentation Session (Abstract #LBA85) at the European Society for Medical Oncology (ESMO) 2023 Congress taking place October 20-24 in Madrid, Spain.[1]

The FA of the MAGNITUDE study included 225 patients with *BRCA*-positive mCRPC (the largest population studied to date), where 113 patients were randomized to niraparib plus abiraterone acetate and prednisone (AAP) and 112 patients were assigned to placebo plus AAP. At 35.9 months median follow-up (9.1 additional months follow-up from the second interim analysis,

presented at ASCO GU 2023), a prespecified MVA, adjusting for baseline imbalances, showed an OS benefit favoring patients who received niraparib plus AAP compared to the placebo plus AAP arm (Hazard Ratio [HR]=0.66; 95 percent Confidence Interval [CI], 0.46-0.95]). Continued trend in improvement in TSP was also observed in patients who received niraparib and AAP compared to patients randomized to placebo plus AAP (HR 0.56; 95 percent CI, 0.37-0.85). Additionally, an evaluation of TCC indicated a favorable trend among patients with *BRCA* mutations treated with niraparib and AAP (HR 0.60; 95 percent CI, 0.39-0.92). Finally, 70 percent of the patients in the niraparib and AAP arm received subsequent life-prolonging therapy compared to 86 percent of the patients assigned to placebo plus AA.

Patient-reported outcomes were also assessed in the FA. Results indicate that patients with *BRCA* mutations treated with niraparib and AAP experienced a trend towards delayed time to worst pain progression (HR 0.81; 95 percent CI, 0.52-1.25) and pain interference progression (HR 0.77; 95 percent CI, 0.48-1.23) compared with the placebo arm.

"The overall survival seen in the MAGNITUDE pre-planned multivariate analysis is promising for patients with *BRCA*-mutated mCRPC, a population more likely to experience poor outcomes," said Kim Chi*, M.D., Medical Oncologist at BC Cancer - Vancouver and principal investigator of the MAGNITUDE study. "These data, with key signals of improvements in overall survival, disease progression, and quality of life measures, underscore the significance of this new treatment option for patients."

The FA observed no new safety signals and no cases of myelodysplastic syndrome or acute myeloid leukemia were observed among patients in the niraparib and AAP arm. Niraparib plus AAP had higher rates of adverse events (AEs) of special interest than the placebo arm, with the most common of any grade including anaemia (52.4 percent versus 22.7 percent) and thrombocytopenia (24.1 percent versus 9.5 percent), respectively. The differences in safety between treatment arms were driven by known hematologic toxicities with niraparib.

"We are dedicated to advancing the science of prostate cancer and developing new targeted treatment options to extend patients' lives," said Angela Lopez-Gitlitz, M.D., Vice President, Late Development Oncology, Prostate Cancer, Janssen Research & Development, LLC. "These data highlight the importance of identifying patients with genetically defined cancer to better inform treatment protocols and ensure they receive available therapies tailored to their unique needs."

About Niraparib

Niraparib is an orally administered, highly 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 (NCT04497844), evaluating the combination of niraparib and AAP in a biomarker-selected patient population with metastatic castration-sensitive prostate cancer (mCSPC).

In April 2016, Janssen Biotech, Inc. entered a worldwide (except Japan) collaboration and license agreement with TESARO, Inc. (acquired by GlaxoSmithKline [GSK] in 2019) for exclusive rights to niraparib in prostate cancer.

In the United States, 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; and for the maintenance treatment of adult patients with deleterious or suspected deleterious germline *BRCA*-positive 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®.

In April 2023, Janssen received approval from the European Commission for AKEEGA™ (niraparib and abiraterone acetate) in the form of a dual action tablet (DAT), plus prednisone or prednisolone, in patients with mCRPC and *BRCA* mutations based on data from the MAGNITUDE study. Health Canada (June 2023) and the U.S. Food and Drug Administration (August 2023) also have authorized/approved AKEEGA™. Reviews are ongoing in other regions.

About abiraterone acetate

Abiraterone acetate is an orally administered androgen biosynthesis inhibitor. In the United States, abiraterone acetate is indicated with prednisone for the treatment of mCRPC and high-risk mCSPC.

About Metastatic Castration-Resistant Prostate Cancer

Metastatic castration-resistant prostate cancer 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 lungs and liver. Prostate cancer is the second most common cancer in men worldwide, behind lung cancer. More than one million patients around

the world are diagnosed with prostate cancer each year. Patients with mCRPC and homologous recombination repair (HRR) gene alterations, of which *BRCA* mutations are the most common, are more likely to have aggressive disease, poor outcomes and a shorter survival time.[Error! Bookmark not defined.,Error! Bookmark not defined.,Error! Bookmark not defined.,Error! Bookmark not defined.]

About MAGNITUDE

MAGNITUDE (NCT03748641) is a Phase 3, randomized, double-blind, placebo-controlled, multi-center clinical study evaluating the safety and efficacy of the combination of niraparib and AAP for patients with mCRPC, with or without certain HRR gene alterations, and who have not received prior therapy for mCRPC except for up to four months of AAP.

The study included patients with (HRR biomarker [BM] positive; *ATM, BRCA1, BRCA2, BRIP1, CDK12, CHEK2, FANCA, HDAC2, PALB2*) and without specified gene alterations (HRR BM negative), who were randomized 1:1 to receive niraparib 200 mg once daily plus AAP or placebo plus AAP.[2] A total of 423 patients with HRR gene alterations were enrolled, 225 (53.2 percent) of whom had *BRCA* mutations.[3,4] The primary endpoint of the MAGNITUDE trial was radiographic progression free survival (rPFS) assessed by blinded independent central review.[5] Secondary endpoints included TCC, TSP and OS. Analysis of the group of patients with *BRCA* alterations was alpha controlled for rPFS and prespecified for other endpoints.

IMPORTANT SAFETY INFORMATION FOR AKEEGA™[4]

WARNINGS AND PRECAUTIONS

The safety population described in the WARNINGS and PRECAUTIONS reflect exposure to AKEEGA™ in combination with prednisone in *BRCA*m patients in Cohort 1 (N=113) of MAGNITUDE.

Myelodysplastic Syndrome/Acute Myeloid Leukemia

AKEEGA™ may cause myelodysplastic syndrome/acute myeloid leukemia (MDS/AML).

MDS/AML, including cases with fatal outcome, has been observed in patients treated with niraparib, a component of AKEEGA™.

All patients treated with niraparib who developed secondary MDS/cancer-therapy-related AML had received previous chemotherapy with platinum agents and/or other DNA-damaging agents, including radiotherapy.

For suspected MDS/AML or prolonged hematological toxicities, refer the patient to a hematologist for further evaluation. Discontinue AKEEGA™ if MDS/AML is confirmed.

Myelosuppression

AKEEGA™ may cause myelosuppression (anemia, thrombocytopenia, or neutropenia).

In MAGNITUDE Cohort 1, Grade 3-4 anemia, thrombocytopenia, and neutropenia were reported, respectively in 28%, 8%, and 7% of patients receiving AKEEGA™. Overall, 27% of patients required a red blood cell transfusion, including 11% who required multiple transfusions. Discontinuation due to anemia occurred in 3% of patients.

Monitor complete blood counts weekly during the first month of AKEEGA™ treatment, every two weeks for the next two months, monthly for the remainder of the first year and then every other month, and as clinically indicated. Do not start AKEEGA™ until patients have adequately recovered from hematologic toxicity caused by previous therapy. If hematologic toxicities do not resolve within 28 days following interruption, discontinue AKEEGA™ and refer the patient to a hematologist for further investigations, including bone marrow analysis and blood sample for cytogenetics.

Hypokalemia, Fluid Retention, and Cardiovascular Adverse Reactions

AKEEGA™ may cause hypokalemia and fluid retention as a consequence of increased mineralocorticoid levels resulting from CYP17 inhibition [see Clinical Pharmacology (12.1)]. In post-marketing experience, QT prolongation and Torsades de Pointes have been observed in patients who develop hypokalemia while taking abiraterone acetate, a component of AKEEGA™. Hypertension and hypertensive crisis have also been reported in patients treated with niraparib, a component of AKEEGA™.

In MAGNITUDE Cohort 1, which used prednisone 10 mg daily in combination with AKEEGA™, Grades 3-4 hypokalemia was detected in 2.7% of patients on the AKEEGA™ arm and Grades 3-4 hypertension were observed in 14% of patients on the AKEEGA™ arm.

The safety of AKEEGA™ in patients with New York Heart Association (NYHA) Class II to IV heart failure has not been established because these patients were excluded from MAGNITUDE.

Monitor patients for hypertension, hypokalemia, and fluid retention at least weekly for the first two months, then once a month. Closely monitor patients whose underlying medical conditions might be compromised by increases in blood pressure, hypokalemia, or fluid retention, such as those with heart failure, recent myocardial infarction, cardiovascular disease, or ventricular arrhythmia. Control hypertension and correct hypokalemia before and during treatment with AKEEGA™.

Discontinue AKEEGA™ in patients who develop hypertensive crisis or other severe cardiovascular adverse reactions.

Hepatotoxicity

AKEEGA™ may cause hepatotoxicity.

Hepatotoxicity in patients receiving abiraterone acetate, a component of AKEEGA™, has been reported in clinical trials. In post-marketing experience, there have been abiraterone acetate-associated severe hepatic toxicity, including fulminant hepatitis, acute liver failure, and deaths.

In MAGNITUDE Cohort 1, Grade 3-4 ALT or AST increases (at least 5 x ULN) were reported in 1.8% of patients. The safety of AKEEGA™ in patients with moderate or severe hepatic impairment has not been established as these patients were excluded from MAGNITUDE.

Measure serum transaminases (ALT and AST) and bilirubin levels prior to starting treatment with AKEEGA™, every two weeks for the first three months of treatment and monthly thereafter. Promptly measure serum total bilirubin, AST, and ALT if clinical symptoms or signs suggestive of hepatotoxicity develop. Elevations of AST, ALT, or bilirubin from the patient's baseline should prompt more frequent monitoring and may require dosage modifications.

Permanently discontinue AKEEGA™ for patients who develop a concurrent elevation of ALT greater than 3 x ULN and total bilirubin greater than 2 x ULN in the absence of biliary obstruction or other causes responsible for the concurrent elevation, or in patients who develop ALT or AST ≥20 x ULN at any time after receiving AKEEGA™.

Adrenocortical Insufficiency

AKEEGA™ may cause adrenal insufficiency.

Adrenocortical insufficiency has been reported in clinical trials in patients receiving abiraterone acetate, a component of AKEEGA™, in combination with prednisone, following interruption of daily steroids and/or with concurrent infection or stress. Monitor patients for symptoms and signs of adrenocortical insufficiency, particularly if patients are withdrawn from prednisone, have prednisone dose reductions, or experience unusual stress. Symptoms and signs of adrenocortical insufficiency may be masked by adverse reactions associated with mineralocorticoid excess seen in patients treated with abiraterone acetate. If clinically indicated, perform appropriate tests to confirm the diagnosis of adrenocortical insufficiency. Increased doses of corticosteroids may be indicated before, during, and after stressful situations.

Hypoglycemia

AKEEGA™ may cause hypoglycemia in patients being treated with other medications for diabetes.

Severe hypoglycemia has been reported when abiraterone acetate, a component of AKEEGA™, was administered to patients receiving medications containing thiazolidinediones (including pioglitazone) or repaglinide.

Monitor blood glucose in patients with diabetes during and after discontinuation of treatment with AKEEGA™. Assess if antidiabetic drug dosage needs to be adjusted to minimize the risk of hypoglycemia.

Increased Fractures and Mortality in Combination with Radium 223 Dichloride

AKEEGA™ with prednisone is not recommended for use in combination with Ra-223 dichloride outside of clinical trials.

The clinical efficacy and safety of concurrent initiation of abiraterone acetate plus prednisone/prednisolone and radium Ra 223 dichloride was assessed in a randomized, placebo-controlled multicenter study (ERA-223 trial) in 806 patients with asymptomatic or mildly symptomatic castration-resistant prostate cancer with bone metastases. The study was unblinded early based on an Independent Data Monitoring Committee recommendation.

At the primary analysis, increased incidences of fractures (29% vs 11%) and deaths (39% vs 36%) have been observed in patients who received abiraterone acetate plus

prednisone/prednisolone in combination with radium Ra 223 dichloride compared to patients who received placebo in combination with abiraterone acetate plus prednisone.
It is recommended that subsequent treatment with Ra-223 not be initiated for at least five days after the last administration of AKEEGA™, in combination with prednisone.

Posterior Reversible Encephalopathy Syndrome
AKEEGA™ may cause Posterior Reversible Encephalopathy Syndrome (PRES).

PRES has been observed in patients treated with niraparib as a single agent at higher than the recommended dose of niraparib included in AKEEGA™.

Monitor all patients treated with AKEEGA™ for signs and symptoms of PRES. If PRES is suspected, promptly discontinue AKEEGA™ and administer appropriate treatment. The safety of reinitiating AKEEGA™ in patients previously experiencing PRES is not known.

Embryo-Fetal Toxicity
The safety and efficacy of AKEEGA™ have not been established in females. Based on animal reproductive studies and mechanism of action, AKEEGA™ can cause fetal harm and loss of pregnancy when administered to a pregnant female.

Niraparib has the potential to cause teratogenicity and/or embryo-fetal death since niraparib is genotoxic and targets actively dividing cells in animals and patients (e.g., bone marrow).

In animal reproduction studies, oral administration of abiraterone acetate to pregnant rats during organogenesis caused adverse developmental effects at maternal exposures approximately ≥0.03 times the human exposure (AUC) at the recommended dose.

Advise males with female partners of reproductive potential to use effective contraception during treatment and for 4 months after the last dose of AKEEGA™. Females who are or may become pregnant should handle AKEEGA™ with protection, e.g., gloves.

Based on animal studies, AKEEGA™ may impair fertility in males of reproductive potential.

ADVERSE REACTIONS
The safety of AKEEGA™ in patients with BRCAm mCRPC was evaluated in Cohort 1 of MAGNITUDE.

The most common adverse reactions (≥10%), including laboratory abnormalities, are decreased hemoglobin, decreased lymphocytes, decreased white blood cells, musculoskeletal pain, fatigue, decreased platelets, increased alkaline phosphatase, constipation, hypertension, nausea, decreased neutrophils, increased creatinine, increased potassium, decreased potassium, increased AST, increased ALT, edema, dyspnea, decreased appetite, vomiting, dizziness, COVID-19, headache, abdominal pain, hemorrhage, urinary tract infection, cough, insomnia, increased bilirubin, weight decreased, arrhythmia, fall, and pyrexia.

Serious adverse reactions reported in >2% of patients included COVID-19 (7%), anemia (4.4%), pneumonia (3.5%), and hemorrhage (3.5%). Fatal adverse reactions occurred in 9% of patients who received AKEEGA™, including COVID-19 (5%), cardiopulmonary arrest (1%), dyspnea (1%), pneumonia (1%), and septic shock (1%).

DRUG INTERACTIONS

Effect of Other Drugs on AKEEGA™

Avoid coadministration with strong CYP3A4 inducers.

Abiraterone is a substrate of CYP3A4. Strong CYP3A4 inducers may decrease abiraterone concentrations, which may reduce the effectiveness of abiraterone.

Effects of AKEEGA™ on Other Drugs

Avoid coadministration unless otherwise recommended in the Prescribing Information for CYP2D6 substrates for which minimal changes in concentration may lead to serious toxicities. If alternative treatments cannot be used, consider a dose reduction of the concomitant CYP2D6 substrate drug.

Abiraterone is a CYP2D6 moderate inhibitor. AKEEGA™ increases the concentration of CYP2D6 substrates, which may increase the risk of adverse reactions related to these substrates.

Monitor patients for signs of toxicity related to a CYP2C8 substrate for which a minimal change in plasma concentration may lead to serious or life-threatening adverse reactions.

Abiraterone is a CYP2C8 inhibitor. AKEEGA™ increases the concentration of CYP2C8 substrates, which may increase the risk of adverse reactions related to these substrates.

Please see the full Prescribing Information for AKEEGA™.

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: Oncology, Immunology, Neuroscience, Cardiovascular, Pulmonary Hypertension, and Retina.

Learn more at www.janssen.com. Follow us at @JNJInnovMed and @JanssenUS. Janssen Biotech, Inc. and Janssen Research & Development, LLC Johnson & Johnson companies.

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., 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; competition, including technological advances, new products and patents attained by competitors; challenges to patents; 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 1, 2023, 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 Janssen Research & Development, LLC, Janssen Biotech, Inc., nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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

[1] Chi KN, et al. Niraparib (NIRA) with abiraterone acetate plus prednisone (AAP) as first-line (1L) therapy in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) and homologous repair (HRR) gene alterations: Three-year update and final analysis (FA) of MAGNITUDE. Oral presentation at ESMO 2023, LBA 85.
[2] 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. Oral presentation, 2022 ASCO GU Annual Meeting.
[3] AKEEGA™ Prescribing Information. Horsham, PA: Janssen Biotech, Inc.
[4] Efstathiou E, et al. Niraparib With Abiraterone Acetate and Prednisone in Patients With Metastatic Castration-Resistant Prostate Cancer and Homologous Recombination Repair Gene Alterations: Second Interim Analysis of MAGNITUDE. Poster presentation, 2023 ASCO GU Annual Meeting. February 16, 2023.