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NEWS RELEASE

Johnson & Johnson leads with first PARP inhibitor combo to improve efficacy in patients with HRR-altered mCSPC

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Results from the Phase 3 AMPLITUDE study show the potential of AKEEGA® (niraparib and abiraterone acetate dual-action tablet) to delay cancer progression and worsening of symptoms

Data show a nearly 50 percent reduction in disease progression in BRCA-altered mCSPC vs. current standard of care

CHICAGO, June 3, 2025 /PRNewswire/ -- Johnson & Johnson announced today first results from the Phase 3, randomized, double-blind, placebo-controlled AMPLITUDE study evaluating the combination of niraparib and abiraterone acetate plus prednisone (AAP) in patients with metastatic castration-sensitive prostate cancer (mCSPC) with homologous recombination repair (HRR) genetic alterations including BRCA. The results show a clinically meaningful and statistically significant improvement in both radiographic progression-free survival (rPFS) and time to symptomatic progression (TSP), with an early trend toward improved overall survival (OS)—highlighting the potential of the combination in this patient population to delay both cancer progression and the worsening of symptoms.[1] This marks the first Phase 3 data to show clinical improvement with a PARP-based combination in mCSPC. The findings are being presented as a late-breaking oral presentation (Abstract #LBA5006) at the **2025 American Society of Clinical Oncology Annual Meeting**. The data have also been selected for Best of ASCO and included in the ASCO Press Program.

"Approximately 25 percent of patients with mCSPC have HRR alterations, with about half being BRCA. These patients typically experience faster disease progression and poorer outcomes," said Gerhardt Attard*, M.D., Ph.D., FRCP, John Black Charitable Foundation Chair of Medical Oncology, University College London Cancer Institute, Research Department of Oncology and presenting author. "The AMPLITUDE trial is the first to show that combining

a PARP inhibitor with an androgen receptor pathway inhibitor both delays disease progression and postpones the onset of symptoms in HRR-altered mCSPC, supporting this combination as a new treatment option for these patients."

"Our aim with the AMPLITUDE study was to determine how long patients could live without their cancer worsening. What we found is that the combination of niraparib, abiraterone acetate, and prednisone is achieving just that, with the goal of offering patients precious quality time before the disease enters a more resistant phase," said Charles Drake, M.D., Ph.D., FAAP, Vice President, Prostate Cancer and Immunotherapy Disease Area Leader, at Johnson & Johnson Innovative Medicine. "This breakthrough highlights the need for early initiation of personalized treatment strategies for patients with mCSPC and HRR alterations, particularly BRCA, who typically face more aggressive disease."

The Phase 3 AMPLITUDE study of 696 patients with mCSPC and HRR alterations met its primary endpoint of rPFS. Patients with BRCA alterations (n=191) showed the greatest benefit of treatment with the combination of niraparib plus AAP, as the median rPFS was not reached compared to 26 months in patients treated with the placebo plus AAP, reducing the risk of radiographic progression or death by 48 percent (hazard ratio [HR] 0.52, 95 percent confidence interval [CI], 0.37-0.72, p<0.0001). In patients with any HRR alteration treated with the niraparib combination, median rPFS was also not reached in comparison to 29.5 months in patients treated with the placebo plus AAP, with a reduction in risk of progression or death by 37 percent (HR 0.63, 95 percent CI, 0.49-0.80, p=0.0001).[1]

These results also showed that treatment with the niraparib combination reduced the risk of symptomatic progression by 56 percent in patients with BRCA alterations (HR 0.44, 95 percent CI, 0.29-0.68, p=0.0001) and 50 percent in patients with HRR alterations (HR 0.50, 95 percent CI, 0.36-0.69, p<0.0001), meaning that patients experienced a longer delay to worsening symptoms and requiring radiation, surgical intervention, or needing a new anti-cancer therapy. The first interim analysis showed an early trend toward improved overall survival (OS) favoring the niraparib/AAP combination with a reduction in risk of death of 25 percent (HR 0.75, 95 percent CI, 0.51-1.11, p=0.15) in patients with BRCA alterations and 21 percent in HRR alterations (HR 0.79, 95 percent CI, 0.59-1.04, p=0.10); follow-up is ongoing for maturity of the data.[1]

Grade 3/4 adverse events (AE) were more frequent with the niraparib combination compared to the placebo group (75 percent vs. 59 percent), with anemia and hypertension being the most common; however, treatment discontinuations due to AEs remained low (14.7 percent vs 10.3 percent). To date, the safety profile of niraparib plus abiraterone acetate and prednisone has been consistent with prior experiences.[1]

New data from the CAPTURE study (Abstract #5094), also being presented at the 2025 ASCO Annual Meeting with simultaneous publication in the **Annals of Oncology**, reinforce that the presence of HRR, specifically BRCA

alterations, among patients with mCSPC are associated with significantly worse prognosis. Despite the availability of life-prolonging ARPIs, patients with HRR-altered mCSPC experience approximately 30 percent faster disease progression and shorter survival, while patients with BRCA-altered mCSPC experience approximately 50 percent faster disease progression and shorter survival—highlighting the importance of genetic testing to inform treatment decisions and the urgent need for novel targeted therapies to improve outcomes and delay progression.[2]

Johnson & Johnson has nearly 20 years of leadership in prostate cancer, treating more than 750,000 patients worldwide. With the AMPLITUDE study, Johnson & Johnson becomes the first to show that a PARP inhibitor combination can benefit patients with mCSPC.[3]

About AMPLITUDE

AMPLITUDE (**NCT04497844**) is an ongoing, phase 3, randomized, double-blind, placebo-controlled, international study evaluating the efficacy and safety of niraparib and abiraterone acetate in a dual-action tablet (DAT) formulation with prednisone plus androgen deprivation therapy (ADT) compared to matching oral placebo/abiraterone acetate with prednisone plus ADT in patients with deleterious germline or somatic homologous recombination repair (HRR) gene-altered metastatic castration-sensitive prostate cancer (mCSPC). The primary endpoint is radiographic progression-free survival (rPFS).

About Metastatic Castration-Sensitive Prostate Cancer

Metastatic castration-sensitive prostate cancer (mCSPC), also known as metastatic hormone-sensitive prostate cancer (mHSPC), refers to prostate cancer that still responds to ADT and has spread to other parts of the body.[4]

About AKEEGA® (niraparib and abiraterone acetate)

AKEEGA® is a combination, in the form of a dual-action tablet (DAT), of niraparib, a highly selective poly (ADP-ribose) polymerase (PARP) inhibitor, and abiraterone acetate, a CYP17 inhibitor. AKEEGA® together with prednisone or prednisolone was approved in **April 2023** by the European Medicines Agency, and in **August 2023** by the U.S. FDA, for the treatment of patients with BRCA-mutated metastatic castration-resistant prostate cancer (mCRPC). Patients are selected for therapy based on an FDA-approved test for genetic alterations. Additional marketing authorization applications are under review across a number of countries globally.

Additional ongoing studies include the Phase 3 AMPLITUDE study evaluating AKEEGA® with prednisone or prednisolone 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.

For more information visit **https://www.akeegahcp.com/.**

AKEEGA® IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

The safety population described in the WARNINGS and PRECAUTIONS reflect exposure to AKEEGA® in combination with prednisone in BRCAm 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. 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 Johnson & Johnson

At Johnson & Johnson, we believe health is everything. Our strength in healthcare innovation empowers us to build a world where complex diseases are prevented, treated, and cured, where treatments are smarter and less invasive, and solutions are personal. Through our expertise in Innovative Medicine and MedTech, we are uniquely positioned to innovate across the full spectrum of healthcare solutions today to deliver the breakthroughs of tomorrow, and profoundly impact health for humanity. Learn more at **https://www.jnj.com/** or

at **www.innovativemedicine.jnj.com**. Follow us at **@JNJInnovMed**. Janssen Research & Development, LLC, Janssen Biotech, Inc., Janssen Global Services, LLC, and Janssen Scientific Affairs, LLC are 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 AKEEGA® (niraparib/abiraterone). The reader is cautioned not to rely on these forward-looking statements. 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 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 most recent Annual Report on Form 10-K, 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. Johnson & Johnson does not undertake to update any forward-looking statement as a result of new information or future events or developments.

*Dr. Attard has provided consulting, advisory, and speaking services to Johnson & Johnson; he has not been paid for any media work.

Media contact:
Oncology Media Relations
Oncology_media_relations@its.jnj.com

Investor contact:
Lauren Johnson
investor-relations@its.jnj.com

U.S. medical inquiries:
+1 800 526-7736

[1] Attard, G., et al. (2025, May). Phase 3 AMPLITUDE trial: Niraparib and abiraterone acetate plus prednisone for metastatic castration-sensitive prostate cancer patients with alterations in homologous recombination repair

genes. Presented at the American Society of Clinical Oncology (ASCO) Annual Meeting, Chicago, IL.
[2] Olmos, D. (2025, May). Impact of somatic/germline homologous recombination repair (HRR) alterations on metastatic hormone-sensitive prostate cancer (mHSPC) outcomes by disease volume. Presented at the American Society of Clinical Oncology (ASCO) Annual Meeting 2025.
[3] Fizazi K, Tran N, Fein L, Matsubara N, Rodriguez-Antolin A, Alekseev BY, Özgüroğlu M, Ye D, Feyerabend S, Protheroe A, Sulur G, Luna Y, Li S, Mundle S, Chi KN. Abiraterone acetate plus prednisone in patients with newly diagnosed high-risk metastatic castration-sensitive prostate cancer (LATITUDE): final overall survival analysis of a randomised, double-blind, phase 3 trial. Lancet Oncol. 2019 May;20(5):686-700. doi: 10.1016/S1470-2045(19)30082-8. Epub 2019 Apr 12. PMID: 30987939.
[4] American Society of Clinical Oncology. ASCO Answers: Prostate Cancer (2018). **http://www.cancer.net/sites/cancer.net/files/asco_answers_guide_prostate.pdf**. Accessed May 2025.

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