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News Release

Media Enquiries:
Magda Palhota
Phone: +351 91 2799282
Email: mpalhota@its.jnj.com

Investor Relations:
Raychel Kruper
Phone: +1 732-524-6164
Email: rkruper@its.jnj.com

Janssen Marks First Approval Worldwide for AKEEGA® (Niraparib and Abiraterone Acetate Dual Action Tablet) with EC Authorisation for the Treatment of Patients with Metastatic Castration Resistant Prostate Cancer with BRCA1/2 Mutations

Approval for AKEEGA® is based on results from the Phase 3 MAGNITUDE study, a prospectively designed precision medicine study that includes the largest cohort to date of BRCA1/2-positive patients with untreated metastatic castration-resistant prostate cancer (mCRPC).[1,2]

Niraparib in combination with abiraterone acetate (AA), plus prednisone or prednisolone, significantly improved radiographic progression-free survival (rPFS) compared to standard of care in untreated mCRPC patients with BRCA1/2 mutations.[3]

BEERSE, Belgium, 21 April 2023 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today that the European Commission (EC) has granted marketing authorisation for AKEEGA® (niraparib and abiraterone acetate [AA]), in the form of a dual action tablet (DAT), given with prednisone or prednisolone, for the treatment of adults with metastatic castration-resistant prostate cancer (mCRPC) and BRCA1/2 mutations (germline and/or somatic) in whom chemotherapy is not clinically indicated.[2]

Prostate cancer is the most common cancer in men in Europe, and the sixth-highest cause of cancer-related death worldwide.[4,5] Despite treatment advances, mCRPC remains an incurable, deadly disease.[6,7] BRCA1/2 gene mutations have been identified in

approximately 10-15 percent of mCRPC patients[8,9] and are more likely to cause aggressive disease, poor outcomes, and a shorter survival time.[10,11,12,13]

"Metastatic castration-resistant prostate cancer remains a lethal disease, with high unmet needs in terms of treatment options, particularly for patients with BRCA1/2 gene mutations," said Professor Gerhardt Attard, Oncologist, University College London (UCL), London, UK*. "We've seen that in these patients, niraparib combined with abiraterone acetate and predniso(lo)ne (AAP) significantly reduced the risk of disease progression or death compared to AAP. The dual action tablet of niraparib with abiraterone acetate is a promising first line targeted treatment option for men with mCRPC and BRCA1/2 mutations."

The EC authorisation, which also marks the first worldwide approval for AKEEGA®, is based on results of the randomised, double-blind, placebo controlled, Phase 3 MAGNITUDE study (NCT03748641).[14] The trial assessed whether the addition of niraparib to AAP improved outcomes in those with untreated mCRPC, with or without alterations in homologous recombination repair (HRR) associated genes (which are involved in the repair of damaged DNA), including BRCA1/2.[1,14] A total of 423 patients with HRR gene alterations were enrolled, 225 (53.2 percent) of whom had BRCA mutations, making it the largest cohort of BRCA1/2-positive patients with first line mCRPC in any clinical study to date.[15]

"The MAGNITUDE trial was prospectively designed as a precision medicine study to identify the specific population of patients who would most benefit from niraparib with abiraterone acetate plus predniso(lo)ne, and potentially increase the likelihood of treatment success," said Martin Vogel, EMEA Therapeutic Area Lead Oncology, Janssen-Cilag GmbH. "The results, on which this European Commission approval is based, reinforce the benefit of this niraparib-based combination in effectively addressing BRCA mutations and changing the outlook for patients with mCRPC."

The primary endpoint for MAGNITUDE was radiographic progression-free survival (rPFS), as analysed by blinded central review.[1,14] Niraparib plus AAP significantly improved rPFS in all HRR-positive patients (Hazard Ratio [HR] 0.73; 95 percent Confidence Interval [CI], 0.56 to 0.96; p=0.022).[3] This improvement was most pronounced in patients with BRCA1/2 gene mutations, where a statistically significant 47 percent risk reduction was observed for rPFS.[3] With additional median follow-up at 24.8 months in the BRCA subgroup, rPFS by central review demonstrated a consistent and clinically meaningful treatment effect favouring niraparib plus AAP, with a median rPFS of 19.5 months compared with 10.9 months for placebo plus AAP.[1] Additionally, there was a trend towards improved overall survival (OS) with niraparib plus AAP, strong improvement in

time to symptomatic progression (TSP) and clinically meaningful improvement in time-to-initiation of cytotoxic chemotherapy (TCC).[1]

The observed safety profile of the combination of niraparib and AAP was consistent with the known safety profile of each agent.[3] Of the patients with HRR gene alterations, 67 percent experienced Grade 3/4 adverse events (AEs) in the combination arm versus 46.4 percent in the control arm.[16] The most common grade 3 AEs were anaemia (28.3 percent versus 7.6 percent) and hypertension (14.6 percent versus 12.3 percent) with niraparib and AAP versus placebo and AAP, respectively.[16] The combination of niraparib and AAP also maintained overall quality of life in comparison with placebo and AAP.[3,16]

"This European milestone, which also marks the first worldwide approval for AKEEGA®, highlights the value of precision medicine and the importance of genetic testing in patients with mCRPC to ensure the right patients receive the right treatment," said Peter Lebowitz, M.D., Ph.D., Global Therapeutic Area Head, Oncology, Janssen Research & Development, LLC. "It also demonstrates our ongoing commitment at Janssen to developing innovative therapeutic approaches to help improve outcomes for patients living with prostate cancer."

Niraparib is a highly selective poly adenosine diphosphate-ribose polymerase (PARP) inhibitor.[14] Together with AA plus prednisone, the combination DAT regimen targets two oncogenic drivers in patients with mCRPC, namely alterations in the androgen receptor axis and in BRCA1/2.[14,17,18] This is the first DAT formulation available in the European Union for patients with mCRPC with BRCA mutations.[2]

Europe is the first region to approve AKEEGA® (niraparib and abiraterone acetate DAT), for the treatment of patients with BRCA-positive mCRPC, globally. In February 2023, Janssen submitted a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) seeking approval of this niraparib-based combination for the treatment of patients with BRCA-positive mCRPC.[19]

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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.[2,20] Additional ongoing studies include the Phase 3 AMPLITUDE study (NCT04497844) evaluating the combination of niraparib and AAP in a homologous recombination repair (HRR) biomarker-selected patient population with metastatic hormone-sensitive prostate cancer (mHSPC).[20]

In April 2016, Janssen Biotech, Inc. entered into a worldwide (except Japan) collaboration and license agreement with TESARO, Inc. (acquired by GSK in 2019),[21] for exclusive rights to niraparib in prostate cancer.[22]

In the European Economic Area (EEA), niraparib is already indicated as monotherapy for the maintenance treatment of adult patients with advanced epithelial high-grade ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response following completion of first-line platinum-based chemotherapy; and as monotherapy for the maintenance treatment of adult patients with platinum-sensitive relapsed high grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in complete or partial response to platinum-based chemotherapy.[17] In these indications, niraparib is currently marketed by GSK as ZEJULA®.[17]

AKEEGA® is a dual action tablet (DAT) combining niraparib and abiraterone acetate (AA). It is available in two dose strengths: regular-strength (100 mg niraparib/500 mg AA) and low-strength (50 mg niraparib/500 mg AA). The recommended dose of AKEEGA® is 200 mg niraparib and 1,000 mg AA daily.[2]

About abiraterone acetate

Abiraterone acetate (AA) is an orally administered androgen biosynthesis inhibitor. In the EEA, AA is indicated with prednisone or prednisolone for the treatment of newly diagnosed high risk mHSPC in adult men in combination with androgen deprivation therapy (ADT); the treatment of metastatic castration-resistant prostate cancer (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.[18]

Janssen-Cilag International NV currently market AA as ZYTIGA®.[18]

About Metastatic Castration-Resistant Prostate Cancer

mCRPC characterises cancer that no longer responds to ADT and has spread to other parts of the body.[23] The most common metastatic sites are bones, followed by the lymph nodes, liver and lungs.[24] Prostate cancer is the most common cancer in men in Europe.[4] In 2020, more than one million men around the world were diagnosed with prostate cancer.[25] Patients with mCRPC and 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.[10,11,12,13]

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About MAGNITUDE

MAGNITUDE (NCT03748641) is a Phase 3 randomised, double-blind, placebo-controlled, multicentre clinical study evaluating the safety and efficacy of the combination of niraparib and AA and predniso(lo)ne (AAP) for patients with mCRPC (n=765), with or without certain HRR gene alterations and who have not received prior therapy for mCRPC except for standard of care, next-generation androgen receptor inhibitors and up to four months of AAP.[14,15] The study includes 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 randomised 1:1 to receive niraparib 200 mg once daily plus AAP or placebo plus AAP.[15,16] A total of 423 patients with HRR gene alterations were enrolled, 225 (53.2 percent) of whom had BRCA mutations.[15,16] Additionally in an open-label cohort of HRR-positive patients, all patients received the DAT formulation of niraparib and AA plus prednisone.[16] The primary endpoint of the MAGNITUDE trial is radiographic progression-free survival (rPFS) assessed by blinded independent central review.[15,16] Secondary endpoints include time-to-initiation of cytotoxic chemotherapy, time to symptomatic progression and overall survival.[15,16]

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 & Retina; 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 Pharmaceutica NV, Janssen-Cilag GmBH and Janssen Research & Development, LLC are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

*Professor Gerhardt Attard 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 materialise, actual results could vary materially from the expectations and projections of Janssen Pharmaceutica NV, Janssen-Cilag GmBH, Janssen Research & Development, LLC, 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 behaviour 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 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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