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ERLEADA™ (apalutamide), a Next-Generation Androgen Receptor Inhibitor, Granted U.S. FDA Approval for the Treatment of Patients with Non-Metastatic Castration-Resistant Prostate Cancer

- *ERLEADA™ is the first FDA-approved therapy to treat patients with non-metastatic castration-resistant prostate cancer*
- *Approval is based on Phase 3 SPARTAN clinical trial data which showed ERLEADA™ decreased the risk of distant metastasis or death by 72 percent and improved median metastasis-free survival by more than two years*
- *The major efficacy outcome was supported by statistically significant improvements for secondary endpoints, including time to metastasis, progression-free survival, and time to symptomatic progression*

HORSHAM, PA, February 14, 2018 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today that the U.S. Food and Drug Administration (FDA) has approved ERLEADA™ (apalutamide), a next-generation androgen receptor inhibitor,[1] for the treatment of patients with non-metastatic castration-resistant prostate cancer (NM-CRPC). ERLEADA™ is the first FDA-approved treatment for these patients. Today's approval follows an FDA Priority Review designation based upon data from the Phase 3 SPARTAN study, which demonstrated a 72 percent reduction in risk of distant metastasis or death, and an increase in median metastasis-free survival (MFS) by more than two years (difference of 24.31 months) in patients with NM-CRPC.

"The need to delay metastasis is critical to the treatment of prostate cancer. Nearly 90 percent of patients with castration-resistant prostate cancer will eventually develop bone metastases, at which point the prognosis sharply worsens," said Mathai Mammen, M.D.,

Ph.D., Global Head, Janssen Research & Development, LLC. "We are excited about what this approval means for patients living with prostate cancer, and that physicians now have an important and much-needed treatment option that has been shown to delay the progression of castration-resistant prostate cancer."

ERLEADA™ received FDA approval based on the Phase 3 data from the SPARTAN clinical trial, which assessed the efficacy and safety of ERLEADA™ versus placebo in patients with NM-CRPC who had a rapidly rising PSA while receiving continuous androgen deprivation therapy.[2] The study was recently presented at the 2018 American Society of Clinical Oncology Genitourinary Cancers Symposium (ASCO GU) on Thursday, February 8, 2018 in San Francisco and published in *The New England Journal of Medicine*.[2,3]

"The SPARTAN trial results demonstrated impressive clinical benefits in patients with non-metastatic castration-resistant prostate cancer," said Matthew Smith, M.D., Ph.D., Director of the Genitourinary Malignancies Program at the Massachusetts General Hospital Cancer Center, Professor of Medicine at Harvard Medical School, and co-principal investigator of the SPARTAN study. "As an oncologist and clinical investigator, I know how devastating it can be for patients and their families to hear that the cancer has spread. With this approval, doctors now have the chance to offer hope for delaying metastases in patients with castration-resistant prostate cancer."

"As the impact of prostate cancer continues to grow, we are reminded every day of the critical need for therapeutic options that offer patients with prostate cancer more time with their loved ones," Mark Scholz, M.D., Executive Director of the Prostate Cancer Research Institute. "Today's approval is significant, as it means that patients with non-metastatic castration-resistant prostate cancer now have a treatment option that offers renewed hope."

SPARTAN, a Phase 3, randomized, double-blind, placebo-controlled, multi-center study, enrolled 1,207 patients with non-metastatic castration-resistant prostate cancer.[4] Patients were randomized 2:1 to receive either ERLEADA™ orally at a dose of 240 mg once daily (n=806), or placebo once daily (n=401).[4] All patients in the SPARTAN trial received a concomitant gonadotropin-releasing hormone (GnRH) analog or had a bilateral orchiectomy.[4]

ERLEADA™ decreased the risk of distant metastasis or death by 72 percent compared to placebo (HR = 0.28; 95% CI, 0.23-0.35; *P*<0.0001).[4] The median MFS was 40.51 months for ERLEADA™ compared to 16.20 months for placebo, prolonging MFS by more than two years (difference of 24.31 months).[4] MFS benefit was consistently seen across patient subgroups including prostate specific antigen doubling time (PSADT) (≤6 months or >6 months), use of a prior bone-sparing agent (yes or no), and locoregional disease (N0 or N1).[4]

The major efficacy outcome was supported by statistically significant improvements for the following secondary endpoints: time to metastasis (TTM), progression-free survival (PFS) and time to symptomatic progression.[4] The median TTM was 40.51 months for ERLEADA™ compared to 16.59 months for placebo (HR=0.27; 95% CI, 0.22-0.34; *P*<0.0001) and the median PFS was 40.51 months compared to 14.72 months for placebo (HR=0.29; 95% CI, 0.24-0.36; *P*<0.0001).[4] Overall survival data were not mature at the time of final MFS analysis (24% of the required number of events).[4]

Warnings and Precautions include seizure, falls and fractures.[4] In the SPARTAN trial, the most common adverse reactions (≥10%) were fatigue, hypertension, rash, diarrhea, nausea, weight decreased, arthralgia, fall, hot flush, decreased appetite, fracture, and peripheral edema.[4]

About Non-Metastatic Castration-Resistant Prostate Cancer

Non-metastatic castration-resistant prostate cancer (NM-CRPC) refers to a disease state when the cancer no longer responds to medical or surgical treatments that lower testosterone, but has not yet been discovered in other parts of the body using a total body bone scan or CT scan.[5] Features include: lack of detectable metastatic disease;[5] rapidly rising prostate-specific antigen while on androgen deprivation therapy (ADT) and serum testosterone level below 50 ng/dL.[6,7] Ninety percent of patients with CRPC will eventually develop bone metastases, which can lead to pain, fractures and spinal cord compression.[8] The relative 5-year survival rate for patients with distant stage prostate cancer is 30 percent.[9] It is critical to delay the onset of metastasis in patients with NM-CRPC.

About ERLEADA™

ERLEADA™ (apalutamide) is an androgen receptor (AR) inhibitor indicated for the treatment of patients with non-metastatic castration-resistant prostate cancer.[4]

ERLEADA™ is an AR inhibitor that binds directly to the ligand-binding domain of the AR. ERLEADA™ inhibits AR nuclear translocation, inhibits DNA binding, and impedes AR-mediated transcription.[4] A major metabolite, N-desmethyl apalutamide, is a less potent inhibitor of AR, and exhibited one-third the activity of ERLEADA™ in an in vitro transcriptional reporter assay.[4] ERLEADA™ administration caused decreased tumor cell proliferation and increased apoptosis leading to decreased tumor volume in mouse xenograft models of prostate cancer.[4]

Full prescribing information will be available soon at www.ERLEADA.com.

Important Safety Information[4]

CONTRAINDICATIONS

Pregnancy - ERLEADA™ can cause fetal harm and potential loss of pregnancy.

WARNINGS AND PRECAUTIONS

Falls and Fractures - In the SPARTAN study, falls and fractures occurred in 16% and 12% of patients treated with ERLEADA™ compared to 9% and 7% treated with placebo respectively. Falls were not associated with loss of consciousness or seizure. Evaluate patients for fracture and fall risk. Monitor and manage patients at risk for fractures according to established treatment guidelines and consider use of bone targeted agents.

Seizure - In a randomized study (SPARTAN), two patients (0.2%) treated with ERLEADA™ experienced a seizure. Permanently discontinue ERLEADA™ in patients who develop a seizure during treatment. It is unknown whether anti-epileptic medications will prevent seizures with ERLEADA™. Advise patients of the risk of developing a seizure while receiving ERLEADA™ and of engaging in any activity where sudden loss of consciousness could cause harm to themselves or others.

ADVERSE REACTIONS

Adverse Reactions - The most common adverse reactions (≥10%) were fatigue, hypertension, rash, diarrhea, nausea, weight decreased, arthralgia, fall, hot flush, decreased appetite, fracture, and peripheral edema.

Laboratory Abnormalities

- Hematology: anemia ERLEADA™ 70% (Grade 3-4 0.4%) placebo 64% (Grade 3-4 0.5%) leukopenia ERLEADA™ 47% (Grade 3-4 0.3%) for, placebo 29% (Grades 3-4 0%), lymphopenia ERLEADA™ 41% (Grade 3-4 2%), placebo 21% (Grade 3-4 2%);
- Chemistry – hypercholesterolemia ERLEADA™ 76%(Grade3-4 0.1%), placebo 46% (Grade 3-4 0%); hypertriglycemia ERLEADA™ 70%(Grade 3-4 2%) Placebo 59% (0.8%); hypertriglyceridemia ERLEADA™ 67%(Grade 3-4 2%) placebo 49%(Grade 3-4 0.8%); Hyperkalemia ERLEADA™ 32%(Grade 3-4 2%) Placebo 22%(Grade 3-4 0.5%)

Rash - Rash was most commonly described as macular or maculo-papular. Adverse reactions were 24% with ERLEADA™ versus 6% with placebo. Grade 3 rashes (defined as covering > 30% body surface area [BSA]) were reported with ERLEADA™ treatment (5%) versus placebo (0.3%).

The onset of rash occurred at a median of 82 days. Rash resolved in 81% of patients within a median of 60 days (range: 2 to 709 days) from onset of rash. Four (4%) of patients treated with ERLEADA™ received systemic corticosteroids. Rash recurred in approximately half of patients who were re-challenged with ERLEADA™.

Hypothyroidism - Hypothyroidism was reported for 8% of patients treated with ERLEADA™ and 2% of patients treated with placebo based on assessments of thyroid-stimulating hormone (TSH) every 4 months. Elevated TSH occurred in 25% of patients treated with ERLEADA™ and 7% of patients treated with placebo. The median onset was Day 113. There were no Grade 3 or 4 adverse reactions. Thyroid replacement therapy, when clinically indicated, should be initiated or dose-adjusted.

Effect of Other Drugs on ERLEADA - Co-administration of a strong CYP2C8 or CYP3A4 inhibitor is predicted to increase the steady-state exposure of the active moieties. No initial dose adjustment is necessary however, reduce the ERLEADA™ dose based on tolerability *[see Dosage and Administration (2.2)].*

DRUG INTERACTIONS

Effect of ERLEADA™ on Other Drugs – ERLEADA™ is a strong inducer of CYP3A4 and CYP2C19, and a weak inducer of CYP2C9 in humans. Concomitant use of ERLEADA™ with

medications that are primarily metabolized by CYP3A4, CYP2C19, or CYP2C9 can result in lower exposure to these medications. Substitution for these medications is recommended when possible or evaluate for loss of activity if medication is continued. Concomitant administration of ERLEADA™ with medications that are substrates of UDP-glucuronosyl transferase (UGT) can result in decreased exposure. Use caution if substrates of UGT must be co-administered with ERLEADA™ and evaluate for loss of activity.

P-gp, BCRP or OATP1B1 substrates - Apalutamide is a weak inducer of P-glycoprotein (P-gp), breast cancer resistance protein (BCRP), and organic anion transporting polypeptide 1B1 (OATP1B1) clinically. Concomitant use of ERLEADA™ with medications that are substrates of P-gp, BCRP, or OATP1B1 can result in lower exposure of these medications. Use caution if substrates of P-gp, BCRP or OATP1B1 must be co-administered with ERLEADA™ and evaluate for loss of activity if medication is continued.

About the Janssen Pharmaceutical Companies of Johnson & Johnson

At the Janssen Pharmaceutical Companies of Johnson & Johnson, we are working to create a world without disease. Transforming lives by finding new and better ways to prevent, intercept, treat and cure disease inspires us. We bring together the best minds and pursue the most promising science.

We are Janssen. We collaborate with the world for the health of everyone in it. Learn more at www.janssen.com. Follow us at www.twitter.com/JanssenGlobal and www.twitter.com/JanssenUS. Janssen Research & Development, LLC is part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

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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 the benefits and availability of ERLEADA™ (apalutamide) for the treatment of certain types of prostate cancer. 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 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 1, 2017, including under "Item 1A. Risk Factors," its most recently filed Quarterly Report on Form 10-Q, including in the section captioned "Cautionary Note Regarding Forward-Looking Statements," 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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