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Long-Term ERLEADA® (apalutamide) Patient-Reported Outcomes Data in Metastatic Castration-Sensitive Prostate Cancer Demonstrate Maintenance of Health-Related Quality of Life for Patients

Results at ASCO from Phase 3 TITAN study final analysis confirm survival benefit achieved with the addition of ERLEADA® to androgen deprivation therapy without significant side effect burden

May 26, 2021 (RARITAN, N.J.) – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced patient-reported outcomes (PRO) data from the pre-specified final analysis of the Phase 3 TITAN study in patients with metastatic castration-sensitive prostate cancer (mCSPC). The TITAN study previously demonstrated statistically significant improvement in overall survival (OS) after a median follow-up of 44 months in patients receiving ERLEADA® plus androgen deprivation therapy (ADT).[1] The new PRO data showed that the addition of ERLEADA® to ADT maintained patients' health-related quality of life (HRQoL) and did not worsen side effect burden, consistent with ADT alone.[1] These data are being presented at the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting, June 4-8 (Abstract #5068).

"Concern about side effects and their resulting burden on quality of life can be a barrier for patients when considering treatment options," said Neeraj Agarwal, M.D., of the University of Utah Huntsman Cancer Institute, and the lead study investigator for TITAN.* "The significant long-term overall survival benefit we've seen demonstrated with ERLEADA, with no impact on quality of life as reported by patients, underscores the important role of this therapy in the treatment of advanced prostate cancer."

No significant differences in quality of life were observed between patients who received ERLEADA® plus ADT and patients who received placebo plus ADT.[1] Overall, patients in both groups reported being relatively asymptomatic with a good baseline HRQoL; the outcomes were assessed using the Brief Pain Inventory-Short Form (BPI-SF) and Functional Assessment of Cancer Therapy-Prostate (FACT-P) questionnaires.[1] On the BPI pain severity scale of zero (no pain/interference in daily activities) to 10 (worst pain/interference), median patient scores were 1.1 in the ERLEADA® group and 1 in the placebo plus ADT group. On the FACT-P HRQoL scale (1-156, higher score = better quality of life), median patient scores were 113 in the ERLEADA® group and 113.3 in the placebo plus ADT group.[1] ERLEADA® plus ADT was also shown to maintain physical, social and family, emotional, functional, and mental well-being beyond two years, as assessed by FACT-P.[1] There were no significant differences between groups in median time to deterioration in any BPI or FACT-P scores, further demonstrating maintenance of quality of life with ERLEADA®.[1]

ERLEADA® has previously shown a statistically significant improvement in OS for both of its approved indications in prostate cancer, specifically mCSPC (TITAN study) and non-metastatic castration-resistant prostate cancer (SPARTAN study).[2] The TITAN final analysis data, presented at the 2021 ASCO Genitourinary Cancers Symposium and recently published in the *Journal of Clinical Oncology,* reaffirmed that the addition of ERLEADA® to ADT continued to provide statistically significant OS benefit after 44 months in patients with mCSPC.[3] ERLEADA® plus ADT reduced the risk of death by 35 percent compared with ADT alone (hazard ratio [HR]=0.65; 95 percent confidence interval [CI], 0.53-0.79; $P<0.0001$).[3] SPARTAN final analysis data were presented at the 2020 ASCO Annual Meeting, showing that ERLEADA® plus ADT prolonged median OS by 14 months (73.9 vs. 59.9 months median OS for ERLEADA® and placebo groups, respectively) and reduced the risk of death by 22 percent (HR=0.78; 95 percent CI, 0.64-0.96; $P=0.016$).[4]

"Patient-reported outcomes provide meaningful input into treatment decisions by giving us insights into the way patients feel and function," said Mary Guckert, RN, MSN, Vice President, Development Leader, Prostate Cancer, Janssen Research & Development, LLC. "It is critically important to offer treatments, such as ERLEADA, that have demonstrated significant survival advantage and that maintain quality of life in patients with metastatic castration-sensitive prostate cancer."

About Metastatic Castration-Sensitive Prostate Cancer

Metastatic castration-sensitive prostate cancer, also known as metastatic hormone-sensitive prostate cancer (mHSPC), refers to prostate cancer that still responds to hormonal therapy and has spread beyond the prostate to other parts of the body.[5]

About the TITAN Study[3]

TITAN (NCT02489318) is a Phase 3, randomized, placebo-controlled, double-blind study in patients with mCSPC. The study included 1,052 patients in 23 countries across 260 sites in North America, Latin America, South America, Europe, and Asia Pacific.[6] Patients with mCSPC were randomized 1:1 and received either ERLEADA® (240 mg) plus ADT (n=524), or placebo plus ADT (n=527). The recruitment period for the study spanned from December 2015 to July 2017.[2] The study included patients with mCSPC with both low- and high-volume disease, those who were newly diagnosed, and those who had received prior definitive local therapy or prior treatment with up to six cycles of docetaxel for mCSPC.[3]

An Independent Data-Monitoring Committee was commissioned by the sponsor to monitor safety and efficacy.[6] Dual primary endpoints of the study were OS and radiographic progression free survival (rPFS). Secondary endpoints included time to cytotoxic chemotherapy, time to pain progression, time to chronic opioid use, and time to skeletal-related events.[6] Exploratory endpoints included time to prostate specific antigen (PSA) progression, second progression free survival (PFS2) and time to symptomatic progression.[6] For additional study information, visit ClinicalTrials.gov.

About ERLEADA® (apalutamide)

ERLEADA® is an androgen receptor inhibitor indicated for the treatment of patients with non-metastatic castration-resistant prostate cancer (nmCRPC) and for the treatment of patients with metastatic castration-sensitive prostate cancer (mCSPC).[2] ERLEADA® received U.S. Food and Drug Administration (FDA) approval for nmCRPC on February 14, 2018 and

was approved for mCSPC on September 17, 2019.[2] To date, more than 25,000 patients worldwide have been treated with ERLEADA®. ERLEADA® is taken orally, once daily, with or without food.[2] The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer include apalutamide (ERLEADA®) with continued androgen deprivation therapy**† as a Category 1 Preferred treatment option for patients with non-metastatic (M0) castration-resistant prostate cancer and a PSADT ≤10 months.[7] The NCCN Clinical Practice Guidelines® also include apalutamide (ERLEADA®) with androgen deprivation**† as a Category 1 Preferred treatment option for patients with metastatic (M1) castration-naive prostate cancer.‡[6] The American Urological Association (AUA) Guidelines for Castration-Resistant Prostate Cancer (CRPC) recommend clinicians offer apalutamide (ERLEADA®) with continued androgen deprivation therapy (ADT) as one of the treatment options for patients with nmCRPC at high risk for developing metastatic disease (Standard; Evidence Level Grade A)***.[8] ERLEADA® is being further studied in two ongoing Phase 3 clinical trials.

For more information about ERLEADA®, visit www.ERLEADA.com.

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***Orchiectomy, LHRH agonist, or LHRH antagonist*

†Use of an LHRH agonist plus a first-generation antiandrogen is an option for patients receiving ADT alone, but is not an option for patients receiving apalutamide.

‡The term "castration-naive" is used to define patients who are not on ADT at the time of progression. The NCCN Prostate Cancer Panel uses the term "castration-naive" even when patients have had neoadjuvant, concurrent, or adjuvant ADT as part of radiation therapy provided they have recovered testicular function.

****Standard: Directive statement that an action should (benefits outweigh risks/burdens) or should not (risks/burdens outweigh benefits) be taken based on Grade A or B evidence.*

****Evidence Level: A designation indicating the certainty of the results as high, moderate, or low (A, B, or C, respectively) based on AUA nomenclature and methodology.*

ERLEADA® IMPORTANT SAFETY INFORMATION
WARNINGS AND PRECAUTIONS

Cerebrovascular and Ischemic Cardiovascular Events — In a randomized study (SPARTAN) of patients with nmCRPC, ischemic cardiovascular events occurred in 4% of patients treated with ERLEADA and 3% of patients treated with placebo. In a randomized study (TITAN) in patients with mCSPC, ischemic cardiovascular events occurred in 4% of patients treated with ERLEADA and 2% of patients treated with placebo. Across the SPARTAN and TITAN studies, 5 patients (0.5%) treated with ERLEADA, and 2 patients (0.2%) treated with placebo died from an ischemic cardiovascular event.

In the SPARTAN study, cerebrovascular events occurred in 4.7% of patients treated with ERLEADA and 0.8% of patients treated with placebo. In the TITAN study, cerebrovascular events occurred in 1.9% of patients treated with ERLEADA and 2.1% of patients treated with placebo. Across the SPARTAN and TITAN studies, 3 patients (0.2%) treated with ERLEADA, and 2 patients (0.2%) treated with placebo died from a cerebrovascular event.

Cerebrovascular and ischemic cardiovascular events, including events leading to death, occurred in patients receiving ERLEADA®. Monitor for signs and symptoms of ischemic heart disease and cerebrovascular disorders. Optimize management of cardiovascular risk factors, such as hypertension, diabetes, or dyslipidemia. Consider discontinuation of ERLEADA® for Grade 3 and 4 events.

Fractures — In a randomized study (SPARTAN) of patients with nmCRPC, fractures occurred in 12% of patients treated with ERLEADA® and in 7% of patients treated with placebo. In a randomized study (TITAN) of patients with mCSPC, fractures occurred in 9% of patients treated with ERLEADA® and in 6% of patients treated with placebo. Evaluate patients for fracture risk. Monitor and manage patients at risk for fractures according to established treatment guidelines and consider use of bone-targeted agents.

Falls — In a randomized study (SPARTAN), falls occurred in 16% of patients treated with ERLEADA® compared with 9% of patients treated with placebo. Falls were not associated with loss of consciousness or seizure. Falls occurred in patients receiving ERLEADA® with increased frequency in the elderly. Evaluate patients for fall risk.

Seizure — In 2 randomized studies (SPARTAN and TITAN), 5 patients (0.4%) treated with ERLEADA® and 1 patient treated with placebo (0.1%) 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.

Embryo-Fetal Toxicity — The safety and efficacy of ERLEADA® have not been established in females. Based on its mechanism of action, ERLEADA® can cause fetal harm and loss of pregnancy when administered to a pregnant female. Advise males with female partners of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of ERLEADA® *[see Use in Specific Populations (8.1, 8.3)]*.

ADVERSE REACTIONS

Adverse Reactions — The most common adverse reactions (≥10%) that occurred more frequently in the ERLEADA®-treated patients (≥ 2% over placebo) from the randomized placebo-controlled clinical trials (TITAN and SPARTAN) were fatigue, arthralgia, rash, decreased appetite, fall, weight decreased, hypertension, hot flush, diarrhea and fracture.

Laboratory Abnormalities — All Grades (Grade 3-4)

- Hematology — In the TITAN study: white blood cell decreased ERLEADA® 27% (0.4%), placebo 19% (0.6%). In the SPARTAN study: anemia ERLEADA® 70% (0.4%), placebo 64% (0.5%); leukopenia ERLEADA® 47% (0.3%), placebo 29% (0%); lymphopenia ERLEADA® 41% (2%), placebo 21% (2%)

- Chemistry — In the TITAN study: hypertriglyceridemia ERLEADA® 17% (3%), placebo 12% (2%). In the SPARTAN study: hypercholesterolemia ERLEADA® 76% (0.1%), placebo 46% (0%); hyperglycemia ERLEADA® 70% (2%), placebo 59% (1%); hypertriglyceridemia ERLEADA® 67% (2%), placebo 49% (0.8%); hyperkalemia ERLEADA® 32% (2%), placebo 22% (0.5%)

Rash — In 2 randomized studies, rash was most commonly described as macular or maculopapular. Adverse reactions of rash were 26% with ERLEADA® vs 8% with placebo. Grade 3 rashes (defined as covering >30% body surface area [BSA]) were reported with ERLEADA® treatment (6%) vs placebo (0.5%).

The onset of rash occurred at a median of 83 days. Rash resolved in 78% of patients within a median of 78 days from onset of rash. Rash was commonly managed with oral antihistamines, topical corticosteroids, and 19% of patients received systemic corticosteroids. Dose reduction or dose interruption occurred in 14% and 28% of patients, respectively. Of the patients who had dose interruption, 59% experienced recurrence of rash upon reintroduction of ERLEADA®.

Hypothyroidism — In 2 randomized studies, 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 at the first scheduled assessment. There were no Grade 3 or 4 adverse reactions. Thyroid replacement therapy, when clinically indicated, should be initiated or dose adjusted.

DRUG INTERACTIONS

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)].*

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.

Please see the full Prescribing Information for ERLEADA®.

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. Follow us at www.twitter.com/JanssenGlobal and www.twitter.com/JanssenUS. Janssen Research & Development, LLC is one of the Janssen Pharmaceutical Companies of Johnson & Johnson.

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*Dr. Agarwal 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 ERLEADA® (apalutamide). 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 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 Report 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. 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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[1] Agarwal, N. et al. Health-related quality of life (HRQoL) and patient-reported outcomes at final analysis of the TITAN study of apalutamide (APA) versus placebo (PBO) in patients (pts) with metastatic castration-sensitive prostate cancer (mCSPC) receiving androgen deprivation therapy (ADT). https://meetinglibrary.asco.org/record/197750/abstract. Accessed May 2021.
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[3] Chi, K, et al. Apalutamide in Patients with Metastatic Castration-Sensitive Prostate Cancer: Final Survival Analysis of the Randomized, Double-Blind, Phase III TITAN Study. *Journal of Clinical Oncology*. Accessed May 2021.
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