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ERLEADA® (apalutamide) Significantly Improved Overall Survival (OS) and Radiographic Progression-Free Survival (rPFS) in Patients with Metastatic Castration-Sensitive Prostate Cancer (mCSPC)

Phase 3 results featured in oral presentation at ASCO 2019, selected for Best of ASCO 2019 Meetings, and simultaneously published in The New England Journal of Medicine

CHICAGO, May 31, 2019 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today findings from the investigational Phase 3 TITAN study, which showed the addition of ERLEADA® (apalutamide) to androgen deprivation therapy (ADT) compared with placebo plus ADT significantly improved the dual primary endpoints of overall survival (OS) and radiographic progression-free survival (rPFS) in patients with metastatic castration-sensitive prostate cancer (mCSPC).[1] The study included patients with mCSPC regardless of extent of disease or prior docetaxel treatment history.[1] Results were presented in an oral session at the American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago (abstract #5006), and simultaneously published online in *The New England Journal of Medicine*. The data were selected for the Best of ASCO 2019 Meetings, which highlight cutting-edge science and reflect leading research in oncology.

ERLEADA plus ADT significantly extended OS compared to placebo plus ADT with a 33 percent reduction in the risk of death (HR=0.67; 95 percent CI, 0.51-0.89; P=0.0053).[1] ERLEADA plus ADT also significantly improved rPFS compared to placebo plus ADT with a 52 percent reduction in risk of radiographic progression or death compared to placebo plus ADT (HR=0.48; 95 percent CI, 0.39-0.60; P<0.0001).[1] The two-year OS rates, after a median follow-up of 22.7 months, were 82 percent for ERLEADA plus ADT compared to 74 percent for placebo plus ADT.[1]

These data formed the basis of a supplemental New Drug Application (sNDA) to the U.S. Food and Drug Administration (FDA) seeking approval of a new indication for ERLEADA for the treatment of patients with mCSPC, which is currently under review through the Real-Time Oncology Review (RTOR) program.

"Patients with metastatic castration-sensitive prostate cancer typically have a poor prognosis, with a median overall survival of less than five years. Despite advances in treatment, there is still a critical need to improve outcomes for these patients," said Dr. Kim Chi, Medical Oncologist at BC Cancer - Vancouver and principal investigator of the study. "These data suggest that apalutamide prolongs overall survival and delays disease progression in patients with metastatic castration-sensitive prostate cancer."

In addition to meeting the primary dual endpoints of OS and rPFS, the secondary endpoint of prolonged time to cytotoxic chemotherapy in patients treated with ERLEADA plus ADT was also met, with a 61 percent risk reduction compared with placebo plus ADT (HR=0.39; 95 percent CI, 0.27-0.56; P<0.0001).[1] In exploratory endpoints, median time to PSA progression was more favorable following ERLEADA plus ADT, compared with placebo plus ADT, and prostate-specific antigen (PSA) reached undetectable levels in 68 percent of patients in the ERLEADA plus ADT arm and 29 percent of patients in the placebo plus ADT arm.[1] Additionally, ERLEADA plus ADT, compared with placebo plus ADT, achieved a 34 percent risk reduction in median time to second progression-free survival (PFS2), defined as time from randomization to either disease progression on first subsequent anticancer therapy or death, whichever occurred first (HR=0.66; 95 percent CI, 0.50-0.87).[1] Although time to pain progression was tested, it did not reach statistical significance. Due to a hierarchical statistical design, no formal testing for further secondary endpoints, including

median time to chronic opioid use and median time to skeletal-related events, were conducted at this time.[1]

Adverse events were generally consistent with the known ERLEADA safety profile. The most common Grade 3/4 adverse events (AEs) for ERLEADA plus ADT, versus placebo plus ADT were similar (42 percent vs. 41 percent).[1] The most common Grade 3 AEs for ERLEADA plus ADT versus placebo plus ADT were hypertension (8.4 percent vs. 9.1 percent) and skin rash (6.3 percent vs. 0.6 percent).[1] Additional reported Grade 3 AEs for ERLEADA plus ADT versus placebo plus ADT were back pain (2.3 percent vs. 2.7 percent), blood alkaline phosphatase increased (0.4 percent vs. 2.5 percent) and anemia (1.7 percent vs. 3.2 percent).[1] Treatment discontinuation due to AEs was 8 percent in the ERLEADA arm compared to 5 percent in the placebo arm.[1] Rash of any grade was more common among patients treated with ERLEADA plus ADT, versus placebo plus ADT (27 percent vs. 9 percent, respectively).[1]

"The TITAN study results demonstrate that the addition of ERLEADA to ADT improves clinical outcomes without compromising health-related quality of life for a broad range of patients with metastatic castration-sensitive prostate cancer," said Craig Tendler, M.D., Vice President, Clinical Development and Global Medical Affairs, Oncology, Janssen Research & Development, LLC. "These data suggest that ADT alone should no longer be considered the standard of care for metastatic castration-sensitive prostate cancer and support Janssen's investigation of ERLEADA in earlier stages of prostate cancer."

About the TITAN Study[1]

TITAN (NCT02489318) is a Phase 3 randomized, placebo-controlled, double-blind study in men with mCSPC regardless of extent of disease or prior docetaxel treatment history. The study included 1,052 patients included in intention-to-treat (ITT) population in 23 countries across 260 sites in North America, Latin America, South America, Europe and Asia Pacific. Patients with mCSPC were randomized 1:1 and received either ERLEADA (240 mg) plus continuous ADT (n=525), or placebo plus ADT (n=527). The recruitment period for the study spanned from December 2015 to July 2017. The study included mCSPC patients with both low- and high-volume disease, those who were newly diagnosed, or those who had received prior definitive local therapy or prior treatment with up to six cycles of docetaxel or up to six months of ADT for mCSPC. Participants were treated until disease progression or the occurrence of unacceptable treatment-related toxicity. An Independent Data-Monitoring

Committee was commissioned by the sponsor to monitor safety and efficacy before unblinding and to make study conduct recommendations. Dual primary endpoints of the study were OS and rPFS. Secondary endpoints included time to cytotoxic chemotherapy, time to pain progression, time to chronic opioid use and time to skeletal-related event. Exploratory endpoints included time to PSA progression, time to PFS2 and time to symptomatic progression.[1] For additional study information, visit ClinicalTrials.gov.

About Metastatic Castration-Sensitive Prostate Cancer

Metastatic castration-sensitive prostate cancer (mCSPC) refers to prostate cancer that still responds to ADT and has spread to other parts of the body.[2,3] Patients with mCSPC tend to have a poor prognosis, with a median OS of less than five years, underscoring the need for new treatment options.[2,3,4]

About ERLEADA

ERLEADA® (apalutamide) is an androgen receptor (AR) inhibitor indicated for the treatment of patients with non-metastatic castration-resistant prostate cancer (nmCRPC). It became the first treatment to receive FDA approval for nmCRPC on February 14, 2018.[5] The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer include apalutamide as a treatment option for patients with non-metastatic (M0) CRPC with a category 1 recommendation for those with a PSA doubling time ≤10 months*.[6] Additionally, the American Urological Association (AUA) Guidelines for Castration-Resistant Prostate Cancer (CRPC) were updated to include apalutamide (ERLEADA) with continued ADT as a treatment option that clinicians should offer to patients with asymptomatic nmCRPC. It is included as one of the options clinicians should offer to patients with nmCRPC who are at high risk for developing metastatic disease (Standard; Evidence Level Grade A)**.[7]

**Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer V.2.2019. © National Comprehensive Cancer Network, Inc. 2018. All rights reserved. Accessed April 23, 2019. To view the most recent and complete version of the NCCN Guidelines®, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use, or application, and disclaims any responsibility for their application or use in any way.*

***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[5]

CONTRAINDICATIONS

Pregnancy — ERLEADA™ (apalutamide) can cause fetal harm and potential loss of pregnancy.

WARNINGS AND PRECAUTIONS

Falls and Fractures — In a randomized study (SPARTAN), 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), 2 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 — All Grades (Grade 3-4)

- Hematology — 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 — 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 — 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 percent of patients treated with ERLEADA™ received systemic corticosteroids. Rash recurred in approximately half of patients who were re-challenged with ERLEADA™.

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.

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. Janssen Research & Development, LLC and Janssen Biotech, Inc. are 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 potential benefits and further benefits of 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, 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 December 30, 2018, 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] Chi, K. First results from TITAN: a phase III double-blind, randomized study of apalutamide (APA) versus placebo (PBO) in patients (pts) with metastatic castration-sensitive prostate cancer (mCSPC) receiving androgen deprivation therapy (ADT). Accessed May 2019.

[2] American Cancer Society. Survival rates for prostate cancer. https://www.cancer.org/cancer/prostate-cancer/detection-diagnosis-staging/survival-rates.html. Accessed May 2019.

[3] Crawford ED, Higano CS, Shore ND, et al. Treating patients with metastatic castration resistant prostate cancer: a comprehensive review of available therapies. *J Urol.* 2015:194;1537-1547.

[4] Fizazi K., et al. Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer. *New England Journal of Medicine*. June 2017.

[5] ERLEADA™ Prescribing Information, February 2018.

[6] National Comprehensive Cancer Network (NCCN) Guidelines. Available at file://znycfp2/ny%20dept/NY%20Health/J&J/Janssen%20Oncology/Apalutamide/2019/Regulatory%20Milestones/NCCN%20Guidelines/PC%20NCCN%20Guidelines%20-%202019.pdf. Accessed May 2019.

[7] American Urological Association. Castration-Resistant Prostate Cancer Guidelines. http://www.auanet.org/guidelines/castration-resistant-prostate-cancer-(2013-amended-2018). Accessed May 2019.