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**ERLEADA® (apalutamide) Significantly Improved Overall Survival in Patients with Non-Metastatic Castration-Resistant Prostate Cancer**

*Final analysis of the Phase 3 SPARTAN study presented during ASCO Virtual Scientific Program suggests 14-month improvement in median overall survival*

**RARITAN, NJ, May 13, 2020** – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today results from the final analysis of the pivotal Phase 3 [SPARTAN](#) study demonstrating ERLEADA® (apalutamide) in combination with androgen deprivation therapy (ADT) significantly improved overall survival (OS), compared to ADT alone, in patients with non-metastatic castration-resistant prostate cancer (nmCRPC) who were at high risk of developing metastases.<sup>1</sup> Results will be presented at the American Society of Clinical Oncology (ASCO) Virtual Scientific Program ([Abstract #5516](#)) beginning May 29<sup>th</sup>.

ERLEADA® in combination with ADT prolonged median overall survival by 14 months and decreased the risk of death by 22 percent.<sup>1</sup> Median OS was significantly longer, with 73.9 months for patients receiving treatment with ERLEADA® in combination with ADT compared to 59.9 months with patients receiving placebo in combination with ADT [HR=0.78; p=0.0161 (to reach statistical significance, a p-value of  $p \leq 0.046$  needed to be observed)].<sup>1</sup> After the study met its primary endpoint of metastasis-free survival (MFS), the SPARTAN

study was unblinded and patients on placebo were allowed to crossover to ERLEADA<sup>®</sup>. The OS results were achieved despite a crossover of 76 randomized placebo patients (19 percent) to ERLEADA<sup>®</sup> treatment.<sup>1</sup> After adjusting for the crossover of patients in the placebo arm, the treatment effect of ERLEADA<sup>®</sup> plus ADT exceeded median OS compared to placebo plus ADT with a difference of 21 months between the two arms (73.9 months vs 52.8 months, respectively, HR=0.69, p=0.0002). Additionally, treatment with ERLEADA<sup>®</sup> in combination with ADT significantly delayed patients' time to cytotoxic chemotherapy compared to placebo in combination with ADT (HR=0.63; p=0.0002).<sup>1</sup>

"Treatment for patients with non-metastatic castration-resistant prostate cancer is primarily focused on delay of metastases and improvement of overall survival," said Eric Small, M.D., FASCO, Professor of Medicine, and Chief Scientific Officer at the Helen Diller Family Comprehensive Cancer Center at the University of California, San Francisco, and lead SPARTAN study investigator. "The final analysis of SPARTAN includes long-term data for each of these treatment parameters and helps to support the earlier use of apalutamide versus ADT alone."

Together with data from the primary analysis, the SPARTAN study has met all primary, secondary and exploratory endpoints. The primary endpoint of the study was MFS; the secondary endpoints were time to metastasis, progression-free survival (PFS), time to symptomatic progression, OS and time to initiation of cytotoxic chemotherapy; and the exploratory endpoints were second progression-free survival (PFS2), prostate specific antigen (PSA) responses and risk of PSA progression.

"This achievement in overall survival adds to the body of clinical data supporting ERLEADA in the treatment of patients diagnosed with non-metastatic castration-resistant prostate cancer," said Margaret Yu, M.D., Vice President, Prostate Cancer Disease Area Leader, Janssen Research & Development, LLC. "Through our five ongoing registrational Phase 3 clinical trials for ERLEADA, we are committed to the development of treatments for patients diagnosed with prostate cancer at various stages of the disease."

Median treatment duration was nearly three times longer for patients treated with ERLEADA<sup>®</sup> plus ADT (33 months) compared with the those treated with placebo plus ADT (12 months).<sup>1</sup> Grade 3/4 treatment-emergent adverse events of special interest were rash (5.2 percent), fractures (4.9 percent), falls (2.7 percent), ischemic heart disease (2.6

percent), hypothyroidism (0 percent) and seizures (0 percent).<sup>1</sup> Safety and tolerability of ERLEADA® is consistent and as reported previously.

Initial results from the SPARTAN trial were [presented](#) at the 2018 American Society of Clinical Oncology Genitourinary Cancers Symposium (ASCO GU) and simultaneously [published](#) in *The New England Journal of Medicine*. The study met its primary endpoint of MFS demonstrating a median MFS of more than two years (difference of 24.31 months) and a 72 percent reduction in risk of distant metastasis in patients with nmCRPC.<sup>2</sup> OS data were not mature at the time of the final MFS analysis (24 percent of the required number of events). Updated results were presented at the European Society for Medical Oncology (ESMO) Annual Congress in 2019 and were simultaneously [published](#) in *Annals of Oncology*.

ERLEADA® became the first FDA-approved therapy for patients with nmCRPC in February 2018. In September 2019, ERLEADA® received FDA approval for the treatment of patients with metastatic castration-sensitive prostate cancer (mCSPC) based on results from the Phase 3 TITAN study, which achieved statistical significance in the dual primary endpoints of OS and radiographic progression-free survival (rPFS). ERLEADA® significantly extends OS across two indications in advanced prostate cancer (nmCRPC and mCSPC). ERLEADA® is currently approved in over 65 countries, and labels are being updated globally to reflect data from the SPARTAN final analysis.

### **About the SPARTAN Study**

SPARTAN ([NCT01946204](#)) is a Phase 3, randomized, registrational, double-blind, placebo-controlled, multicenter study that evaluated ERLEADA® in combination with ADT in men with nmCRPC with a rapidly rising PSA (PSA Doubling Time  $\leq 10$  months).<sup>3</sup> The SPARTAN study enrolled 1,207 patients who were randomized 2:1 to receive either ERLEADA® orally at a dose of 240 mg once daily in combination with ADT (n=806) or placebo once daily in combination with ADT (n=401).<sup>3</sup>

Warnings and Precautions include ischemic cardiovascular events, fractures, falls, seizure and embryo-fetal toxicity.<sup>3</sup> In the SPARTAN study, the most common adverse reactions ( $\geq 10$  percent) were fatigue, hypertension, rash, diarrhea, nausea, weight decreased, arthralgia, falls, hot flush, decreased appetite, fracture and peripheral edema.<sup>3</sup>

### **About Non-Metastatic Castration-Resistant Prostate Cancer**

Non-metastatic castration-resistant prostate cancer (nmCRPC) refers to a disease stage in which the cancer no longer responds to treatments that lower testosterone but has not yet been discovered in other parts of the body using a total body bone scan and/or CT/MRI scan.<sup>4</sup> Features include: lack of detectable metastatic disease using conventional radiographic imaging and rapidly rising PSA while on ADT with serum testosterone level below 50 ng/dL.<sup>5,6</sup> Ninety percent of patients with nmCRPC will eventually develop metastases, which can lead to pain, fractures and other symptoms.<sup>7</sup> The relative five-year survival rate for patients diagnosed with a distant-stage prostate cancer is 31 percent.<sup>8</sup> It is critical to delay the development of metastasis in patients with nmCRPC.

### **About ERLEADA<sup>®</sup>**

ERLEADA<sup>®</sup> (apalutamide) is an androgen receptor (AR) inhibitor indicated for the treatment of patients with nmCRPC and for the treatment of patients with mCSPC.<sup>3</sup> ERLEADA<sup>®</sup> received FDA approval for nmCRPC on [February 14, 2018](#), and was approved for mCSPC on [September 17, 2019](#).<sup>3</sup> ERLEADA<sup>®</sup> is taken orally, once daily, with or without food.<sup>3</sup> The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines<sup>®</sup>) for Prostate Cancer include apalutamide (ERLEADA<sup>®</sup>) with continued androgen deprivation therapy<sup>\*\*†</sup> as a Category 1 Preferred treatment option for patients with non-metastatic (M0) castration-resistant prostate cancer and a PSADT ≤10 months.<sup>\*9</sup> The NCCN Guidelines<sup>®</sup> also include apalutamide (ERLEADA<sup>®</sup>) with androgen deprivation<sup>\*\*†</sup> as a Category 1 Preferred treatment option for patients with metastatic (M1) castration-naïve prostate cancer.<sup>‡\*9</sup> The American Urological Association (AUA) Guidelines for Castration-Resistant Prostate Cancer (CRPC) recommend clinicians offer apalutamide (ERLEADA<sup>®</sup>) 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)<sup>\*\*\*.10</sup> ERLEADA<sup>®</sup> is being studied in five registrational Phase 3 clinical trials.

*\* Referenced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines<sup>®</sup>) for Prostate Cancer V.1.2020. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed March 16, 2020. To view the most recent and complete version of the NCCN Guidelines<sup>®</sup>, 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.*

*\*\*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<sup>3</sup>**

### **WARNINGS AND PRECAUTIONS**

**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, 6 patients (0.5%) treated with ERLEADA® and 2 patients (0.2%) treated with placebo died from an ischemic cardiovascular event. Patients with current evidence of unstable angina, myocardial infarction, or congestive heart failure within six months of randomization were excluded from the SPARTAN and TITAN studies.

Ischemic cardiovascular events, including events leading to death, occurred in patients receiving ERLEADA®. Monitor for signs and symptoms of ischemic heart disease. 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<sup>®</sup> 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<sup>®</sup> compared to 9% of patients treated with placebo. Falls were not associated with loss of consciousness or seizure. Falls occurred in patients receiving ERLEADA<sup>®</sup> with increased frequency in the elderly. Evaluate patients for fall risk.

**Seizure** — In two randomized studies (SPARTAN and TITAN), five patients (0.4%) treated with ERLEADA<sup>®</sup> and one patient treated with placebo (0.1%) experienced a seizure. Permanently discontinue ERLEADA<sup>®</sup> in patients who develop a seizure during treatment. It is unknown whether anti-epileptic medications will prevent seizures with ERLEADA<sup>®</sup>. Advise patients of the risk of developing a seizure while receiving ERLEADA<sup>®</sup> 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<sup>®</sup> have not been established in females. Based on its mechanism of action, ERLEADA<sup>®</sup> 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<sup>®</sup> [see *Use in Specific Populations (8.1, 8.3)*].

## **ADVERSE REACTIONS**

**Adverse Reactions** — The most common adverse reactions ( $\geq 10\%$ ) that occurred more frequently in the ERLEADA<sup>®</sup>-treated patients ( $\geq 2\%$  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 TITAN study, white blood cell decreased ERLEADA<sup>®</sup> 27% (0.4%), placebo 19% (0.6%). In SPARTAN study anemia ERLEADA<sup>®</sup> 70% (0.4%), placebo 64% (0.5%); leukopenia ERLEADA<sup>®</sup> 47% (0.3%), placebo 29% (0%); lymphopenia ERLEADA<sup>®</sup> 41% (2%), placebo 21% (2%)

- Chemistry — In TITAN study, hypertriglyceridemia ERLEADA® 17% (3%), placebo 12% (2%). In 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 two randomized studies, rash was most commonly described as macular or maculo-papular. Adverse reactions of rash were 26% with ERLEADA® versus 8% with placebo. Grade 3 rashes (defined as covering >30% body surface area [BSA]) were reported with ERLEADA® treatment (6%) versus 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 two 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<sup>®</sup> 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<sup>®</sup> 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<sup>®</sup> 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<sup>®</sup> and evaluate for loss of activity if medication is continued.

Please see the full [Prescribing Information](#) for ERLEADA<sup>®</sup>.

### **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](http://www.janssen.com). Follow us at [www.twitter.com/JanssenGlobal](https://www.twitter.com/JanssenGlobal) and [www.twitter.com/JanssenUS](https://www.twitter.com/JanssenUS). Janssen Research & Development, LLC is one 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 product development and the potential benefits and treatment impact of ERLEADA<sup>®</sup> (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 December 29, 2019, 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](http://www.sec.gov), [www.jnj.com](http://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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<sup>1</sup> Small, E. et al. Final Survival Results From SPARTAN, a Phase 3 Study of Apalutamide (APA) vs Placebo (PBO) in Patients (pts) With Nonmetastatic Castration-Resistant Prostate Cancer (nmCRPC). <https://meetinglibrary.asco.org/record/187437/abstract>.

<sup>2</sup> Small E., et al. SPARTAN, a phase 3 double-blind, randomized study of apalutamide (APA) vs placebo (PBO). in patients (pts) with nonmetastatic castration-resistant prostate cancer (nmCRPC). Abstract #161.

<sup>3</sup> ERLEADA® Prescribing Information, September 2019.

<sup>4</sup> Scher HI, et al. Design and end points of clinical trials for patients with progressive prostate cancer and castrate levels of testosterone: recommendations of the Prostate Cancer Clinical Trials Working Group. J Clin Oncol. 2008;26:1148-1159. Accessed May 2020.

<sup>5</sup> Scher HI, et al. Trial Design and Objectives for Castration-Resistant Prostate Cancer: Updated Recommendations From the Prostate Cancer Clinical Trials Working Group 3. J Clin Oncol. 2016;34:1402-1418. Accessed May 2020.

<sup>6</sup> Virgo K, et al. Second-Line Hormonal Therapy for Men with Chemotherapy-Naive, Castration-Resistant Prostate Cancer: American Society of Clinical Oncology Provisional Clinical Opinion. Journal of Clinical Oncology. 2017; 0732-183X/17/3599-1. Accessed May 2020.

<sup>7</sup> Saad F, et al. The 2015 CUA0CUOG guidelines for the management of castration-resistant prostate cancer (CRPC). Can Urol Assoc J. 2015;9(3-4):90-96. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4455631/>. Accessed May 2020.

<sup>8</sup> American Cancer Society. Cancer Facts & Figures. Available at: <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2020/cancer-facts-and-figures-2020.pdf>. Accessed May 2020.

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<sup>9</sup> NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines<sup>®</sup>) for Prostate Cancer V.4.2019. National Comprehensive Cancer Network, Inc. 2019. All rights reserved. Updated August 2019.

<sup>10</sup> American Urological Association. Castration-Resistant Prostate Cancer Guidelines. [http://www.auanet.org/guidelines/castration-resistant-prostate-cancer-\(2013-amended-2018\)](http://www.auanet.org/guidelines/castration-resistant-prostate-cancer-(2013-amended-2018)). Accessed May 2020.