



News Release

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New ERLEADA® (apalutamide) Analysis Demonstrates Rapid, Deep Prostate-Specific Antigen (PSA) Response in Patients with Metastatic Castration-Sensitive Prostate Cancer (mCSPC)

Real-world evidence study demonstrates majority of patients with mCSPC achieved over 90 percent decline in PSA by six months after initiation of ERLEADA®

Rapid and deep PSA decline is associated with improved health-related quality of life in advanced prostate cancer as shown by separate post-hoc analysis of patient-reported outcomes from Phase 3 SPARTAN and TITAN studies

SAN FRANCISCO, Feb. 14, 2022 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced new real-world evidence data showing the initiation of ERLEADA® (apalutamide) results in high rates of rapid and deep prostate-specific antigen (PSA) response among patients with metastatic castration-sensitive prostate cancer (mCSPC). In a separate post-hoc analysis of the registrational Phase 3 SPARTAN and TITAN studies, rapid and deep PSA responses with ERLEADA® were associated with improvement in patient-reported outcomes (PROs) related to quality of life, physical wellbeing, pain, and fatigue intensity. These findings will be presented during the American Society of Clinical Oncology's Genitourinary (ASCO GU) Cancers Symposium, taking place in San Francisco and virtually from February 17-19, 2022.

The real-world evidence study evaluating PSA response (Abstract 43, Poster B9) included data from 186 patients treated with ERLEADA® and 165 treated with enzalutamide from 69 community urology practices in the United States. By six months, 69.3 percent of patients with mCSPC initiated on ERLEADA® attained PSA90 response and 55.6 percent for enzalutamide (HR=1.56; p=0.014). PSA90 response is defined as the patient's earliest attainment of ≥90 percent decline in PSA relative to their baseline PSA at treatment initiation. At nine months and by the end of follow-up, 70.4 percent of patients treated with ERLEADA® achieved PSA90 and 62.5 percent for enzalutamide (HR=1.49; p=0.024). The median time to PSA90 response was 3.1 months for patients treated with ERLEADA® and to 5.2 months for enzalutamide.^{1*}

“Deep PSA response is an important early prognostic factor for achieving longer radiographic progression-free survival and overall survival in patients with metastatic castration-sensitive prostate cancer,” said Benjamin Lowentritt, M.D., Director Prostate Cancer Care Program, Chesapeake Urology, and Past President, AUA, Mid-Atlantic Region, and lead study investigator.** “These real-world data are consistent with and reinforce the benefit of ERLEADA as reported in the clinical trial setting, providing prescribers with important insights regarding time to and durability of PSA90 responses for commonly prescribed mCSPC medications.”

Patients included in the analysis had at least 12 months of clinical activity to assess baseline characteristics and were classified into treatment cohorts based on their first filled prescription for ERLEADA® or enzalutamide after Dec. 16, 2019. Patients were followed from their first filled prescription date until the earliest of one of the following events: regimen discontinuation, treatment switch, end of clinical activity or end of data availability (March 5, 2021).

A separate ERLEADA® poster presentation evaluating PROs data (Abstract 73, Poster D1) demonstrated an association between rapid and deep PSA decline and improved health-related quality of life PROs as reported from the Phase 3 SPARTAN and TITAN studies. Patient-reported outcomes were assessed using tools including the Functional Assessment of Cancer Therapy-Prostate (FACT-P; TITAN and SPARTAN), Brief Pain Inventory-Short Form (BPI-SF; TITAN only), and Brief Fatigue Inventory (BFI; TITAN only):

- A landmark analysis at three months after treatment initiation evaluated the association between deep PSA decline (≤ 0.2 ng/mL) and delay in deterioration in PROs (defined as decrease ≥ 10 points FACT-P total, ≥ 3 points Physical Wellbeing, ≥ 30 percent baseline for BPI-SF worst pain, or ≥ 2 points for BFI worst fatigue).²
- Patients in both studies who achieved a deep PSA decline maintained FACT-P total (SPARTAN: HR=0.83; TITAN: HR=0.54) or FACT-P Physical Wellbeing (SPARTAN: HR=0.70; TITAN: HR=0.63) levels longer.²
- Patients in TITAN who achieved a deep PSA decline had a lower risk of increasing pain or worsening fatigue; as assessed by the BPI-SF worst pain intensity progression (HR=0.70) or BFI worst fatigue intensity progression (HR=0.76), respectively.²

“This analysis demonstrates that the rapid and deep PSA responses shown in the SPARTAN and TITAN pivotal studies translate into improved quality of life for patients,” said Tracy McGowan, M.D., Therapeutic Area Head, U.S. Medical Affairs, Janssen Scientific Affairs, LLC. “We are dedicated to continually expanding the body of research for ERLEADA by providing important information that may help patients and their physicians make treatment decisions that work best for them.”

To date, published results on ERLEADA[®] include data from more than 2,000 patients across three Phase 3 clinical studies. ERLEADA[®] has shown a statistically significant improvement in overall survival with a consistent safety profile, while maintaining patients’ health-related quality of life in both approved indications of mCSPC and non-metastatic castration resistant prostate cancer (nmCRPC).³ ERLEADA[®] is currently approved in more than 74 countries.

About ERLEADA[®]

ERLEADA[®] is an androgen receptor inhibitor indicated for the treatment of patients with nmCRPC and for the treatment of patients with mCSPC.⁴ 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](#).⁴ To date, more than 50,000 patients worldwide have been treated with ERLEADA[®]. ERLEADA[®] is taken orally, once daily, with or without food.⁴ 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.⁴ 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.^{‡5} 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)^{***.5} ERLEADA® is being further studied in two ongoing Phase 3 clinical trials.

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

**© National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed December 11, 2020. 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.*

***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 3.7% of patients treated with ERLEADA® and 2% of patients treated with placebo. In a randomized

study (TITAN) in patients with mCSPC, ischemic cardiovascular events occurred in 4.4% of patients treated with ERLEADA[®] and 1.5% of patients treated with placebo. Across the SPARTAN and TITAN studies, 4 patients (0.3%) treated with ERLEADA[®] and 2 patients (0.2%) treated with placebo died from an ischemic cardiovascular event. Patients with history of unstable angina, myocardial infarction, congestive heart failure, stroke, or transient ischemic attack within 6 months of randomization were excluded from the SPARTAN and TITAN studies.

In the SPARTAN study, cerebrovascular events occurred in 2.5% of patients treated with ERLEADA[®] and 1% 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 two 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 findings from animals and 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

The most common adverse reactions ($\geq 10\%$) that occurred more frequently in the ERLEADA[®]-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 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% (1.8%), placebo 21% (1.6%)
- **Chemistry** — In the TITAN study: hypertriglyceridemia ERLEADA[®] 17% (2.5%), placebo 12% (2.3%). In the SPARTAN study: hypercholesterolemia ERLEADA[®] 76% (0.1%), placebo 46% (0%); hyperglycemia ERLEADA[®] 70% (2%), placebo 59% (1.0%); hypertriglyceridemia ERLEADA[®] 67% (1.6%), placebo 49% (0.8%); hyperkalemia ERLEADA[®] 32% (1.9%), placebo 22% (0.5%)

Rash — In 2 randomized studies (SPARTAN and TITAN), 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 (SPARTAN and TITAN), hypothyroidism was reported for 8% of patients treated with ERLEADA® and 1.5% 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

CYP3A4, CYP2C9, CYP2C19, and UGT Substrates — 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 [@JanssenUS](#) and [@JanssenGlobal](#). Janssen Biotech, Inc. and Janssen Research & Development, LLC are part the Janssen Pharmaceutical Companies of Johnson & Johnson.

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*While this study utilized robust methodology, it did not address whether these findings represent a clinically meaningful difference or whether they translate into differences in longer term outcomes (e.g.: overall survival).

**Dr. Lowentritt 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 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, Janssen Biotech, Inc., or any 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 2, 2022, 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.

¹ Lowentritt et al. Attainment of Early, Deep Prostate-Specific Antigen Response in Metastatic Castration-Sensitive Prostate Cancer: A Comparison of Patients Initiated on Apalutamide or Enzalutamide. ASCO GU 2022.

² Small et al. Association Between Patient-Reported Outcomes (PROs) and Changes in Prostate-Specific Antigen (PSA) in Patients (pts) with Advanced Prostate Cancer Treated with Apalutamide (APA) in the SPARTAN and TITAN Studies. ASCO GU 2022.

³ ERLEADA® U.S. Prescribing Information, November 2021.

⁴ NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer V.3.2020. National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed January 2022.

⁵ 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 January 2022.