Media Inquiries:
Suzanne Frost
Phone: 1-416-317-0304

Brian Kenney
Phone: 1-215-628-7010

Investor Relations:
Christopher DelOrefice
Phone: 1-732-524-2955

Lesley Fishman
Phone: 1-732-524-3922

U.S. Medical Inquiries:
1-800-526-7736

Updated Results of the SPARTAN Study Show 25 Percent Reduction in the Risk of Death in Patients with Non-Metastatic Castration-Resistant Prostate Cancer (nmCRPC) Treated with ERLEADA® (apalutamide)

Results from the second interim analysis of the Phase 3 SPARTAN study featured in an oral presentation at ESMO 2019 and simultaneously published in Annals of Oncology

BARCELONA, SPAIN, September 27, 2019 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today updated, longer-term results from the pivotal Phase 3 SPARTAN study following a second interim analysis. Treatment with ERLEADA® (apalutamide) plus androgen deprivation therapy (ADT) resulted in a 25 percent reduction in the risk of death compared with placebo plus ADT in patients with non-metastatic castration-resistant prostate cancer (nmCRPC) who were at high risk of developing metastases.[1]

The updated findings showed overall survival (OS) results supported the first interim analysis, despite a crossover of patients receiving placebo to the ERLEADA® treatment group.[1] Results were presented in an oral session at the 2019 European Society for Medical

Oncology (ESMO) Annual Congress (abstract #843O), and simultaneously published in *Annals of Oncology*.

At the second interim analysis, a longer median follow-up of 41 months, four-year OS rates were 72.1 percent for patients treated with ERLEADA® and 64.7 percent for patients treated with placebo.[1] Overall, a 25 percent reduction in the risk of death was observed for patients receiving ERLEADA® compared with placebo [HR=0.75; 95 percent CI, 0.59-0.96; p=0.0197 (to reach statistical significance, a p-value of p<0.0121 needed to be observed)].[1] The OS benefit of ERLEADA® was consistent across baseline subgroups, such as race, prior treatments, baseline PSA and performance status.[1]

This interim analysis took place when 67 percent of the required OS events had been observed, compared with the original report when only 24 percent of required OS events had occurred (HR=0.70; 95 percent CI, 0.47-1.04; p=0.07).[1] After unblinding the study and prior to the second interim analysis, 76 non-progressing patients in the placebo group (19 percent of all placebo patients) crossed over to open-label ERLEADA®; the OS rates in the placebo group included those patients who were crossed over to ERLEADA® treatment.[1] The rates of treatment-emergent adverse events for ERLEADA® at the second interim analysis were consistent with rates previously reported.[1] In the SPARTAN study, the most common adverse events (≥10 percent) were fatigue, hypertension, rash, diarrhea, nausea, weight decreased, arthralgia, falls, hot flush, decreased appetite, fracture and peripheral edema.[2]

"Longer-term analyses help to present a more complete picture of a medication's benefits and potential risks over time. This updated SPARTAN analysis shows an important survival benefit," 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. "These results add to the evidence supporting apalutamide as a standard option for treating patients with non-metastatic castration-resistant prostate cancer who remain at high risk of their cancer spreading."

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.*

"While there have been advances in the treatment of prostate cancer over the years, it is still a lethal illness, particularly when patients progress to later stages of metastatic disease," said Margaret Yu, M.D., Vice President, Prostate Cancer Disease Area Leader, Janssen Research & Development, LLC. "ERLEADA® is now being studied in five Phase 3 randomized controlled trials as part of the largest clinical program of androgen receptor inhibitors. Together, these trials highlight Janssen's commitment to making prostate cancer a manageable disease."

About the SPARTAN Study

SPARTAN (NCT01946204) was 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 ≤10 months).[2] 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). Study results were initially reported at the 2018 ASCO Genitourinary Cancers Symposium and published in *The New England Journal of Medicine*.

Warnings and Precautions include ischemic cardiovascular events, fractures, falls, seizure and embryo-fetal toxicity.[2] In the SPARTAN study, the most common adverse reactions (≥10 percent) were fatigue, hypertension, rash, diarrhea, nausea, weight decreased, arthralgia, falls, hot flush, decreased appetite, fracture and peripheral edema.[2]

About Non-Metastatic Castration-Resistant Prostate Cancer

Non-metastatic castration-resistant prostate cancer (nmCRPC) refers to a disease stage when 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 CT/MRI scan.[3] 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.[4,5] Ninety percent of patients with nmCRPC will eventually develop metastases, which can lead to pain, fractures and other symptoms.[6] The relative five-year survival rate for patients diagnosed at a distant-stage prostate cancer is 30 percent.[7] It is critical to delay the development of metastasis in patients with nmCRPC.

About ERLEADA®

ERLEADA® (apalutamide) is an androgen receptor (AR) inhibitor indicated for the treatment of patients with nmCRPC and for the treatment of patients with metastatic castration-sensitive prostate cancer (mCSPC). ERLEADA® received FDA approval for nmCRPC on February 14, 2018 and was approved for mCSPC on September 17, 2019.[2] ERLEADA® was approved by the European Commission for the treatment of nmCRPC on January 12, 2019 and Janssen has submitted an application in Europe seeking approval for mCSPC. ERLEADA® is taken orally, once daily, with or without food. The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer include apalutamide (ERLEADA®) 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*.[8] The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) include apalutamide (ERLEADA®) with androgen deprivation** as a Category 1 treatment option for patients with metastatic (M1) castration-naive prostate cancer.[†8] The American Urological Association (AUA) Guidelines for Castration-Resistant Prostate Cancer (CRPC) recommend clinicians offer apalutamide (ERLEADA®) with 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)***.[9] ERLEADA® is being studied in five Phase 3 clinical trials.

**Referenced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer V.4.2019. © National Comprehensive Cancer Network, Inc. 2019. All rights reserved. Accessed September 16, 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.*

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

[†] 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[2]
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 6 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® 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 two 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.

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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 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. Neither the Janssen Pharmaceutical Companies of Johnson & Johnson 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] Smith, M, et al. Apalutamide and Overall Survival in Patients with Nonmetastatic Castration-Resistant Prostate Cancer (nmCRPC): Updated Results from the Phase 3 SPARTAN Study. https://oncologypro.esmo.org/Meeting-Resources/ESMO-2019-Congress/Apalutamide-APA-and-Overall-Survival-OS-in-Patients-pts-With-Nonmetastatic-Castration-Resistant-Prostate-Cancer-nmCRPC-Updated-Results-From-the-Phase-3-SPARTAN-Study. Accessed September 2019.

[2] ERLEADA® Prescribing Information, September 2019.

[3] 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 September 2019.

[4] 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 September 2019.

[5] Virgo K, et al. Second-Line Hormonal Therapy for Men with Chemotherapy-Naïve, Castration-Resistant Prostate Cancer: American Society of Clinical Oncology Provisional Clinical Opinion. Journal of Clinical Oncology. 2017; 0732-183X/17/3599-1. Accessed September 2019.

[6] 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 September 2019.

[7] 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/2018/cancer-facts-and-figures-2018.pdf. Accessed September 2019.

[8] NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer V.4.2019. National Comprehensive Cancer Network, Inc. 2019. All rights reserved. Updated August 2019.

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