PRESS RELEASE
FOR UK MEDICAL AND TRADE MEDIA ONLY
Embargoed until 00:01 Wednesday 8 September

Media Contact:
Preetika Ramjoorawon
PRamjoor@ITS.JNJ.com
+44 (0) 7920 417930

NICE backs Janssen's Erleada®▼ (apalutamide) for Hormone-Sensitive Metastatic and Hormone-Relapsed Non-Metastatic Prostate Cancer

- *Apalutamide has been shown to increase the time until the disease progresses and how long patients live, according to data from the Phase III TITAN and SPARTAN studies*[1,2]
- *Eligible prostate cancer patients will now have access to apalutamide via the National Health Service (NHS) in England and Wales*[3,4]

High Wycombe, 8th September 2021 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced that the National Institute of Health and Care Excellence (NICE) has reconsidered its previous decision for Erleada®▼ (apalutamide), and today published two positive Final Appraisal Determinations (FADs) recommending the use of apalutamide in combination with androgen deprivation therapy (ADT) to treat prostate cancer.[3,4] Apalutamide plus ADT is recommended for two indications within its marketing authorisation:

- As an option for treating hormone-sensitive metastatic prostate cancer (mHSPC) in adults, only if docetaxel is not suitable or cannot be tolerated[3]
- As an option for treating hormone-relapsed non-metastatic prostate cancer (nmHRPC)* that is at high risk** of metastasising in adults.[4]

The decision means eligible prostate cancer patients with mHSPC and nmHRPC will now have access to apalutamide via the National Health Service (NHS) in England and Wales.

There are over 42,500 people diagnosed with prostate cancer each year in England and Wales.[5] It is estimated that 13 percent have metastatic disease at diagnosis, and those with mHSPC also tend to have a poor prognosis, with a median overall survival (OS) of approximately 45 months in three large randomised controlled trials when starting standard androgen deprivation therapy (ADT).[7,6] However, there are some patients who cannot tolerate or are unsuitable for docetaxel plus ADT.[3] NICE concluded that identifying people for whom docetaxel was contraindicated or unsuitable would be based on a clinical framework considering individual patient risk.[3] Now apalutamide plus ADT has been recommended for use when docetaxel is unsuitable or cannot be tolerated, these patients can now access an alternative treatment option that is generally better tolerated than docetaxel plus ADT and is likely to be more effective than ADT alone.[3]

Approximately 87 percent of those with prostate cancer suffer from the non-metastatic form of the disease at diagnosis – meaning that the cancer has not spread to other parts

of the body.[7] If the disease is hormone-relapsed (also known as castration-resistant), it no longer responds to medical or surgical treatments that lower testosterone.[8] Around 90 percent of patients with hormone-relapsed prostate cancer will eventually develop bone metastases, which can be a key cause of complications and death.[8] Extending the period without metastases is therefore an important treatment goal.

"Despite significant advances in treatment options through research in advanced prostate cancer management, unfortunately in some patients the prognosis can be poor," said Professor Amit Bahl***, Consultant Clinical Oncologist and Uro-oncology Research Lead at Bristol Haematology & Oncology Centre. "The addition of apalutamide to the treatment pathway provides eligible prostate cancer patients with a therapy option with significant survival benefit as shown in clinical trials. It is a vital step towards improving outcomes in prostate cancer and enabling patients to have a better prognosis."

NICE's decision for mHSPC is based on data from the phase III TITAN study, which concluded that apalutamide plus ADT is clinically effective compared with placebo plus ADT.[3] NICE also concluded that the data showed that median radiographic progression-free survival for people randomised to apalutamide plus ADT was not reached and for people randomised to placebo plus ADT, it was 22.1 months (hazard ratio 0.5, 95% CI 0.4 to 0.6).[3]

Published data from TITAN confirmed that the safety profiles for apalutamide plus ADT, versus placebo plus ADT, were similar with 42 percent versus 41 percent of Grade 3/4 AEs observed respectively.[1] The most common Grade ≥3 AEs for apalutamide 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] Treatment discontinuation due to AEs was 8 percent in the apalutamide arm compared to 5 percent in the placebo arm.[1] Overall, the NICE committee concluded that adverse effects with apalutamide plus ADT are tolerable.[3]

In addition, NICE's decision around the nmHRPC indication is based on the results of the phase III SPARTAN trial.[4] In the trial median metastases-free survival for people randomised to apalutamide plus ADT was 40.5 months and for people randomised to placebo plus ADT it was 15.7 months (hazard ratio 0.30, 95% confidence interval [CI] 0.24 to 0.36). Furthermore, median overall survival (OS) for people given apalutamide plus ADT was 73.9 months, compared to 59.9 months in the placebo group.[4] Apalutamide plus ADT also improved median time to second progression (progression on next treatment), 55.6 months, compared to the control group (41.2 months).[4] Finally, mean change in EQ-5D-3L visual analogue score showed improvements in the apalutamide plus ADT arm compared with the placebo plus ADT arm at cycles 21 (mean difference 3.03) and 25 (mean difference 3.28), $p<0.05$.[4]

The most common Grade 3/4 treatment-emergent adverse events (AEs) in the SPARTAN study were hypertension (14.3 percent vs. 11.8 percent), rash (5.2 percent vs. 0.3 percent), fall (1.7 percent vs. 0.8 percent) and fracture (2.7 percent vs. 0.8 percent).[2] Treatment discontinuation due to adverse events was 10.6 percent in the apalutamide arm compared to 7 percent in the placebo arm.[2] Rates of serious adverse events were similar in the apalutamide in combination with ADT arm versus placebo in combination with ADT

arm (24.8 percent vs. 23.1 percent respectively).[2] Overall, the NICE committee concluded that adverse effects with apalutamide plus ADT are tolerable.[4]

"Today's positive recommendation for apalutamide marks a significant milestone in our mission to bring new therapeutic options to patients with mHSPC and nmHRPC," said Sarah Scanlon, Business Unit Director, Oncology, Haematology and Pulmonary Hypertension. "We are delighted that NICE has given the green light for apalutamide for both indications and look forward to seeing these groups of patients benefit from a new treatment option."

*Hormone-relapsed non-metastatic prostate cancer (nmHRPC) can also be referred to as castration-resistant non-metastatic prostate cancer (nmCRPC).
**High risk is defined as a blood prostate specific antigen (PSA) level that has doubled in 10 months or less on continuous ADT.[4]
*** Professor Amit Bahl has not received consultancy honoraria from Janssen. He has not been compensated for any media work.

#ENDS#

About apalutamide
Apalutamide is a next-generation oral androgen receptor (AR) inhibitor that blocks the androgen signalling pathway in prostate cancer cells.[9] Apalutamide inhibits the growth of cancer cells in three ways: by preventing the binding of androgen to the AR; by inhibiting AR nuclear translocation and DNA binding; and prevents AR-mediated gene transcription.[2]

It is indicated for use in the UK for the treatment of patients with non-metastatic hormone-relapsed prostate cancer (nmHRPC) who are at high risk of developing metastatic disease, and in adult men with metastatic hormone-sensitive prostate cancer (mHSPC) in combination with androgen deprivation therapy (ADT).[10] nmHRPC can also be referred to as castration-resistant non-metastatic prostate cancer (nmCRPC).[4]

Important safety information
For a full list of side effects and information on dosage and administration, contraindications and other precautions when using apalutamide please refer to the Summary of Product Characteristics for further information.

Adverse events should be reported.▼ This medicinal product is subject to additional monitoring and it is therefore important to report any suspected adverse events related to this medicinal product. Healthcare professionals are asked to report any suspected adverse events via the MHRA. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/ or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Janssen-Cilag Limited on 01494 567447 or at dsafety@its.jnj.com.

About the TITAN study[1]
TITAN is a Phase III randomised, placebo-controlled, double-blind study in men with mHSPC regardless of extent of disease or prior docetaxel treatment history. The study included 1,052 patients 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 mHSPC were randomised 1:1 and received either apalutamide (240 mg) plus continuous androgen deprivation therapy (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 mHSPC 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 mHSPC. Participants were treated until disease progression or the occurrence of unacceptable treatment-related toxicity.

In the TITAN study, apalutamide plus ADT was found to be clinically effective compared with placebo plus ADT in the treatment of mHSPC. The percentage of patients with radiographic progression–free survival at 24 months was 68.2 percent in the apalutamide group and 47.5 percent in the placebo group. Overall survival at 24 months was also greater with apalutamide than with placebo (82.4 percent in the apalutamide group versus 73.5 percent in the placebo group).

An independent data-monitoring committee was commissioned by the sponsor to monitor safety and efficacy before unblinding and 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 second progression-free survival and time to symptomatic progression. For additional study information, visit ClinicalTrials.gov.

About the SPARTAN study[2]
SPARTAN is a Phase III randomised, placebo-controlled, double-blind study that evaluated apalutamide in combination with ADT in men with nmHRPC with a rapidly rising prostate-specific antigen (PSA) (PSA Doubling Time ≤10 months). The SPARTAN study enrolled 1,207 patients who were randomised 2:1 to receive either apalutamide 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).

The SPARTAN clinical study showed that apalutamide, when added to ADT, significantly reduced the risk of developing distant metastasis or death (metastasis free survival [MFS]) by 72 percent, compared to placebo in combination with ADT (hazard ratio [HR] = 0.28; 95% CI, 0.23-0.35; P < 0.001). The median MFS was improved by over two years (40.5 months vs 16.2 months) in patients with nmHRPC with a PSA doubling time of less or equal to 10 months.

The most common Grade 3/4 treatment-emergent adverse events in the SPARTAN study comparing APA+ADT vs the placebo (PBO)+ADT were hypertension (14.3 percent vs. 11.8 percent), rash (5.2 percent vs. 0.3 percent), fall (1.7 percent vs. 0.8 percent) and fracture (2.7 percent vs. 0.8 percent).

About metastatic hormone-sensitive prostate cancer
Metastatic hormone-sensitive prostate cancer (mHSPC) refers to prostate cancer that still responds to androgen deprivation therapy (ADT) and has spread to other parts of the

body. Patients with mHSPC tend to have a poor prognosis, with a median overall survival (OS) of approximately 45 months, underscoring the need for new treatment options.[6]

About non-metastatic hormone-relapsed prostate cancer

Non-metastatic hormone-relapsed prostate cancer (nmHRPC) refers to a disease stage when the cancer no longer responds to medical or surgical treatments that lower testosterone, but has not yet been discovered in other parts of the body using a bone scan or CT scan.[11] Features include: lack of detectable metastatic disease; rapidly rising prostate-specific antigen while on androgen deprivation therapy (ADT) and serum testosterone level below 50 ng/dLa.[11] 90 percent of patients with nmHRPC will eventually develop bone metastases, which can lead to pain, fractures and spinal cord compression.[9]

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.

Janssen-Cilag Limited is a Janssen Pharmaceutical Company of Johnson & Johnson.
Learn more at www.janssen.com/uk. Follow us at www.twitter.com/JanssenUK.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding 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 materialise, 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

PRESS RELEASE
FOR UK MEDICAL AND TRADE MEDIA ONLY
Embargoed until 00:01 Wednesday 8 September

Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

References:

[1] Chi, Kim N., et al. Apalutamide for Metastatic, Castration-Sensitive Prostate Cancer. *The New England Journal of Medicine,* vol. 381, no. 1, 2019, pp. 13–24.

[2] Smith, Matthew R., et al. Apalutamide Treatment and Metastasis-Free Survival in Prostate Cancer. The *New England Journal of Medicine*, vol. 378, no. 15, 2018, pp. 1408–1418.

[3] National Institute for Health and Care Excellence. Final appraisal document. Apalutamide with androgen deprivation therapy for treating hormone-sensitive metastatic prostate cancer. Available at: https://www.nice.org.uk/guidance/gid-ta10423/documents/. Last accessed September 2021.

[4] National Institute for Health and Care Excellence. Final appraisal document. Apalutamide with androgen deprivation therapy for treating high-risk hormone-relapsed non-metastatic prostate cancer. Available at: https://www.nice.org.uk/guidance/gid-ta10423/documents/. Last accessed September 2021.

[5] Prostate Cancer UK. About Prostate Cancer. Available at: https://prostatecanceruk.org/prostate-information/about-prostate-cancer. Last accessed September 2021.

[6] European Association of Urology. Updated guidelines for metastatic hormone-sensitive prostate cancer: abiraterone acetate combined with castration is another standard. Available at: https://uroweb.org/wp-content/uploads/Mottet-N.-et-al.-Eur-Urol-733316-321.-Updated-Guidelines-for-Metastatic-Hormone-sensitive-PCa-Abiraterone-Acetate.pdf. Last accessed September 2021.

[7] National Prostate Cancer Audit. Annual Report 2020: Results of the NPCA Prospective Audit in England and Wales for men diagnosed from 1 April 2018 to 31 March 2019. January 2021. Available at: https://www.npca.org.uk/content/uploads/2021/01/NPCA-Annual-Report-2020_Final_140121.pdf. Last accessed September 2021.

[8] Saad. F. Guidelines for the management of castrate-resistant prostate cancer. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2997826/ Last accessed September 2021.

[9] Clegg, Nicola J., et al. ARN-509: A Novel Antiandrogen for Prostate Cancer Treatment. *Cancer Research,* vol. 72, no. 6, 2012, pp. 1494–1503.

[10] EMC. Summary of Product Characteristics. Erleada 60 mg film coated tablets. Available at: https://www.medicines.org.uk/emc/product/9832/smpc#gref. Last accessed September 2021.

[11] Luo, Jia, et al. Treatment of Nonmetastatic Castration-Resistant Prostate Cancer. *Oncology*, vol. 30, no. 4, 2016, pp. 336–344.

Date of preparation: September 2021
Job code: EM-70506