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Janssen Submits Marketing Authorisation Application for Apalutamide to Treat Patients with High-Risk Non-Metastatic Castration-Resistant Prostate Cancer

- *Phase 3 SPARTAN data showed apalutamide improved median metastasis-free survival by over two years compared to placebo*
- *Data presented at ASCO GU 2018 (Abstract #161) and published in* The New England Journal of Medicine

BEERSE, BELGIUM, 8th February, 2018 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced that it has submitted a Marketing Authorisation Application to the European Medicines Agency (EMA) for apalutamide, an investigational, next generation oral androgen receptor (AR) inhibitor for the treatment of patients with high-risk non-metastatic castration-resistant prostate cancer (nmCRPC).

The submission is based on data from the pivotal SPARTAN Phase 3 clinical trial which assessed the safety and efficacy of apalutamide versus placebo in men with nmCRPC who have a rapidly rising prostate specific antigen (PSA) level, despite receiving continuous androgen deprivation therapy (ADT). The SPARTAN clinical trial showed a significantly decreased risk of distant metastasis or death (definition of the primary endpoint, metastasis free survival) by 72 percent, compared to placebo in combination with ADT (HR = 0.28; 95% CI, 0.23-0.35; p < 0.0001) and improved median metastasis-free survival (MFS) by over two years (difference of 24.3 months) in patients with nmCRPC whose PSA is rapidly rising. The results were presented at the American Society of Clinical Oncology Genitourinary Cancers Symposium (ASCO GU) in San Francisco (Abstract 161). Study findings were simultaneously published in *The New England Journal of Medicine*.

“The results of the SPARTAN trial are the first to show that metastases can be delayed in patients with castration-resistant prostate cancer, suggesting that apalutamide could become a new

standard of care for patients with high-risk non-metastatic CRPC," said Dr Simon Chowdhury, Consultant Medical Oncologist, Guy's and St Thomas' Hospitals, and a SPARTAN study investigator.

SPARTAN, a Phase 3, randomised, double-blind, placebo-controlled, multicenter study, enrolled 1,207 patients with non-metastatic castration-resistant prostate cancer and was conducted at 332 sites in 26 countries in North America, Europe, Asia-Pacific and Australia. Patients were randomised 2:1 to receive apalutamide in combination with androgen deprivation therapy (ADT) (n = 806), or placebo in combination with ADT (n = 401).

Apalutamide in combination with ADT decreased the risk of distant metastasis or death by 72 percent, compared to placebo in combination with ADT (HR = 0.28; 95% CI, 0.23-0.35; P < 0.0001).[1] The median MFS was 40.5 months for apalutamide in combination with ADT compared to 16.2 months for placebo in combination with ADT, prolonging MFS by over two years. MFS benefit was consistently seen across all subgroups of patients.[1]

"At Janssen we are committed to transforming prostate cancer management. By treating earlier and delaying the cancer from spreading we aim to improve outcomes for patients with this devastating disease," said Dr Ivo Winiger-Candolfi, Oncology Solid Tumor Therapy Area Lead, Janssen-Cilag International NV. "We look forward to working with the European Medicines Agency to bring this potential new treatment option to patients in the European Union as soon as possible."

"Delaying prostate cancer from metastasising is critical. Once the cancer starts to spread, a patient's overall health, well-being and prognosis change drastically," said Peter Lebowitz, M.D., Ph.D., Global Therapeutic Area Head of Oncology at Janssen Research & Development, LLC. "It's exciting to see apalutamide data at ASCO GU and these strong results truly underscore Janssen's commitment to addressing unmet needs for treatment across all stages of disease progression."

In addition to significantly improving metastasis free survival, apalutamide in combination with ADT, compared to placebo in combination with ADT, demonstrated clinical improvement across all secondary endpoints, with statistically significant improvements in time to metastasis (TTM; median of 40.5 months in the apalutamide arm compared to median of 16.6 months in the placebo arm) and progression-free survival (PFS; median of 40.5 months compared to median of 14.7 months in the placebo arm). Treatment with apalutamide significantly decreased the risk of symptomatic progression by 55 percent compared with placebo (HR = 0.447; 95% CI: 0.315, 0.634; P <0.0001).

Apalutamide was associated with a 30 percent risk reduction of death compared to placebo at this early interim analysis for overall survival (OS) (HR = 0.70; p = 0.07).[1] In exploratory endpoints, apalutamide in combination with ADT, compared to placebo in combination with ADT, also achieved a 94 percent risk reduction in time to PSA progression (HR = 0.06; 95% CI, 0.05-0.08; P <0.0001), and a 51 percent risk reduction in second progression-free survival (PFS2) (HR = 0.49; p < 0.001). The combination of apalutamide and ADT was tolerable, with maintenance of overall health-related quality of life.

The most common Grade 3/4 treatment-emergent adverse events (TEAEs) for apalutamide in combination with ADT versus placebo in combination with ADT were 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). Treatment discontinuation due to adverse events was 11 percent in the apalutamide arm compared to 7 percent in the placebo arm. Rates of serious adverse events (SAEs) were similar in the apalutamide in combination with ADT arm versus placebo in combination with ADT arm (25 percent vs. 23 percent respectively).

About Non-Metastatic Castration-Resistant Prostate Cancer

Non-metastatic castration-resistant prostate cancer (CRPC) 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.[2] 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/dL.[2] Ninety percent of patients with non-metastatic CRPC will eventually develop bone metastases, which can lead to pain, fractures and spinal cord compression.[3] The relative 5-year survival rate for patients with distant stage castration sensitive or castration resistant prostate cancer is 30 percent.[4,5] While it is critical to delay the onset of metastasis in patients with non-metastatic CRPC, there are currently no FDA or EMA approved treatments.[6]

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About Apalutamide

Apalutamide is an investigational, next-generation oral androgen receptor (AR) inhibitor that blocks the androgen signaling pathway in prostate cancer cells. Apalutamide inhibits the growth of cancer cells in three ways: by preventing the binding of androgen to the AR; by stopping the AR from entering the cancer cells; and by preventing the AR from binding to the DNA of the cancer cell.[7]

About the Janssen Pharmaceutical Companies of Johnson & Johnson

At the Janssen Pharmaceutical Companies of Johnson & Johnson, we are working to create a world without disease. Transforming lives by finding new and better ways to prevent, intercept, treat and cure disease inspires us. We bring together the best minds and pursue the most promising science. We are Janssen. We collaborate with the world for the health of everyone in it. Janssen-Cilag International NV is part of the Janssen Pharmaceutical Companies of Johnson & Johnson. Learn more at www.janssen.com/emea. Follow us at http://www.twitter.com/janssenEMEA.

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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 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-Cilag International NV, 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 behaviour and spending patterns or financial distress 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 1, 2017, including under "Item 1A. Risk Factors," its most recently filed Quarterly Report on Form 10-Q, including under the caption "Cautionary Note Regarding

Forward-Looking Statements," 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 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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