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**Janssen Submits Supplemental New Drug Application to U.S. FDA for ZYTIGA®
(abiraterone acetate) to Treat Men with Earlier Stages of Metastatic Prostate Cancer**

*Filing Supported by Data from Pivotal LATITUDE Trial Evaluating ZYTIGA® in Combination with
Prednisone and Androgen Deprivation Therapy (ADT)*

HORSHAM, PA, September 14, 2017 – Janssen Biotech, Inc. today announced the submission of a supplemental New Drug Application (sNDA) to the U.S. Food and Drug Administration (FDA) seeking to expand the indication of ZYTIGA® in combination with prednisone and ADT to include treatment of patients with high-risk metastatic hormone naïve prostate cancer (HNPC) or newly diagnosed, high-risk metastatic hormone sensitive prostate cancer (HSPC). The filing is based on Phase 3 data from the pivotal LATITUDE clinical trial, which found that in newly diagnosed patients with high-risk mHNPC, ZYTIGA® in combination with prednisone and ADT significantly increased overall survival (OS) and radiographic progression-free survival (rPFS), compared to placebo plus ADT.

“We are excited about the promising results from the LATITUDE study which suggest that ZYTIGA® can benefit men with newly diagnosed, high-risk metastatic prostate cancer, rather than waiting for them to become resistant to conventional hormonal treatments,” said Craig Tendler, M.D., Vice President, Late-Stage Development and Global Medical Affairs for Oncology, Hematology and Supportive Care at Janssen. “We look forward to working with the FDA on the review of this application to provide a new therapeutic option for men with newly diagnosed, high-risk metastatic prostate cancer.”

LATITUDE was a multinational, multicenter, randomized, double-blind, placebo-controlled clinical trial which examined the use of ZYTIGA® 1,000 mg once daily in combination with prednisone 5 mg once daily and ADT, compared to placebo plus ADT (N=1,199) in patients with newly diagnosed, high-risk mHNPC. [The study](#) was presented at the plenary session of the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago, and simultaneously published in the [New England Journal of Medicine](#).¹ [Additional data](#) from the study were presented at the 2017 European Society for Medical Oncology (ESMO) Annual Conference on September 8 in Madrid, Spain.²

The LATITUDE study showed ZYTIGA® in combination with prednisone and ADT reduced the risk of death by 38 percent compared to placebo plus ADT (median OS not reached vs. 34.7 months, respectively; hazard ratio: 0.62; 95% confidence interval [CI], 0.51 to 0.76; P<0.001) in patients with mHNPC. Additional study results found patients with mHSPC who received ZYTIGA® in combination with prednisone and ADT had a 53 percent lower risk of radiographic progression or death, compared to placebo plus ADT (median rPFS 33.0 months vs. 14.8 months, respectively, HR: 0.47; 95% CI, 0.39 to 0.55; P<0.001). Concerning the secondary end points, ZYTIGA® in combination with prednisone and ADT, reduced the risk of pain progression by 31 percent (HR=0.695; 95% CI: 0.583, 0.829; P<0.0001) and skeletal-related events by 30 percent (HR=0.703; 95% CI: 0.539, 0.916; p=0.0086) and reduced the risk of needing to start chemotherapy by 56 percent (HR=0.443; 95% CI: 0.349, 0.561, P<0.0001) compared to placebo plus ADT.

Additional data, presented at ESMO, demonstrated clinically meaningful and statistically significant improvements in patient reported outcomes (PRO) in patients with high-risk mHNPC who received ZYTIGA® in combination with prednisone and ADT compared to placebo plus ADT alone. ZYTIGA® in combination with prednisone and ADT, significantly delayed the time to health-related quality of life degradation by 15 percent (HR=0.853; 0.736, 0.989; p=0.0322) and significantly delayed the time to worst fatigue intensity progression by 35 percent (HR=0.652; 95% CI: 0.527, 0.805; P=0.0001) for patients with mHNPC.

Overall, the safety profile of ZYTIGA® in combination with prednisone and ADT, was similar to prior studies in patients with metastatic castration resistant prostate cancer (mCRPC). Grade 3/4 events reported in ≥5 percent of patients were hypertension (20%/0% vs. 10%/0.2%), hypokalemia (10%/0.8% vs. 1%/0.2%) and increase in alanine aminotransferase (5%/0.3% vs. 1%/0%) in ZYTIGA® in combination with prednisone and ADT vs. placebo plus ADT groups, respectively.

Since its first approval in the U.S. in 2011, ZYTIGA® has been approved in combination with prednisone or prednisolone in 105 countries. In April 2017, Janssen submitted a Type II variation application to the European Medicines Agency (EMA), seeking to expand the existing marketing authorization for ZYTIGA® in combination with prednisone or prednisolone to include the treatment of men with mHNPC. Similar submissions have been made in Japan, Canada, Mexico, Brazil, Switzerland, Taiwan, Singapore, and the Philippines. If approved, these submissions will broaden the use of ZYTIGA® in combination with prednisone or prednisolone to include an earlier stage of prostate cancer than its current indications.

Metastatic prostate cancer is cancer that has spread to another part of the body.³ **Metastatic hormone-naïve prostate cancer (mHNPC)** refers to prostate cancer that is metastatic, but has not been previously treated with ADT⁴, and therefore, not castration resistant. **Metastatic hormone-sensitive prostate cancer (mHSPC)** refers to prostate cancer that still responds to testosterone suppression therapy.³ Patients with newly diagnosed metastatic disease and high-risk disease characteristics tend to have a poorer prognosis.⁵

About the LATITUDE Clinical Trial⁶

The Phase 3, multinational, multicenter, randomized, double-blind, placebo-controlled LATITUDE study enrolled 1,199 newly diagnosed patients with high-risk mHNPC and was conducted at 235 sites in 34 countries in Europe, Asia-Pacific, Latin America, and Canada. A total number of 597 patients were randomized to receive ADT in combination with abiraterone acetate and prednisone (n=597), while 602 patients were randomized to receive ADT and placebo (n=602). Patients included had high-risk mHNPC documented by positive bone scan or metastatic lesions at the time of diagnosis on computed tomography (CT) or magnetic resonance imaging (MRI). Additionally, patients had to have at least two of the three following high-risk factors associated with poor prognosis: Gleason score ≥ 8 , ≥ 3 bone lesions and/or presence of measurable visceral metastases.

About ZYTIGA®

ZYTIGA® (abiraterone acetate) is indicated in combination with prednisone for the treatment of patients with metastatic castration-resistant prostate cancer (mCRPC). ZYTIGA® blocks CYP17-mediated androgen production, which fuels prostate cancer growth, at three sources: in the testes, adrenals and the prostate tumor tissue. It has proven efficacy in patients with mCRPC who have progressed on androgen deprivation therapy.

Since its first approval in the U.S. in 2011, ZYTIGA[®] has been approved in combination with prednisone/prednisolone in 105 countries. More than 330,000 men worldwide, including 113,000 in the U.S., have received treatment with it, and it was the number one prescribed oral medication in the U.S. for men with mCRPC in 2016.

For more information about ZYTIGA[®], visit www.ZYTIGA.com.

Important Safety Information

CONTRAINDICATIONS - ZYTIGA[®] (abiraterone acetate) is not indicated for use in women. ZYTIGA[®] can cause fetal harm (Pregnancy Category X) when administered to a pregnant woman and is contraindicated in women who are or may become pregnant.

Hypertension, Hypokalemia and Fluid Retention Due to Mineralocorticoid Excess - Use with caution in patients with a history of cardiovascular disease or with medical conditions that might be compromised by increases in blood pressure, hypokalemia, or fluid retention. ZYTIGA[®] may cause hypertension, hypokalemia, and fluid retention as a consequence of increased mineralocorticoid levels resulting from CYP17 inhibition. Safety has not been established in patients with LVEF <50% or New York Heart Association (NYHA) Class III or IV heart failure (in Study 1) or NYHA Class II to IV heart failure (in Study 2) because these patients were excluded from these randomized clinical trials. Control hypertension and correct hypokalemia before and during treatment. Monitor blood pressure, serum potassium, and symptoms of fluid retention at least monthly.

Adrenocortical Insufficiency (AI) - AI was reported in patients receiving ZYTIGA[®] in combination with prednisone, after an interruption of daily steroids and/or with concurrent infection or stress. Use caution and monitor for symptoms and signs of AI if prednisone is stopped or withdrawn, if prednisone dose is reduced, or if the patient experiences unusual stress. Symptoms and signs of AI may be masked by adverse reactions associated with mineralocorticoid excess seen in patients treated with ZYTIGA[®]. Perform appropriate tests, if indicated, to confirm AI. Increased dosages of corticosteroids may be used before, during, and after stressful situations.

Hepatotoxicity - In post-marketing experience, there have been ZYTIGA[®]-associated severe hepatic toxicities, including fulminant hepatitis, acute liver failure and deaths. Monitor liver function and modify, withhold, or discontinue ZYTIGA[®] dosing as recommended (see Prescribing Information for more information). Measure serum transaminases [alanine aminotransferase (ALT) and

aspartate aminotransferase (AST)] and bilirubin levels prior to starting treatment with ZYTIGA[®], every two weeks for the first three months of treatment, and monthly thereafter. Promptly measure serum total bilirubin, AST, and ALT if clinical symptoms or signs suggestive of hepatotoxicity develop. Elevations of AST, ALT, or bilirubin from the patient's baseline should prompt more frequent monitoring. If at any time AST or ALT rise above five times the upper limit of normal (ULN) or the bilirubin rises above three times the ULN, interrupt ZYTIGA[®] treatment and closely monitor liver function. Re-treatment with ZYTIGA[®] at a reduced dose level may take place only after return of liver function tests to the patient's baseline or to AST and ALT less than or equal to 2.5X ULN and total bilirubin less than or equal to 1.5X ULN.

Permanently discontinue ZYTIGA[®] for patients who develop a concurrent elevation of ALT greater than 3X ULN and total bilirubin greater than 2X ULN in the absence of biliary obstruction or other causes responsible for the concurrent elevation.

Adverse Reactions - The most common adverse reactions ($\geq 10\%$) are fatigue, joint swelling or discomfort, edema, hot flush, diarrhea, vomiting, cough, hypertension, dyspnea, urinary tract infection and contusion.

The most common laboratory abnormalities ($>20\%$) are anemia, elevated alkaline phosphatase, hypertriglyceridemia, lymphopenia, hypercholesterolemia, hyperglycemia, elevated AST, hypophosphatemia, elevated ALT and hypokalemia.

Drug Interactions - Based on in vitro data, ZYTIGA[®] is a substrate of CYP3A4. In a drug interaction trial, co-administration of rifampin, a strong CYP3A4 inducer, decreased exposure of abiraterone by 55%. Avoid concomitant strong CYP3A4 inducers during ZYTIGA[®] treatment. If a strong CYP3A4 inducer must be co-administered, increase the ZYTIGA[®] dosing frequency only during the co-administration period [see Dosage and Administration (2.3)]. In a dedicated drug interaction trial, co-administration of ketoconazole, a strong inhibitor of CYP3A4, had no clinically meaningful effect on the pharmacokinetics of abiraterone.

ZYTIGA[®] is an inhibitor of the hepatic drug-metabolizing enzymes CYP2D6 and CYP2C8. Avoid co-administration with CYP2D6 substrates with a narrow therapeutic index. If alternative treatments cannot be used, exercise caution and consider a dose reduction of the CYP2D6 substrate drug. In a CYP2C8 drug interaction trial in healthy subjects, the AUC of pioglitazone, a CYP2C8 substrate, was increased by 46% when administered with a single dose of ZYTIGA[®]. Patients should be monitored



closely for signs of toxicity related to a CYP2C8 substrate with a narrow therapeutic index if used concomitantly with ZYTIGA®.

Use in Specific Populations - Do not use ZYTIGA® in patients with baseline severe hepatic impairment (Child-Pugh Class C).

About the Janssen Pharmaceutical Companies

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. Learn more at www.janssen.com. Follow us at www.twitter.com/JanssenUS and www.twitter.com/JanssenGlobal.

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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, including the potential expanded use of ZYTIGA® in combination with prednisone. 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 Biotech, Inc., 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 1, 2017, including under "Item 1A. Risk Factors," its most recently filed Quarterly Report on Form 10-Q, including in the section captioned "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.

¹ Fizazi K., et al. Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer. *New England Journal of Medicine*. June 2017.

² Chi K. Benefits of Abiraterone Acetate Plus Prednisone (AA+P) When Added to Androgen Deprivation Therapy (ADT) in LATITUDE on Patient (Pt) Reported Outcomes (PRO). Abstract 783O. Presented at the 2017 European Society for Medical Oncology (ESMO) Annual Meeting, 8th September 2017. Available at: <http://www.esmo.org/content/download/117241/2057634/file/ESMO-2017-Abstract-Book.pdf> Accessed September 2017.

³ American Society of Clinical Oncology. Prostate Cancer: Treatment Options. <http://www.cancer.net/cancer-types/prostate-cancer/treatment-options> . Accessed September 2017.

⁴ Harvard University. Prostate Cancer Knowledge. Androgen-Independent Prostate Cancer. Available at: <http://www.harvardprostateknowledge.org/androgen-independent-prostate-cancer>. Accessed September 2017.

⁵ Fizazi K., et al. LATITUDE: A phase III, double-blind, randomized trial of androgen deprivation therapy with abiraterone acetate plus prednisone or placebos in newly diagnosed high-risk metastatic hormone-naïve prostate cancer. ASCO 2017. Abstract #LBA3.

⁶ Clinical trials.gov. A Study of Abiraterone Acetate Plus Low-Dose Prednisone Plus Androgen Deprivation Therapy (ADT) Versus ADT Alone in Newly Diagnosed Participants With High-Risk, Metastatic Hormone-Naïve Prostate Cancer (mHNPC). Available at: <https://clinicaltrials.gov/ct2/show/NCT01715285>. Accessed September 2017.