NEWS RELEASE

FDA Approves Label Update for ZYTIGA® to Include Statistically Significant Overall Survival Results in Chemotherapy-Naïve Men with Metastatic Castration-Resistant Prostate Cancer

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HORSHAM, PA, March 30, 2015 - The U.S. Food and Drug Administration (FDA) has approved a label update for ZYTIGA® (abiraterone acetate) plus prednisone based on the final analysis of the Phase 3, randomized, double-blind, placebo-controlled COU-AA-302 study, which showed that ZYTIGA plus prednisone significantly prolonged median overall survival (OS), compared to placebo plus prednisone, in chemotherapy-naïve men with metastatic castration-resistant prostate cancer (mCRPC). After a median follow-up of more than four years (49.2 months), the Janssen Research & Development, LLC ("Janssen")-sponsored registration study demonstrated a median OS of almost three years (34.7 months) in the patients randomized to ZYTIGA plus prednisone compared to 30.3 months in the placebo plus prednisone arm (median OS, 34.7 vs. 30.3 months, respectively; HR= 0.81 [95% CI, 0.70-0.93]; p = 0.0033).

"The statistically significant improvement in overall survival demonstrated in the final analysis and resulting label update help affirm the established efficacy, safety and tolerability that physicians treating men with metastatic castration-resistant prostate cancer have seen with ZYTIGA," said Charles Ryan, M.D., Professor of Clinical Medicine, Urology at the University of California, San Francisco, and lead investigator of the COU-AA-302 study. "Representing a median follow-up of four years, this analysis adds to the robust body of clinical data supporting ZYTIGA as an important treatment option for men with metastatic castration-resistant prostate cancer."

Overall survival is particularly meaningful in this final analysis because 65 percent of men in the ZYTIGA plus prednisone arm and 78 percent in the control placebo plus prednisone arm received subsequent therapy that may prolong OS in mCRPC. This includes 44 percent of men in the control arm who subsequently received ZYTIGA plus

prednisone. Additionally, with a median of 49 months of follow-up, there were no notable changes in the safety profile of ZYTIGA since the previously reported interim analyses.[i]

"Since its launch in 2011, ZYTIGA has helped change the treatment paradigm for metastatic castration-resistant prostate cancer, treating more than 150,000 men worldwide," said Cynthia Guzzo, M.D., Vice President, Medical Affairs, Janssen Scientific Affairs, LLC. "This label update marks an exciting milestone for ZYTIGA and Janssen as we continue to focus on our commitment to patient care in the prostate cancer treatment space."

The final analysis data was recently published in the February 2015 issue of **The Lancet Oncology**[i] with an independent **commentary**.[ii] Additionally, Janssen first presented these **data** at the European Society for Medical Oncology (ESMO) 2014 Congress in Madrid, Spain (September 26-30, 2014). Based on the results from the final analysis, Janssen is working with relevant global health authorities to revise the label for ZYTIGA to include the final analysis results.

The U.S. FDA based its approval of ZYTIGA plus prednisone for treating men with mCRPC prior to chemotherapy on the results from a planned second interim analysis of COU-AA-302, which is an international, randomized, double-blind, placebo controlled Phase 3 study that included 1,088 men with mCRPC who had not received prior chemotherapy, and were randomized 1:1 to receive ZYTIGA® (abiraterone acetate) 1,000 milligrams (mg) administered orally once daily plus prednisone 5 mg administered twice daily or placebo plus prednisone 5 mg administered twice daily. The co-primary endpoints of the study were radiographic progression-free survival (rPFS) and OS. Key secondary endpoints included time to opiate use and time to initiation of chemotherapy.

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.

Adverse Reactions - The most common adverse reactions (≥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.

Increased ZYTIGA® Exposures With Food - ZYTIGA® must be taken on an empty stomach. No food should be eaten for at least two hours before the dose of ZYTIGA® is taken and for at least one hour after the dose of

ZYTIGA® is taken. Abiraterone Cmax and AUC0-∞ (exposure) were increased up to 17- and 10-fold higher, respectively, when a single dose of abiraterone acetate was administered with a meal compared to a fasted state.

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.

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.

Hepatotoxicity - Monitor liver function and modify, withhold, or discontinue ZYTIGA® dosing as recommended (see Prescribing Information for more information). Measure serum transaminases (ALT and 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.

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 Prostate Cancer

Prostate cancer occurs in men when cancerous cells form in the tissues of the prostate, a gland that is located around the urethra and produces part of the seminal fluid.[iii] During the course of the illness, it may progress to castration-resistant prostate cancer (CRPC), which is resistant to medical or surgical treatments that lower testosterone (e.g., androgen deprivation therapy).[iv] CRPC that spreads to other areas of the body is called metastatic castration-resistant prostate cancer or mCRPC.[v] Research has shown that prostate cancer tumor cells develop adaptive mechanisms including the capability of producing androgen, which helps to fuel their survival, suggesting that reducing androgen production is key to helping men with mCRPC manage their illness.[vi]

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 - and has proven efficacy in patients with mCRPC who have progressed on androgen deprivation therapy.

Since its first approval in the U.S. in 2011, more than 60,000 men in the U.S. have been prescribed ZYTIGA® and more than 150,000 patients worldwide have received treatment with this important therapeutic option.

Janssen is committed to supporting access to ZYTIGA® for appropriate patients who are prescribed this medicine. ZytigaOne™ Support provides enhanced support to physician offices and personalized care coordination services to patients, including the ZytigaOne™ Instant Savings Program, which can help commercially insured patients with out-of-pocket co-pays and coinsurance. For more information on ZytigaOne™ Support, contact 1-855-ZYTIGA-1.

More information about ZYTIGA® can be found at **www.ZYTIGA.com**.

About Janssen Research & Development, LLC

At Janssen, we are dedicated to addressing and solving some of the most important unmet medical needs of our time in oncology, immunology, neuroscience, infectious diseases and vaccines, and cardiovascular and metabolic diseases. Driven by our commitment to patients, we develop innovative products, services and healthcare solutions

to help people throughout the world. Janssen Research & Development is part of the Janssen Pharmaceutical Companies. Please visit **www.janssenrnd.com** for more information.

Janssen in Oncology

In oncology, our goal is to fundamentally alter the way cancer is understood, diagnosed, and managed, reinforcing our commitment to the patients who inspire us. In looking to find innovative ways to address the cancer challenge, our primary efforts focus on several treatment and prevention solutions. These include a focus on hematologic malignancies, prostate cancer and lung cancer; cancer interception with the goal of developing products that interrupt the carcinogenic process; biomarkers that may help guide targeted, individualized use of our therapies; as well as safe and effective identification and treatment of early changes in the tumor microenvironment.

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[i] Ryan CJ, Smith MR, Fizazi K, et al. Abiraterone acetate plus prednisone versus placebo plus prednisone in chemotherapy-naïve men with metastatic castration-resistant prostate cancer (COU-AA-302): final overall survival analysis of a randomised, double-blind, placebo-controlled phase 3 study. Lancet Oncol. 2015;16(2):152-160.

[ii] Madan, R. & Dahut, W. Abiraterone's efficacy confirmed; time to aim higher. Lancet Oncol. 2015;16(2):119-121.

[iii] National Cancer Institute. What you need to know about prostate cancer. **http://www.cancer.gov/publications/patient-education/prostate.pdf**. Accessed January 2015.

[iv] American Cancer Society. Prostate Cancer. **http://www.cancer.org/cancer/prostatecancer/detailedguide/prostate-cancer-treating-recurrence**. Accessed January 2015.

[v] American Society of Clinical Oncology. **http://www.cancer.net/research-and-advocacy/asco-care-and-treatment-recommendations-patients/treatment-metastatic-castration-resistant-prostate-cancer**. Accessed January 2015

[vi] Locke JA, Guns ES, Lubik AA, et al. Androgen levels increase by intratumoral de novo steroidogenesis during progression of castration-resistant prostate cancer. Cancer Res 2008;68:6407-15.

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