# IMAAGEN Data Demonstrate that Abiraterone Acetate Plus Prednisone (5mg once daily) Lowers PSA Levels in Men with High-Risk Non-Metastatic Castration-Resistant Prostate Cancer (M0-CRPC)

June 2, 2014

HORSHAM, PA, June 2, 2014 - Abiraterone acetate (ZYTIGA®) plus prednisone demonstrated statistically significant reductions in PSA levels at six months, the primary endpoint of the IMAAGEN trial, which evaluates the investigational use of abiraterone acetate plus prednisone (5 mg once daily) in patients with non-metastatic castration-resistant prostate cancer (M0-CRPC) at high risk of developing metastatic disease.

Janssen Biotech, Inc. today announced the results from this study, which also found significant reductions in testosterone levels, a key secondary endpoint.

Median baseline PSA was 11.9 ng/mL (range 1.3-167.8 ng/mL). Of the 131 patients enrolled, 122 patients were evaluable for the analysis of PSA response. At the end of six cycles of treatment, 87 percent (106/122; 95% CI 80.9-92.9; P<0.0001) of patients had a 50 percent or greater reduction in PSA and 60 percent (73/122; 95% CI 50.5-61.6) of patients had a 90 percent or greater reduction in PSA. No patient had his prednisone dose increased to greater than 5 mg to manage symptoms of mineralocorticoid excess. The safety profile in this study is consistent with the known safety profile of abiraterone acetate.

The IMAAGEN study is a Phase 2, multi-center, open-label, single arm, U.S.-based study that evaluated the effect of abiraterone acetate plus prednisone on the PSA levels in patients with high risk M0-CRPC with PSA values ≥10 ng/mL or with a PSA doubling time of ≤10 months at screening. Of the 131 patients, 14.5 percent were African-American, 1.5 percent were Asian and 82.4 percent were Caucasian. Patients in the study were administered 1,000 mg of abiraterone acetate plus prednisone (5 mg once daily) for the duration of the study and PSA assessment and imaging scans were conducted every three months. The primary endpoint was the proportion of patients with a 50 percent or greater reduction in PSA during cycles 1-6 of treatment. Key secondary endpoints included assessment of testosterone levels, description of safety profile, time to PSA progression and time to radiographic disease progression.

"Patients with non-metastatic CRPC frequently progress to metastatic CRPC. The patients in this study had clinical features placing them at higher risk of developing metastatic disease. We sought to understand the impact of treatment with abiraterone acetate plus prednisone (5 mg once daily) on PSA response, which is one factor to consider when evaluating disease progression," said Charles Ryan, M.D., Professor of Clinical Medicine, Urology at the University of California, San Francisco, and the steering committee chair for IMAAGEN. "This study adds important new insights to the scientific understanding of abiraterone acetate in this patient population on the cusp of disease progression."

The IMAAGEN data (Abstract #5086) will be presented at the American Society of Clinical Oncology (ASCO) meeting in Chicago, IL during the Genitourinary (Prostate) Cancer General Poster Session on Monday, June 2nd (1:15 p.m.-5:00 p.m.).

**Ongoing Research in Prostate Cancer**

Advanced prostate cancer is an area of focus and commitment for Janssen, as exemplified by the recent Johnson & Johnson acquisition of Aragon Pharmaceuticals, Inc. and ARN-509, an investigational second-generation androgen receptor signaling inhibitor. Janssen is currently enrolling patients in the initial Phase 3 SPARTAN trial, which will evaluate ARN-509 in men with high-risk M0-CRPC, providing an option that may address the unmet needs across a broad range of patients with prostate cancer.

**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.[1] 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). CRPC that spreads to other areas of the body is called metastatic castration-resistant prostate cancer or mCRPC.[2] Research has shown that prostate cancer tumor cells are capable of producing androgen, which helps to fuel their survival, suggesting that reducing androgen production is key to helping men with mCRPC manage their illness.[3]

**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 50,000 men in the U.S. have been prescribed ZYTIGA® and more than 120,000 patients worldwide have received treatment with this important therapeutic option.

Janssen Biotech 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.

**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** - 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.

**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.

**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.

**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 enzyme CYP2D6. 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 vitro, ZYTIGA® inhibits CYP2C8. There are no clinical data on the use of ZYTIGA® with drugs that are substrates of CYP2C8. Patients should be monitored closely for signs of toxicity related to the CYP2C8 substrate if used concomitantly with abiraterone acetate.

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

**About Janssen Biotech, Inc.**
Janssen Biotech, Inc. redefines the standard of care in immunology, oncology, urology and nephrology. Built upon a rich legacy of innovative firsts, Janssen Biotech has delivered on the promise of new treatments and ways to improve the health of individuals with serious disease. Beyond its innovative medicines, Janssen Biotech is at the forefront of developing education and public policy initiatives to ensure patients and their families, caregivers, advocates and health care professionals have access to the latest treatment information, support services and quality care. For more information on Janssen Biotech, Inc. or its products, visit www.janssenbiotech.com.

Janssen Biotech is one of the Janssen Pharmaceutical Companies of Johnson & Johnson, which are dedicated to addressing and solving some of the most important unmet medical needs in oncology, immunology, neuroscience, infectious diseases and vaccines, and cardiovascular and metabolic diseases. Driven by our commitment to patients, we work together to bring innovative ideas, products, services and solutions to people throughout the world. Follow us on Twitter at www.twitter.com/JanssenUS.

**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.

*(This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding product development. 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 unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of Janssen Biotech, Inc. or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges inherent in new product development, including obtaining regulatory approvals; competition, including technological advances, new products and patents attained by competitors; challenges to patents; changes in behavior and spending patterns or financial distress of purchasers of health care products and services; changes to governmental laws and regulations and domestic and foreign health care reforms; general industry conditions including trends toward health care cost containment; and increased scrutiny of the health care industry by government agencies. A further list and description 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 29, 2013, including in Exhibit 99 thereto, and our 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 or Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.)*

[1]National Cancer Institute. What you need to know about prostate cancer. http://www.cancer.gov/cancertopics/wyntk/prostate/prostate.pdf. Accessed April 2014.
[2]American Cancer Society. Prostate Cancer. http://www.cancer.org/cancer/prostatecancer/detailedguide/prostate-cancer-treating-recurrence. Accessed April 2014.
[3]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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