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**ENZALUTAMIDE PHASE 2 TERRAIN TRIAL DEMONSTRATED STATISTICALLY SIGNIFICANT INCREASE IN PFS AS COMPARED TO BICALUTAMIDE IN METASTATIC PROSTATE CANCER**

SAN FRANCISCO, CA and TOKYO, JAPAN – January 22, 2015 – Medivation, Inc. (NASDAQ: MDVN) and Astellas Pharma Inc. (TSE: 4503) today announced topline results from the Phase 2 TERRAIN trial comparing enzalutamide with bicalutamide in men with metastatic castration-resistant prostate cancer. The study achieved its primary endpoint demonstrating a statistically significant increase in progression-free survival (PFS) for enzalutamide compared to bicalutamide (Hazard Ratio = 0.44; 95% Confidence Interval, 0.34-0.57;  $p < 0.0001$ ). Median PFS was 15.7 months in the enzalutamide group compared to 5.8 months in the bicalutamide group.

The median time on treatment in TERRAIN was 11.7 months in the enzalutamide group versus 5.8 months in the bicalutamide group. Serious adverse events were reported in 31.1% of enzalutamide-treated patients and 23.3% of bicalutamide-treated patients. Grade 3 or higher cardiac adverse events were reported in 5.5% of enzalutamide-treated patients versus 2.1% of bicalutamide-treated patients. Two seizures were reported in the enzalutamide group and one in the bicalutamide group. The most common side effects occurring during treatment and more common in the enzalutamide-treated versus bicalutamide-treated patients included fatigue, hot flush, hypertension, diarrhea, weight decreased and pain in extremity.

“The results of this study showed that enzalutamide provides a longer duration of disease control in the studied patient population compared to bicalutamide,” said Neal Shore, MD, co-principal investigator of the TERRAIN study and Medical Director, Carolina Urologic Research Center. “This robust data set adds to an impressive and consistent body of data for enzalutamide across multiple studies and stages of prostate cancer.”

Additional data from the Phase 2 TERRAIN trial, including the secondary endpoints and further safety data, will be submitted for presentation at an upcoming medical conference

**About TERRAIN**

The Phase 2 TERRAIN trial enrolled 375 patients in North America and Europe. The trial involved patients with metastatic prostate cancer whose disease progressed despite treatment with a luteinizing hormone-releasing hormone (LHRH) analogue therapy or following surgical castration. The primary endpoint of the trial was progression-free survival, defined as time from

randomization to centrally confirmed radiographic progression, skeletal related event, initiation of new anti-neoplastic therapy or death, whichever occurs first. The trial was designed to evaluate enzalutamide at a dose of 160 mg taken once daily versus bicalutamide at a dose of 50 mg taken once daily, the approved dose in combination with a LHRH analogue. Targeted enrollment was completed in July 2013.

### **About XTANDI® (enzalutamide) capsules**

XTANDI is approved by the U.S. Food and Drug Administration for the treatment of patients with metastatic castration-resistant prostate cancer (CRPC).

### **Enzalutamide Mechanism of Action**

Enzalutamide is an androgen receptor inhibitor that acts on three different steps in the androgen receptor signaling pathway.

### **Important Safety Information (from currently approved U.S. prescribing information)**

**Contraindications:** XTANDI (enzalutamide) capsules can cause fetal harm when administered to a pregnant woman based on its mechanism of action and findings in animals. XTANDI is not indicated for use in women. XTANDI is contraindicated in women who are or may become pregnant.

**Warnings and Precautions:** In Study 1, conducted in patients with metastatic castration-resistant prostate cancer (CRPC) who previously received docetaxel, seizure occurred in 0.9% of patients who were treated with XTANDI and 0% treated with placebo. In Study 2, conducted in patients with chemotherapy-naïve metastatic CRPC, seizure occurred in 0.1% of patients who were treated with XTANDI and 0.1% treated with placebo. Patients experiencing a seizure were permanently discontinued from therapy and all seizure events resolved. There is no clinical trial experience re-administering XTANDI to patients who experienced a seizure, and limited clinical trial experience in patients with predisposing factors for seizure. Study 1 excluded the use of concomitant medications that may lower threshold, whereas Study 2 permitted the use of these medications. Because of the risk of seizure associated with XTANDI use, patients should be advised of the risk of engaging in any activity during which sudden loss of consciousness could cause serious harm to themselves or others. Permanently discontinue XTANDI in patients who develop a seizure during treatment.

**Adverse Reactions:** The most common adverse reactions ( $\geq 10\%$ ) reported from the two combined clinical trials that occurred more commonly ( $\geq 2\%$  over placebo) in the XTANDI-treated patients were asthenia/fatigue, back pain, decreased appetite, constipation, arthralgia, diarrhea, hot flush, upper respiratory tract infection, peripheral edema, dyspnea, musculoskeletal pain, weight decreased, headache, hypertension, and dizziness/vertigo.

Other Adverse Reactions include:

- **Laboratory Abnormalities:** In the two studies, Grade 1-4 neutropenia occurred in 15% of patients treated with XTANDI (1% Grade 3-4) and in 6% of patients treated with placebo (0.5% Grade 3-4). The incidence of Grade 1-4 thrombocytopenia was 6% of patients treated with XTANDI (0.3% Grade 3-4) and 5% of patients on placebo (0.5% Grade 3-4). Grade 1-4 elevations in ALT occurred in 10% of patients treated with XTANDI (0.2% Grade 3-4) and 16% of patients treated with placebo (0.2% Grade 3-4). Grade 1-4 elevations in bilirubin occurred in 3% of patients treated with XTANDI (0.1% Grade 3-4) and 2% of patients treated with placebo (no Grade 3-4).
- **Infections:** In Study 1, 1% of XTANDI versus 0.3% of placebo patients and in Study 2, 1 patient in each treatment group (0.1%) had an infection resulting in death.

- Falls: In the two studies, falls including fall-related injuries occurred in 9% of XTANDI patients vs 4% treated with placebo. Falls were not associated with loss of consciousness or seizure. Fall-related injuries were more severe in XTANDI patients and included non-pathologic fractures, joint injuries, and hematomas.
- Hypertension: In the two studies, hypertension was reported in 11% of patients receiving XTANDI and 4% of patients receiving placebo. No patients experienced hypertensive crisis. Medical history of hypertension was balanced between arms. Hypertension led to study discontinuation in < 1% of XTANDI or placebo treated patients.

#### **Drug Interactions:**

- Effect of Other Drugs on XTANDI - Administration of strong CYP2C8 inhibitors can increase the plasma exposure to XTANDI. Co-administration of XTANDI with strong CYP2C8 inhibitors should be avoided if possible. If co-administration of XTANDI cannot be avoided, reduce the dose of XTANDI. Co-administration of XTANDI with strong or moderate CYP3A4 and CYP2C8 inducers may alter the plasma exposure of XTANDI and should be avoided if possible.
- Effect of XTANDI on Other Drugs -XTANDI is a strong CYP3A4 inducer and a moderate CYP2C9 and CYP2C19 inducer in humans. Avoid CYP3A4, CYP2C9 and CYP2C19 substrates with a narrow therapeutic index, as XTANDI may decrease the plasma exposures of these drugs. If XTANDI is co-administered with warfarin (CYP2C9 substrate), conduct additional INR monitoring.

For Full Prescribing Information for XTANDI (enzalutamide) capsules, please visit [www.XtandiHCP.com/PI](http://www.XtandiHCP.com/PI)

#### **About Astellas Pharma Inc.**

Astellas Pharma Inc. is a pharmaceutical company dedicated to improving the health of people around the world through provision of innovative and reliable pharmaceuticals. The organization is committed to being a global category leader in Oncology and Urology, and has several oncology compounds in development in addition to enzalutamide. For more information on Astellas Pharma Inc., please visit our website at [www.astellas.com/en](http://www.astellas.com/en).

#### **About Medivation Inc.**

Medivation, Inc. is a biopharmaceutical company focused on the rapid development of medically innovative therapies to treat serious diseases for which there are limited treatment options. Medivation aims to transform the treatment of these diseases and offer hope to critically ill patients and their families. For more information, please visit us at <http://www.medivation.com>.

#### **About the Medivation/Astellas Collaboration**

In October 2009, Medivation (NASDAQ: MDVN) and Astellas (TSE: 4503) entered into a global agreement to jointly develop and commercialize enzalutamide. The companies are collaborating on a comprehensive development program that includes studies to develop enzalutamide across the full spectrum of advanced prostate cancer as well as advanced breast cancer. The companies jointly commercialize XTANDI in the United States and Astellas has responsibility for manufacturing and all additional regulatory filings globally, as well as commercializing XTANDI outside the United States.

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