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**ASTELLAS AND MEDIVATION RECEIVE PRIORITY REVIEW FROM FDA FOR XTANDI®  
(ENZALUTAMIDE) CAPSULES IN CHEMOTHERAPY-NAIVE  
ADVANCED PROSTATE CANCER**

TOKYO, JAPAN and SAN FRANCISCO, CA – MAY 6, 2014 – Astellas Pharma Inc. (TSE: 4503) and Medivation Inc. (NASDAQ: MDVN) today announced that the U.S. Food and Drug Administration (FDA) has accepted for filing the supplemental New Drug Application (sNDA) to extend the indication for XTANDI® (enzalutamide) capsules for the treatment of men with metastatic castration-resistant prostate cancer (mCRPC) who have not received chemotherapy. This sNDA application was granted Priority Review designation with a stated FDA Prescription Drug User Fee Act (PDUFA) review date of September 18, 2014. XTANDI is currently approved for the treatment of patients with mCRPC who have previously received docetaxel chemotherapy.

The sNDA application is based on the results from the Phase 3 PREVAIL trial evaluating XTANDI as compared to placebo in more than 1,700 chemotherapy-naïve mCRPC patients. A variation application to amend the European Marketing Authorization Application was submitted to the European Medicines Agency on April 2, 2014.

The FDA's acceptance of the sNDA triggers a milestone payment to Medivation under its collaboration agreement with Astellas.

**About the PREVAIL Trial**

The Phase 3 PREVAIL trial is a randomized, double-blind, placebo-controlled, multi-national trial that enrolled more than 1,700 patients at sites in the United States, Canada, Europe, Australia, Russia, Israel and Asian countries including Japan. The trial enrolled patients with chemotherapy-naïve metastatic prostate cancer whose disease progressed on a luteinizing hormone-releasing hormone analogue or after bilateral orchiectomy. The co-primary endpoints of the trial were overall survival and radiographic progression-free survival. The trial was designed to evaluate enzalutamide at a dose of 160 mg taken orally once daily versus placebo.

**Enzalutamide Mechanism of Action**

Enzalutamide is an androgen receptor inhibitor that acts on different steps in the androgen receptor signaling pathway. Enzalutamide has been shown to competitively inhibit androgen binding to androgen receptors, and inhibit androgen receptor nuclear translocation and interaction with DNA.

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

XTANDI was approved by the FDA on August 31, 2012 and is indicated for the treatment of patients with metastatic castration-resistant prostate cancer (mCRPC) who have previously received docetaxel.

### **Important Safety Information for XTANDI (from the approved prescribing information)**

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

**Warnings and Precautions:** In the randomized clinical trial, seizure occurred in 0.9% of patients on XTANDI. No patients on the placebo arm experienced seizure. Patients experiencing a seizure were permanently discontinued from therapy. All seizures resolved. Patients with a history of seizure, taking medications known to decrease the seizure threshold, or with other risk factors for seizure were excluded from the clinical trial. Because of the risk of seizure associated with XTANDI use, patients should be advised of the risk of engaging in any activity where sudden loss of consciousness could cause serious harm to themselves or others.

**Adverse Reactions:** The most common adverse drug reactions ( $\geq 5\%$ ) reported in patients receiving XTANDI in the randomized clinical trial were asthenia/fatigue, back pain, diarrhea, arthralgia, hot flush, peripheral edema, musculoskeletal pain, headache, upper respiratory infection, muscular weakness, dizziness, insomnia, lower respiratory infection, spinal cord compression and cauda equina syndrome, hematuria, paresthesia, anxiety, and hypertension. Grade 1-4 neutropenia occurred in 15% of XTANDI patients (1% Grade 3-4) and in 6% on placebo (no Grade 3-4). Grade 1-4 elevations in bilirubin occurred in 3% of XTANDI patients and 2% on placebo. One percent of XTANDI patients compared to 0.3% on placebo died from infections or sepsis. Falls or injuries related to falls occurred in 4.6% of XTANDI patients versus 1.3% on 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. Grade 1 or 2 hallucinations occurred in 1.6% of XTANDI patients and 0.3% on placebo, with the majority on opioid-containing medications at the time of the event.

**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 can 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](http://www.XtandiHCP.com).

### **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**

Medivation, Inc. is a biopharmaceutical company focused on the rapid development of novel small molecule drugs 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 [www.medivation.com](http://www.medivation.com).

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

In October 2009, Astellas and Medivation 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 will have responsibility for manufacturing and all additional regulatory filings globally, as well as commercializing XTANDI outside the United States.

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