



August 31, 2012

## **U.S. FDA Approves XTANDI(R) (enzalutamide) After Priority Review for Patients With Metastatic Castration-Resistant Prostate Cancer Previously Treated With Docetaxel**

### **Medivation to Host Conference Call Today at 11:45am PT**

SAN FRANCISCO, CA and TOKYO -- (Marketwire) -- 08/31/12 -- Medivation, Inc. (NASDAQ: MDVN) and Astellas Pharma Inc. (TSE: 4503) today announced that the U.S. Food and Drug Administration (FDA) has granted approval to XTANDI® (enzalutamide) capsules for the treatment of patients with metastatic castration-resistant prostate cancer who have previously received docetaxel. XTANDI is an oral, once-daily androgen receptor inhibitor.

The FDA accepted the XTANDI New Drug Application (NDA) on July 23, 2012, and granted the filing Priority Review Designation with a Prescription Drug User Fee Act (PDUFA) action date of November 22, 2012. Medivation and Astellas expect to make XTANDI available to patients in the United States in mid-September 2012, and the specific availability date will be announced on [www.XtandiHCP.com](http://www.XtandiHCP.com) as soon as it is known. Separately, a Marketing Authorization Application for XTANDI has been accepted for review by the European Medicines Agency (EMA).

"Today's approval marks a significant accomplishment for Medivation. We are proud to be in a position to offer a new treatment, XTANDI, for this patient population for which there is a significant unmet medical need," said David Hung, M.D., co-founder, president and CEO, Medivation, Inc. "I would like to extend my thanks to the patients, physicians, and their study teams who participated in the clinical trials, and to our employees, and those of our partner Astellas, who have been instrumental in helping us reach this important milestone."

"Enzalutamide provides an exciting new option for physicians that can prolong the lives of patients with metastatic prostate cancer who have received chemotherapy," said Howard I. Scher, M.D., chief, Genitourinary Oncology Service, Sidney Kimmel Center for Prostate and Urologic Cancers, Memorial Sloan-Kettering Cancer Center, and the co-principal investigator of the AFFIRM pivotal study. "It is extremely gratifying to have led the clinical trial of enzalutamide, having followed the development of this drug from its early inception in the laboratory to the clinic."

"We believe XTANDI has the potential to play an important role in the treatment of advanced prostate cancer," said Stephen Eck, M.D., Ph.D., Vice President of Medical Oncology, Astellas Pharma Global Development. "We're eager to work with Medivation to make this much-needed new treatment available to medical professionals and patients in September."

The recommended dose of XTANDI is 160 mg (four 40 mg capsules) administered orally once daily. XTANDI can be taken with or without food and does not require concomitant steroid (e.g., prednisone) use. In the phase 3 clinical trial, 48% of XTANDI patients and 46% of patients in the placebo arm were treated with glucocorticoids.

As a post-marketing requirement, Medivation and Astellas have agreed with the FDA to conduct an open-label safety study of XTANDI (160 mg/day) in patients who are at high risk for seizure. Medivation and Astellas have agreed to provide the data from this study in 2019.

#### *About XTANDI*

XTANDI is an androgen receptor inhibitor indicated for the treatment of patients with metastatic castration-resistant prostate cancer (mCRPC) who have previously received docetaxel. The efficacy and safety of XTANDI were assessed in a randomized, placebo-controlled, multicenter phase 3 clinical trial. A total of 1,199 patients with mCRPC who had previously received docetaxel were randomized 2:1 to receive either XTANDI orally at a dose of 160 mg once daily (N = 800) or placebo (N = 399). 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. The primary endpoint of the trial was overall survival.

XTANDI-treated patients had a statistically-significant improvement in median overall survival compared to the placebo group: 18.4 months in the XTANDI group versus 13.6 months in the placebo group (P < 0.0001). XTANDI provided a 37% reduction in risk of death compared to placebo (hazard ratio = 0.631). Seizure occurred in 0.9% of patients on XTANDI and 0% of the placebo-treated patients. The most common adverse reactions (≥ 5%) are 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 3 and higher adverse reactions were reported among 47% of XTANDI-treated patients and 53% of

placebo-treated patients.

### *XTANDI Mechanism of Action*

XTANDI (enzalutamide) is an androgen receptor inhibitor that acts on different steps in the androgen receptor signaling pathway. XTANDI has been shown to competitively inhibit androgen binding to androgen receptors and inhibit androgen receptor nuclear translocation and interaction with DNA. A major metabolite, N-desmethyl enzalutamide, exhibited similar in vitro activity to XTANDI. XTANDI decreased proliferation and induced cell death of prostate cancer cells in vitro, and decreased tumor volume in a mouse prostate cancer xenograft model.

### *Important Safety Information for XTANDI*

**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.

**Warning 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.

**Drug Interactions-** Enzalutamide is a strong CYP3A4 inducer and a moderate CYP2C9 and CYP2C19 inducer in humans. 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 CYP3A4 and CYP2C8 inducers may decrease the plasma exposure of XTANDI and should be avoided if possible. 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, please visit [www.XtandiHCP.com](http://www.XtandiHCP.com).

### *Conference Call Information*

Medivation will host a live conference call and webcast at 11:45am PT today, August, 31, 2012. To access the call, please dial 877-303-2523 from the United States or +1-253-237-1755 internationally. Individuals may access the live audio webcast by visiting [www.medivation.com](http://www.medivation.com) and going to the Investor Relations section. A replay of the webcast will be available on the Company's website for 30 days following the live event.

### *About Medivation*

Medivation, Inc. is a biopharmaceutical company focused on the rapid development of novel 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 [www.medivation.com](http://www.medivation.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 becoming a global category leader in oncology, and has several oncology compounds in development in addition to XTANDI. For more information on Astellas Pharma Inc., please visit our website at [www.astellas.com/en](http://www.astellas.com/en).

### *Forward-Looking Statements*

This press release contains forward-looking statements that are made pursuant to the safe harbor provisions of the federal securities laws, including statements regarding the expected launch and commercialization of XTANDI and the timing thereof. Any statements contained in this press release that are not statements of historical fact may be deemed to be forward-looking statements. Forward-looking statements involve risks and uncertainties that could cause Medivation's actual results to differ

significantly from those projected, including, without limitation, the risk that unanticipated developments could delay or prevent the launch and commercialization of XTANDI, as well as other risks detailed in Medivation's filings with the Securities and Exchange Commission, including its quarterly report on Form 10-Q for the quarter ended June 30, 2012, filed on August 9, 2012 with the SEC. You are cautioned not to place undue reliance on the forward-looking statements, which speak only as of the date of this release. Medivation disclaims any obligation or undertaking to update or revise any forward-looking statements contained in this press release.

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