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**Medivation and Astellas Announce FINAL Results from the Phase 3 PREVAIL Trial of Enzalutamide in Men with Metastatic Prostate Cancer Progressing on Androgen deprivation THERAPY**

**--Study demonstrates statistically significant benefits in overall survival, radiographic progression-free survival, and a delay (17 months) in the time to initiation of chemotherapy--**

SAN FRANCISCO, CA AND TOKYO, JAPAN – January 28, 2014 – Medivation Inc. (NASDAQ: MDVN) and Astellas Pharma Inc. (TSE: 4503) announced final results on the primary and secondary efficacy endpoints from the Phase 3 PREVAIL trial of enzalutamide in patients with chemotherapy-naïve metastatic prostate cancer who have failed androgen deprivation therapy and have few or no symptoms. Data will be shared in a late-breaking oral presentation at the upcoming American Society of Clinical Oncology (ASCO) 2014 Genitourinary (GU) Cancers Symposium in San Francisco on Thursday, January 30, 2014.[[1]](#endnote-1)

”Xtandi används idag för patienter som progredierat i sin prostatacancer under eller efter behandling med kemoterapi. Nu har en studie med Xtandi visat goda resultat före kemoterapi, vilket gör att behandlingen blir ett alternativ till kemoterapi som första behandling när vanlig hormonbehandling sviktar. Detta är en patientgrupp med allvarlig prognos och vi har därför behov av flera olika behandlingsalternativ. Den optimala ordningsföljden av behandlingar för den enskilde patienten är emellertid ännu oklar. Vi hoppas nu att Xtandi så snart som möjligt får myndigheternas godkännande för att användas även i detta tidigare skede i sjukdomsförloppet, säger Göran Ahlgren, Urolog på Skånes Universitetssjukhus i Malmö.”

“This is a significant step forward in prostate cancer therapy for men whose cancer has progressed, despite treatment with androgen deprivation therapy” said Professor Bertrand Tombal, MD, PhD, Chairman of the Division of the Urology, Cliniques Universitaires Saint Luc, Université Catholique de Louvain (UCL) and European Principal Investigator for PREVAIL. “As well as the clear efficacy benefits, what impressed me most about the results is that treatment with enzalutamide delays the time to initiation of chemotherapy, a key factor in maintaining quality of life in men with advanced prostate cancer.”

The PREVAIL study results in men with metastatic prostate cancer who have progressed on androgen deprivation therapy are as follows:

* Treatment with enzalutamide demonstrated a statistically significant overall survival benefit compared with placebo treatment. Enzalutamide reduced the risk of death by 29% (HR=0.71; p<0.0001), compared with placebo. This benefit was observed despite substantial use of subsequent therapies (40% in the enzalutamide and 70% in the placebo groups).i
* Treatment with enzalutamide significantly reduced the risk of radiographic progression or death by 81% compared with placebo treatment (HR=0.19; p<0.0001).i
* Consistent benefits on these co-primary endpoints of overall survival and radiographic progression-free survival were observed across patient subgroups.i
* Men taking enzalutamide experienced a 17-month delay in the time to initiation of chemotherapy compared with men taking placebo (28.0 months versus 10.8 months; HR=0.35; p<0.0001).i
* The majority of men (58.8%) with soft tissue metastatic disease treated with enzalutamide versus 5% of patients treated with placebo had objective responses (complete responses or partial responses) including complete responses in 19.7% of enzalutamide patients compared with 1% of placebo patients.i
* Enzalutamide extended the median time to PSA progression from 2.8 months (placebo) to 11.2 months (HR=0.169; p<0.0001).ii
* Nearly 4 out of 5 patients in the enzalutamide group experienced a PSA decline of 50% or more, compared to less than 4% in the placebo group (78% vs. 3.5%; p<0.0001).ii
* The median times to deterioration in a measure of prostate cancer-specific quality of life, the Functional Assessment of Cancer Therapy-Prostate or FACT-P, were 11.3 months for the enzalutamide-treated patients and 5.6 months for the placebo patients (HR= 0.625, p<0.0001).ii
* The median treatment duration for enzalutamide was more than 3 times longer than for placebo (16.6 versus 4.6 months).ii
* Common side effects occurring during treatment and more common in the enzalutamide treated men included fatigue, back pain, constipation and arthralgia. Hypertension was observed in 13.4% of enzalutamide versus 4.1% of placebo-treated patients. Grade 3 or higher cardiac adverse events were reported in 2.8% of enzalutamide versus 2.1% of placebo-treated patients. Investigators reported zero seizures in the enzalutamide-treated group and one in the placebo group prior to the data cut-off date. One seizure was reported in the enzalutamide group after the data cut-off date.i

“Medivation's primary mission is to develop and make available to patients medically innovative therapies that provide clinically meaningful benefits and address major medical unmet needs among a spectrum of serious diseases,” said David Hung, M.D., founder, president and CEO of Medivation. “Should enzalutamide be approved for use in this patient population, it will be a meaningful advance in the field of prostate cancer therapy.”

"We are very excited about these results and the potential to offer a new treatment option for patients with metastatic castration resistant prostate cancer, in the pre-chemotherapy setting," said Dr Ayad Abdulahad, Senior Vice President, Medical Affairs Health Economics, APEL. "There remains a high unmet patient need for a new treatment that offers patients with advanced prostate cancer, not only the opportunity to live for longer, but to do so with a good quality of life. We are committed to work with our partners, Medivation, to seek the necessary European regulatory approval for this expanded use of enzalutamide, based on the results of PREVAIL.”

Details of the presentation are as follows:

***Title:*** Enzalutamide in men with chemotherapy-naïve metastatic prostate cancer (mCRPC): Results of Phase 3 PREVAIL Study

***Presenter:*** Tomasz M. Beer, M.D., F.A.C.P., Knight Cancer Institute, Oregon Health & Science University

* Session Detail: Welcome and General Session 1: Integrating Androgen Axis Therapy across the Disease Spectrum
* Session Date/Time: January 30, 2014 from 7:45 a.m - 9:45 a.m.

**About the PREVAIL Trial**

The Phase 3 PREVAIL trial is a randomised, 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 metastatic prostate cancer whose disease progressed despite treatment with androgen deprivation therapy and had not yet received chemotherapy. 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. Targeted enrollment was completed in May 2012 and the pre-specified interim analysis was conducted after 516 events (patient deaths).[[2]](#endnote-2)i

**Enzalutamide Mechanism of Action**

XTANDI (enzalutamide) is a novel, oral, once-daily androgen receptor signalling inhibitor which works in three distinct ways: it inhibits testosterone binding to androgen receptors, nuclear translocation of androgen receptors; and DNA binding and activation by androgen receptors.iv

**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.

Enzalutamide is currently licensed in Europe for the treatment of adult men with metastatic castration-resistant prostate cancer whose disease has progressed on or after docetaxel therapy.iv

**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 randomised 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 (≥ 5%) reported in patients receiving XTANDI in the randomised clinical trial were asthenia/fatigue, back pain, diarrhoea, 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.

**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.

**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 organisation 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.

1. Beer T, et al. Enzalutamide Decreases Risk of Death and Delays Progression in Phase 3 Trial of Men with Metastatic Prostate Cancer. Presentation ASCO GU 2014
ii Phung, et al. PREVAIL results, APGD Leadership Team Presentation [↑](#endnote-ref-1)
2. http://clinicaltrials.gov/ct2/show/NCT01212991. Last accessed January 2014
iv European Medicines Agency, XTANDI, (enzalutamide) Summary of Product Characteristics, 2013 [↑](#endnote-ref-2)