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Enzalutamide Data Presented at ASCO GU Symposium

-- Six Abstracts Presented Include Data from Phase II Study Investigating XTANDI® (enzalutamide) Capsules in Hormone-Naïve Prostate Cancer --

SAN FRANCISCO, CA AND TOKYO – February 13, 2013 – Medivation, Inc. (NASDAQ: MDVN) and Astellas Pharma Inc. (Tokyo: 4503) announced that data for enzalutamide, an oral androgen receptor inhibitor, will be presented at the American Society of Clinical Oncology (ASCO) 2013 Genitourinary (GU) Cancers Symposium in Orlando, Florida.

Title: Enzalutamide monotherapy: Phase 2 study results in hormone-naïve prostate cancer patients (Abstract #18)

This phase 2 study assessed the efficacy and safety of enzalutamide monotherapy (160 mg) in 67 patients who had never received hormone therapy and presented with normal testosterone levels (≥ 230 ng/dL). The analysis showed:

- Ninety-three percent of study participants experienced a $\geq 80\%$ PSA decrease at week 25.
- Median change in PSA was -99.6% (range -100% to -86.5%).
- Serum testosterone increased by a mean of 114% at week 25 compared with baseline.
- Frequent treatment-emergent adverse events (AEs) were mostly Grade 1 or 2 and included gynecomastia (36%), fatigue (34%), nipple pain (19%), and hot flush (18%).
- Endocrine level changes and the most common drug-related AEs were consistent with potent AR signaling inhibition.

Title: Enzalutamide in combination with docetaxel in men with metastatic castration-resistant prostate cancer (mCRPC): preliminary results from a phase 1 study (Abstract #63)

- A phase I study of enzalutamide given in combination with docetaxel in men with metastatic castration-resistant prostate cancer (mCRPC) who are on androgen deprivation therapy is currently ongoing. Preliminary data suggest that enzalutamide does not affect tolerability of docetaxel or have a clinically meaningful impact on docetaxel pharmacokinetics in this patient population.
- Overall, enzalutamide was well tolerated with no patients discontinuing because of an enzalutamide-related adverse event.

Title: Impact of on-study corticosteroid use on efficacy and safety in the phase 3 AFFIRM study of enzalutamide, an androgen receptor inhibitor (Abstract #6)

- A *post-hoc* analysis of AFFIRM, a randomized, multinational, placebo-controlled phase 3 study among patients with mCRPC who had previously received docetaxel, showed that concomitant corticosteroid (CS) use was associated with reduced overall survival (median of 12.8 months in the CS group vs. median not met in the no CS group) and higher rates of grade 3-4 adverse events (63.3% in the CS group vs. 34.4% in the no CS group) in this population.

Title: Improved outcomes in elderly patients with metastatic castration-resistant prostate cancer (mCRPC) treated with the androgen receptor inhibitor enzalutamide: results from the Phase 3 AFFIRM trial (Abstract #16)

- A *post-hoc* analysis of the phase 3 AFFIRM study showed that outcomes in elderly (≥ 75 years) and younger (< 75 years) patients with post-docetaxel mCRPC treated with enzalutamide were comparable and significantly improved over placebo.
- Safety and tolerability findings were comparable between the two age groups.

Title: Enzalutamide improves health-related quality of life (HRQoL) in men with metastatic castration-resistant prostate cancer (mCRPC) following docetaxel-based therapy: results from the AFFIRM study (Abstract #17)

- An analysis of patients enrolled in the enzalutamide phase 3 AFFIRM study showed that a greater percentage of patients on enzalutamide reported health-related quality of life (HRQoL) improvement compared to placebo (42.2% vs. 14.5%; $p < 0.001$).
- Both enzalutamide and placebo groups reported deterioration at some point during the study. However, compared with patients receiving placebo, patients receiving enzalutamide had a significantly prolonged time to HRQoL deterioration.

Title: Long-term responders to enzalutamide (ENZA) during the phase 3 AFFIRM trial: baseline characteristics and efficacy outcomes (Abstract #20)

- In this *post hoc* analysis of AFFIRM data, 35% of patients remained on enzalutamide for ≥ 12 months and 22% for ≥ 18 months.

Compared with the all-enzalutamide group and the placebo group, patients in the long-term exposure subgroup had somewhat less disease burden at baseline, lower concomitant steroid use, and improved efficacy outcomes consistently across multiple endpoints.

About XTANDI®

XTANDI® (enzalutamide) capsules is an oral, once-daily androgen receptor inhibitor. XTANDI was approved by the FDA on August 31, 2012 for the treatment of metastatic castration-resistant prostate cancer for patients who have previously received docetaxel (chemotherapy).

A Marketing Authorization Application for XTANDI is currently under review by the European Medicines Agency (EMA).

The efficacy and safety of XTANDI were assessed in the randomized, placebo-controlled, global phase 3 AFFIRM 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 OS.

XTANDI-treated patients had a statistically-significant improvement in median OS 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.

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.

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, 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

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 vs 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, please visit www.XtandiHCP.com.

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.

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