



Pfizer and Astellas Announce Top-Line Results from Phase 4 PLATO Trial of XTANDI® (enzalutamide) Capsules in Patients with Metastatic Castration-Resistant Prostate Cancer

Wednesday, December 14, 2016 - 11:15am

“Current and emerging treatments in the management of castration-resistant prostate cancer.”

Pfizer Inc. (NYSE:PFE) and Astellas Pharma Inc. (TSE:4503) today announced the Phase 4 PLATO study, evaluating the efficacy and safety of continued treatment with XTANDI® (enzalutamide), plus abiraterone acetate and prednisone as compared to treatment with abiraterone acetate and prednisone alone, did not meet its primary endpoint of improvement in progression-free survival (PFS) in patients with chemotherapy-naïve metastatic castration-resistant prostate cancer (CRPC) whose prostate-specific antigen (PSA) has previously progressed on XTANDI.

“While the PLATO trial did not meet its primary endpoint, it is critical that we continue to focus on addressing the unmet needs of men with metastatic CRPC, who have a poor prognosis despite treatment advances,” said Mohammad Hirmand, M.D., interim chief medical officer at Medivation, Inc., which is now part of Pfizer. “We will continue to analyze these data to better understand the results with the goal of further helping these patients.”

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“XTANDI continues to remain an important treatment option for men with metastatic CRPC and their physicians. We are committed to continuing to explore the clinical potential of XTANDI across the disease continuum,” said Steven Benner, M.D., senior vice president, therapeutic area head for oncology development, Astellas.

XTANDI is approved by the U.S. Food and Drug Administration for the treatment of patients with metastatic castrate-resistant prostate cancer (CRPC), based on clinical studies showing statistically significant overall survival benefit versus placebo.

About PLATO

The Phase 4 PLATO trial (NCT01995513) is a global randomized, double-blind, placebo-controlled, two-period study designed to evaluate the efficacy and safety of continued treatment with XTANDI plus abiraterone acetate and prednisone at the time of confirmed PSA progression, as compared to treatment with abiraterone acetate and prednisone alone at the time of PSA progression. The study enrolled 509 patients with chemotherapy-naïve metastatic CRPC who received open label XTANDI during period 1 of the study, until PSA progression was confirmed. Eligible patients were then randomized to one of the two treatments and assessed for the primary endpoint of the study, PFS, defined by either: 1) radiographic progression or 2) unequivocal clinical progression or 3) death during the study.

Period 1 patients were treated with XTANDI 160mg/day orally and period 2 patients were treated with blinded XTANDI 160 mg/day orally in combination with abiraterone at a dose of 1,000 mg/day administered orally and prednisone at a dose of 5 mg administered orally twice daily, versus placebo plus the same doses of abiraterone acetate and prednisone.

For additional information regarding the PLATO trial, visit clinicaltrials.gov.

About Metastatic Castration-Resistant Prostate Cancer (CRPC)

Metastatic castration-resistant prostate cancer (CRPC) refers to prostate cancer that has spread to parts of the body other than the prostate, and continues to spread despite treatment.¹ Up to 40 percent of men diagnosed with prostate cancer who undergo therapy develop metastatic, or advanced, prostate cancer.² In the U.S., the five-year relative survival rate for prostate cancer patients with metastatic disease is 28 percent, compared with 100 percent for prostate cancer patients with non-metastatic disease.³

About XTANDI® (enzalutamide) capsules

XTANDI (enzalutamide) is an androgen receptor inhibitor that blocks multiple steps in the androgen receptor signaling pathway within the tumor cell. In preclinical studies, enzalutamide has been shown to competitively inhibit androgen binding to androgen receptors, and inhibit androgen receptor nuclear translocation and interaction with DNA. The clinical significance of this mechanism of action (MOA) is unknown.

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

Important Safety Information

Contraindications

XTANDI is not indicated for women. XTANDI can cause fetal harm and potential loss of pregnancy.

Warnings and Precautions

Seizure occurred in 0.5% of patients receiving XTANDI in clinical studies. In placebo-controlled studies, 8 of 1671 (0.5%) patients treated with XTANDI and 1 of 1243 (0.1%) patients treated with placebo experienced a seizure. In patients who previously received docetaxel, 7 of 800 (0.9%) patients treated with XTANDI experienced a seizure and no patients treated with placebo experienced a seizure. In a placebo-controlled study in chemotherapy-naïve patients, 1 of 871 (0.1%) treated with XTANDI and 1 of 844 (0.1%) patients treated with placebo experienced a seizure. In bicalutamide-controlled studies conducted in chemotherapy-naïve patients, 3 of 380 (0.8%) patients treated with XTANDI and 1 of 387 (0.3%) patients treated with bicalutamide experienced a seizure.

Permanently discontinue XTANDI in patients who develop a seizure during treatment.

Posterior Reversible Encephalopathy Syndrome (PRES) In post approval use, there have been reports of PRES in patients receiving XTANDI. PRES is a neurological disorder which can present with rapidly evolving symptoms including seizure, headache, lethargy, confusion, blindness, and other visual and neurological disturbances, with or without associated hypertension. A diagnosis of PRES requires confirmation by brain imaging, preferably MRI. Discontinue XTANDI in patients who develop PRES.

Adverse Reactions

The most common adverse reactions ($\geq 10\%$) that occurred more commonly ($\geq 2\%$ over placebo) in the XTANDI patients from the two placebo-controlled clinical trials 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. In the bicalutamide-controlled study of chemotherapy naïve patients, the most common adverse reactions ($\geq 10\%$) reported in XTANDI patients were asthenia/fatigue, back pain, musculoskeletal pain, hot flush, hypertension, nausea, constipation, upper respiratory tract infection, diarrhea, and weight loss.

In the study of patients taking XTANDI who previously received docetaxel, Grade 3 and higher adverse reactions were reported among 47% of XTANDI patients and 53% of placebo patients. Discontinuations due to adverse events were reported for 16% of XTANDI patients and 18% of placebo patients. In the placebo-controlled study of chemotherapy-naïve patients, Grade 3-4 adverse reactions were reported in 44% of XTANDI patients and 37% of placebo patients. Discontinuations due to adverse events were reported for 6% of both study groups. In the bicalutamide-controlled study of chemotherapy naïve patients, Grade 3-4 adverse reactions were reported in 38.8% of XTANDI patients and 37.6% of bicalutamide patients. Discontinuations due to adverse events were reported for 7.6% of XTANDI patients and 6.3% of bicalutamide patients.

Lab Abnormalities: In the two placebo-controlled trials Grade 1-4 neutropenia occurred in 15% of XTANDI patients (1% Grade 3-4) and 6% of placebo patients (0.5% Grade 3-4). Grade 1-4 thrombocytopenia occurred in 6% of XTANDI patients (0.3% Grade 3-4) and 5% of placebo patients (0.5% Grade 3-4). Grade 1-4 elevations in ALT occurred in 10% of XTANDI patients (0.2% Grade 3-4) and 16% of placebo patients (0.2% Grade 3-4). Grade 1-4 elevations in bilirubin occurred in 3% of XTANDI patients (0.1% Grade 3-4) and 2% of placebo patients (no Grade 3-4).

Infections: In a study of patients taking XTANDI who previously received docetaxel, 1% of XTANDI patients compared to 0.3% of placebo patients died from infections or sepsis. In the placebo-controlled study of chemotherapy-naïve patients, 1 patient in each treatment group (0.1%) had an infection resulting in death.

Falls (including fall-related injuries) occurred in 9% of XTANDI patients and 4% of placebo patients in the two placebo-controlled trials. 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 occurred in 11% of XTANDI patients and 4% of placebo patients in the two placebo-controlled trials. No patients experienced hypertensive crisis. Medical history of hypertension was balanced between arms. Hypertension led to study discontinuation in <

1% of all patients in each arm.

Drug Interactions

Effect of Other Drugs on XTANDI Avoid strong CYP2C8 inhibitors, as they can increase the plasma exposure to XTANDI. If co-administration is necessary, reduce the dose of XTANDI.

Avoid strong CYP3A4 inducers as they can decrease the plasma exposure to XTANDI. If co-administration is necessary, increase the dose of XTANDI.

Effect of XTANDI on Other Drugs 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.

Please see Full Prescribing Information at <https://www.astellas.us/docs/us/12A005-ENZ-WPI.pdf?v=1> for additional safety information.

You are encouraged to report negative side effects of prescription drugs to the FDA.

Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

About Pfizer Oncology

Pfizer Oncology is committed to pursuing innovative treatments that have a meaningful impact on those living with cancer. As a leader in oncology speeding cures and accessible breakthrough medicines to patients, Pfizer Oncology is helping to redefine life with cancer. Our strong pipeline of biologics, small molecules and immunotherapies, one of the most robust in the industry, is studied with precise focus on identifying and translating the best scientific breakthroughs into clinical application for patients across a wide range of cancers. By working collaboratively with academic institutions, individual researchers, cooperative research groups, governments and licensing partners, Pfizer Oncology strives to cure or control cancer with its breakthrough medicines. Because Pfizer Oncology knows that success in oncology is not measured solely by the medicines you manufacture, but rather by the meaningful partnerships you make to have a more positive impact on people's lives. Learn more about how Pfizer Oncology is applying innovative approaches to improve the outlook for people living with cancer at http://www.pfizer.com/research/therapeutic_areas/oncology.

About Astellas

Astellas Pharma Inc., based in Tokyo, Japan, is a company dedicated to improving the health of people around the world through the provision of innovative and reliable pharmaceutical products. We focus on Urology, Oncology, Immunology, Nephrology and Neuroscience as prioritized therapeutic areas while advancing new therapeutic areas and discovery research leveraging new technologies/modalities. We are also creating new value by combining internal capabilities and external expertise in the medical/healthcare business. Astellas is on the forefront of healthcare change to turn innovative science into value for patients. For more information, please visit our website at www.astellas.com/en.

About the Pfizer/Astellas Collaboration

In October 2009, Medivation, Inc., which is now part of Pfizer (NYSE:PFE), 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.

Pfizer Disclosure Notice

The information contained in this release is as of December 14, 2016. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about XTANDI® (enzalutamide) that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, uncertainties regarding the commercial impact of the results of the PLATO study; the uncertainties inherent in research and development, including the possibility of unfavorable clinical trial results, including unfavorable new clinical data and additional analyses of existing clinical data; decisions by regulatory authorities regarding labeling, safety, and other matters that could affect the availability or commercial potential of XTANDI; risks related to the ability to sustain and increase the rate of growth in revenues for XTANDI despite increasing competitive, reimbursement and economic challenges; dependence on the efforts and funding by Astellas Pharma Inc. for the development, manufacturing and commercialization of XTANDI; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2015 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

Astellas Forward-Looking Statement

In this press release, statements made with respect to current plans, estimates, strategies and beliefs and other statements that are not historical facts are forward-looking statements about the future performance of Astellas. These statements are based on management's current assumptions and beliefs in light of the information currently available to it and involve known and unknown risks and uncertainties. A number of factors could cause actual results to differ materially from those discussed in the forward-looking statements. Such factors include, but are not limited to: (i) changes in general economic conditions and in laws and regulations, relating to pharmaceutical markets, (ii) currency exchange rate fluctuations, (iii) delays in new product launches, (iv) the inability of Astellas to market existing and new products effectively, (v) the inability of Astellas to continue to effectively research and develop products accepted by customers in highly competitive markets, and (vi) infringements of Astellas' intellectual property rights by third parties.

Information about pharmaceutical products (including products currently in development), which is included in this press release is not intended to constitute an advertisement or medical advice.

1 Cancer.net. Treatment of Metastatic Castration-Resistant Prostate Cancer. <http://www.cancer.net/research-and-advocacy/asco-care-and-treatment-recommendations-patients/treatment-metastatic-castration-resistant-prostate-cancer>. Accessed 12-14-2016.

2 "Current and emerging treatments in the management of castration-resistant prostate cancer." David Shapiro and Basir Tareen. *Expert Rev Anticancer Ther.* 2012;12(7):951-964.

3 National Cancer Institute. SEER Cancer Statistics Factsheets: Prostate Cancer. Available at seer.cancer.gov/statfacts/html/prost.html. Accessed 12-14-2016.

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