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Pfizer and Astellas Announce Positive Top-Line Results from Phase 3 PROSPER Trial of XTANDI (enzalutamide) in Patients with Non-Metastatic Castration-Resistant Prostate Cancer

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Enzalutamide is the first androgen receptor-inhibitor to demonstrate a statistically significant improvement in metastasis-free survival (MFS) in this patient population in a randomized, controlled clinical trial

Pfizer Inc. (NYSE:PFE) and Astellas Pharma Inc. (TSE: 4503, President and CEO: Yoshihiko Hatanaka, "Astellas") announced today that the Phase 3 PROSPER trial evaluating XTANDI® (enzalutamide) plus androgen deprivation therapy (ADT) versus ADT alone in patients with non-metastatic (M0) Castration-Resistant Prostate Cancer (CRPC) met its primary endpoint of improved metastasis-free survival (MFS). The preliminary safety analysis of the PROSPER trial appears consistent with the safety profile of XTANDI in previous clinical trials.

"Many prostate cancer patients who initiate androgen deprivation therapy will experience disease progression illustrated by a rising PSA level, and currently, there are no FDA-approved treatment options for patients with non-metastatic CRPC until they develop confirmed radiographic metastatic disease," said Neal Shore, M.D., director, CPI, Carolina Urologic Research Center.

Based on the results of PROSPER, the companies intend to discuss the data with global health authorities to potentially support expanding the label for XTANDI to cover all patients with CRPC.

"We are delighted with the significant results seen in the PROSPER study, showing that XTANDI plus ADT delayed clinically detectable metastases compared to ADT alone in patients with non-metastatic CRPC whose only sign of underlying disease was a rapidly rising prostate-specific antigen (PSA) level. We look forward to discussing the data with regulatory authorities," said Mace Rothenberg, M.D., chief development officer, Oncology, Pfizer Global Product Development. "XTANDI is already established as a standard of care for men with metastatic CRPC based on the results of prior studies, such as AFFIRM and PREVAIL, which demonstrated that XTANDI delayed disease progression and improved overall survival in men with clinically detectable metastatic disease."

"We want to thank the patients, family members and clinicians who participated in the PROSPER trial and helped advance the scientific understanding of the potential role for XTANDI in this prevalent disease," said Steven Benner, M.D., senior vice president and global therapeutic area head, oncology development, Astellas. "We look forward to further analyzing the detailed efficacy and safety results from PROSPER, and submitting

them for presentation at an upcoming major medical meeting."

As part of Pfizer and Astellas' ongoing commitment to the clinical development of enzalutamide in areas of greatest unmet need, the companies initiated the PROSPER trial to evaluate the potential benefits of XTANDI in men with non-metastatic CRPC, an earlier stage of prostate cancer where there are currently no FDA-approved treatment options. On June 9, 2017, the companies announced an amendment to the PROSPER protocol, which accelerated the clinical trial completion date by two years.

XTANDI is currently approved for the treatment of metastatic CRPC based on clinical data from previous studies that showed a statistically significant overall survival benefit for XTANDI versus placebo in the metastatic CRPC setting. XTANDI has been prescribed to more than 185,000 patients globally since its first approval in 2012.

About PROSPER

The Phase 3 randomized, double-blind, placebo-controlled, multi-national trial enrolled approximately 1,400 patients with non-metastatic castration-resistant prostate cancer (CRPC) at sites in the United States, Canada, Europe, South America and the Asia Pacific region. PROSPER enrolled patients with prostate cancer that had progressed, based on a rising prostate-specific antigen (PSA) level despite androgen deprivation therapy (ADT), but who had no symptoms with no prior or present evidence of metastatic disease. The primary objective of the trial was metastasis-free survival (MFS). MFS is a measure of the amount of time that passes until a cancer can be radiographically detected as having metastasized, or spread, to other parts of the body. The trial evaluated enzalutamide at a dose of 160 mg taken orally once daily plus ADT, versus placebo plus ADT. For more information on the PROSPER trial go to www.clinicaltrials.gov.

XTANDI has not yet been evaluated by the FDA for the treatment of patients with non-metastatic CRPC.

About Non-Metastatic Castration-Resistant Prostate Cancer

According to the American Cancer Society, more than 161,000 men are estimated to be diagnosed with prostate cancer in 2017.[i] Castration-resistant prostate cancer (CRPC) refers to the subset of men whose prostate cancer progresses despite androgen deprivation therapy.[ii] Non-metastatic CRPC means there is no clinically detectable evidence of the cancer spreading to other parts of the body (metastases), and there is a rising prostate-specific antigen (PSA) level.[iii] Many men with non-metastatic CRPC will go on to develop metastatic CRPC.[iv]

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). Additional ongoing studies, such as the ARCHES trial in metastatic hormone-sensitive prostate cancer and the EMBARK trial in non-metastatic hormone-sensitive prostate cancer, are continuing to evaluate the potential of enzalutamide to help patients in need.

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 a study of patients with predisposing factors, seizures were reported in 2.2% of patients. See section 5.1 of the Prescribing Information for the list of predisposing factors. It is unknown whether anti-epileptic medications will prevent seizures with XTANDI. 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 (? 10%) that occurred more commonly (? 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 (? 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 placebo-controlled 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 the 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 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 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 for additional safety information.

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 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 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 other cancers. 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 September 14, 2017. 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) and a potential indication in patients with non-metastatic castration-resistant prostate cancer, including their potential benefits, 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, the uncertainties inherent in research and development, including the ability to meet anticipated clinical trial completion dates and regulatory submission dates, as well as the possibility of unfavorable clinical trial results, including unfavorable new clinical data and additional analyses of existing clinical data;the risk that clinical trial data are subject to differing interpretations, and, even when we view data as sufficient to support the safety and/or effectiveness of a product candidate, regulatory authorities may not share our views and may require additional data or may deny approval altogether; whether regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when any supplemental drug applications may be filed for XTANDI for the potential indication; whether and when regulatory authorities may approve any such applications, which will depend on the assessment by such regulatory authority of the benefit-risk profile suggested by the totality of the efficacy and safety information submitted; decisions by regulatory authorities regarding labeling, safety, and other matters that could affect the availability or commercial potential of XTANDI; risks related to 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, 2016 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.

[i] American Cancer Society. Key Statistics for Prostate Cancer (01-05-2017). https://www.cancer.org/cancer/prostate-cancer/about/key-statistics.html. Accessed 01-31-2017.
[ii] Urology Care Foundation. Advanced Prostate Cancer Patient Guide. www.urologyhealth.org/educational-materials. Accessed 02-16-2017.
[iii] Luo J, Beer T, Graff J. Treatment of Non-metastatic Castration Resistant Prostate Cancer. Oncology. April 2016, 30(4):336-344.
[iv] Kirby M, Hirst C, Crawford ED. Characterising the castration-resistant prostate cancer population: a systematic review. Int J Clin Pract 2011;65(11):1180-1192.

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