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U.S. FDA Grants Priority Review for a Supplemental New Drug Application (sNDA) for XTANDI® (enzalutamide) in Non-Metastatic Castration-Resistant Prostate Cancer (CRPC)

sNDA Seeks to Expand the Indication of XTANDI to include Men with Non-metastatic CRPC

NEW YORK and TOKYO, March 19, 2018 – Pfizer Inc. (NYSE: PFE) and Astellas Pharma Inc. (TSE: 4503, President and CEO: Yoshihiko Hatanaka, "Astellas") announced today that a supplemental New Drug Application (sNDA) for XTANDI® (enzalutamide) has been accepted for filing and granted Priority Review designation by the U.S. Food and Drug Administration (FDA). If approved, the sNDA would expand the indication of XTANDI to include men with non-metastatic Castration-Resistant Prostate Cancer (CRPC), based on data from the Phase 3 PROSPER trial. XTANDI is currently indicated for the treatment of patients with metastatic CRPC.

The FDA grants Priority Review designation to applications for drugs that, if approved, may offer significant improvements in the safety and effectiveness of the treatment of serious conditions when compared to standard applications. Under Priority Review, the FDA aims to take action on an application within six months of receipt, as compared to ten months under standard review. The Prescription Drug User Fee Act (PDUFA) goal date assigned by the FDA is July 2018. In addition, the European Medicines Agency (EMA) has validated the Type II Variation submitted for XTANDI seeking to expand the current indication to the same patient population and started the review process on March 5.

"Once cancer spreads and metastasizes, men with castration-resistant prostate cancer face a daunting prognosis and challenging odds," said Steven Benner, M.D., senior vice president and global therapeutic area head, Oncology Development, Astellas. "We're pleased to see the FDA's Priority Review designation as we work to potentially bring XTANDI to men living with non-metastatic CRPC."

“Treatment options have been limited for men with non-metastatic CRPC, in whom the only evidence of progressive disease is a rapidly rising PSA,” 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. This milestone marks an important step toward our ability to bring XTANDI to CRPC patients in an earlier setting.”

The PROSPER trial evaluated XTANDI plus androgen deprivation therapy (ADT) versus ADT alone in 1,401 patients with non-metastatic CRPC. The study met its primary endpoint, demonstrating that the use of XTANDI plus ADT significantly reduced the risk of developing metastasis or death compared to ADT alone. Adverse events in the PROSPER trial were higher in the enzalutamide plus ADT arm compared to ADT alone (87% vs. 77%), and were generally consistent with those reported in prior enzalutamide clinical trials in patients with metastatic CRPC. Results from the PROSPER trial were presented at the 2018 Genitourinary Cancers Symposium (ASCO GU) in February.[1] For more information on the PROSPER trial, go to www.clinicaltrials.gov.

The FDA approved XTANDI in 2012 for the treatment of patients with metastatic CRPC who had previously received docetaxel. In 2014, the FDA approved XTANDI to treat patients with metastatic CRPC.

About Prostate Cancer

Prostate cancer is the second most common cancer in men worldwide.[2] More than 164,000 men in the United States are estimated to be newly diagnosed with prostate cancer in 2018.[3] In the European Union, the estimated number of new prostate cancer cases in 2015 was 365,000.[4]

Castration-resistant prostate cancer (CRPC) refers to the subset of men whose prostate cancer progresses despite castration levels of testosterone.[5] 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.[6] Many men with non-metastatic CRPC and a rapidly rising PSA level go on to develop metastatic CRPC.[7]

About XTANDI® (enzalutamide) capsules

XTANDI (enzalutamide) is an androgen receptor inhibitor indicated for the treatment of patients with metastatic castration-resistant prostate cancer.

Important Safety Information for XTANDI®

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 the Enzalutamide Development Program
Pfizer and Astellas are collaborating on a comprehensive development program that includes studies of enzalutamide across the full spectrum of advanced prostate cancer. Ongoing studies of enzalutamide in prostate cancer include the ARCHES trial in metastatic hormone-sensitive prostate cancer and the EMBARK trial in non-metastatic hormone-sensitive prostate cancer.

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 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 March 19, 2018. 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; the risks associated with interim data; whether and when any supplemental drug applications may be filed for XTANDI for the potential indication in any other jurisdictions; whether and when the FDA and the EMA may approve the pending applications and whether and when regulatory authorities in any other jurisdictions may approve any such other applications, which will depend on the assessment by such regulatory authorities of the benefit-risk profile suggested by the totality of the efficacy and safety information submitted and, if approved, whether XTANDI for the potential indication will be commercially successful; 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, 2017 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.

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[1] Hussain M, Fizazi K, Saad F, et al. PROSPER: a phase 3, randomized, double-blind, placebo (PBO)-controlled study of enzalutamide (ENZA) in men with nonmetastatic castration-resistant prostate cancer (M0 CRPC). ASCO GU Meeting Library. https://meetinglibrary.asco.org/record/157683/abstract. Accessed 02-07-2018.
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[3] American Cancer Society. Key Statistics for Prostate Cancer. https://www.cancer.org/cancer/prostate-cancer/about/keystatistics.html. Accessed 01-08-2018.
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[6] Luo J, Beer T, Graff J. Treatment of nonmetastatic castration-resistant prostate cancer. *Oncology* 2016;30(4):336-44.
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