FDA Approves Supplemental New Drug Application for XTANDI® (enzalutamide) Capsules in Advanced Prostate Cancer

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- TERRAIN Trial Showed Improved Radiographic Progression-Free Survival with Enzalutamide Versus Bicalutamide in Men with Metastatic Castration-Resistant Prostate Cancer -

Astellas Pharma Inc. (TSE: 4503) and Pfizer Inc. (NYSE: PFE) today announced the U.S. Food and Drug Administration (FDA) approved a supplemental New Drug Application (sNDA) to update the U.S. product labeling for XTANDI® (enzalutamide) capsules to include new clinical data versus bicalutamide from the TERRAIN study. The data demonstrate improvement in radiographic progression-free survival (rPFS) in patients with metastatic castration-resistant prostate cancer (CRPC) who were treated with enzalutamide compared to patients who were treated with bicalutamide.

The TERRAIN study evaluated men with metastatic CRPC and the results from this study were published in the Lancet Oncology. The updated label includes data that enzalutamide reduces the risk of radiographic progression or death by 40% compared with bicalutamide, showing a median rPFS of 19.5 months for the enzalutamide group versus a median of 13.4 months for the bicalutamide group (hazard ratio = 0.60 [0.43, 0.83]; 95% confidence interval) based on an analysis recommended by the FDA. The safety profile of enzalutamide was consistent with results of earlier enzalutamide trials.

"The addition of data from the TERRAIN trial continues to build the body of evidence that demonstrates the clinical impact XTANDI can have for patients living with metastatic CRPC," said Steven Benner, M.D., senior vice president, therapeutic area head for oncology development, Astellas. "Advances in scientific knowledge as seen through

clinical trials like TERRAIN would not be possible without the participation of hundreds of patients, family members and clinical investigators, and we thank them for their valuable contributions."

According to the American Cancer Society, each year approximately 181,000 new cases of prostate cancer will be diagnosed and an estimated 26,000 men will die of the disease in 2016.1 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

"We are pleased with the FDA's decision to update the XTANDI label with these data from the first and largest comparative trial that demonstrated safety and efficacy of enzalutamide compared to bicalutamide," said Mohammad Hirmand, M.D., interim chief medical officer at Medivation, Inc., which is now part of Pfizer. "We believe these data will help physicians better understand the differences between enzalutamide and bicalutamide for their patients living with metastatic CRPC."

The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) issued a positive opinion onApril 1, 2016 recommending approval of a type II variation to include data from the TERRAIN trials in the European label for XTANDI.

About the TERRAIN trial The Phase II TERRAIN trial enrolled 375 chemotherapy-naïve patients with metastatic CRPC in North America and Europe. Radiographic progression-free survival was defined as the time from randomization to the first objective evidence of radiographic progression as assessed by Independent Central Review or death, whichever occurred first. The trial was designed to evaluate patients who were randomized 1:1 to receive enzalutamide at a dose of 160 mg taken orally once daily versus bicalutamide at a dose of 50 mg taken once daily.

Grade 3-4 adverse reactions were reported in 38.8% of enzalutamide-treated patients and 37.6% of bicalutamide-treated patients. Individual Grade 3 or higher adverse events largely occurred at a similar rate (<1% difference) between the enzalutamide vs. bicalutamide treatment groups, with the exception of hypertension (7.1% vs. 4.4%), diarrhea (0% vs. 1.1%) and back pain (2.7% vs. 1.6%). Two seizures were reported in the enzalutamide group and one in the bicalutamide group. The most common Grade 1-4 adverse reactions (incidence ≥10%) occurring during treatment and more common in the enzalutamide-treated versus bicalutamide-treated patients included asthenic conditions, back pain, musculoskeletal pain, hot flush, hypertension, diarrhea, upper respiratory tract infection, and weight loss.

About XTANDI® (enzalutamide) capsules XTANDI (enzalutamide) capsules 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 (≥ 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 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 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.

Pfizer Disclosure Notice The information contained in this release is as of October 21, 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) capsules and a label update to include the results of the TERRAIN study, 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,uncertainties regarding the commercial impact of the label update; the uncertainties inherent in research and development, including the ability to meet anticipated clinical trial commencement and 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; whether and when any drug applications may be filed for any potential additional indications for XTANDI; whether and when any such applications may be approved by regulatory authorities, 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; decisions by regulatory authorities regarding labeling 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.

References

American Cancer Society. "Cancer Facts and Figures: 2016." "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. National Cancer Institute. SEER Cancer Statistics Factsheets: Prostate Cancer. Available at seer.cancer.gov/statfacts/html/prost.html. Accessed October 5, 2016.
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