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U.S. FDA Grants XTANDI® (enzalutamide) Application Priority Review for the Treatment of Men with Metastatic Hormone-Sensitive Prostate Cancer

XTANDI Supplemental New Drug Application (sNDA) Seeks to Add an Indication for Men with Prostate Cancer that Has Spread but Is Sensitive to Hormone Therapy

TOKYO and NEW YORK, August 21, 2019 – Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D., "Astellas") and Pfizer Inc. (NYSE: PFE) announced today that the U.S. Food and Drug Administration (FDA) has accepted for review the filing of a supplemental New Drug Application (sNDA) for XTANDI® (enzalutamide) to add an indication for the treatment of men with metastatic hormone-sensitive prostate cancer (mHSPC). The application has also been granted Priority Review, a designation given to those applications for drugs that, if approved, may offer significant improvements in the safety or effectiveness of the treatment, diagnosis or prevention of serious conditions when compared to standard applications. XTANDI is currently indicated in the U.S. for the treatment of patients with castration-resistant prostate cancer (CRPC).

The submission is based on results from the Phase 3 ARCHES trial presented at the 2019 Genitourinary Cancers Symposium (ASCO GU) in February and published in *The Journal of Clinical Oncology* in July 2019. The study evaluated the efficacy and safety of XTANDI plus androgen deprivation therapy (ADT) versus ADT plus placebo in men with mHSPC. The primary endpoint of radiographic progression-free survival (rPFS) was met in the study.

Additionally, the submission is supported by data from ENZAMET, an Astellas-supported, investigator-sponsored Phase 3 research study led by the Australian and New Zealand Urogenital and Prostate Cancer Trials Group (ANZUP) and sponsored by the University of Sydney. The ENZAMET trial evaluated XTANDI plus ADT versus ADT plus a standard nonsteroidal antiandrogen therapy (bicalutamide, nilutamide or flutamide) in men with mHSPC to provide an active control. The results were presented during the Plenary Session at the 2019 American Society of Clinical Oncology (ASCO) Annual Meeting in June and simultaneously published in *The New England Journal of Medicine*. The primary endpoint of

overall survival (OS) was met in the ENZAMET trial. The safety analyses of the ARCHES and ENZAMET trials appear consistent with the safety profile of enzalutamide in previous clinical trials in CRPC.

“We are pleased to receive the Priority Review designation, which reflects the need for more treatment options for men living with metastatic hormone-sensitive prostate cancer,” said Chris Boshoff, M.D., Ph.D., Chief Development Officer, Oncology, Pfizer Global Product Development. “The submission is supported by a strong data package, including two Phase 3 trials investigating XTANDI in men living with this form of prostate cancer.”

“The complementary data from the ARCHES and ENZAMET trials in men with mHSPC take us another step closer to understanding XTANDI's full potential in helping address unmet needs in prostate cancer,” said Andrew Krivoshik, M.D., Ph.D., Senior Vice President and Oncology Therapeutic Area Head at Astellas. “XTANDI is a current standard of care in castration-resistant prostate cancer and we look forward to working with the FDA to potentially make XTANDI available to men earlier in their prostate cancer journey.”

Data from the ARCHES and ENZAMET studies have also been submitted to the European Medicines Agency (EMA) and to the Pharmaceuticals and Medical Devices Agency (PMDA) in Japan to potentially support an indication for XTANDI that includes men with mHSPC.

The FDA has set a Prescription Drug User Fee Act (PDUFA) date, or target action date, in Q4 2019.

About Metastatic Hormone-Sensitive Prostate Cancer
In men with prostate cancer, the disease is considered metastatic once the cancer has spread outside of the prostate gland to other parts of the body, such as the bones, lymph nodes, bladder and rectum.[1] Men are considered hormone (or castration) sensitive if their disease still responds to medical or surgical treatment to lower testosterone levels.[2] The prevalence of mHSPC in the U.S. in 2019 is estimated to be just over 40,000.[3]

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

Important Safety Information for XTANDI® for Castration-Resistant Prostate Cancer (CRPC)

Warnings and Precautions
Seizure occurred in 0.4% of patients receiving XTANDI in clinical studies. In a study of patients with predisposing factors for seizure, 2.2% of XTANDI-treated patients experienced a seizure. Patients in the study had one or more of the following pre-disposing factors: use of medications that may lower the seizure threshold; history of traumatic brain or head injury, cerebrovascular accident or transient ischemic attack, Alzheimer's disease, meningioma, or leptomeningeal disease from prostate cancer, unexplained loss of consciousness within the last 12 months, history of seizure, presence of a space occupying lesion of the brain, history of arteriovenous malformation, or history of brain infection. It is unknown whether anti-epileptic medications will prevent seizures with XTANDI. Advise patients of the risk of developing a seizure while taking XTANDI and of engaging in any activity where sudden loss of

consciousness could cause serious harm to themselves or others. 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.

Hypersensitivity reactions, including edema of the face (0.5%), tongue (0.1%), or lip (0.1%) have been observed with XTANDI in clinical trials. Pharyngeal edema has been reported in post-marketing cases. Advise patients who experience any symptoms of hypersensitivity to temporarily discontinue XTANDI and promptly seek medical care. Permanently discontinue XTANDI for serious hypersensitivity reactions.

Ischemic Heart Disease In the placebo-controlled clinical studies, ischemic heart disease occurred more commonly in patients on the XTANDI arm compared to patients on the placebo arm (2.7% vs 1.2%). Grade 3-4 ischemic events occurred in 1.2% of patients on XTANDI versus 0.5% on placebo. Ischemic events led to death in 0.4% of patients on XTANDI compared to 0.1% on placebo. Monitor for signs and symptoms of ischemic heart disease. Optimize management of cardiovascular risk factors, such as hypertension, diabetes, or dyslipidemia. Discontinue XTANDI for Grade 3-4 ischemic heart disease.

Falls and Fractures In the placebo-controlled clinical studies, falls occurred in 10% of patients treated with XTANDI compared to 4% of patients treated with placebo. Fractures occurred in 8% of patients treated with XTANDI and in 3% of patients treated with placebo. Evaluate patients for fracture and fall risk. Monitor and manage patients at risk for fractures according to established treatment guidelines and consider use of bone-targeted agents.

Embryo-Fetal Toxicity Safety and efficacy of XTANDI have not been established in females. XTANDI can cause fetal harm and loss of pregnancy when administered to a pregnant female. Advise males with female partners of reproductive potential to use effective contraception during treatment with XTANDI and for 3 months after the last dose of XTANDI. XTANDI should not be handled by females who are or may become pregnant.

Adverse Reactions

The most common adverse reactions (≥ 10%) that occurred more frequently (≥ 2% over placebo) in the XTANDI patients from the randomized placebo-controlled trials were asthenia/fatigue, decreased appetite, hot flush, arthralgia, dizziness/vertigo, hypertension, headache and weight decreased. In the bicalutamide-controlled study, the most common adverse reactions (≥ 10%) reported in XTANDI patients were asthenia/fatigue, back pain, musculoskeletal pain, hot flush, hypertension, nausea, constipation, diarrhea, upper respiratory tract infection, and weight loss.

In the placebo-controlled study of metastatic CRPC (mCRPC) 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 mCRPC 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 placebo-controlled study of non-metastatic CRPC (nmCRPC) patients, Grade 3 or higher adverse reactions were reported in 31% of XTANDI patients and 23% of placebo patients. Discontinuations with an adverse event as the primary reason were reported for 9% of XTANDI patients and 6% of placebo patients. In the bicalutamide-controlled study of chemotherapy-naïve mCRPC patients, Grade 3-4 adverse reactions were reported in 39% of XTANDI patients and 38% of bicalutamide patients. Discontinuations with an AE as the primary reason were reported for 8% of XTANDI patients and 6% of bicalutamide patients.

Lab Abnormalities: In the two placebo-controlled trials in patients with mCRPC, Grade 1-4 neutropenia occurred in 15% of XTANDI patients (1% Grade 3-4) and 6% of placebo patients (0.5% Grade 3-4). In the placebo-controlled trial in patients with nmCRPC, Grade 1-4 neutropenia occurred in 8% of patients receiving XTANDI (0.5% Grade 3-4) and in 5% of patients receiving placebo (0.2% Grade 3-4).

Hypertension: In the two placebo-controlled trials in patients with mCRPC, hypertension was reported in 11% of XTANDI patients and 4% of placebo patients. Hypertension led to study discontinuation in <1% of patients in each arm. In the placebo-controlled trial in patients with nmCRPC, hypertension was reported in 12% of patients receiving XTANDI and 5% of patients receiving placebo.

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
As part of Pfizer and Astellas' ongoing commitment to the clinical development of enzalutamide, XTANDI is also being evaluated in the EMBARK trial, in men with high-risk non-metastatic HSPC. Details about EMBARK (NCT02319837) are available on www.clinicaltrials.gov.

About Pfizer Oncology
At Pfizer Oncology, we are committed to advancing medicines wherever we believe we can make a meaningful difference in the lives of patients. Today, Pfizer Oncology has an industry-leading portfolio of 21 approved innovative cancer medicines and biosimilars across more than 30 indications, including breast, prostate, kidney and lung cancers, as well as leukemia and melanoma. Pfizer Oncology is striving to change the trajectory of cancer.

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. For more information, please visit our website at https://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 August 21, 2019. 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 new indication for the treatment of men with metastatic hormone-sensitive 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, uncertainties regarding the commercial success of XTANDI; the uncertainties inherent in research and development, including the ability to meet anticipated clinical endpoints, commencement and/or completion dates for our clinical trials, regulatory submission dates, regulatory approval dates and/or launch dates, as well as the possibility of unfavorable new clinical data and further analyses of existing clinical data; the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities; whether regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when drug applications for the potential new indication for XTANDI may be filed in any other jurisdictions and whether and when drug applications for any other potential indications for XTANDI may be filed in any jurisdictions; whether and when the FDA may approve the sNDA for the potential new indication and whether and when regulatory authorities in any jurisdictions may approve any such other applications that may be pending or filed, which will depend on myriad factors, including making a determination as to whether the product's benefits outweigh its known risks and determination of the product's efficacy and, if approved, whether XTANDI for any such potential new indications will be commercially successful; decisions by regulatory authorities impacting labeling, manufacturing processes, safety and/or other matters that could affect the availability or commercial potential of XTANDI, including for the potential new indications; 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, 2018 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] American Society of Clinical Oncology. ASCO Answers: Prostate Cancer (2018). http://www.cancer.net/sites/cancer.net/files/asco_answers_guide_prostate.pdf Accessed 11-13-2018.
[2] Cancer.net. Prostate Cancer: Types of Treatment (03-2018). https://www.cancer.net/cancer-types/prostate-cancer/types-treatment. Accessed 11-7-2018.
[3] Supplement to: Scher HI, Solo K, Valant J, Todd MB, Mehra M. Prevalence of prostate cancer clinical states and mortality in the United States: estimates using a dynamic progression model. PLoS One 2015;10(10):e0139440.