Pfizer Logo

XTANDI® (enzalutamide) Demonstrates Significant Improvement in Overall Survival in Phase 3 PROSPER Trial of Patients with nmCRPC

Tuesday, February 11, 2020 - 10:00am

TOKYO and NEW YORK, February 11, 2020 – Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D., "Astellas") and Pfizer Inc. (NYSE: PFE) announced today results of the final overall survival (OS) analysis from the Phase 3 PROSPER trial, which evaluated XTANDI® (enzalutamide) plus androgen deprivation therapy (ADT) versus placebo plus ADT in men with non-metastatic castration-resistant prostate cancer (nmCRPC).

The results demonstrated a statistically significant improvement in OS in patients with nmCRPC who were treated with XTANDI plus ADT. OS was a key secondary endpoint of the trial. In a preliminary analysis, adverse events were generally consistent with those previously reported from PROSPER. Detailed efficacy and safety results from the final PROSPER OS analysis will be shared at a later date.

In 2018, Astellas and Pfizer announced that the PROSPER trial met its primary endpoint of metastasis-free survival (MFS). These results were presented at the Genitourinary Cancers Symposium (ASCO GU) and later published in the *New England Journal of Medicine*.[1]

PROSPER efficacy and safety data at the time of the MFS analysis are included in the XTANDI labels in the U.S., Europe and Japan and are currently under review in China.

About Non-Metastatic Castration-Resistant Prostate Cancer

Castration-resistant prostate cancer (CRPC) refers to the subset of men whose prostate cancer progresses on androgen deprivation therapy (ADT) despite castrate levels of testosterone (i.e., less than 50 ng/dL).[2] 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.[3] Many men with non-metastatic CRPC and a rapidly rising PSA level go on to develop metastatic CRPC.[4]

PROSPER Trial

The Phase 3 randomized, double-blind, placebo-controlled, multi-national trial enrolled approximately 1,400 patients with nmCRPC 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 PSA level despite ADT, but who had no symptoms and no prior or present evidence of metastatic disease. The trial evaluated enzalutamide at a dose of 160 mg taken orally once daily plus ADT, versus placebo plus ADT.

The primary endpoint of the PROSPER trial, metastasis-free survival (MFS), was measured as the time from patients entering the trial until their cancer was radiographically detected as having metastasized, or until death, within 112 days of treatment discontinuation. Key secondary endpoints included overall survival, time to PSA progression and time to first use of antineoplastic therapy.

For more information on the PROSPER trial, go to www.clinicaltrials.gov.

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

Important Safety Information for XTANDI®

Warnings and Precautions

Seizure occurred in 0.5% of patients receiving XTANDI in seven randomized clinical trials. In a study of patients with predisposing factors for seizure, 2.2% of XTANDI-treated patients experienced a seizure. It is unknown whether anti-epileptic medications will prevent seizures with XTANDI. Patients in the study had one or more of the following predisposing factors: use of medications that may lower the seizure threshold, history of traumatic brain or head injury, history of cerebrovascular accident or transient ischemic attack, and 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. 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) There have been reports of PRES in patients receiving XTANDI. PRES is a neurological disorder that 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 seven randomized 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 combined data of four randomized, placebo-controlled clinical studies, ischemic heart disease occurred more commonly in patients on the XTANDI arm compared to patients on the placebo arm (2.9% vs 1.3%). Grade 3-4 ischemic events occurred in 1.4% of patients on XTANDI versus 0.7% 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 occurred in patients receiving XTANDI. 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. In the combined data of four randomized, placebo-controlled clinical studies, falls occurred in 11% of patients treated with XTANDI compared to 4% of patients treated with placebo. Fractures occurred in 10% of patients treated with XTANDI and in 4% of patients treated with placebo.

Embryo-Fetal Toxicity The 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.

Adverse Reactions (ARs)

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

In AFFIRM, the placebo-controlled study of metastatic CRPC (mCRPC) patients who previously received docetaxel, Grade 3 and higher ARs were reported among 47% of XTANDI-treated patients. Discontinuations due to adverse events (AEs) were reported for 16% of XTANDI-treated patients. In PREVAIL, the placebo-controlled study of chemotherapy-naive mCRPC patients, Grade 3-4 ARs were reported in 44% of XTANDI patients and 37% of placebo patients. Discontinuations due to AEs were reported for 6% of XTANDI-treated patients. In TERRAIN, the bicalutamide-controlled study of chemotherapy-naive mCRPC patients, Grade 3-4 ARs 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.

In PROSPER, the placebo-controlled study of non-metastatic CRPC (nmCRPC) patients, Grade 3 or higher ARs were reported in 31% of XTANDI patients and 23% of placebo patients. Discontinuations with an AE as the primary reason were reported for 9% of XTANDI patients and 6% of placebo patients.

In ARCHES, the placebo-controlled study of metastatic CSPC (mCSPC) patients, Grade 3 or higher AEs were reported in 24% of XTANDI-treated patients. Permanent discontinuation due to AEs as the primary reason was reported in 5% of XTANDI patients and 4% of placebo patients.

Lab Abnormalities: Lab abnormalities that occurred in ? 5% of patients, and more frequently (> 2%) in the XTANDI arm compared to placebo in the pooled, randomized, placebo-controlled studies are neutrophil count decreased, white blood cell decreased, hyperglycemia, hypermagnesemia, hyponatremia, and hypercalcemia.

Hypertension: In the combined data from four randomized placebo-controlled clinical trials, hypertension was reported in 12% of XTANDI patients and 5% of placebo patients. 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 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 22 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 February 11, 2020. 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), including its 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 XTANDI may be filed in any other jurisdictions; whether and when regulatory authorities in any jurisdictions where applications may be pending or filed may approve any such applications, 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 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; 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.

###

[1] Hussain M, Fizazi K, Saad F, et al. Enzalutamide in Men with Nonmetastatic, Castration-Resistant Prostate Cancer. *New England Journal of Medicine*. 2018;378(26):2465-2474. doi:10.1056/nejmoa1800536.

[2] Kirby M, Hirst C, Crawford ED. Characterising the castration-resistant prostate cancer population: a systematic review. *Int J Clin Pract* 2011;65(11):1180-92.

[3] Luo J, Beer T, Graff J. Treatment of nonmetastatic castration-resistant prostate cancer. *Oncology* 2016;30(4):336-44.

[4] Smith MR, Kabbinavar F, Saad F, et al. Natural history of rising serum prostate-specific antigen in men with castrate nonmetastatic prostate cancer. *J Clin Oncol* 2005;23(13):2918-25.

Pfizer Contacts:
For Media:
Jessica Smith
212-733-6213
Jessica.M.Smith@pfizer.com

For Investors:
Ryan Crowe
212-733-8160
Ryan.Crowe@pfizer.com

Astellas Contacts:
For Media:
Chris Goldrick
847-224-3014
chris.goldrick@astellas.com

For Investors:
Shin Okubo
81-3-3244-3202
shin.ohkubo@astellas.com