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Phase 3 ARCHES Trial Shows XTANDI® (enzalutamide) Significantly Improved Radiographic Progression-Free Survival in Men with Metastatic Hormone-Sensitive Prostate Cancer

Monday, February 11, 2019 - 12:00pm

Data to be presented at the 2019 Genitourinary Cancers Symposium

NEW YORK & TOKYO--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) and Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D., "Astellas") announced today results from the Phase 3 ARCHES trial in men with metastatic hormone-sensitive prostate cancer (mHSPC). Prostate cancer is considered metastatic once the cancer has spread outside of the prostate gland to other parts of the body.[1] Men are considered hormone (or castration) sensitive if their disease still responds to medical or surgical treatment to lower testosterone levels.[2]

The results show that XTANDI® (enzalutamide) plus androgen deprivation therapy (ADT) met the primary endpoint by significantly reducing the risk of radiographic progression or death by 61% versus ADT alone (n=1,150; HR=0.39 [95% CI: 0.30-0.50]; p<0.0001). These data will be presented in an oral session at the 2019 Genitourinary Cancers Symposium in San Francisco (Abstract #687; Thursday, February 14th, 1:55 PM PT).

"The ARCHES trial demonstrated that XTANDI plus standard hormonal therapy delayed disease progression, and if approved, has the potential to be an important treatment option for men with prostate cancer that has spread but has not yet become hormone resistant," said Andrew Armstrong, M.D., Professor of Medicine, Surgery, Pharmacology and Cancer Biology, and Director of Research in the Duke Cancer Institute's Center for Prostate and Urologic Cancers.

Median time to a radiographic progression-free survival (rPFS) event was not reached in the XTANDI plus ADT arm, while median time to an rPFS event in the ADT alone arm was 19.4 months. Significant improvements in rPFS were also observed in all prespecified subgroups including disease volume, pattern of disease localization at baseline, geographic region, and prior docetaxel use (HRs=0.24-0.53). Secondary endpoints reported in the abstract showed that XTANDI plus ADT reduced the risk of PSA progression (HR=0.19 [95% CI: 0.13-0.26]; p<0.0001) and reduced the risk of starting a new antineoplastic therapy (HR=0.28 [95% CI: 0.20-0.40]; p<0.0001) compared to ADT alone. Undetectable PSA and objective response rates were also higher in men treated with XTANDI plus ADT versus ADT alone (68.1% versus 17.6%; p<0.0001 and 83.1% versus 63.7%; p<0.0001, respectively). Treatment with XTANDI plus ADT did not significantly reduce the risk of deterioration in urinary symptoms compared to ADT alone. At the time of

the analysis, overall survival (OS) data were not mature.

Adverse events (AEs) in the ARCHES clinical trial were generally consistent with those reported in enzalutamide clinical trials in patients with castration-resistant prostate cancer (CRPC). Grade 3 or 4 AEs were reported in 23.6 percent of men receiving XTANDI plus ADT versus 24.7 percent of men receiving ADT alone. Common AEs (occurring in at least 5 percent of patients) that were reported more often in patients treated with XTANDI plus ADT versus those treated with ADT alone included hot flush, fatigue, arthralgia, hypertension, nausea, musculoskeletal pain, diarrhea, asthenia and dizziness.

Based on the ARCHES results, the companies intend to discuss these data with global health authorities to potentially support a new indication for XTANDI in men with mHSPC. XTANDI is currently approved in the U.S. and Japan for the treatment of CRPC and in the EU for the treatment of metastatic and high-risk non-metastatic CRPC.

Seven additional abstracts evaluating XTANDI will also be presented at the 2019 Genitourinary Cancers Symposium.

About ARCHES

The Phase 3, randomized, double-blind, placebo-controlled, multi-national trial enrolled 1,150 patients with metastatic hormone-sensitive prostate cancer (mHSPC) at sites in the United States, Canada, Europe, South America and the Asia-Pacific region. Patients in the ARCHES trial were randomized to receive XTANDI 160 mg daily or placebo and continued on a luteinizing hormone-releasing hormone (LHRH) agonist or antagonist or had a history of bilateral orchiectomy. The ARCHES trial included patients with both low- and high-volume disease and both newly diagnosed patients with mHSPC and patients who had prior definitive therapy and subsequently developed metastatic disease. The trial also included some patients who had received recent treatment with docetaxel for mHSPC, but whose disease had not progressed. The primary endpoint of the trial was radiographic progression-free survival (rPFS), defined as the time from randomization to the first objective evidence of radiographic disease progression as assessed by central review, or death within 24 weeks of treatment discontinuation. For more information on the ARCHES (NCT02677896) trial, go to www.clinicaltrials.gov.

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] Approximately 38,000 men in the U.S. develop metastatic HSPC every year.[3,4]

About XTANDI® (enzalutamide) capsules

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

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.

Important Safety Information for XTANDI® in 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 Pfizer Oncology

At Pfizer Oncology, we are committed to advancing medicines wherever we believe we can make a meaningful difference on the lives of patients. Today, Pfizer Oncology has an industry-leading portfolio of 17 approved innovative cancer medicines and biosimilars across more than 20 indications, including breast, prostate, kidney, lung and hematology. We also have several assets in mid to late-stage development for the treatment of cancer or as supportive care. 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/us/.

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.

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.

Pfizer Disclosure Notice

The information contained in this release is as of February 11, 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 potential new indications being evaluated for the treatment of men with metastatic hormone-sensitive prostate cancer and the treatment of men with high-risk non-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 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; the risks associated with interim data; whether and when drug applications for any of the potential new indications for XTANDI or any potential indications for XTANDI may be filed in any jurisdictions; whether and when regulatory authorities in any jurisdictions 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 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, 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.

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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] Scher HI, Solo K, Valant J, Todd MB, Mehra M et al. Prevalence of Prostate Cancer Clinical States and Mortality in the United States: Estimates Using a Dynamic Progression Model. PLoS One. 2015; 10(10): 1-2.

[4] Siegel RL, Miller KD, Jemal A, Cancer statistics, 2018. CA Cancer Journal for Clinicians. 2018;68:7–30.

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