Press Release

XTANDI® (enzalutamide) Approved by Japan MHLW for the Treatment of Prostate Cancer with Distant Metastasis

XTANDI is now MHLW-approved for both metastatic hormone-sensitive prostate cancer and castration-resistant prostate cancer in Japan

TOKYO, May 29, 2020 – Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D., "Astellas") today announced that the Japan Ministry of Health, Labour and Welfare (MHLW) has approved XTANDI® (enzalutamide), an oral androgen receptor signaling inhibitor, for the treatment of prostate cancer patients with distant metastasis. With this approval, XTANDI is now indicated for the treatment of metastatic hormone-sensitive prostate cancer (mHSPC), a form of prostate cancer that has spread to other parts of the body and still responds to a medical or surgical treatment that lowers testosterone.[1,2] This is in addition to an existing indication for castration-resistant prostate cancer (CRPC).

The approval for mHSPC is based on results from the ARCHES trial[i], a randomized multi-national Phase 3 study which evaluated enzalutamide plus androgen deprivation therapy (ADT) versus placebo plus ADT in 1,150 men with mHSPC and met its primary endpoint of radiographic progression-free survival (rPFS).[3] It is also supported by data from the ENZAMET trial[ii], an overseas Phase 3 study evaluating enzalutamide plus ADT versus ADT plus a standard nonsteroidal antiandrogen therapy (bicalutamide, nilutamide or flutamide) in men with mHSPC.[4]

"Enzalutamide with androgen deprivation therapy led to a significant delay in the risk of progression of metastatic disease or death, and this delay was associated with maintained quality of life and a reduced need for subsequent therapies over time. These endpoints are all critically important to men with metastatic prostate cancer," said Andrew Armstrong, M.D., Professor of Medicine, Surgery, Pharmacology and Cancer Biology, Director of Research in the Duke Cancer Institute's Center for Prostate and Urologic Cancers and lead investigator of the ARCHES trial. "The research supporting the approval provides compelling evidence to consider enzalutamide as a treatment option for men with mHSPC."

Data from the ARCHES trial showed enzalutamide plus ADT significantly reduced the risk of radiographic progression or death by 61% versus placebo plus ADT in men with mHSPC.[5] The ENZAMET trial demonstrated a 33% reduction in the risk of death in men with mHSPC receiving enzalutamide plus ADT compared to those who took a nonsteroidal antiandrogen therapy plus ADT.[6]

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[i] Referred to as the Multinational Phase III study in the Japan Package Insert
[ii] Referred to as the Overseas Phase III study in the Japan Package Insert

The safety analyses of the ARCHES and ENZAMET trials were generally consistent with the safety profile of enzalutamide in previous clinical trials in CRPC. In the ARCHES trial, adverse drug reactions were reported in 53.0% of patients. Major adverse drug reactions with an incidence of more than 10% were hot flush (20.5%) and fatigue (14.9%). In the ENZAMET trial, serious adverse drug reactions were reported in 3.0% of patients. Serious adverse drug reactions observed in 2 or more patients were seizure (0.9%), hypertension (0.5%) and fatigue (0.4%).

“Today’s MHLW approval of XTANDI marks continued progress to provide a treatment option to men earlier in their advanced prostate cancer treatment journey,” said Andrew Krivoshik, M.D., Ph.D., Senior Vice President and Global Therapeutic Area Head, Oncology Development. “At Astellas, we have made a commitment to fight cancer and continue to build a robust oncology portfolio to help meet the needs of patients.”

About metastatic Hormone-Sensitive Prostate Cancer (mHSPC)
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. Men are considered hormone- (or castration-) sensitive if their disease still responds to medical or surgical treatment that lowers testosterone.

About the ARCHES trial
The company-sponsored, Phase 3, randomized, multinational, double-blind, placebo-controlled, ARCHES trial (NCT02677896) enrolled 1,150 patients with mHSPC at sites in the U.S., Canada, Europe, South America, and the Asia-Pacific region. Patients in the trial were randomized to receive enzalutamide 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 primary endpoint of the trial was radiographic progression-free survival (rPFS) assessed by blinded independent central review. rPFS was defined as the time from randomization to radiographic disease progression at any time or death within 24 weeks after study drug discontinuation. Patients were stratified by volume of disease (low vs high) and prior docetaxel therapy for prostate cancer (no prior docetaxel, 1-5 cycles, or 6 prior cycles).[3]

About the ENZAMET trial
ENZAMET is an overseas Phase 3 study funded by Astellas and sponsored by the University of Sydney with trial sites in Australia, Canada, Ireland, New Zealand, UK and U.S. The trial evaluated the potential of enzalutamide plus androgen deprivation therapy (ADT) versus a conventional non-steroidal anti androgen (NSAA) plus ADT in 1,125 men with mHSPC. The primary endpoint for the trial is overall survival (OS; 3-years). Additional details about ENZAMET (NCT02446405) are available on www.clinicaltrials.gov.[4]

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

Important Safety Information
For important Safety Information for enzalutamide please see the Package Insert

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 enzalutamide in the United States and Astellas has responsibility for manufacturing and all additional regulatory filings globally, as well as commercializing enzalutamide outside the United States.

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[1] Cancer.net. Prostate Cancer: Types of Treatment (03-2018). https://www.cancer.net/cancer-types/prostate-cancer/types-treatment. Accessed May 2020.
[2] American Society of Clinical Oncology. ASCO Answers: Prostate Cancer (2018). http://www.cancer.net/sites/cancer.net/files/asco_answers_guide_prostate.pdf. Accessed May 2020.
[3] A Study of Enzalutamide Plus Androgen Deprivation Therapy (ADT) Versus Placebo Plus ADT in Patients With Metastatic Hormone Sensitive Prostate Cancer (mHSPC) (ARCHES). https://clinicaltrials.gov/ct2/show/NCT02677896. Accessed April 2020.
[4] Enzalutamide in First Line Androgen Deprivation Therapy for Metastatic Prostate Cancer (ENZAMET). https://clinicaltrials.gov/ct2/show/NCT02446405. Accessed April 2020.
[5] Enzalutamide Plus ADT Significantly Reduces Risk of Progression in Metastatic Hormone-Sensitive Prostate Cancer. https://www.targetedonc.com/news/enzalutamide-plus-adt-significantly-reduces-risk-of-progression-in-metastatic-hormonesensitive-prostate-cancer. Accessed April 2020.
[6] Current Treatment Options for Metastatic Hormone-Sensitive Prostate Cancer. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6770296/. Accessed April 2020.