Press Release

Astellas' XTANDI™ (Enzalutamide) Granted European Commission Approval for Use in Additional Recurrent Early Prostate Cancer Treatment Setting

- *XTANDI is now the first and only novel hormone therapy available for the treatment of high-risk biochemical recurrent non-metastatic hormone-sensitive prostate cancer in the European Union (EU)*

- *XTANDI can be given alone or in combination with androgen deprivation therapy*

- *Approval is based on results from the positive Phase 3 EMBARK study which showed XTANDI alone or in combination with leuprolide reduced the risk of metastasis or death*

TOKYO, April 23, 2024 – Astellas Pharma Inc. (TSE: 4503, President and CEO: Naoki Okamura, "Astellas") today announced the European Commission (EC) has approved a label extension for XTANDI™ (enzalutamide) as monotherapy or in combination with androgen deprivation therapy (ADT) for the treatment of adult men with high-risk biochemical recurrent (BCR) non-metastatic hormone-sensitive prostate cancer (nmHSPC) who are unsuitable for salvage-radiotherapy.

The extended approval for XTANDI is based on results from the Phase 3 EMBARK trial in 1,068 men with high-risk BCR nmHSPC, in whom levels of prostate-specific antigen (PSA), the biomarker which can be indicative of prostate cancer activity, doubled in nine months or less. The study showed patients treated with XTANDI in combination with leuprolide had a 57.6% lower chance of their cancer spreading or dying compared to those treated with leuprolide alone. Participants who were treated with XTANDI alone had a 36.9% reduction in risk.[1]

The European Association of Urology (EAU) revised their treatment guidelines in April 2024, recommending enzalutamide for men with high-risk BCR nmHSPC with or without ADT, after radiation therapy or surgery. Up until now, there has been no consensus on the standard of care for men in this setting.[2]

Dr. Antonio Alcaraz, Chairman of the Department of Urology at the University Hospital Clinic of Barcelona:
"When non-metastatic hormone-sensitive prostate cancer recurs and is allowed to evolve, it could potentially lead to metastasis. Facing a particularly high risk and poorer outcomes in this stage of prostate cancer are men with a rapidly rising PSA, where PSA levels double within 9 months. It is critical to manage the cancer carefully then, and I urge clinicians not to delay treatment in this setting. With this expanded approval for enzalutamide, clinicians now have an important new option to treat men with non-metastatic hormone-sensitive prostate cancer at high risk of metastasizing, which could become a new standard of care."

Ernst-Günther Carl, Chairman, Europa Uomo:
"There is a desperate need for additional effective treatment options for those living with advanced prostate cancer. Many men with hormone-sensitive prostate cancer undergo arduous surgery and rounds of radiotherapy, which can be a successful way to keep their cancer at bay. It is devastating then, when up to four in ten of those will go on to develop a recurrence that puts them at significantly greater risk of their cancer spreading and early death. The patient community welcomes any ongoing therapeutic research advances that may benefit those living with prostate cancer in progress."

Ahsan Arozullah, MD, MPH, Senior Vice President and Head of Oncology Development, Astellas:
"This expanded approval for XTANDI is a vitally important advance for patients with nmHSPC with high-risk BCR and is a testament to our long and ongoing collaboration with a global network of dedicated clinical trial investigators, patient groups, clinical trial participants and their families. Efficacy and safety results from the EMBARK study demonstrate the potential for XTANDI as a new option for treatment in the early, recurrent hormone-sensitive prostate cancer setting. Astellas is in active discussions with regulatory authorities around the world to bring XTANDI to those who may benefit."

The EC approval follows the positive opinion issued by the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) in March 2024, recommending approval of XTANDI in the high risk BCR nmHSPC setting.[3]

XTANDI was approved by the U.S. Food and Drug Administration (FDA) for the treatment of patients with non-metastatic castration-sensitive prostate cancer (nmCSPC; also known as nmHSPC) with BCR at high risk for metastasis in November 2023.

Astellas will reflect the impact from this matter in its financial forecast of the fiscal year ending March 31, 2025 that is scheduled to be disclosed on April 25, 2024.

For more information, please see the press releases "Astellas Receives Positive CHMP Opinion for XTANDI™ in Additional Recurrent Early Prostate Cancer Treatment Setting" issued on March 25, 2024, and "European Medicines Agency Validates Type II Variation for Astellas' XTANDI® (enzalutamide) for Treatment of Non-Metastatic Hormone-Sensitive Prostate Cancer with High-Risk Biochemical Recurrence" issued on September 12, 2023.

About EMBARK

The Astellas- and Pfizer-led Phase 3, randomized, double-blind, placebo-controlled, multi-national trial enrolled 1,068 patients with nonmetastatic hormone- (or castration-) sensitive prostate cancer (nmHSPC or nmCSPC) with high-risk BCR at sites in the U.S., Canada, Europe, South America, and the Asia-Pacific region. Patients who were considered to experience high-risk BCR had a prostate-specific antigen doubling time (PSA-DT) ≤ 9 months; serum testosterone ≥ 150 ng/dL (5.2 nmol/L); and screening PSA by the central laboratory ≥ 1 ng/mL if they had a radical prostatectomy (with or without radiotherapy) as primary treatment for prostate cancer, or at least 2 ng/mL above the nadir if they had radiotherapy only as primary treatment for prostate cancer. Patients in the EMBARK trial were randomized to receive enzalutamide 160 mg daily plus leuprolide (n=355), enzalutamide 160 mg as a single agent (n=355), or placebo plus leuprolide (n=358). Leuprolide 22.5 mg was administered every 12 weeks.

EMBARK met its primary endpoint of metastasis-free survival (MFS) for the XTANDI plus leuprolide arm, demonstrating a statistically significant reduction in the risk of metastasis or death over placebo plus leuprolide. MFS is defined as the duration of time in months between randomization and the earliest objective evidence of radiographic progression by central imaging or death due to any cause, whichever occurred first.

The study also met a key secondary endpoint, by demonstrating that patients treated with XTANDI (single agent) had a statistically significant reduction in the risk of metastasis or death versus placebo plus leuprolide, meeting its MFS endpoint.

In EMBARK, Grade 3 or higher adverse events (AEs) were reported in 46% of XTANDI plus leuprolide patients, 50% of patients treated with XTANDI (single agent), and 43% of patients receiving placebo plus leuprolide. Permanent discontinuation due to AEs as the primary reason was reported in 21% of XTANDI plus leuprolide patients, 18% in XTANDI (single agent) patients, and 10% in placebo plus leuprolide patients.

For more information on the EMBARK trial (NCT02319837) go to www.clinicaltrials.gov.

About High Risk Biochemical Recurrent Non-Metastatic Hormone Sensitive Prostate Cancer

In non-metastatic hormone (or castration-) sensitive prostate cancer (nmHSPC or nmCSPC), no evidence of the cancer spreading to distant parts of the body (metastases) is detectable with conventional radiological methods (CT/MRI), and the cancer still responds to medical or surgical treatment designed to lower testosterone levels.[4] Of men who have undergone definitive prostate cancer treatment, including radical prostatectomy, radiotherapy, or both, an estimated 20-40% will experience a BCR within 10 years.[5] About 9 out of 10 men with high-risk BCR will develop metastatic disease, and 1 in 3 will die as a result of their metastatic prostate cancer.[6] The EMBARK trial focused on men with high-risk BCR. Per the EMBARK protocol, patients with nmHSPC and high-risk BCR are those initially treated by radical prostatectomy or radiotherapy, or both, with a PSA-DT ≤ 9 months. High-risk BCR patients with a PSA-DT of ≤ 9 months have a higher risk of metastases and death.[7]

About XTANDI™ (enzalutamide)

XTANDI (enzalutamide) is an androgen receptor signaling inhibitor. Enzalutamide is a standard of care and has received regulatory approvals in one or more countries around the world for use in men with metastatic hormone-sensitive prostate cancer (mHSPC), metastatic castration-resistant prostate cancer (mCRPC), non-metastatic castration-resistant prostate cancer (nmCRPC) and non-metastatic hormone-sensitive prostate cancer (nmHSPC) with high-risk biochemical recurrence (BCR). Enzalutamide is currently approved for one or more of these indications in more than 90 countries, including in the United

States, European Union and Japan. Over one million patients have been treated with enzalutamide globally.[8]

About XTANDI™ (enzalutamide) in the E.U.[9]
Enzalutamide is an androgen receptor signaling inhibitor indicated in the E.U.:

- as monotherapy or in combination with androgen deprivation therapy for the treatment of adult men with high-risk biochemical recurrent (BCR) non-metastatic hormone-sensitive prostate cancer (nmHSPC) who are unsuitable for salvage-radiotherapy.
- in combination with androgen deprivation therapy for the treatment of adult men with metastatic hormone-sensitive prostate cancer (mHSPC).
- for the treatment of adult men with high-risk non-metastatic castration-resistant prostate cancer (CRPC).
- for the treatment of adult men with metastatic CRPC who are asymptomatic or mildly symptomatic after failure of androgen deprivation therapy in whom chemotherapy is not yet clinically indicated.
- for the treatment of adult men with metastatic CRPC whose disease has progressed on or after docetaxel therapy.

Important Safety Information
For Important Safety Information for enzalutamide please see the full Summary of Product Characteristics at: https://www.ema.europa.eu/en/documents/product-information/xtandi-epar-product-information_en.pdf

About Astellas
Astellas Pharma Inc. is a pharmaceutical company conducting business in more than 70 countries around the world. We are promoting the Focus Area Approach that is designed to identify opportunities for the continuous creation of new drugs to address diseases with high unmet medical needs by focusing on Biology and Modality. Furthermore, we are also looking beyond our foundational Rx focus to create Rx+® healthcare solutions that combine our expertise and knowledge with cutting-edge technology in different fields of external partners. Through these efforts, Astellas stands on the forefront of healthcare change to turn innovative science into VALUE for patients. For more information, please visit our website at https://www.astellas.com/

Cautionary Notes
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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