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Astellas and Pfizer's XTANDI™ (enzalutamide) Shows Long-Term Overall Survival in Metastatic Hormone-Sensitive Prostate Cancer

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- *Five-year follow-up data from the Phase 3 ARCHES trial shows XTANDI (enzalutamide) plus androgen deprivation therapy (ADT) reduces risk of death by 30%*
- *After a median follow-up of 61.4 months, treatment with XTANDI (enzalutamide) plus ADT was associated with a 66% probability of survival at five years compared to 53% probability of survival with placebo plus ADT*
- *XTANDI (enzalutamide) is the first and only androgen receptor inhibitor to demonstrate an overall survival benefit at five years in men with metastatic hormone-sensitive prostate cancer*
- *Data continue to show wide-ranging effect of treatment with XTANDI (enzalutamide) plus ADT across various patient subgroups, notably those with high-volume disease, no prior docetaxel use, and synchronous disease*
- *Long-term data reinforce XTANDI (enzalutamide) plus ADT as a standard of care*

TOKYO and NEW YORK, May 22, 2025 — Astellas Pharma Inc. (TSE: 4503, President and CEO: Naoki Okamura, "Astellas") and Pfizer Inc. (NYSE: PFE) today announced longer-term follow-up results from an open-label extension of the Phase 3 ARCHES (NCT02677896) study, reporting a five-year follow up of overall survival (OS) benefits and a 30% reduction in the risk of death in men with metastatic hormone-sensitive prostate cancer (mHSPC) treated with XTANDI™ (enzalutamide), an androgen receptor pathway inhibitor (ARPI), plus androgen deprivation therapy (ADT) compared to placebo plus ADT. These data will be presented during an oral presentation (Abstract #5005) at the American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago (Tuesday, June 3, 9:45 a.m.- 12:45 p.m. US CT).

"Historically, the likelihood of survival at five years for men with metastatic hormone-sensitive prostate cancer was low, but with advancements in initial treatment intensification like what we've seen with XTANDI, this is now becoming the standard," *said Andrew J. Armstrong, MD, ScM, Director of Research at the Center for Prostate & Urologic Cancers, Duke Cancer Institute, Durham, NC, and ARCHES primary investigator*. "In our five-year follow up of the global ARCHES trial, two-thirds of men are now surviving five years, representing a 13% absolute and 30% relative improvement over standard hormonal therapy alone, with benefits in patients with high and low disease burden that are meaningful to our patients."

In patients with high-volume disease (HR: 0.70; 95% CI: 0.56-0.88) a 36-month improvement in median OS was observed. Additional clinically relevant subgroups of patients were evaluated, showing consistently improved survival: low-volume disease (HR: 0.71; 95% CI, 0.49-1.05); patients who had previously received docetaxel therapy (HR: 0.67; 95% CI, 0.43- 1.05) and those who had not received prior docetaxel therapy (HR: 0.71; 95% CI, 0.57-0.88). The incidence of treatment-emergent adverse events in the five-year follow-up is consistent with

prior ARCHES analyses and no new safety signals were identified.

“The survival benefits of intervention with XTANDI in advanced prostate cancer are well-recognized,” *added Shontelle Dodson, Executive Vice President, Head of Medical Affairs, Astellas*. “The collective – and growing – body of data for XTANDI continues to reinforce its long-term efficacy and patient impact in prostate cancer, including in the metastatic setting, and shows that XTANDI is changing the trajectory of those living with the disease.”

These results of the five-year follow-up from the ARCHES study will be submitted for publication in a peer-reviewed journal in the near future.

“Until recently, patients with metastatic hormone-sensitive prostate cancer faced a poor prognosis, particularly in advanced stages, often due to treatment resistance,” *said Johanna Bendell, M.D., Oncology Chief Development Officer, Pfizer*. “As the only androgen receptor inhibitor demonstrating sustained five-year survival in this patient population, these data further reinforce XTANDI combined with androgen deprivation therapy as the standard-of-care for treating this advanced disease.”

In addition to five-year data from the follow-up ARCHES study, eight-year data from the ENZAMET study assessing outcomes of enzalutamide versus non-steroidal anti-androgen (NSAA) – both plus testosterone suppression with or without docetaxel – in mHSPC will also be presented during a poster session at ASCO (Monday, June 2, 9:00 a.m. US CT). This independent, Phase 3 trial sponsored by the University of Sydney (NCT02446405), led by the Australian and New Zealand Urogenital and Prostate Cancer Trials Group Limited (ANZUP), demonstrated a reduction in risk of death in men with mHSPC.

“Data from the eight-year follow-up of XTANDI are highly encouraging, as they show the progression-free survival and overall survival benefits are sustained out to at least eight years,” *said Christopher Sweeney, MBBS, DHS, FRACP, ANZUP Cancer Trials Group Limited, Sydney, Australia, and ENZAMET follow-up primary investigator*. “These results further support the value of XTANDI as a treatment regimen for metastatic hormone-sensitive prostate cancer.”

With a median follow-up of 98 months, patients with mHSPC were treated with XTANDI plus testosterone suppression or NSAA plus testosterone suppression, each group with or without docetaxel. The median OS in the XTANDI group was 8.0 years and 5.8 years in the NSAA group (HR: 0.73; 95% CI, 0.63-0.86). OS at 96 months was 50% with XTANDI and 40% for NSAA; progression-free survival (PFS) also favored XTANDI over NSAA (HR: 0.49; 95% CI, 0.42-0.57). Prostate cancer accounted for 468 of all 622 deaths and were less frequent among those assigned XTANDI than NSAA (207 versus 261). Other causes accounted for a total of 154 deaths and were similarly frequent among those assigned XTANDI versus NSAA (78 versus 76). Mean duration of treatment was longer for XTANDI (58 months) than NSAA (36 months), with 33% remaining on XTANDI and 88% of these patients remained at the full dose of 160 mg.

XTANDI is currently approved in more than 90 countries, including in the United States, European Union and Japan. Since its initial approval in 2012, over one million patients have been treated with XTANDI globally.[1]

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About Metastatic Hormone-Sensitive Prostate Cancer (mHSPC)
Metastatic hormone-sensitive prostate cancer, also known as metastatic castration-sensitive prostate cancer, refers to prostate cancer that still responds to hormonal therapy and has spread outside of the prostate gland to other parts of the body, such as the lymph nodes, bones, lungs and liver.[2]

About the ARCHES Study
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.

In addition to the key secondary endpoint of overall survival at final analysis, a post hoc 5-year analysis was executed with the intent to further quantify long-term overall survival at a clinically meaningful landmark follow-up of five years.

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

About ENZAMET
ENZAMET is a trial led by ANZUP Cancer Trials Group Limited in collaboration with the NHMRC (National Health and Medical Research Council) Clinical Trials Centre at the University of Sydney with trial sites in Australia, Canada, Ireland, New Zealand, UK and United States. The trial evaluates 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). Additional details about ENZAMET (NCT02446405) are available on www.clinicaltrials.gov. Astellas provided funding and support for the ENZAMET trial.

About XTANDI™ (enzalutamide)
XTANDI (enzalutamide) is an androgen receptor signaling inhibitor. XTANDI 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). XTANDI 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 XTANDI globally.[1]

About XTANDI (enzalutamide) and Important Safety Information

XTANDI (enzalutamide) is indicated for the treatment of patients with:

- castration-resistant prostate cancer (CRPC)
- metastatic castration-sensitive prostate cancer (mCSPC)
- nonmetastatic castration sensitive prostate cancer (nmCSPC) with biochemical recurrence at high risk for metastasis (high-risk BCR)

Important Safety Information

Warnings and Precautions
Seizure?occurred in 0.6% of patients receiving XTANDI in eight 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 eight 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 five randomized, placebo-controlled clinical studies, ischemic heart disease occurred more commonly in patients on the XTANDI arm compared to patients on the placebo arm (3.5% vs 2%). Grade 3-4 ischemic events occurred in 1.8% of patients on XTANDI versus 1.1% 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 five randomized, placebo-controlled clinical studies, falls occurred in 12% of patients treated with XTANDI compared to 6% of patients treated with placebo. Fractures occurred in 13% of patients treated with XTANDI and in 6% 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.

Dysphagia or Choking Severe dysphagia or choking, including events that could be life-threatening requiring medical intervention or fatal, can occur due to XTANDI product size. Advise patients to take each capsule or tablet whole with a sufficient amount of water to ensure that all medication is successfully swallowed. Consider use of a smaller tablet size of XTANDI in patients who have difficulty swallowing. Discontinue XTANDI for patients who cannot swallow capsules or tablets.

Adverse Reactions (ARs)
In the data from the five randomized placebo-controlled trials, the most common ARs (? 10%) that occurred more frequently (? 2% over placebo) in XTANDI-treated patients were musculoskeletal pain, fatigue, hot flush, constipation, decreased appetite, diarrhea, hypertension, hemorrhage, fall, fracture, and headache. 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 ARCHES, the placebo-controlled study of metastatic CSPC (mCSPC) patients, Grade 3 or higher ARs were reported in 24% of XTANDI-treated patients. Permanent discontinuation due to ARs 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 hemoglobin decrease, neutrophil count decreased, white blood cell decreased, hyperglycemia, hypermagnesemia, hyponatremia, hypophosphatemia, and hypercalcemia.

Hypertension: In the combined data from five randomized placebo-controlled clinical trials, hypertension was reported in 14.2% of XTANDI patients and 7.4% of placebo patients. Hypertension led to study discontinuation in < 1% of patients in each arm.

Drug Interactions
Effect of Other Drugs on XTANDI?Avoid coadministration with strong CYP2C8 inhibitors. If coadministration cannot be avoided, reduce the dosage of XTANDI.

Avoid coadministration with strong CYP3A4 inducers. If coadministration cannot be avoided, increase the dosage of XTANDI.

Effect of XTANDI on Other Drugs Avoid coadministration with certain CYP3A4, CYP2C9, and CYP2C19 substrates for which minimal decrease in concentration may lead to therapeutic failure of the substrate. If coadministration cannot be avoided, increase the dosage of these substrates in accordance with their Prescribing Information. In cases where active metabolites are formed, there may be increased exposure to the active metabolites.

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/en.

About Pfizer Oncology
At Pfizer Oncology, we are at the forefront of a new era in cancer care. Our industry-leading portfolio and extensive pipeline includes three core mechanisms of action to attack cancer from multiple angles, including small molecules, antibody-drug conjugates (ADCs), and bispecific antibodies, including other immune-oncology biologics. We are focused on delivering transformative therapies in some of the world's most common cancers, including breast cancer, genitourinary cancer, hematology-oncology, and thoracic cancers, which includes lung cancer. Driven by science, we are committed to accelerating breakthroughs to help people with cancer live better and longer lives.

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 XTANDI (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 May 22, 2025. 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 new indication in the U.S. for the treatment of patients with nonmetastatic castration-sensitive prostate cancer with biochemical recurrence at high risk for metastasis (high-risk BCR), 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 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; whether the EMBARK trial will meet the secondary endpoint of overall survival; 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 the clinical studies; whether and when drug applications for XTANDI may be filed in other jurisdictions; whether and when regulatory authorities in any jurisdictions may approve any such applications that may be pending or filed for XTANDI (including the application pending with the European Medicines Agency), which will depend on a myriad of 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 potential indication 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 new indication; dependence on the efforts and funding by Astellas Pharma Inc. for the development, manufacturing and commercialization of XTANDI; uncertainties regarding the impact of COVID-19 on Pfizer's business, operations and financial results; 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, 2024, 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 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.

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[1] Astellas. Data on File. XTANDI patient. January 2023.
[2] Sartor, O., de Bono, J., Chi, K. N., Fizazi, K., Herrmann, K., Piulats, J. M., ... & Hussain, M. (2021). Lutetium-177-PSMA-617 for Metastatic Castration-Resistant Prostate Cancer. New England Journal of Medicine, 385(12), 1091-1103.

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