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Pfizer’s TALZENNA Plus XTANDI FDA-Approved for an Earlier Metastatic Prostate Cancer Treatment Setting

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TALZENNA plus XTANDI is now approved for HRR gene-mutated metastatic androgen pathway modulation-naïve or -sensitive prostate cancer, offering a potential new standard of care earlier in the course of disease

Approval based on pivotal Phase 3 TALAPRO-3 data, which showed an estimated 52% reduction in the risk of radiographic progression or death

NEW YORK--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) today announced that the U.S. Food and Drug Administration (FDA) has expanded approval of TALZENNA® (talazoparib) in combination with XTANDI® (enzalutamide) to the treatment of men with metastatic androgen pathway modulation-naïve or -sensitive (mAPMN/S) prostate cancer (PC) with homologous recombination repair (HRR) gene mutations, including both BRCA and non-BRCA mutations. mAPMN/S is also known as metastatic hormone-sensitive prostate cancer (mHSPC). This approval makes TALZENNA, an oral poly ADP-ribose polymerase (PARP inhibitor), plus XTANDI, an androgen receptor pathway inhibitor (ARPI), available in an earlier line, providing an opportunity to delay disease progression at a critical stage when more patients may experience greater benefit.

“Today’s approval of TALZENNA plus XTANDI builds on its established role as a standard-of-care option for men with advanced prostate cancer. Moving this targeted therapy into the androgen pathway modulation-naïve or -sensitive setting further reflects our commitment to men with HRR-mutated metastatic prostate cancer, providing a new option at a stage where it may have a greater impact to delay progression.”

- Aamir Malik, Executive Vice President, Chief U.S. Commercial Officer, Pfizer

“This approval represents a critical advancement for patients with newly diagnosed metastatic prostate cancer with HRR gene mutations, who face a more aggressive disease, worse prognosis, and limited treatment options. In the TALAPRO-3 trial, clinical benefits were consistent for patients with BRCA and non-BRCA HRR gene mutations, addressing a long-standing unmet need – and reinforcing the importance of biomarker testing at the time of diagnosis.”

- Neeraj Agarwal, M.D., FASCO, Co-director of Prostate Cancer Program at Harvard Cancer Consortium, faculty medical oncologist at Dana-Farber Cancer Institute, and global lead investigator for TALAPRO-3

TALZENNA plus XTANDI was first approved in the U.S. in 2023 for men with metastatic androgen pathway modulation resistant (mAPMR) PC with HRR gene mutations, also known as HRRm metastatic castration-resistant prostate cancer (mCRPC). The application to expand the indication was reviewed under FDA Priority Review and was supported by results from the Phase 3 TALAPRO-3 study.

Key Results from the Pivotal Phase 3 TALAPRO-3 Study

- **Improved Radiographic Progression-Free Survival (rPFS)**: TALZENNA plus XTANDI reduced the risk of radiographic progression or death by 52% vs. placebo plus XTANDI (Hazard Ratio [HR] of 0.48; 95% Confidence Interval [CI], 0.36–0.65; p ? 0.0001) in patients with mAPMN/S PC with HRR gene mutations and an estimated 77% of patients remained progression-free at three years. Consistent benefit was observed across patients with *BRCA* and non- *BRCA* HRR gene mutations.
- **Consistent Safety Profile:** The safety profile was consistent with the known profiles of each agent, and no new safety signals were identified. The most common treatment-emergent adverse events (TEAEs) in the TALZENNA plus XTANDI group were anemia, fatigue, decreased neutrophil count, and asthenia. The most common grade 3 or higher TEAE was anemia, reported by 51% in the TALZENNA plus XTANDI group and 3% in the control group. Five percent of patients discontinued TALZENNA due to anemia. TEAEs were generally manageable with dose modifications and supportive care as needed.
- **Published Previously:** These results were presented at the 2026 American Society of Clinical Oncology (ASCO) Annual Meeting and simultaneously published in *The New England Journal of Medicine*.

About the TALAPRO-3 Phase 3 Study

- TALAPRO-3 (NCT04821622) is a multicenter, randomized, double-blind, placebo-controlled study that enrolled 599 patients with mAPMN/S PC with ?3 months of androgen deprivation therapy (ADT) [chemical or surgical] with or without an approved ARPI in the mAPMN/S setting at sites in the U.S., Canada, Europe, South America, and the Asia-Pacific region.
- Patients were randomized to receive TALZENNA 0.5 mg/day plus XTANDI 160mg/day, or placebo plus XTANDI 160mg/day.
- The primary endpoint is investigator-assessed rPFS, defined as the time from the date of randomization to radiographic progression in soft tissue per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1), or in bone per Prostate Cancer Working Group 3 (PCWG3) criteria by investigator assessment, or death, whichever occurs first.

About mAPMN/S PC (mHSPC)

- mAPMN/S PC is a form of advanced prostate cancer that has spread beyond the prostate but is still sensitive to androgen deprivation therapy. [1]
- Approximately 25% of patients with mAPMN/S PC (mHSPC) harbor HRR gene mutations. [2]

Advancing Pfizer’s Leadership in Genitourinary Cancers

This milestone reflects Pfizer's 20-year commitment to driving advances in genitourinary cancers, and its efforts to advance precision medicines into earlier stages of disease, where they may have even more impact for patients. TALZENNA plus XTANDI is an established standard of care for HRR gene-mutated mAPMR PC and this FDA approval brings the combination to men at an earlier stage of disease, when delaying disease progression may have an even greater impact. An application is also under review by the European Medicines Agency (EMA), with additional global regulatory filings planned or underway. The FDA conducted their review of TALZENNA plus XTANDI under Project Orbis, an Oncology Center of Excellence initiative that provides a framework for concurrent submission and review of oncology drugs among international partners.

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- https://www.nejm.org/doi/full/10.1056/NEJMoa2604126

About TALZENNA® (talazoparib)
TALZENNA is an oral inhibitor of poly ADP-ribose polymerase (PARP), which plays a role in DNA damage repair. Preclinical studies have demonstrated that TALZENNA blocks PARP enzyme activity and traps PARP at the site of DNA damage, leading to decreased cancer cell growth and cancer cell death.

TALZENNA was initially approved in the U.S., EU, and multiple other regions as a single agent for the treatment of adult patients with deleterious or suspected deleterious gBRCAm HER2-negative locally advanced or metastatic breast cancer.

TALZENNA in combination with XTANDI was approved by the U.S. Food and Drug Administration (FDA) for the treatment of adult patients with HRR gene-mutated metastatic androgen pathway modulation resistant (mAPMR) PC in June 2023. The combination was also approved by the European Commission in January 2024 for the treatment of adult patients with mCRPC in whom chemotherapy is not clinically indicated. TALZENNA in combination with XTANDI is approved in more than 60 countries; indications vary by country.

About XTANDI® (enzalutamide)
XTANDI (enzalutamide) is an androgen receptor pathway inhibitor. XTANDI is a standard of care and has received regulatory approvals around the world for use in men with metastatic hormone-sensitive prostate cancer (mHSPC), 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 80 countries, including in the United States, European Union, and Japan. Over 1.5 million patients have been treated with XTANDI globally.[3]

XTANDI® is jointly developed and commercialized by Pfizer and Astellas in the United States.

TALZENNA® (talazoparib) Indications in the U.S.

TALZENNA is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated for:

Breast Cancer:
As a single agent, for the treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) HER2?negative locally advanced or metastatic breast cancer. Select patients for therapy based on an FDA?authorized companion diagnostic for TALZENNA.

Prostate Cancer:
In combination with enzalutamide for the treatment of adult patients with:

- metastatic androgen pathway modulation-resistant (mAPMR) prostate cancer with homologous recombination repair (HRR) gene mutations, as detected by an FDA-authorized test.
- metastatic androgen pathway modulation-naïve or -sensitive (mAPMN/S) prostate cancer with HRR gene mutations, as detected by an FDA-authorized test.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML), including cases with a fatal outcome, has been reported in patients who received TALZENNA. In clinical studies, among 1,096 patients treated with TALZENNA as a single agent or as part of a combination regimen with enzalutamide, the cumulative incidence of MDS/AML was approximately 1% including 0.6% with fatal outcomes. The incidence of MDS/AML among patients treated with active control or with placebo in combination with enzalutamide was 0.2%. The median duration of therapy with TALZENNA in patients who developed MDS/AML was approximately 2.8 years (range: 1 to 5.8 years).

Do not start TALZENNA until patients have adequately recovered from hematological toxicity caused by previous chemotherapy. Monitor blood counts monthly during treatment with TALZENNA. For prolonged hematological toxicities, interrupt TALZENNA and monitor blood counts weekly until recovery. If counts do not recover within 4 weeks, refer the patient to a hematologist for further investigations including bone marrow analysis and blood sample for cytogenetics. If MDS/AML is confirmed, discontinue TALZENNA.

Myelosuppression consisting of anemia, leukopenia/neutropenia, and/or thrombocytopenia has been reported in patients treated with TALZENNA. Grade ? 3 anemia, neutropenia, and thrombocytopenia were reported, respectively, in 49%, 19%, and 9% of patients receiving TALZENNA in combination with enzalutamide. Forty-one percent of patients required a red blood cell transfusion, including 25% who required more than one transfusion. Discontinuation due to anemia, neutropenia, and thrombocytopenia occurred, respectively, in 7%, 4%, and 1% of patients.

Withhold TALZENNA until patients have adequately recovered from hematological toxicity caused by previous therapy. Monitor blood counts monthly during treatment with TALZENNA. If hematological toxicities do not resolve within 28 days, discontinue TALZENNA and refer the patient to a hematologist for further investigations including bone marrow analysis and blood sample for cytogenetics.

Embryo-Fetal Toxicity TALZENNA can cause fetal harm when administered to a pregnant woman. Advise male patients with female partners of reproductive potential or who are pregnant to use effective contraception during treatment and for 4 months following the last dose of TALZENNA.

ADVERSE REACTIONS

In the pooled safety population of 810 patients with prostate cancer, the most common (? 20%) adverse reactions including laboratory abnormalities were decreased hemoglobin (86%), decreased neutrophils (68%), decreased lymphocytes (62%), decreased platelets (54%), fatigue (48%), decreased albumin (26%), decreased calcium (26%), back pain (24%), decreased appetite (22%), and nausea (21%).

DRUG INTERACTIONS

Coadministration With P-gp Inhibitors The effect of coadministration of P-gp inhibitors on talazoparib exposure when TALZENNA is taken with enzalutamide has not been studied. Monitor patients for increased adverse reactions and modify the dosage as recommended for adverse reactions when TALZENNA is coadministered with a P-gp inhibitor.

Coadministration With BCRP Inhibitors Monitor patients for increased adverse reactions and modify the dosage as recommended for adverse reactions when TALZENNA is coadministered with a BCRP inhibitor. Coadministration of TALZENNA with BCRP inhibitors may increase talazoparib exposure, which may increase the risk of adverse reactions.

USE IN SPECIFIC POPULATIONS

Males of Reproductive Potential Based on animal studies, TALZENNA may impair fertility.

Renal Impairment Reduce the recommended dosage of TALZENNA in patients with moderate (CLcr 30 - 59 mL/min) and severe (CLcr 15 - 29 mL/min) renal impairment. No dose adjustment is required for patients with mild renal impairment. TALZENNA has not been studied in patients requiring hemodialysis.

INDICATIONS

TALZENNA is indicated in combination with enzalutamide for the treatment of adult patients with:

- Metastatic androgen pathway modulation-resistant (mAPMR) prostate cancer with homologous recombination repair gene mutations (HRRm), as detected by an FDA-authorized test
- Metastatic androgen pathway modulation-naïve or -sensitive (mAPMN/S) prostate cancer with homologous recombination repair gene mutations (HRRm), as detected by an FDA-authorized test

Please see the Full Prescribing Information for TALZENNA. There may be a delay as the document is updated with the latest information. It will be available as soon as possible. Please check back for the updated full information shortly.

XTANDI® (enzalutamide) Indications in the U.S.
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)

XTANDI® (enzalutamide) U.S. 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.

Interference with Immunoassay Measurement of Digoxin XTANDI can interfere with certain digoxin immunoassays (e.g., Chemiluminescent Microparticle Immunoassays), resulting in falsely elevated digoxin plasma concentration results. Notify the laboratory conducting the digoxin plasma concentration assay to use an appropriate method in patients receiving XTANDI and digoxin.

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 EMBARK, the placebo-controlled study of nonmetastatic CSPC (nmCSPC) with high-risk biochemical recurrence (BCR) patients, Grade 3 or higher adverse reactions during the total duration of treatment were reported in 46% of patients treated with XTANDI plus leuprolide, 50% of patients receiving XTANDI as a single agent, and 43% of patients receiving placebo plus leuprolide. Permanent treatment discontinuation due to adverse reactions during the total duration of treatment as the primary reason was reported in 21% of patients treated with XTANDI plus leuprolide, 18% of patients receiving XTANDI as a single agent, and 10% of patients receiving placebo plus leuprolide.

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.

Please access this link for XTANDI's U.S. Full Prescribing Information for additional safety information.

About Pfizer: Breakthroughs That Change Patients' Lives
At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products, including innovative medicines and vaccines. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 175 years, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.Pfizer.com. In addition, to learn more, please visit us on www.Pfizer.com and follow us on X at @Pfizer and @Pfizer_News, LinkedIn, YouTube and like us on Facebook at www.facebook.com/Pfizer/.

Disclosure Notice
The information contained in this release is as of October 26, 2026. 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 Pfizer Oncology, TALZENNA and XTANDI, including their potential benefits, the TALAPRO-3 results, an approval in the U.S. for TALZENNA in combination with XTANDI to expand the use of TALZENNA plus XTANDI to the treatment of men with HRR gene-mutated metastatic androgen pathway modulation-naïve or -sensitive prostate cancer and additional global regulatory filings planned or underway, 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 TALZENNA in combination with 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; whether the TALAPRO-3 trial will meet the key secondary endpoint for overall survival; risks associated with initial, preliminary or interim 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 applications for TALZENNA, XTANDI or a combination may be filed in particular jurisdictions for any potential indications; whether and when any such applications for TALZENNA, XTANDI or a combination that may be pending or filed may be approved by regulatory authorities (including the application under review by the EMA for TALZENNA in combination with XTANDI for men with HRR gene-mutated mAPMN/S PC), 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 TALZENNA, XTANDI or a combination 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 TALZENNA, XTANDI or a combination; risks and uncertainties related to issued or future executive orders or other new, or changes in, laws or regulations; 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, 2025, 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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3. Data on file. Northbrook, IL: Astellas Inc

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