Pfizer Logo

Pfizer’s TALZENNA® in Combination with XTANDI® Improves Survival Outcomes in Metastatic Castration Resistant Prostate Cancer

Thursday, February 13, 2025 - 10:00am

- *TALZENNA + XTANDI is the first PARP inhibitor plus ARPI combination to demonstrate statistically significant and clinically meaningful improvement in overall survival (OS) in patients with metastatic castration-resistant prostate cancer (mCRPC) regardless of HRR mutation status*
- *TALZENNA + XTANDI improved median OS by almost 9 months in unselected patients (Cohort 1) and by 14 months in patients selected for HRR mutations (Cohort 2) versus standard of care XTANDI*

NEW YORK--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) today announced positive results from the Phase 3 TALAPRO-2 study of TALZENNA® (talazoparib), an oral poly ADP-ribose polymerase (PARP) inhibitor, in combination with XTANDI® (enzalutamide), an androgen receptor pathway inhibitor (ARPI), demonstrating a statistically significant and clinically meaningful improvement in overall survival (OS) compared to placebo plus XTANDI in patients with metastatic castration-resistant prostate cancer (mCRPC), with or without homologous recombination repair (HRR) gene mutations. The TALAPRO-2 results will be presented at the American Society of Clinical Oncology Genitourinary (ASCO GU) Cancers Symposium in San Francisco and featured in the ASCO GU official Press Program.

The TALAPRO-2 study evaluated two sets of patients, unselected (cohort 1) and selected for HRR gene-mutations (cohort 2). Overall survival was a prespecified, alpha-protected key secondary endpoint. After more than four years of median follow-up (52.5 months), the median OS in cohort 1 was 45.8 months with TALZENNA in combination with XTANDI, and 37.0 months with XTANDI and placebo (Hazard Ratio [HR] of 0.80; 95% Confidence Interval [CI], 0.66-0.96; p=0.015), representing a 20% reduction in the risk of death. This represents a nearly 9-month gain in median OS versus standard of care XTANDI. Data from cohort 1 will be presented today at ASCO GU in an oral presentation (Abstract LBA18) by Dr. Neeraj Agarwal, global lead investigator for TALAPRO-2.

In Cohort 2, a statistically significant and clinically meaningful improvement in OS was observed in patients with HRR-mutated mCRPC. At a median follow-up of 44.2 months, the median OS was 45.1 months with TALZENNA in combination with XTANDI, and 31.1 months with XTANDI and placebo (HR of 0.62; 95% CI, 0.48-0.81; p=0.0005), a 38% reduction in the risk of death. This result represents a 14-month gain in median OS versus standard of care XTANDI in a patient population with a historically poor prognosis. The OS improvement in the HRR-mutated population was observed in patients in both BRCA and non-BRCA gene alterations. Dr. Karim Fizazi, Institut Gustave Roussy, University of Paris-Saclay will share data from Cohort 2 at ASCO GU today (Abstract LBA141).

“Since its approval, TALZENNA in combination with XTANDI has redefined the standard of care for those living with homologous recombination repair gene-mutated mCRPC. These latest data from TALAPRO-2 are extremely compelling, demonstrating that the combination significantly extended overall survival, in patients selected and unselected for HRR gene alterations, potentially shifting the treatment paradigm for all men living with mCRPC,” said Roger Dansey, M.D., Chief Oncology Officer, Pfizer. “Although definitive conclusions cannot be drawn across studies, these results appear to represent the longest median overall survival reported in a randomized, controlled Phase 3 trial in mCRPC. We look forward to continuing to work with global authorities to potentially update the TALZENNA label with these results.”

“TALAPRO-2 is the first study demonstrating a significant and clinically meaningful survival benefit using a combination of PARP and androgen receptor inhibitors in mCRPC,” said Neeraj Agarwal, M.D., FASCO, Professor and Presidential Endowed Chair of Cancer Research at Huntsman Cancer Institute, University of Utah, and global lead investigator for TALAPRO-2. “Survival rates in metastatic castration-resistant prostate cancer are poor due to the advanced and aggressive stage of the disease. Today’s results demonstrate the potential for TALZENNA in combination with XTANDI to be a practice-changing treatment to help improve patient survival in mCRPC.”

At the time of the final analysis, updated radiographic progression free survival (rPFS) and other secondary efficacy endpoints demonstrated maintained clinical benefit in both cohorts and were consistent with the primary analyses previously reported and published in *The Lancet* and *Nature Medicine* .

In addition to the FDA, these data have been shared with the European Medicines Agency (EMA) and other global health authorities to support potential updates of the approved labels for TALZENNA.

The safety profile of TALZENNA plus XTANDI was generally consistent with the known safety profile of each medicine. The most common all-cause adverse events in the TALZENNA group (?30% of patients) were anemia, neutropenia, and fatigue, and the most common (?10% of patients) grade 3–4 adverse events were anemia (49%) and neutropenia (19.3%). Adverse events were generally manageable with dose modification and supportive care.

About Metastatic Castration-Resistant Prostate Cancer

Prostate cancer is the second most common cancer in men and the fifth most common cause of cancer death among men worldwide, with an estimated 1.4 million new cases diagnosed in 2022.[1] In the U.S., it is the most common cancer in men.[2] mCRPC is a cancer that has spread beyond the prostate gland and has progressed despite medical or surgical treatment to lower testosterone. Approximately 10–20% of prostate cancer patients develop mCRPC within 5?7 years of diagnosis.[3] Between 1.2–2.1% of all prostate cancer cases globally are mCRPC.[4]

About TALAPRO-2

The Phase 3 TALAPRO-2 trial is a multicenter, randomized, double-blind, placebo-controlled study that enrolled 1,035 unique patients with mCRPC who had not received new life-prolonging systemic treatments after documentation of mCRPC at sites in the U.S., Canada, Europe, South America, and the Asia-Pacific region. The study included two patient cohorts: unselected (n=805, of whom 169 had HRR mutations and 636 did not) and those with HRR gene mutations (n=399, including 169 patients from Cohort 1 and 230 subsequently enrolled to comprise Cohort 2). Patients with castrate testosterone levels were randomized to receive TALZENNA 0.5 mg/day plus XTANDI 160mg/day, or placebo plus XTANDI 160mg/day.

The primary endpoint of the trial was rPFS, defined as the time from the date of randomization to first objective evidence of radiographic progression by blinded independent central review (BICR), or death, whichever occurred first, in both Cohort 1 (unselected) and Cohort 2 (those with HRRm). Secondary endpoints included OS, objective response rate (ORR), duration of response (DoR), prostate-specific antigen (PSA) response, time to cytotoxic chemotherapy and PFS2.

For more information on the TALAPRO-2 trial (NCT03395197), go to www.clinicaltrials.gov.

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 mCRPC 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 is the first and only PARP inhibitor licensed in the European Union for use with XTANDI for patients with mCRPC, with or without gene mutations. TALZENNA in combination with XTANDI is now approved in more than 40 countries globally for patients with mCRPC, indications vary by country.

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

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

HRR gene-mutated mCRPC:

- In combination with enzalutamide for the treatment of adult patients with homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer (mCRPC).

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-approved companion diagnostic for TALZENNA.

TALZENNA® (talazoparib) 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. Overall, MDS/AML has been reported in 0.4% (3 out of 788) of solid tumor patients treated with TALZENNA as a single agent in clinical studies. In TALAPRO-2, MDS/AML occurred in 2 out of 511 (0.4%) patients treated with TALZENNA and enzalutamide and in 0 out of 517 (0%) patients treated with placebo and enzalutamide. The durations of TALZENNA treatment in these five patients prior to developing MDS/AML were 0.3, 1, 2, 3, and 5 years, respectively. Most of these patients had

received previous chemotherapy with platinum agents and/or other DNA damaging agents including radiotherapy.

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, neutropenia, and/or thrombocytopenia have been reported in patients treated with TALZENNA. In TALAPRO-2, Grade ?3 anemia, neutropenia, and thrombocytopenia were reported, respectively, in 45%, 18%, and 8% of patients receiving TALZENNA and enzalutamide. Overall, 39% of patients (199/511) required a red blood cell transfusion, including 22% (111/511) who required multiple transfusions. Discontinuation due to anemia, neutropenia, and thrombocytopenia occurred, respectively, in 7%, 3%, and 0.4% 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 pregnant women. Advise male patients with female partners of reproductive potential or who are pregnant to use effective contraception during treatment with TALZENNA and for 4 months after receiving the last dose.

ADVERSE REACTIONS

In TALAPRO-2, serious adverse reactions reported in >2% of patients included anemia (9%) and fracture (3%). Fatal adverse reactions occurred in 1.5% of patients, including pneumonia, COVID infection, and sepsis (1 patient each).

The most common adverse reactions (? 10%, all Grades), including laboratory abnormalities, for patients in the TALAPRO-2 study who received TALZENNA in combination with enzalutamide vs patients receiving placebo with enzalutamide were hemoglobin decreased (79% vs 34%), neutrophils decreased (60% vs 18%), lymphocytes decreased (58% vs 36%), fatigue (49% vs 40%), platelets decreased (45% vs 8%), calcium decreased (25% vs 11%), nausea (21% vs 17%), decreased appetite (20% vs 14%), sodium decreased (22% vs 20%), phosphate decreased (17% vs 13%), fractures (14% vs 10%), magnesium decreased (14% vs 12%), dizziness (13% vs 9%), bilirubin increased (11% vs 7%), potassium decreased (11% vs 7%), and dysgeusia (10% vs 4.5%).

Clinically relevant adverse reactions in <10% of patients who received TALZENNA with enzalutamide included abdominal pain (9%), vomiting (9%), alopecia (7%), dyspepsia (4%), venous thromboembolism (3%) and stomatitis (2%).

Based on animal studies, TALZENNA may impair fertility in males of reproductive potential.

DRUG INTERACTIONS

Coadministration with P-gp inhibitors The effect of coadministration of P-gp inhibitors on talazoparib exposure when TALZENNA is taken in combination 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

Renal Impairment The recommended dosage of TALZENNA for patients with moderate renal impairment (CLcr 30 - 59 mL/min) is 0.35 mg taken orally once daily in combination with enzalutamide. The recommended dosage of TALZENNA for patients with severe renal impairment (CLcr 15 - 29 mL/min) is 0.25 mg taken orally once daily in combination with enzalutamide. No dose adjustment is required for patients with mild renal impairment. TALZENNA has not been studied in patients requiring hemodialysis.

Please see full U.S. Prescribing Information and Patient Information for TALZENNA® (talazoparib) at www.TALZENNA.com.

About XTANDI® (enzalutamide) and Important Safety Information

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 castration-sensitive prostate cancer (mCSPC; also known as metastatic hormone-sensitive prostate cancer or mHSPC), metastatic castration-resistant prostate cancer (mCRPC), non-metastatic castration-resistant prostate cancer (nmCRPC) and nonmetastatic castration-sensitive prostate cancer (nmCSPC) with biochemical recurrence at high risk for metastasis (high-risk BCR). XTANDI is currently approved for one or more of these indications in more than 90 countries, including in the U.S., EU, and Japan. Over one million patients have been treated with XTANDI globally.[6]

What should I tell my doctor before taking XTANDI?

Tell your doctor about all your medical conditions, including if you:

- Have a history of seizures, brain injury, stroke, or brain tumors.
- Have a history of heart disease, have high blood pressure, or have abnormal amounts of fat or cholesterol in your blood (dyslipidemia).
- Are pregnant or plan to become pregnant. XTANDI can cause harm to your unborn baby and loss of pregnancy (miscarriage).
- Have a partner who is pregnant or may become pregnant.
    - Males who have female partners who are able to become pregnant should use effective birth control (contraception) during treatment with XTANDI and for 3 months after the last dose.
    - Males must use a condom during sex with a pregnant female.
- Are breastfeeding or plan to breastfeed. It is not known if XTANDI passes into your breast milk.
- **Take other medicines.**XTANDI may affect the way other medicines work, and other medicines may affect how XTANDI works. These include prescription and over-the-counter medicines, vitamins, and herbal supplements. Do not start or stop any medicine without talking to your doctor.

How should I take XTANDI?

- **Take XTANDI exactly as your doctor tells you.**Take your prescribed dose once a day, at the same time each day. XTANDI can be taken with or without food. Swallow XTANDI capsules or tablets whole with enough water to make sure that you can swallow all of the medicine successfully. Do not chew, dissolve, or open the capsules. Do not cut, crush or chew the tablets. Your doctor may change your dose if needed. Your doctor may also change your pill size or stop treatment if you have swallowing problems.
- Do not change or stop taking your prescribed dose of XTANDI without talking with your doctor first.
- If you are receiving gonadotropin-releasing hormone (GnRH) therapy, you should continue with this treatment while taking XTANDI unless you have had surgery to lower the amount of testosterone in your body (surgical castration).
- **If you miss a dose of XTANDI:**Take your prescribed dose as soon as you remember that day. If you miss your daily dose, take your prescribed dose at your regular time the next day. Do not take more than your prescribed dose of XTANDI each day.
- **If you take too much XTANDI:**Call your doctor or go to the nearest emergency room right away. You may have an increased risk of seizure if you take too much XTANDI.

What are the possible side effects of XTANDI?

XTANDI may cause serious side effects including:

- **Seizure.**If you take XTANDI, you may be at risk of having a seizure. Avoid activities where a sudden loss of consciousness could seriously harm you or someone else. Tell your doctor right away if you lose consciousness or have a seizure.
- **Posterior Reversible Encephalopathy Syndrome (PRES).**If you take XTANDI you may be at risk of developing a condition involving the brain called PRES. Tell your doctor right away if you have a seizure or quickly worsening symptoms such as headache, decreased alertness, confusion, reduced eyesight, blurred vision or other visual problems. Your doctor will do a test to check for PRES.
- **Allergic Reactions.** Allergic reactions have happened in people who take XTANDI. Stop taking XTANDI and get medical help right away if you develop swelling of the face, tongue, lip or throat.
- **Heart Disease.**Blockage of the arteries in the heart (ischemic heart disease) that can lead to death has happened in some people during treatment with XTANDI. Your doctor will monitor you for signs and symptoms of heart problems during your treatment. Call your doctor or go to the emergency room right away if you get chest pain or discomfort at rest or with activity or shortness of breath during your treatment with XTANDI.
- **Falls and Bone Fractures.**XTANDI treatment may increase your risk for falls and bone fractures. Falls were not caused by loss of consciousness or seizures. Your doctor will monitor your risks for falls and bone fractures during treatment with XTANDI.
- **Swallowing problems or choking.**Severe swallowing problems or choking, including life-threatening problems or death can happen in people during treatment with XTANDI, because of the size of the XTANDI capsules and tablets. Swallow each XTANDI capsule or tablet whole with enough water to make sure that you can swallow all of the medicine successfully.

Your doctor will stop treatment with XTANDI if you have serious side effects.

The most common side effects of XTANDI include:

- Muscle and joint pain
- Feeling more tired than usual
- Hot flashes
- Constipation
- Decreased appetite

- Diarrhea
- High blood pressure
- Bleeding problems
- Falls
- Bone fractures
- Headache

XTANDI may cause fertility problems in males, which may affect the ability to father children. Talk to your doctor if you have concerns about fertility.

These are not all the possible side effects of XTANDI. For more information, talk to your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch .

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 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 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 Facebook.com/Pfizer.

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.

Disclosure Notice

The information contained in this release is as of February 13, 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 Pfizer Oncology, TALZENNA and XTANDI, including their potential benefits, the TALAPRO-2 results, and potential updates of the approved labels for TALZENNA 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; 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 any jurisdictions for any potential indications; whether and when any applications for TALZENNA, XTANDI or a combination that may be pending or filed may be approved by regulatory authorities, 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; 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, 2023, 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.

References

1. Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries.*CA: A Cancer Journal for Clinicians*. 2024;74(3):229-263. Published 2024 April 4. doi:10.3322/caac.21834
2. American Cancer Society.Key Statistics for Prostate Cancer. Accessed August 2024. *other than non-melanoma skin cancer
3. Kirby M, Hirst C, Crawford ED. Characterising the castration-resistant prostate cancer population: a systematic review. Int J Clin Pract. 2011 Nov;65(11):1180-92. doi:10.1111/j.1742-1241.2011.02799.x. PMID: 21995694.
4. Shore N, Oliver L, Shui I, Gayle A, Wong OY, Kim J, Payne S, Amin S, Ghate S. Systematic Literature Review of the Epidemiology of Advanced Prostate Cancer and Associated Homologous Recombination Repair Gene Alterations. J Urol. 2021 Apr;205(4):977-986. doi: 10.1097/JU.0000000000001570. Epub 2020 Dec 17. PMID: 33332152.https://www.auajournals.org/doi/10.1097/JU.0000000000001570
5. National Cancer Institute.*Surveillance, Epidemiology, and End Results Program*. Cancer Stat Facts: Prostate Cancer, Bethesda, MD, USA (2022); USA. Accessed December 2024. https://seer.cancer.gov/statfacts/html/prost.html.
6. Data on file. Northbrook, IL: Astellas Inc.

Media Contact:
+1 (212) 733-1226
PfizerMediaRelations@Pfizer.com

Investor Contact:
+1 (212) 733-4848
IR@Pfizer.com

Source: Pfizer Inc.