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First Participant Dosed in Pfizer's Pivotal Phase 3 TALAPRO-3 Combination Study of Talazoparib and Enzalutamide in Metastatic Castration-Sensitive Prostate Cancer (mCSPC)

Wednesday, June 23, 2021 - 06:45am

Study explores combination in patients with DNA damage response alterations before prostate cancer becomes castration resistant

NEW YORK--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) today announced that the first participant has been dosed in TALAPRO-3, a global, randomized, double-blind, placebo-controlled Phase 3 clinical trial. The study will evaluate the efficacy and safety of talazoparib, an oral poly (ADP-ribose) polymerase (PARP) inhibitor, in combination with enzalutamide, an androgen receptor inhibitor, compared with placebo plus enzalutamide in men with DNA damage response (DDR)-deficient metastatic castration-sensitive prostate cancer (mCSPC). The first patient was dosed at a site in Glendale, California.

"The prognosis for men with advanced prostate cancer has significantly improved since the introduction of novel hormone therapies, but additional therapeutic options are needed for the approximately 25 percent of men with tumors harboring DNA damage response (DDR) gene mutations, who may have poorer outcomes," said Chris Boshoff, M.D., Ph.D., Chief Development Officer, Oncology, Pfizer Global Product Development. "By combining enzalutamide, which has a proven clinical benefit in men with metastatic castration-sensitive prostate cancer, with talazoparib, our PARP inhibitor that is active in DDR-mutated cancer, we may be able to offer a new treatment option that targets the underlying genetic mechanisms associated with DDR-mutated mCSPC."

The TALAPRO-3 trial will enroll approximately 550 men with DDR-deficient mCSPC across 285 clinical trial sites in 28 countries. The primary endpoint of the study is radiographic progression-free survival (rPFS), and overall survival (OS) is a secondary endpoint. The anticipated primary completion date is late-2024.

"With the introduction of PARP inhibitors in the metastatic castration-resistant prostate cancer setting, it is important to explore how a combination approach may impact outcomes for men with metastatic castration-sensitive disease," said Neeraj Agarwal, M.D., Professor of Oncology at the University of Utah School of Medicine, Senior Director for Clinical Research Innovation at Huntsman Cancer Institute and member of the TALAPRO-3 steering committee. "It's exciting to be at the forefront of landmark studies like TALAPRO-3, which are helping to further our understanding of how different approaches may advance care for these men."

More information about the TALAPRO-3 trial and participating sites may be found at www.clinicaltrials.gov (NCT04821622).

Talazoparib is currently approved under the brand name TALZENNA® for the treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) HER2-negative locally advanced or metastatic breast cancer. Selection of patients for therapy is based on an FDA-approved companion diagnostic for TALZENNA. Talazoparib is not approved for the treatment of prostate cancer. Enzalutamide is an androgen receptor inhibitor currently approved under the brand name XTANDI® and is indicated for the treatment of patients with castration-resistant prostate cancer (CRPC) and mCSPC. As part of a global agreement, Pfizer and Astellas 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.

In addition to the TALAPRO-3 trial, the combination of enzalutamide plus talazoparib is being investigated in TALAPRO-2 (NCT03395197), a two-part, Phase 3, randomized, double-blind, placebo-controlled study in men with metastatic CRPC (with and without DDR defects).

About TALAPRO-3 Trial

The Phase 3, randomized, double-blind, placebo-controlled, global TALAPRO-3 trial (NCT04821622) will enroll 550 men with DDR-deficient mCSPC across approximately 285 clinical trial sites in 28 countries. In the study, participants will be randomly assigned to one of the two treatment groups and receive either talazoparib (0.50 mg once daily) in combination with enzalutamide (160 mg once daily) or placebo capsules identical to talazoparib in combination with enzalutamide. Men with moderate renal impairment at screening may be enrolled and given a lower dose of either talazoparib (0.35 mg once daily) or the placebo.

The primary endpoint of the study is radiographic progression-free survival (rPFS), which is defined as the time from the date of randomization to first objective evidence of radiographic progression or death, whichever occurs first.

About Metastatic Castration-Sensitive Prostate Cancer

Prostate cancer is considered metastatic once it has spread outside of the prostate gland to other parts of the body, such as the lymph nodes, bones, lungs, and liver.[i] Men are considered castration-sensitive if their disease still responds to medical or surgical treatment to lower testosterone levels.[ii] The prevalence of mCSPC in the U.S. in 2020 was estimated to be just over 41,000.[iii] Studies have shown that DDR defects are found in 23%-27% of metastatic prostate cancers.[iv,v]

About talazoparib

Talazoparib is an inhibitor of PARP enzymes, which play a role in DNA response. Preclinical studies have demonstrated that talazoparib blocks PARP enzyme activity and traps PARP at the site of DNA damage, leading to decreased cancer cell growth and cancer cell death. Talazoparib is being evaluated in several ongoing clinical trials in prostate cancer, as well as other novel combinations with targeted therapies in various solid tumors.

About XTANDI® (enzalutamide)

XTANDI (enzalutamide) is an androgen receptor inhibitor indicated for the treatment of patients with castration-resistant prostate cancer (CRPC) and metastatic castration-sensitive prostate cancer (mCSPC).

Prescribing Information for XTANDI® and TALZENNA®

Please see Full Prescribing Information for XTANDI® (enzalutamide) at www.Xtandi.com.

Please see Full Prescribing Information for TALZENNA® (talazoparib) at www.Talzenna.com.

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.

About Pfizer Oncology

At Pfizer Oncology, we are committed to advancing medicines wherever we believe we can make a meaningful difference in the lives of people living with cancer. Today, we have an industry-leading portfolio of 24 approved innovative cancer medicines and biosimilars across more than 30 indications, including breast, genitourinary, colorectal, blood and lung cancers, as well as melanoma.

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 170 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 Twitter at @Pfizer and @Pfizer News, LinkedIn, YouTube and like us on Facebook at Facebook.com/Pfizer.

DISCLOSURE NOTICE: The information contained in this release is as of June 23, 2021. 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 talazoparib, including its potential benefits and a potential indication in men with DNA damage response (DDR)-deficient metastatic castration-sensitive prostate cancer, 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, 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 talazoparib may be filed in any jurisdictions for the potential indication or for any other indications; whether and when any such applications for talazoparib 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 talazoparib 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 talazoparib; uncertainties regarding the impact of COVID-19 of our 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, 2020 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.

[i] American Society of Clinical Oncology. ASCO Answers: Prostate Cancer (2018). https://www.cancer.net/sites/cancer.net/files/asco_answers_guide_prostate.pdf. Accessed 04-05-2021.
[ii] Cancer.net. Prostate Cancer: Types of Treatment (03-2018). https://www.cancer.net/cancer-types/prostate-cancer/types-treatment. Accessed 04-05-2021.
[iii] Supplement to: Scher HI, Solo K, Valant J, Todd MB, Mehra M. Prevalence of prostate cancer clinical states and mortality in the United States: estimates using a dynamic progression model. PLoS One 2015;10(10):e0139440.
[iv] Robinson, D., Van Allen, E. M., Wu, Y. M., Schultz, N., Lonigro, R. J., Mosquera, J. M. et al. Integrative clinical genomics of advanced prostate cancer. Cell 161, 1215–1228 (2015).
[v] Armenia, J., Wankowicz, S. A. M., Liu, D., Gao, J., Kundra, R., Reznik, E. et al. The long tail of oncogenic drivers in prostate cancer. Nat. Genet. 50, 645–651 (2018).

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Source: Pfizer Inc.