Investor News

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U.S. FDA approves darolutamide, a new treatment for men with non-metastatic castration-resistant prostate cancer

- Darolutamide was approved in the U.S. under the FDA Priority Review designation; approval granted three months ahead of target FDA action date
- Approval based on Phase III ARAMIS trial evaluating the efficacy and safety of darolutamide plus androgen deprivation therapy (ADT) compared to placebo plus ADT

Leverkusen, Germany, July 31, 2019 –

Berlin, July 31, 2019 – The U.S. Food and Drug Administration (FDA) has approved darolutamide, a non-steroidal androgen receptor inhibitor (ARi), under the brand name Nubeqa®. The FDA approval is for the treatment of patients with non-metastatic castration-resistant prostate cancer (nmCRPC) and is based on the Phase III ARAMIS trial evaluating darolutamide plus androgen deprivation therapy (ADT), which demonstrated a highly significant improvement in the primary efficacy endpoint of metastasis-free survival (MFS), with a median of 40.4 months versus 18.4 months for placebo plus ADT ($p<0.0001$). MFS is defined as the time from randomization to the time of first evidence of blinded independent central review (BICR)-confirmed distant metastasis or death from any cause within 33 weeks after the last evaluable scan, whichever occurred first. The compound, which is developed jointly by Bayer and Orion Corporation, a globally operating Finnish pharmaceutical company, was approved under the FDA Priority Review designation, which is reserved for medicines that may provide significant improvements in the safety or effectiveness of the treatment for serious conditions. The androgen receptor inhibitor has a distinct chemical structure that binds to the receptor with high affinity and exhibits strong antagonistic activity, thereby inhibiting the receptor function and the growth of prostate cancer cells.

“Patients at this stage of prostate cancer typically don’t have symptoms of the disease. The overarching goals of treatment in this setting are to delay the spread of prostate

cancer and limit the burdensome side effects of therapy," said Matthew Smith, M.D., Ph.D., Director of the Genitourinary Malignancies Program, Massachusetts General Hospital Cancer Center. "This approval marks an important new option for the prostate cancer community."

Prostate cancer that is treated with ADT but keeps progressing even when the amount of testosterone is reduced to very low levels in the body is known as castration-resistant prostate cancer (CRPC). In the U.S., over 73,000 men are estimated to have a CRPC diagnosis in 2019. About one-third of men with non-metastatic CRPC go on to develop metastases within two years.

"With the approval of darolutamide, we now have a new therapy that extends MFS and allows physicians greater flexibility to treat men living with nmCRPC,," said Robert LaCaze, Member of the Executive Committee of Bayer's Pharmaceuticals Division and Head of the Oncology Strategic Business Unit. "Bayer is proud to take this latest step forward in the nmCRPC treatment landscape. Darolutamide is the newest addition to our prostate cancer portfolio and reflects Bayer's commitment to finding treatments for men at different stages along the prostate cancer continuum."

In the ARAMIS trial, overall survival (OS) and time to pain progression were additional secondary efficacy endpoints. A positive trend in OS was observed; OS data were not yet mature at the time of final MFS analysis. The MFS result was additionally supported by a delay in time to pain progression as compared to placebo plus ADT. All other secondary endpoints, time to cytotoxic chemotherapy, and time to a symptomatic skeletal event, demonstrated a benefit in favor of darolutamide.

The only adverse reactions occurring more frequently in the darolutamide plus ADT arm (≥2% over placebo plus ADT) were fatigue (16% vs. 11%), pain in extremity (6% vs. 3%), and rash (3% vs. 1%). Discontinuation due to adverse events occurred in 9% of patients in both arms of the study.

Preclinical studies showed that darolutamide has a lower blood-brain barrier penetration compared to other currently available AR inhibitors. A high concentration of these compounds in the central nervous system (CNS) may lead to undesired side effects.

Bayer has filed for approval of the compound in the European Union (EU), Japan and with other health authorities.

About the ARAMIS trial

The FDA approval of darolutamide is based on the ARAMIS trial, a randomized (2:1), double-blind, placebo-controlled, multi-center Phase III study which evaluated the safety and efficacy of the compound in patients with nmCRPC who are currently being treated with androgen deprivation therapy (ADT) and are at high risk for developing metastatic disease. In the clinical study, 1,509 patients were randomized in a 2:1 ratio to receive 600 mg of darolutamide orally twice daily or placebo along with ADT. Patients with a history of seizure were allowed in the study.

About darolutamide

Darolutamide is an androgen receptor inhibitor (ARi) with a distinct chemical structure that binds to the receptor with high affinity and exhibits strong antagonistic activity, thereby inhibiting the receptor function and the growth of prostate cancer cells. The compound is also being investigated in a Phase III study in metastatic hormone-sensitive prostate cancer (ARASENS). Information about these trials can be found at http://www.clinicaltrials.gov.

Darolutamide has been approved in the U.S. under the brand name Nubeqa®. It has not been approved by the European Medicines Agency or any other health authority outside the U.S.

About castration-resistant prostate cancer (CRPC)

Prostate cancer is the second most commonly diagnosed malignancy in men worldwide. In 2018, an estimated 1.2 million men were diagnosed with prostate cancer, and about 358,000 died from the disease worldwide. Prostate cancer is the fifth leading cause of death from cancer in men. Prostate cancer results from the abnormal proliferation of cells within the prostate gland, which is part of a man’s reproductive system. It mainly affects men over the age of 50, and the risk increases with age.

Treatment options range from surgery to radiation treatment to therapy using hormone-receptor antagonists, i.e., substances that stop the formation of testosterone or prevent its effect at the target location. However, in nearly all cases, the cancer eventually becomes

resistant to conventional hormone therapy.

CRPC is an advanced form of the disease where the cancer keeps progressing despite ADT treatment, even when the amount of testosterone is reduced to very low levels in the body. The field of treatment options for castration-resistant patients is evolving rapidly, but until two years ago, there have been no FDA-approved effective treatment options for CRPC patients who have rising prostate-specific antigen (PSA) levels while on ADT and no detectable metastases. In men with progressive nmCRPC, a rapid PSA doubling time has been consistently associated with reduced time to first metastasis and death.

About Oncology at Bayer
Bayer is committed to delivering science for a better life by advancing a portfolio of innovative treatments. The oncology franchise at Bayer now expands to six marketed products and several other assets in various stages of clinical development. Together, these products reflect the company's approach to research, which prioritizes targets and pathways with the potential to impact the way that cancer is treated.

About Bayer
Bayer is a global enterprise with core competencies in the life science fields of health care and nutrition. Its products and services are designed to benefit people by supporting efforts to overcome the major challenges presented by a growing and aging global population. At the same time, the Group aims to increase its earning power and create value through innovation and growth. Bayer is committed to the principles of sustainable development, and the Bayer brand stands for trust, reliability and quality throughout the world. In fiscal 2018, the Group employed around 117,000 people and had sales of 39.6 billion euros. Capital expenditures amounted to 2.6 billion euros, R&D expenses to 5.2 billion euros. For more information, go to www.bayer.com.

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Forward-Looking Statements
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