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News Release

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Bayer receives approval for darolutamide in Japan

Marketing authorization granted for the treatment of men with non-metastatic castration-resistant prostate cancer

Berlin, January 23, 2020 – Bayer announced today that the Japanese Ministry of Health, Labor and Welfare (MHLW) has granted marketing authorization for darolutamide, under the brand name Nubeqa®, for the treatment of men with non-metastatic castration-resistant prostate cancer (nmCRPC). The approval is based on the Phase III ARAMIS trial evaluating the efficacy and safety of darolutamide plus androgen deprivation therapy (ADT) compared to placebo plus ADT, showing a highly significant improvement in the primary efficacy endpoint of metastasis-free survival (MFS), with a median 40.4 months for darolutamide plus ADT versus 18.4 months for placebo plus ADT (HR=0.41, 95% CI 0.34-0.50; P<0.001). The androgen receptor inhibitor (ARi), which is jointly developed by Bayer and Orion Corporation, a globally operating Finnish pharmaceutical company, is already approved in the U.S. and Brazil and filings in the European Union and other regions are underway or planned.

“NmCRPC patients typically don’t have symptoms of the disease and in many cases, they are on treatment for a long time. Despite recent advances in nmCRPC treatments, there remains a high unmet need for new therapeutic options that not only delay the time to distant metastases, but also have a favorable safety profile”, said Kazuhiro Suzuki, Professor, Department of Urology, Gunma University, Maebashi, Japan. “More treatment options are needed for physicians and patients to be able to select a drug and treatment strategy based on each patients’ life style and preferences.”

“The number of prostate cancer cases in Japan continues to grow. Bayer is committed to addressing important unmet needs of this large and growing patient population in Japan, and we look forward to providing more patients and physicians with a new and

differentiated treatment option", said Dr. Scott Z. Fields, Senior Vice President and Head of Oncology Development.

In Japan, over 89,000 men are estimated to be diagnosed with prostate cancer annually, making it the second most-common cancer diagnosis in Japanese men (after stomach cancer). 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).[1] In men with progressive nmCRPC, a rapid prostate specific antigen (PSA) doubling time has been consistently associated with reduced time to first metastasis and death.[1]

In the ARAMIS trial, overall survival (OS) and time to pain progression were additional secondary efficacy endpoints. At the time of final MFS analysis, a positive trend in OS was observed; OS data were not yet mature. 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 (SSE), demonstrated a benefit in favor of darolutamide.

Adverse reactions occurring more frequently in the darolutamide plus ADT arm (≥2% absolute increase in frequency compared to 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.

About the ARAMIS trial

The approval of darolutamide in Japan is based on the results of 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 www.clinicaltrials.gov.

The product is also approved in the U.S. and Brazil under the brand name Nubeqa®. It has not been approved by the European Medicines Agency.

About castration-resistant prostate cancer (CRPC)

Prostate cancer is the second most commonly diagnosed malignancy in men worldwide.[2] In 2018, an estimated 1.2 million men were diagnosed with prostate cancer, and about 358,000 died from the disease worldwide.[2] Prostate cancer is the fifth leading cause of death from cancer in men.[2] Prostate cancer results from the abnormal proliferation of cells within the prostate gland, which is part of a man's reproductive system.[3] It mainly affects men over the age of 50, and the risk increases with age.[4]

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.[5] However, in nearly all cases, the cancer eventually becomes resistant to conventional hormone therapy.[6]

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.[1,7] In men with progressive nmCRPC, a rapid prostate specific antigen (PSA) doubling time has been consistently associated with reduced time to first metastasis and death.[1]

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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