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News Release

Not intended for U.S. and UK Media

Bayer completes rolling submission for darolutamide in U.S.

Berlin, February 27, 2019 – Bayer today announced the completion of the rolling submission of a New Drug Application (NDA) for darolutamide to the U.S. Food and Drug Administration (FDA). The submission, which was initiated in December 2018, is based on data from the Phase III ARAMIS trial in men with non-metastatic castration-resistant prostate cancer (nmCRPC) showing a statistically significant improvement in metastasis-free survival (MFS) for darolutamide plus androgen deprivation therapy (ADT). Darolutamide plus ADT has shown a favorable safety profile compared to placebo plus ADT.[1] These data were recently presented at the American Society of Clinical Oncology Genitourinary Cancers Symposium (ASCO GU) in San Francisco and published simultaneously in *The New England Journal of Medicine*.

“Despite recent advances in nmCRPC treatment, there remains a high unmet need for new therapeutic options that not only delay the time to metastases, but also have a favorable safety profile, that allows patients to continue their daily life. Maintaining quality of life is particularly important for this patient population who are generally asymptomatic”, said Scott Z. Fields, M.D., senior vice president and head of Oncology Development at Bayer's Pharmaceutical Division. “This NDA submission is a key milestone bringing us one step closer to providing darolutamide as a potential new treatment option for men with nmCRPC.”

Bayer has been granted Fast Track designation by the U.S. Food and Drug Administration (FDA) for darolutamide in men with nmCRPC. Bayer is also in discussions with other health authorities regarding a submission for darolutamide. The compound is being developed jointly by Bayer and Orion Corporation, a globally operating Finnish pharmaceutical company.

About ARAMIS

The ARAMIS trial is a randomized, Phase III, multi-center, double-blind, placebo-controlled trial evaluating the safety and efficacy of oral darolutamide in patients with nmCRPC who are currently being treated with ADT and are at high risk for developing metastatic disease. 1,509 patients were randomized in a 2:1 ratio to receive 600 mg of darolutamide twice a day or placebo along with ADT.

About darolutamide

Darolutamide is a non-steroidal androgen receptor (AR) antagonist 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. In preclinical studies, darolutamide demonstrated lower blood-brain barrier penetration compared to other currently available AR antagonists.[2] This may also explain the overall low incidence of central nervous system (CNS)-related adverse events seen in the ARAMIS Phase III study.[1]

In addition to the Phase III trial ARAMIS in men with nmCRPC, darolutamide 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.

Darolutamide is not approved by the U.S. FDA, the European Medicines Agency or any other health authority.

About castration-resistant prostate cancer (CRPC)

Prostate cancer is the second most commonly diagnosed malignancy in men worldwide.[3] In 2018, an estimated 1.2 million men were diagnosed with prostate cancer, and about 358,000 died from the disease worldwide.[3] Prostate cancer is the fifth leading cause of death from cancer in men.[3] Prostate cancer results from the abnormal proliferation of cells within the prostate gland, which is part of a man´s reproductive system.[4] It mainly affects men over the age of 50, and the risk increases with age.[5] 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.[6] However, in nearly all cases, the cancer eventually becomes resistant to conventional hormone therapy.[7]

CRPC is an advanced form of the disease where the cancer keeps progressing 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 recently, there have been no approved 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 short PSA doubling time has been consistently associated with reduced time to first metastasis and death.[8]

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 includes five 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.

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7) Nakazawa, Mary; Paller, Channing; Kyprianou, Natasha. Mechanisms of Therapeutic Resistance in Prostate Cancer. *Curr Oncol Rep* (2017) 19:13.
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About Bayer
Bayer is a global enterprise with core competencies in the Life Science fields of health care and agriculture. Its products and services are designed to benefit people and improve their quality of life. At the same time, the Group aims to create value through innovation, growth and high earning power. Bayer is committed to the principles of sustainable development and to its social and ethical responsibilities as a corporate citizen. In fiscal 2017, the Group employed around 99,800 people and had sales of EUR 35.0 billion. Capital expenditures amounted to EUR 2.4 billion, R&D expenses to EUR 4.5 billion. For more information, go to www.bayer.com.

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