Not intended for U.S. and UK Media

U.S. FDA accepts New Drug Application and grants Priority Review for darolutamide

Leverkusen, Germany, April 29, 2019 – Bayer today announced the U.S. Food and Drug Administration (FDA) has accepted the New Drug Application (NDA) and granted Priority Review to darolutamide for the treatment of non-metastatic castration-resistant prostate cancer (nmCRPC). The NDA and Priority Review status were based on data from the Phase III ARAMIS trial in men with nmCRPC.[1] Darolutamide is an investigational, non-steroidal androgen receptor (AR) antagonist with a distinct chemical structure that binds with high affinity to the receptor, inhibiting the growth of prostate cancer cells.

“Bayer is committed to addressing treatment gaps that exist along the continuum of care for men with prostate cancer,” said Scott Z. Fields, M.D., senior vice president and head of Oncology Development at Bayer's Pharmaceutical Division. “With the NDA acceptance and Priority Review designation, we are an important step closer to bringing darolutamide to patients as quickly as possible.”

The FDA grants Priority Review for the applications of medicines that, if approved, would provide significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions when compared to standard applications. Bayer has also been granted Fast Track designation by the FDA for darolutamide in men with nmCRPC.

Bayer recently submitted an application to the European Medicines Agency and the Ministry of Health, Labor and Welfare (MHLW) in Japan. Bayer is also in discussions with other health authorities regarding submissions.

Darolutamide 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]

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 rapid 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.

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.

Bayer Investor Relations Team

Bayer AG
Investor Relations
51368 Leverkusen, Germany
E-mail: ir@bayer.com
Internet: http://www.investor.bayer.com

References

1. Fizazi, Karim; Shore, Neal; Tammela, Teuvo, et al. Darolutamide in Nonmetastatic Castration-Resistant Prostate Cancer. *N Engl J Med.* 2019; doi: 10.1056/NEJMoa1815671.
2. Moilanen, Anu-Maarit; Riikonen, Reetta; Oksala, Riikka, et al. Discovery of ODM-201, a new-generation androgen receptor inhibitor targeting resistance mechanisms to androgen signaling-directed prostate cancer therapies. *Sci Rep.* 2015;5:12007
3. GLOBOCAN 2018: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2018. Prostate Cancer. http://gco.iarc.fr/today/data/pdf/fact-sheets/cancers/cancer-fact-sheets-19.pdf. Accessed February 2019.
4. American Cancer Society. What is Prostate Cancer? https://www.cancer.org/content/dam/CRC/PDF/Public/8793.00.pdf. Accessed February 2019.
5. American Cancer Society. Prostate Cancer Risk Factors. https://www.cancer.org/content/dam/CRC/PDF/Public/8794.00.pdf. Accessed February 2019.
6. National Cancer Institute. Hormone Therapy for Prostate Cancer. https://www.cancer.gov/types/prostate/prostate-hormone-therapy-fact-sheet. Accessed February 2019.
7. Nakazawa, Mary; Paller, Channing; Kyprianou, Natasha. Mechanisms of Therapeutic Resistance in Prostate Cancer. *Curr Oncol Rep* (2017) 19:13.
8. Howard, Lauren; Moreira, Daniel M; DeHoedt, Amanda; Aronson, William J., et al. Thresholds for PSA doubling time in men with non-metastatic castration-resistant prostate cancer. *BJU Int* 2017;120: E80-E86.