



Bayer AG
Investor Relations
51368 Leverkusen
Germany
www.investor.bayer.com

Investor News

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Bayer submits European marketing authorization application for darolutamide

- Third submission for darolutamide in two weeks underscores Bayer's commitment to fill an unmet need for men with nmCRPC worldwide
 - Regulatory submission based on positive data from Phase III study ARAMIS
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Leverkusen, Germany, March 8, 2019 – Bayer has submitted a marketing authorization application (MAA) to the European Medicines Agency (EMA) for darolutamide for the treatment of patients with non-metastatic castration-resistant prostate cancer (nmCRPC).

“Men are typically asymptomatic at this stage of prostate cancer. Therefore, it is critical that they have treatment options, which not only delay the development of metastases, but also limit burdensome side effects of therapy, so that these men can continue with their day-to-day lives,” said Scott Z. Fields, M.D., senior vice president and head of Oncology Development of Bayer AG's Pharmaceutical Division. “With this submission, we are taking an important step toward providing patients, caregivers, and physicians with a potential new treatment option for nmCRPC.”

The submission to the EMA is based on data from the Phase III ARAMIS trial in men with nmCRPC, which 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*, showing a statistically significant improvement in metastasis-free survival (MFS) for darolutamide plus androgen deprivation therapy (ADT).¹

Bayer recently completed the rolling submission of a New Drug Application to the United States Food and Drug Administration (FDA) and submitted an application to the Ministry of Health, Labor and Welfare (MHLW) in Japan. Bayer is also in discussions with other health authorities regarding submissions.

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

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.

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4. American Cancer Society. What is Prostate Cancer? <https://www.cancer.org/content/dam/CRC/PDF/Public/8793.00.pdf>. Accessed February 2019.
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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.

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>

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