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

Investor News

Not intended for U.S. and UK Media

Bayer submits darolutamide for marketing authorization in Japan

Regulatory submission based on positive data from Phase III ARAMIS study

Leverkusen, Germany, March 5, 2019 – Bayer has submitted an application for marketing authorization to the Ministry of Health, Labor and Welfare (MHLW) in Japan for darolutamide for the treatment of patients with castration-resistant prostate cancer (CRPC)**.**

“In the early stage of prostate cancer, patients are typically asymptomatic. Thus, it is critically important for men to have treatment options that significantly delay the development of metastases while limiting burdensome side effects of therapy, which allow them to continue their day-to-day lives,” said Scott Z. Fields, M.D., senior vice president and head of Oncology Development at Bayer's Pharmaceutical Division. “With this submission, we are one step closer to providing patients and physicians in Japan with a potential new treatment option for CRPC.”

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

Bayer recently completed the rolling submission of a New Drug Application to the United States Food and Drug Administration (FDA) and 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 non-metastatic castration-resistant prostate cancer (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.

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. Letzter Zugriff Februar 2019.
4. American Cancer Society. What is Prostate Cancer? https://www.cancer.org/content/dam/CRC/PDF/Public/8793.00.pdf. Letzter Zugriff Februar 2019.
5. American Cancer Society. Prostate Cancer Risk Factors. https://www.cancer.org/content/dam/CRC/PDF/Public/8794.00.pdf. Letzter Zugriff Februar 2019.
6. National Cancer Institute. Hormone Therapy for Prostate Cancer. https://www.cancer.gov/types/prostate/prostate-hormone-therapy-fact-sheet. Letzter Zugriff Februar 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.

Bayer Investor Relations Team

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

Forward-Looking Statements
This release may contain forward-looking statements based on current assumptions and forecasts made by Bayer management. Various known and unknown risks, uncertainties and other factors could lead to material differences between the actual future results, financial situation, development or performance of the company and the estimates given here. These factors include those discussed in Bayer's public reports which are available on the Bayer website at www.bayer.com. The company assumes no liability whatsoever to update these forward-looking statements or to conform them to future events or developments.