MEDIA & INVESTOR RELEASE

Novartis receives positive CHMP opinion for Pluvicto® for patients with progressive, PSMA-positive metastatic castration-resistant prostate cancer

- Phase III VISION trial showed Pluvicto® plus best standard of care significantly improved survival for patients with pre-treated PSMA-positive mCRPC

- Approximately 473,000 prostate cancer cases and 108,000 prostate cancer-related deaths occurred across Europe in 2020; Metastatic prostate cancer has a 5-year survival rate of approximately 30%

- Two Phase III trials are underway to evaluate Pluvicto® for treatment in earlier stages of metastatic prostate cancer

Basel, October 14, 2022 — Novartis announced today that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a positive opinion and recommended granting a marketing authorization for Pluvicto® (INN: lutetium (177)Lu) vipivotide tetraxetan) (formerly referred to as 177Lu-PSMA-617), a radioligand therapy, in combination with androgen deprivation therapy (ADT) with or without androgen receptor (AR) pathway inhibition, for the treatment of adult patients with progressive prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) who have been treated with AR pathway inhibition and taxane based chemotherapy.

“People at this advanced stage of disease have already received many different treatments and have few alternatives left,” said Prof. Karim Fizazi, MD, PhD, VISION trial investigator and Head of Medical Oncology at Gustave Roussy, first European cancer center based in Villejuif, France. “If approved in Europe, Pluvicto® would represent a new type of precision medicine targeting a biomarker broadly expressed in prostate cancer patients and provide a therapeutic option with demonstrated potential to improve outcomes. As a clinician this gives me hope for patients facing a very difficult situation.”

The positive CHMP opinion is based on data from the Phase III VISION study, in which Pluvicto® plus best standard of care (BSoC) demonstrated significantly improved overall survival in PSMA-positive mCRPC patients previously treated with AR pathway inhibition and taxane-based chemotherapy compared to BSoC alone.

Results from the VISION trial demonstrated that participants treated with Pluvicto® plus BSoC had a 38% reduction in risk of death and a 60% reduction in the risk of radiographic disease progression or death (rPFS) compared to BSoC alone. In addition, approximately a third (29.8%) of patients with evaluable disease at baseline demonstrated an overall response (per RECIST 1.1) with Pluvicto® plus BSoC, compared to 1.7% in the BSoC alone arm. The most common adverse events (all grades) in the Pluvicto® arm of the study were fatigue (43%), dry mouth (39%), nausea (35%), anemia (low red blood cell counts) (32%), decreased appetite (21%), and constipation (20%).
“This positive CHMP opinion for Pluvicto® is an important step forward in our goal of bringing transformative innovation to more patients around the world,” said Marie-France Tschudin, President, Innovative Medicines International & Chief Commercial Officer, Novartis. “If approved by the European Commission, Pluvicto® would be the first and only commercial radioligand therapy for people with advanced prostate cancer in Europe. We are committed to exploring the potential of radioligand therapy to address unmet needs in prostate cancer, including in earlier stages of disease.”

The CHMP’s positive opinion on Pluvicto® in PSMA–positive mCRPC patients will be referred to the European Commission (EC), which will deliver a final decision in approximately two months. The decision will be applicable to all 27 EU member states plus Iceland, Norway, Northern Ireland and Liechtenstein.

About Pluvicto® (lutetium (¹⁷⁷)Lu) vipivotide tetraxetan
Despite advances in prostate cancer care, there is a high unmet need for new targeted treatment options to improve outcomes for patients with mCRPC1. Pluvicto® is a radioligand therapy combining a targeting compound (ligand, in this case directed to PSMA) with a therapeutic radioisotope (a radioactive particle, in this case lutetium-177)¹. Pluvicto® delivers radiation to PSMA-positive cells and the surrounding microenvironment1. Pluvicto® was approved by the FDA in March 2022.

Two additional Phase III trials in earlier lines of treatment for metastatic prostate cancer are ongoing, investigating potential clinical utility in the mCRPC pre-taxane setting (PSMAfore)¹¹ and in the metastatic hormone-sensitive setting (PSMAddition)¹². Novartis is also evaluating opportunities to investigate Pluvicto® radioligand therapy in earlier stages of prostate cancer.

About VISION
VISION is an international, prospective, randomized, open-label, multicenter, phase III study that assessed the efficacy and safety of Pluvicto® (lutetium (¹⁷⁷)Lu) vipivotide tetraxetan) (7.4 GBq administered by IV infusion every 6 weeks for a maximum of 6 cycles) plus investigator-chosen standard of care (BSoS) in the investigational arm, versus BSoS in the control arm¹. Patients with PSMA PET-scan positive mCRPC who have received androgen receptor (AR) pathway inhibition and taxane-based chemotherapy, were randomized in a 2:1 ratio in favor of the investigational arm¹. The alternate primary endpoints were rPFS and OS¹. The study enrolled 831 patients¹.

Novartis and Prostate Cancer
With more 1.4 million new cases and 375,000 deaths in 2020 alone, prostate cancer is the most frequently diagnosed cancer in 112 countries—more than half the world¹³.

At Novartis, we are harnessing the innovation of our world-class scientists, strategic partnerships, and one of the industry’s most competitive pipelines to explore the potential of new, targeted therapies and precision medicine platforms to address the greatest unmet needs in prostate cancer.

Through the bold science of targeted therapies, our goal is to reduce the global disease burden, extend the lives of patients with prostate cancer, and elevate current standards of care.

About Phenotypic Precision Medicine in advanced prostate cancer
More than 80% of patients with prostate cancer highly express a phenotypic biomarker⁴ called prostate-specific membrane antigen (PSMA)⁴-⁸, making it a promising diagnostic (through positron emission tomography (PET) scan imaging) and therapeutic target for radioligand therapy⁹. This differs from ‘genotypic’ precision medicine which targets specific genetic alterations in cancer cells¹⁰.
Disclaimer
This press release contains forward-looking statements within the meaning of the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements can generally be identified by words such as “potential,” “can,” “will,” “plan,” “may,” “could,” “would,” “expect,” “anticipate,” “seek,” “look forward,” “believe,” “committed,” “investigational,” “pipeline,” “launch,” or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for the investigational or approved products described in this press release, or regarding potential future revenues from such products. You should not place undue reliance on these statements. Such forward-looking statements are based on our current beliefs and expectations regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no guarantee that the investigational or approved products described in this press release will be submitted or approved for sale or for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that such products will be commercially successful in the future. In particular, our expectations regarding such products could be affected by, among other things, the uncertainties inherent in research and development, including clinical trial results and additional analysis of existing clinical data; regulatory actions or delays or government regulation generally; global trends toward health care cost containment, including government, payor and general public pricing and reimbursement pressures and requirements for increased pricing transparency; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; general political, economic and business conditions, including the effects of and efforts to mitigate pandemic diseases such as COVID-19; safety, quality, data integrity or manufacturing issues; potential or actual data security and data privacy breaches, or disruptions of our information technology systems, and other risks and factors referred to in Novartis AG’s current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

About Novartis
Novartis is reimagining medicine to improve and extend people’s lives. As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. In our quest to find new medicines, we consistently rank among the world’s top companies investing in research and development. Novartis products reach nearly 800 million people globally and we are finding innovative ways to expand access to our latest treatments. About 108,000 people of more than 140 nationalities work at Novartis around the world. Find out more at https://www.novartis.com.

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