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MEDIA UPDATE

Novartis receives European Commission approval for Pluvicto® as the first targeted radioligand therapy for treatment of progressive PSMA–positive metastatic castration-resistant prostate cancer

- *EC approval based on results from pivotal Phase III VISION trial, in which Pluvicto® plus best standard of care (BSoC) significantly improved overall survival and radiographic progression-free survival in patients with pre-treated PSMA–positive mCRPC[1]*

- *Pluvicto® becomes the first targeted radioligand therapy commercially available for people with advanced prostate cancer, addressing a significant unmet need for new treatment option to improve therapeutic outcomes[2]*

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

- *Novartis is advancing a broad portfolio of radioligand therapies to treat cancer and is investing in manufacturing capacity to meet the growing global demand for treatment*

Basel, December 13, 2022 — Novartis today announced the European Commission (EC) approved Pluvicto® (INN: lutetium (^{177}Lu) vipivotide tetraxetan), a targeted radioligand therapy. Pluvicto® is approved in combination with androgen deprivation therapy (ADT) with or without androgen receptor (AR) pathway inhibition, for the treatment of adult patients with prostate-specific membrane antigen (PSMA)–positive metastatic castration-resistant prostate cancer (mCRPC)[3]. These patients have been treated with AR pathway inhibition and taxane-based chemotherapy[3].

The approval follows a positive opinion issued in October by the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) and is applicable to all 27 European Union member states plus Iceland, Norway, Northern Ireland and Liechtenstein.

The EC approval was granted based on results from the pivotal Phase III VISION trial, where participants, previously treated with AR pathway inhibition and taxane based chemotherapy, receiving Pluvicto® plus best standard of care (BSoC) had a 38% reduction in the risk of death and a statistically significant reduction (60%) in the risk of radiographic disease progression or death (rPFS) compared to BSoC alone[1]. About a third (30%) of patients with evaluable disease at baseline demonstrated an objective response (per RECIST 1.1) with Pluvicto® plus BSoC, compared to the 2% in the BSoC-alone arm[1].

“Today’s approval of Pluvicto® by the European Commission marks a major milestone for patients with advanced prostate cancer who have few alternative treatments at this stage of their disease,” said Haseeb Ahmad, President Europe, Novartis. “We are excited by the potential of Pluvicto® to bring groundbreaking clinical benefits to these patients, transforming cancer care for the third-most diagnosed cancer globally[4].”

Approximately 473,300 prostate cancer cases and 108,000 prostate cancer-related deaths occurred across Europe in 2020[5]. Patients with metastatic prostate cancer have an approximate 3 in 10 chances of surviving 5 years[6], indicating a high unmet need for new targeted treatment options for these patients[2]. Novartis is committed to addressing this need by reimagining cancer care with radioligand therapy and precision medicine, with a goal to reduce the global disease burden, extend the lives of patients with prostate cancer and elevate current standards of care.

About Pluvicto® (lutetium (^{177}Lu) vipivotide tetraxetan)
Pluvicto® is an intravenous radioligand therapy combining a targeting compound (a ligand) with a therapeutic radionuclide (a radioactive particle, in this case lutetium-177)[1]. After administration into the bloodstream, Pluvicto® binds to target cells, including prostate cancer cells that express PSMA, a transmembrane protein[1]. Once bound, energy emissions from the radioisotope damage the target cells and nearby cells disrupting their ability to replicate and/or triggering cell death[3].

Pluvicto® is approved in the US and other countries including Great Britain and Canada to treat adults with a type of advanced cancer called prostate-specific membrane antigen–positive metastatic castration-resistant prostate cancer (PSMA–positive mCRPC) and who have already been treated with other anticancer treatments (androgen receptor pathway inhibition and taxane-based chemotherapy)[3,7,8].

Novartis is also evaluating opportunities to investigate Pluvicto® radioligand therapy in earlier stages of prostate cancer[9,10].

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 (BSoC) in the investigational arm, versus BSoC in the control arm[1]. 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 arm[1]. The alternate primary endpoints were rPFS and OS[1]. The study enrolled 831 patients[1].

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 men in 112 countries—more than half the world[5].

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.

Novartis and Radioligand Therapy (RLT)
Novartis is reimagining cancer care with radioligand therapy for patients with advanced

cancers. By harnessing the power of radioactive atoms and applying it to advanced cancers, RLT is theoretically able to deliver radiation to target cells anywhere in the body[11,12]. Novartis has established global expertise, specialized supply chain and manufacturing capabilities across its network of radioligand therapy production sites. In order to support growing demand for our RLT platform, we are investing in the expansion of our RLT production capabilities in Millburn, New Jersey (US), Zaragosa (Spain) and Ivrea (Italy), as well as building a new radioligand manufacturing facility in Indianapolis, Indiana (US), that is planned to be operational in 2023. We are continually evaluating additional opportunities to expand capacity.

About Phenotypic Precision Medicine in advanced prostate cancer

Despite advances in prostate cancer care, there is a high unmet need for new targeted treatment options to improve outcomes for patients with mCRPC. More than 80% of patients with prostate cancer highly express a phenotypic biomarker[13] called prostate-specific membrane antigen (PSMA)[13-17], making it a promising diagnostic (through positron emission tomography (PET) scan imaging) and therapeutic target for radioligand therapy[18]. This differs from 'genotypic' precision medicine which targets specific genetic alterations in cancer cells[19].

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About Novartis

Novartis is reimagining medicine to improve and extend people's lives. We deliver high-value medicines that alleviate society's greatest disease burdens through technology leadership in R&D and novel access approaches. In our quest to find new medicines, we consistently rank among the world's top companies investing in research and development. About 108,000 people of more than 140 nationalities work together to bring Novartis products to nearly 800 million people around the world. Find out more at https://www.novartis.com

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