

Novartis Pluvicto™ approved by FDA as first targeted radioligand therapy for treatment of progressive, PSMA-positive metastatic castration-resistant prostate cancer

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- FDA also approved complementary diagnostic imaging agent, Locametz®, after radiolabeling with gallium-68 for the identification of PSMA-positive lesions²
- Metastatic prostate cancer has a 5-year survival rate of less than 30%³; mCRPC patients who progress on multiple lines of therapy have limited treatment options
- FDA approval was based on pivotal Phase III VISION trial, where patients with pre-treated PSMA-positive mCRPC who received Pluvicto plus standard of care had a statistically significant reduction in risk of death¹; both alternate primary endpoints of overall survival and radiographic progression free survival were met¹
- Novartis is committed to reimagining medicine in prostate cancer with targeted radioligand therapy - a type of precision cancer treatment combining a targeting compound (ligand) with a therapeutic radioisotope (a radioactive particle)
- Two pivotal Phase III studies evaluating Pluvicto in earlier lines of treatment for metastatic prostate cancer are underway, with a goal to move into earlier stages of disease

EAST HANOVER, N.J., March 23, 2022 -- Novartis announced today that the US Food and Drug Administration (FDA) approved Pluvicto™ (lutetium Lu 177 vipivotide tetraxetan) (formerly referred to as 177Lu-PSMA-617) for the treatment of adult patients with a certain type of advanced cancer called prostate-specific membrane antigen-positive metastatic castration-resistant prostate cancer (PSMA-positive mCRPC) that has spread to other parts of the body (metastatic)¹. These patients have already been treated with other anti-cancer treatments (androgen receptor pathway inhibition and taxane-based chemotherapy)¹.

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"The approval of Pluvicto is an important clinical advancement for people with progressing mCRPC, as it can significantly improve survival rates for those who have limited treatment options," said Oliver Sartor, MD, Medical Director at Tulane Cancer Center. "Pluvicto is a step forward in the evolution of precision medicine for prostate cancer."

Pluvicto is the first FDA-approved targeted radioligand therapy (RLT) for eligible patients with mCRPC that combines a targeting compound (ligand) with a therapeutic radioisotope (a radioactive particle)¹. Pluvicto is expected to be available to physicians and patients within weeks.

The FDA has also approved Locametz® (kit for the preparation of gallium Ga 68 gozetotide injection)². After radiolabeling, this imaging agent may be used to identify PSMA-positive lesions in adult patients with mCRPC through a positron emission tomography (PET) scan². Gallium-68 labeled Locametz can identify tumor lesions expressing the PSMA biomarker and locate where in the body tumors may have spread (eg, in soft tissue, lymph nodes, or bone), identifying patients eligible for targeted treatment with Pluvicto^{1,2}. PSMA is highly expressed in more than 80 percent of patients with prostate cancer, making it an important phenotypic biomarker for assessing the progression of metastatic prostate cancer¹⁰. Locametz is expected to be available to physicians and patients within weeks.

"With our unique strategy to tackle cancer by leveraging four therapeutic platforms, I am thrilled that with Pluvicto, we are bringing the targeted RLT platform to bear for treating eligible patients with mCRPC," said Susanne Schaffert, PhD, President, Novartis Oncology. "Today's approval builds upon our history in prostate cancer, a devastating disease where we believe our innovation can make a meaningful difference to patients."

FDA approval of Pluvicto is based on the results of the Phase III VISION trial which demonstrated that PSMA-positive mCRPC patients previously treated with androgen receptor (AR) pathway inhibition and taxane-based chemotherapy who received Pluvicto plus standard of care (SOC) had improved overall survival compared to SOC alone¹. Participants treated with Pluvicto plus SOC had a 38% reduction in risk of death and a statistically significant reduction in the risk of radiographic disease progression or death (rPFS) compared to SOC alone¹. Interpretation of the magnitude of the rPFS effect was limited due to a high degree of censoring from early drop out in the control arm¹.

In addition, about a third (30%) of patients with evaluable disease at baseline demonstrated an overall response (per RECIST 1.1) with Pluvicto plus SOC, compared to 2% in the SOC alone arm¹. 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%)¹.

"Prostate cancer is the second leading cause of cancer-related death in Americans with a prostate gland¹³. Although the treatment landscape for mCRPC continues to evolve, there is a high unmet need for additional precision medicine treatment options to improve outcomes for these patients," said Jamie Bearse, CEO and President at ZERO – The End of Prostate Cancer. "The approval of Pluvicto offers new hope to the mCRPC community."

Pluvicto and Locametz are registered products of Advanced Accelerator Applications, the radioligand business of Novartis, approved in the United States for physicians to prescribe to appropriate patients. Additional safety details for [Pluvicto](#) and [Locametz](#), and full Prescribing Information can be found on the Novartis website.

About Pluvicto

Pluvicto™ (lutetium Lu 177 vipivotide tetraxetan) is indicated for the treatment of adult patients with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) who have already been treated with other anticancer treatments (androgen receptor pathway inhibition (ARPI) and taxane-based chemotherapy)¹. It is a type of precision cancer treatment combining a targeting compound (ligand) with a therapeutic radioisotope (a radioactive particle)¹. After administration into the bloodstream, Pluvicto binds to target cells, including prostate cancer cells that express PSMA, a transmembrane protein¹. Once bound, energy emissions from the radioisotope damage the target cells and nearby cells disrupting their ability to replicate and/or triggering cell death¹.

Novartis has submitted marketing authorization for Pluvicto to the European Medicines Agency and other health authorities.

About Locametz

Locametz® (gallium Ga 68 gozetotide), diagnostic kit for radiopharmaceutical injectable preparation is indicated for positron emission tomography (PET) of PSMA-positive lesions with prostate cancer with suspected metastasis who are candidates for initial definitive therapy; with suspected recurrence based on elevated serum prostate-specific antigen (PSA) level; and for selection of patients with metastatic prostate cancer, for whom lutetium Lu 177 vipivotide tetraxetan PSMA-directed therapy is indicated².

Novartis has submitted marketing authorization for Locametz to the European Medicines Agency and other health authorities.

About VISION

VISION is an international, prospective, randomized, open-label, multicenter, phase III study that assessed the efficacy and safety of Pluvicto (lutetium Lu 177 vipivotide tetraxetan) (7.4 GBq administered by IV infusion every 6 weeks for a maximum of 6 cycles) plus investigator-chosen standard of care (SOC) in the investigational arm, versus

SOC 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.

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 biomarker⁹ called prostate specific membrane antigen (PSMA)^{4-6,9,10}, making it a promising diagnostic (through positron emission tomography (PET) scan imaging) and therapeutic target for radioligand therapy¹⁰. This differs from 'genotypic' precision medicine which targets specific genetic alterations in cancer cells⁷.

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 world¹².

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.

Pluvicto Indication

PLUVICTO™ (lutetium Lu 177 vipivotide tetraxetan) is a radiopharmaceutical used to treat adults with an advanced cancer called prostate-specific membrane antigen–positive metastatic castration-resistant prostate cancer (PSMA-positive mCRPC) that has spread to other parts of the body (metastatic), and has already been treated with other anticancer treatments.

Pluvicto Important Safety Information

Use of PLUVICTO involves exposure to radioactivity. Long-term, accruing radiation exposure is associated with increased risk for cancer. To minimize radiation exposure to others following administration of PLUVICTO, patients are advised to limit close contact (less than 3 feet) with household contacts for 2 days or with children and pregnant women for 7 days, to refrain from sexual activity for 7 days, and to sleep in a separate bedroom from household contacts for 3 days, from children for 7 days, or from pregnant women for 15 days.

PLUVICTO may cause low level of blood cell counts. Patients should tell their doctor right away if they develop any new or worsening symptoms, including tiredness or weakness, pale skin, shortness of breath, bleeding or bruising more easily than normal or difficulty to stop bleeding, or frequent infections with signs such as fever, chills, sore throat, or mouth ulcers. PLUVICTO may also cause problems with kidneys. Patients should tell their doctor right away if they develop any new or worsening symptoms, including passing urine less often or passing much smaller amounts of urine than usual.

Before receiving PLUVICTO, patients should tell their doctor if they have low level of blood cell counts (hemoglobin, white blood cell count, absolute neutrophil count, platelet count); if they have or have had tiredness, weakness, pale skin, shortness of breath, bleeding or bruising more easily than normal or difficulty stopping bleeding, or frequent infections with signs such as fever, chills, sore throat, or mouth ulcers (possible signs of myelosuppression); if they have or have had kidney problems; if they have or have had any other type of cancer or treatment for cancer, as PLUVICTO contributes to long-term cumulative radiation exposure; and if they are sexually active, as all radiopharmaceuticals, including PLUVICTO, have the potential to cause harm to an unborn baby. Patients should use effective contraception for intercourse during treatment with PLUVICTO and for 14 weeks after the last dose. PLUVICTO may cause temporary or permanent infertility.

Before administration of PLUVICTO patients should drink plenty of water in order to urinate as often as possible during the first hours after administration.

The most common side effects of PLUVICTO include tiredness, dry mouth, nausea, low red blood cell count, loss of appetite, changes in bowel movements (constipation or diarrhea), vomiting, low blood platelet count, urinary tract infection, weight loss, and abdominal pain.

Please see full Prescribing Information for PLUVICTO at <https://www.novartis.us/sites/www.novartis.us/files/pluvicto.pdf>.

Locametz Indication

LOCAMETZ® (kit for the preparation of gallium Ga 68 gozetotide injection), after radiolabeling with gallium-68, is indicated for positron emission tomography (PET) of prostate-specific membrane antigen (PSMA)-positive lesions in men with prostate cancer:

- with suspected metastasis who are candidates for initial definitive therapy
- with suspected recurrence based on elevated serum prostate-specific antigen (PSA) level
- for selection of patients with metastatic prostate cancer for whom lutetium Lu 177 vipivotide tetraxetan PSMA-directed therapy is indicated

Locametz Important Safety Information

LOCAMETZ PET images can be misinterpreted. Gallium Ga 68 gozetotide may be taken up into other types of cancerous and noncancerous tissue. Corroborating approaches, which may include histopathology, are recommended.

Gallium Ga 68 gozetotide contributes to a patient's long-term cumulative radiation exposure, which is associated with an increased risk of cancer. Safe handling and preparation procedures must be ensured to protect patients and health care workers from unintentional radiation exposure. Patients should be well hydrated prior to administration and urinate immediately prior to and frequently during the first hours after image acquisition to reduce radiation exposure.

Adverse reactions that occurred at a rate of 0.5% or greater in the VISION study were fatigue, nausea, constipation, and vomiting; at a rate less than 0.5%, diarrhea, dry mouth, injection site reactions, and chills.

Please see full Prescribing Information for LOCAMETZ at <https://www.novartis.us/sites/www.novartis.us/files/locametz.pdf>.

Patient Access and Support

Novartis is committed to helping ensure that our medicines are accessible to as many patients as possible. With the approval of Pluvicto in the United States, we offer support and services to address a range of needs through AAA PatientCONNECT™. AAA PatientCONNECT™ is a support center staffed by dedicated case managers who can help eligible patients throughout their treatment journey to start and stay on treatment. Patients or providers can call 1-844-638-7222 or visit AAApatientconnect.com to enroll and learn more about AAA PatientCONNECT™.

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About Advanced Accelerator Applications

Advanced Accelerator Applications (AAA), a Novartis company, specializes in targeted radioligand therapies and precision imaging radioligands for oncology indications. We are committed to transforming patients' lives by leading innovation in nuclear medicine. AAA has a legacy as a leader in radiopharmaceutical drugs for Positron Emission tomography (PET) and Single-Photon Emission Computed Tomography (SPECT) diagnostic imaging. For more information, please visit: <https://www.adacap.com>.

About Novartis

Located in East Hanover, NJ Novartis Pharmaceuticals Corporation – an affiliate of 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 employs nearly 15,500 people in the United States. For more information, please visit <https://www.novartis.us>.

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List of links present in page

1. <https://qa1.novartis.us/news/media-releases/novartis-pluvictotm-approved-fda-first-targeted-radioligand-therapy-treatment-progressive-psma-positive-metastatic-castration-resistant-prostate-cancer>
2. <https://www.multivu.com/players/English/8969951-novartis-pluvicto-fda-approval-prostate-cancer/>
3. <https://c212.net/c/link/?t=0&l=en&o=3471040-1&h=667812225&u=https%3A/www.novartis.us/sites/www.novartis.us/files/pluvicto.pdf&a=Pluvicto>
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13. <mailto:media.relations@novartis.com>
14. <https://seer.cancer.gov/statfacts/html/prost.html>
15. <https://www.cancer.org/cancer/prostate-cancer/about/key-statistics.html>
16. <mailto:media.relations@novartis.com>
17. <mailto:julie.masow@novartis.com>
18. <mailto:rachel.levine@novartis.com>
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