Category

Best Pharmaceutical Product

General Information

Company Name *

Novartis

Product/Solution Name *

PLUVICTO®

Compound/Tech Name*

lutetium Lu 177 vipivotide tetraxetan

Trade Name *

PLUVICTO®

Corporate Name *

PLUVICTO®

Date of Approval *

2022-03-23

Indications *

PLUVICTO is indicated for the treatment of adult patients with prostate-specific membrane antigen (PSMA)-positive
metastatic castration-resistant prostate cancer (mCRPC) who have been treated with androgen receptor pathway inhibitor
(ARPI) therapy, and
• are considered appropriate to delay taxane-based chemotherapy, or
• have received prior taxane-based chemotherapy.

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454

Therapeutic Areas *

Oncology (Genitourinary Cancers)

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497

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Attached Files:

- Pluvicto US label_updated March 2025.pdf

Background information and need for drug / device
(please be as specific as possible in your description; limit 500 words)

.This year in the US, about 1 in 8 men will be diagnosed with prostate cancer and 1 in 44 men will die from prostate cancer. In Europe, 470,000 new cases with 110,000 deaths were estimated for 2020. More than half of these lives are claimed within 2 years of mCRPC diagnosis, and more than half of patients will only receive one life-prolonging therapy.[Shore; Freedland] In the face of this growing crisis, innovation is essential.

Traditional treatment options after metastatic progression, like chemotherapy and androgen receptor inhibitors, are not targeted and/or are limited to earlier use, potential systemic toxicities, and cross-resistance. Chemotherapy is generally regarded as effective but with potentially significant deterioration of quality of life (QoL).

There is an urgent need for novel targeted treatments to provide additional options in mCRPC. More than 80% of prostate cancers overexpress PSMA-a biomarker target hiding in plain sight.

Enter PLUVICTO: a radioligand therapy (RLT) that is comprised of a radionuclide and PSMA-targeting ligand, unleashing DNA-breaking radiation directly into PSMA+ cells. This breakthrough offers hope to most patients with mCRPC-PLUVICTO is where precision meets power.

PLUVICTO received its first US and European approval in men with PSMA+ mCRPC after ARPI and taxane therapy. Approval was based on positive results from the landmark VISION trial, the first to investigate an RLT in mCRPC. VISION (NCT03511664) was an international, prospective, open-label, multicenter, randomized Phase 3 study of PLUVICTO + SoC vs SoC alone in men with PSMA+ mCRPC previously treated with at least 1 ARPI and 1-2 taxanes.

After PLUVICTO achieved positive outcomes in the post-ARPI, post-chemotherapy mCRPC setting, Novartis recognized the opportunity to help more patients earlier. Men treated with chemotherapy experience significant QoL deterioration caused by rapid disease progression. With this in mind, Novartis rapidly initiated the next Phase 3 trial called PSMAfore.

PSMAfore (NCT04689828) was an international, prospective, open-label, multicenter, randomized study of PLUVICTO vs a change in ARPI in patients with PSMA+ mCRPC who progressed after 1 ARPI and were considered appropriate to delay taxane-based chemotherapy.

With significant efficacy and a consistent and favorable safety profile, PLUVICTO received a second approval in the US, now becoming a pioneer as the first and only PSMA-targeted RLT approved in the post-ARPI, pre-chemotherapy setting. [PI] This allowed PLUVICTO to triple the number of eligible patients and also enabled use in the oncology and urology community beyond academic medical centers.

These studies established PLUVICTO as the first and only PSMA-targeted RLT to improve efficacy and have a well-tolerated and manageable safety profile both pre- and post-chemotherapy in mCRPC. The

new indication was included in the NCCN guidelines in an ad-hoc meeting within 2 weeks of US approval (Category 2a useful in certain circumstances).

With each trial, PLUVICTO aims to treat appropriate patients earlier in their prostate cancer journey. Interim positive results were recently announced for PSMAddition, which enrolled men with PSMA+ hormone-sensitive prostate cancer, an even larger patient population.

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History of the development of the solution/product *
(please be as specific as possible in your description; 500 words)

Radioligand therapies, like PLUVICTO, are the result of decades of innovation and research. One of the first targeted radiotherapies was iodine-131 for the treatment of thyroid cancer-developed rationally, based on the naturally occurring, metabolic accumulation of iodine in the thyroid. Scientists have since built onto this concept by engineering RLTs that can specifically target markers expressed in cancers, including PSMA, an actionable target for countless patients with prostate cancers.

The ligand PSMA-617 was initially developed by the German Cancer Research Center, Deutsches Krebsforschungszentrum (DKFZ), in collaboration with University Hospital Heidelberg. Following initial preclinical development of PSMA-617, the compound was licensed to ABX GmbH in Germany. Endocyte, Inc. assumed responsibility for global development of PSMA-617 in 2017. Novartis acquired Advanced Accelerator Applications in January 2018 and Endocyte, Inc. in December 2018, enabling significant resources to be committed to the clinical development, clinical validation, and commercialization of PLUVICTO.

VISION (NCT03511664), the first pivotal study of PLUVICTO, was conducted in heavily pre-treated patients with PSMA+ mCRPC. Both alternate primary endpoints were met, supporting the first US and European approval of PLUVICTO, with clinically meaningful and statistically significant improvements in OS (38% risk reduction) and rPFS (60% risk reduction) for the PLUVICTO arm (PLUVICTO + SoC) vs control arm (SoC alone). There were no unexpected safety concerns; the most common all-grade AEs (≥20%) were fatigue, dry mouth, nausea, anemia, back pain, arthralgia, decreased appetite, and constipation.

In PSMAfore (NCT04689828), the primary endpoint was met, with a statistically significant and clinically meaningful improvement in rPFS for the PLUVICTO arm (PLUVICTO) vs control arm (a change in ARPI). In the primary analysis, HR=0.41 (95% CI, 0.29-0.56; P<0.0001) and in an updated exploratory analysis, HR=0.49 (95% CI, 0.39-0.61). At the final OS analysis, a positive trend was observed for the PLUVICTO arm towards improved OS (a key secondary endpoint). Safety was consistent with the VISION study.

In the US, these results supported the second US approval of PLUVICTO, meaning patients have the opportunity to receive earlier, targeted treatment with PLUVICTO.

Potentially expanding the patient population even further, PLUVICTO is currently being studied in two ongoing Phase 3 studies. The PSMAddition study is investigating the efficacy and safety of PLUVICTO in patients with PSMA+ hormone-sensitive metastatic prostate cancer, an even earlier patient population. Interim results for PSMAddition were recently announced that PLUVICTO demonstrated statistically significant and clinically meaningful rPFS benefit in this population.

PSMA-DC (Delay Castration) will investigate PLUVICTO in patients with oligometastatic prostate cancer as assessed by PSMA PET. These studies both have potential to bring RLT benefits to a significantly larger group of patients with prostate cancer.

With over 450 unique RLT clinical and preclinical projects in development across a broad range of potential cancers-including genitourinary, gastrointestinal, neurological, lung, breast, hematological, gastroenteropancreatic neuroendocrine tumors (GEP-NETs), and other solid tumors-the future of RLT can transform cancer care.

With each new innovation, more patients can live longer lives doing the things they love with the people they love.

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Why this drug or device is innovative, the broad implications for future research, and/or how it will improve the human condition *

PLUVICTO and innovation are one in the same. First and foremost, the PLUVICTO mechanism of action (MOA) has first-in-class status and can effectively target PSMA, a biomarker widely expressed in prostate cancer. PLUVICTO delivers targeted, ionizing radiation directly to PSMA+ cells, regardless of where they are in the body. This theranostic concept combines diagnostic imaging for PSMA and targeted radiation treatment in a single therapeutic strategy.

With proven efficacy and a favorable safety profile, plus a specialized manufacturing system built to deliver within 5-days, PLUVICTO is effective and widely accessible in the US.

The MOA for PLUVICTO is an innovative approach to cancer treatment that delivers targeted ionizing radiation directly to PSMA+ cells, regardless of where they are in the body.

PLUVICTO is comprised of 2 key components: Lutetium-177, a cytotoxic radionuclide, and PSMA-617, a PSMA-targeting ligand. After binding to PSMA, PLUVICTO is brought into the cell, emitting DNA-breaking radiation within the cell. This results in single- and double-stranded DNA breaks and cell death.

PLUVICTO has been shown to improve outcomes while maintaining QoL for thousands of men with mCRPC. By precisely targeting PSMA+ cells, the aim is to reduce exposure to healthy cells, which can

compromise QoL and create other issues for patients.

The two current approvals of PLUVICTO demonstrate clear, proven clinical benefits, including a manageable safety profile, for radiopharmaceutical intervention in PSMA+ mCRPC both pre- and post-taxane.

Innovation in delivery is essential for PLUVICTO, as RLT manufacturing requires highly specialized associates racing against the clock every day, advancing the Novartis mission of reimagining medicine for patients. Novartis currently has manufacturing sites in New Jersey, Indiana, and soon, a planned expansion to California to keep up with current and future patient needs.

Educational innovation is also a core part of PLUVICTO, which led to the development of the RLT Institute. Novartis launched the RLT Institute to demystify RLT facilities and demonstrate how to use RLT through educational 3D models, videos, and VR goggle capabilities.

In response to marketplace needs, Novartis introduced a patient-ready dose in a pre-filled syringe, now available to all customers in the US. This practical innovation is expected to become the standard in RLT therapy and helps treatment staff and community healthcare providers offer these treatments to their patients.

RLT has established a firm footing in cancer care, with Novartis leading the way. With PLUVICTO alone, more than 20K patients have been treated-in total, Novartis RLTs have reached nearly 40K patients with cancer. An exciting future awaits regarding how far the theranostic concept will take the field of oncology and further enhance patients' lives.

The future also looks bright for RLT innovation at Novartis with more trials planned with PLUVICTO and beyond as Novartis seeks to continue filling key evidence gaps for patients to deliver efficacious medicines with tolerable safety and QoL for patients.

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Please provide appropriate references (PubMed, Abstract, Website) *

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