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Novartis strengthens its position as Pluvicto gets FDA clearance for pre-chemo mCRPC

Market Event Summary

Joan Tur, Ph.D. | April 2025

Pluvicto offers an effective and well-tolerated option for first-line mCRPC

Background

- **Novartis's Pluvicto is a radioligand therapy** that binds to PSMA on tumor cells, delivering beta radiation to damage their DNA.
- Previously, Pluvicto was approved only for metastatic castration-resistant prostate cancer (mCRPC) patients who had received at least one taxane and one androgen receptor pathway inhibitor (ARPI).
- **An unmet need** existed for first-line mCRPC: most patients cannot tolerate or refuse chemotherapy, ARPIs are often ineffective due to prior exposure, and few patients have DNA repair gene alterations to be eligible for PARP inhibitors.

Event

- After delays, **the FDA approved Pluvicto** in March 2025 based on **PSMAfore**, making it the first PSMA-targeted radioligand therapy for pre-taxane mCRPC.
- **The Phase 3 PSMAfore trial** tested Pluvicto vs. a change in ARPI in taxane-naive, mCRPC patients previously treated with an ARPI.
- **Pluvicto reduced the risk of progression or death** by 59%, with a median PFS of 11.6 vs. 5.6 months. **OS was confounded** by a 60% crossover from the control arm (HR 0.9; HR 0.6 adjusted for crossover).
- **Pluvicto was very well tolerated**, with fewer grade 3-5 adverse events than the ARPI change arm.

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Clarivate's takeaways

Unlocking a lucrative market

This label expansion allows patients to get Pluvicto without prior chemotherapy, tripling its eligible patient pool. With high efficacy and tolerability, we expect robust uptake—coupled with its high price, Pluvicto is set to become the top-selling agent in first-line mCRPC by 2033.

Ex-U.S. regulatory uncertainty and market access barriers

While the FDA has approved the label expansion, uncertainty remains in other regions due to the lack of clear survival benefit and the use of a weak control arm (ARPIchange) in PSMAfore. These factors raise concerns about how European regulators will assess Pluvicto's value. Moreover, major European payers (e.g., in U.K., Spain) have declined reimbursement under the current label, creating significant barriers to market adoption.

What's next? Expanding potential, rising competition

Ongoing trials in earlier disease stages—including PSMAddition and PSMA-DC—could further expand Pluvicto's reach and drive sales higher. Although Pluvicto has the first-mover advantage, competition in the prostate cancer radioligand space is intensifying. Lutetium-based agents like PSMA-I&T and TLX-591 are expected to enter the pre-taxane mCRPC setting, directly challenging Pluvicto, while next-generation radioligand therapies using actinium and other isotopes are advancing into Phase 3 posing a longer-term threat.

About the author

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Dr. Tur is a pharmaceutical industry analyst at Clarivate. He conducts market research and forecasting in various oncology indications, including urologic tumors, colorectal cancer, and hematological malignancies. Dr. Tur has published market assessment articles in *Nature Reviews Drug Discovery*, authored multi-indication reports, and written the flagship *Cortellis Drugs to Watch* reports. Before his tenure at Clarivate, he was an academic researcher specialized in macrophage biology. He holds a Ph.D. in biomedicine, an M.Sc. in immunology, and a B.Sc. in biology from the University of Barcelona.

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