## Pluvicto™ (lutetium Lu 177 vipivotide tetraxetan) – New drug approval

- On March 23, 2022, Novartis announced the FDA approval of Pluvicto (lutetium Lu 177 vipivotide tetraxetan), 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 (AR) pathway inhibition and taxane-based chemotherapy.

- Pluvicto is the first FDA-approved targeted radioligand therapy that combines a targeting compound (ligand) with a therapeutic radioisotope (a radioactive particle).

- The efficacy of Pluvicto was established in VISION, a randomized, open-label study in 831 patients with progressive, PSMA-positive mCRPC. Patients received Pluvicto plus best standard of care (BSoC) or BSoC alone. The major efficacy outcome measures were overall survival (OS) and radiographic progression-free survival (rPFS). An additional efficacy outcome measure included was overall response rate (ORR).

    - Median OS was 15.3 months and 11.3 months for Pluvicto plus BSoC and BSoC alone, respectively (hazard ratio [HR] 0.62, 95% CI: 0.52, 0.74; $p < 0.001$).
    - The ORR was 30% (95% CI: 25, 35) and 2% (95% CI: 0, 6) for Pluvicto plus BSoC and BSoC, respectively ($p < 0.001$).
    - Interpretation of the magnitude of the rPFS effect was limited due to a high degree of censoring from early drop out in the control arm.

- Warnings and precautions for Pluvicto include risk from radiation exposure; myelosuppression; renal toxicity; embryo-fetal toxicity; and infertility.

- The most common adverse reactions (≥ 20%) with Pluvicto use were fatigue, dry mouth, nausea, anemia, decreased appetite, and constipation. The most common laboratory abnormalities (≥ 30%) were decreased lymphocytes, decreased hemoglobin, decreased leukocytes, decreased platelets, decreased calcium, and decreased sodium.

- The recommended Pluvicto dosage is 7.4 GBq (200 mCi) intravenously every 6 weeks for up to 6 doses, or until disease progression, or unacceptable toxicity.

    - Patients with previously treated mCRPC should be selected for treatment with Pluvicto using LOCAMETZ or another approved PSMA-11 imaging agent based on PSMA expression in tumors.
    - Pluvicto is a radiopharmaceutical and should be handled with appropriate safety measures to minimize radiation exposure.

    - Novartis plans to launch Pluvicto within weeks. Pluvicto will be available as a 1,000 MBq/mL (27 mCi/mL) single-dose vial.