Enhertu® (trastuzumab deruxtecan) – Expanded indication

- On January 27, 2025, AstraZeneca and Daiichi Sankyo announced the FDA approval of Enhertu (trastuzumab deruxtecan), for the treatment of adult patients with **unresectable or metastatic hormone receptor (HR)-positive, HER2-low (IHC 1+ or IHC 2+/ISH-) or HER2-ultralow (IHC 0 with membrane staining) breast cancer**, as determined by an FDA-approved test, that has progressed on one or more endocrine therapies in the metastatic setting.

- Enhertu has several other approvals across breast cancer, non-small cell lung cancer, gastric cancer, and solid tumors. Refer to the drug label for complete listing of its indications and uses.

- The approval of Enhertu for the expanded indication was based on DESTINY-Breast06, a randomized, open-label study in 866 adult patients with advanced or metastatic HR-positive breast cancer with HER2-low (IHC 1+ or IHC 2+/ISH-) or HER2-ultralow (IHC 0 with membrane staining) expression. Patients were randomized to receive either Enhertu or physician's choice of single agent chemotherapy. The major outcome measure was progression-free survival (PFS) in patients with HER2-low breast cancer. Additional outcome measures were PFS assessed in the overall population, overall survival (OS) in HER2-low patients, and OS in the overall population.

    - In the HER-2 low population, median PFS was 13.2 months and 8.1 months in the Enhertu and chemotherapy arms, respectively (hazard ratio [HR] 0.62, 95% CI: 0.52, 0.75; $p < 0.0001$).
    - In the overall population, median PFS was 13.2 months and 8.1 months in the Enhertu and chemotherapy arms, respectively (HR 0.64, 95% CI: 0.54, 0.76; $p < 0.0001$).
    - At the time of the PFS final analysis, OS data was immature, and a total of 335 (39%) of patients had died across both study arms in the overall population.

- Enhertu carries a boxed warning for interstitial lung disease and embryo-fetal toxicity.

- The recommended dose of Enhertu for the treatment of breast cancer is **5.4 mg/kg given as an intravenous infusion once every 3 weeks** (21-day cycle) until disease progression or unacceptable toxicity.

    - Refer to the Enhertu drug label for dosing for all its other indications.