

To estimate the **Potential Peak Sales** for fam-trastuzumab deruxtecan-nxki (Enhertu) in the specified indication (unresectable or metastatic HER2-low breast cancer) in the US, EU5 (France, Germany, Italy, Spain, UK), China, and Japan, as well as the **\$ value of 1% share of treated patients** in these geographies, we need to follow a structured approach based on available data, assumptions, and market analysis. Since exact numbers may not be publicly available, I will outline the methodology and provide reasonable estimates based on typical market dynamics for oncology drugs.

## **Step 1: Define the Target Population**

The indication is for adult patients with **unresectable or metastatic HER2-low breast cancer (IHC 1+ or IHC 2+/ISH-)** who have received prior chemotherapy in the metastatic setting or had recurrence during or within six months of adjuvant chemotherapy.

- **HER2-low breast cancer** accounts for approximately 40-50% of all breast cancer cases (as opposed to HER2-positive, which is ~15-20%, and triple-negative, ~10-15%).

- **Metastatic breast cancer (mBC)** represents about 5-10% of breast cancer patients at initial diagnosis, with an additional 20-30% of early-stage patients progressing to metastatic disease over time.

- For simplicity, we will focus on the prevalent population of metastatic HER2-low patients eligible for treatment in a given year.

#### Incidence and Prevalence Estimates (Annual Eligible Patients):

- **US:** Breast cancer incidence is ~280,000 new cases/year. Approximately 40-50% are HER2-low (~112,000-140,000). Of these, ~10-15% are metastatic at diagnosis or progress to metastatic (~11,200-21,000). Assuming ~50% have prior chemotherapy or recurrence within 6 months, the eligible population is ~5,600-10,500 patients/year.

- **EU5:** Combined breast cancer incidence is ~350,000/year. HER2-low (~140,000-175,000), metastatic (~14,000-26,250), eligible after prior therapy (~7,000-13,125 patients/year).

- **China:** Breast cancer incidence is ~300,000/year. HER2-low (~120,000-150,000), metastatic (~12,000-22,500), eligible (~6,000-11,250 patients/year).

- **Japan:** Breast cancer incidence is ~90,000/year. HER2-low (~36,000-45,000), metastatic (~3,600-6,750), eligible (~1,800-3,375 patients/year).

**Total Eligible Patients (Midpoint Estimates):**

- US: ~8,000 patients/year

- EU5: ~10,000 patients/year

- China: ~8,500 patients/year

- Japan: ~2,500 patients/year

- **Total:** ~29,000 patients/year

## **Step 2: Market Penetration (20%-30% Share of Treated Patients)**

The problem assumes a 20%-30% share of treated patients for Enhertu in this indication. This accounts for competition, physician adoption, and patient eligibility.

- **Low-end (20%):**  $29,000 * 0.2 = 5,800$  treated patients/year
- **High-end (30%):**  $29,000 * 0.3 = 8,700$  treated patients/year

**Breakdown by Geography (Midpoint of 25%):**

- US:  $8,000 * 0.25 = 2,000$  treated patients/year
- EU5:  $10,000 * 0.25 = 2,500$  treated patients/year
- China:  $8,500 * 0.25 = 2,125$  treated patients/year
- Japan:  $2,500 * 0.25 = 625$  treated patients/year

### **Step 3: Pricing and Treatment Duration**

Enhertu is a high-cost oncology drug administered intravenously. Pricing varies by region due to healthcare systems and reimbursement policies.

- **US:** Annual cost of Enhertu is approximately \$150,000-\$180,000 per patient (based on reported costs for similar antibody-drug conjugates like trastuzumab-based therapies).
- **EU5:** Pricing is typically 30-50% lower than the US due to negotiations and health technology assessments. Assume ~\$90,000-\$120,000/year.
- **Japan:** Pricing is often aligned with EU levels, ~\$90,000-\$120,000/year.
- **China:** Pricing is significantly lower due to market access challenges and local policies. Assume ~\$30,000-\$50,000/year.
- **Treatment Duration:** Patients with metastatic breast cancer may receive treatment for 6-12 months on average, depending on progression-free survival (PFS). Enhertu has shown a median PFS of ~10 months in trials (e.g., DESTINY-Breast04). For simplicity, assume annual cost reflects full-year treatment.

**Average Annual Cost per Patient (Midpoint Estimates):**

- US: \$165,000
- EU5: \$105,000
- China: \$40,000
- Japan: \$105,000

### **Step 4: Potential Peak Sales Calculation**

Peak sales are calculated as the number of treated patients multiplied by the annual cost per patient.

#### At 25% Market Share (Midpoint):

- **US:**  $2,000 \text{ patients} * \$165,000 = \$330 \text{ million/year}$
- **EU5:**  $2,500 \text{ patients} * \$105,000 = \$262.5 \text{ million/year}$
- **China:**  $2,125 \text{ patients} * \$40,000 = \$85 \text{ million/year}$

- **Japan:** 625 patients \* \$105,000 = **\$65.6 million/year**
- **Total Peak Sales (25%):** \$330M + \$262.5M + \$85M + \$65.6M = **~\$743 million/year**

#### Range (20%-30% Market Share):

- **20% Share:** ~5,800 patients \* weighted average cost (~\$94,000 across regions) = **~\$545 million/year**
- **30% Share:** ~8,700 patients \* weighted average cost (~\$94,000) = **~\$818 million/year**

**Potential Peak Sales Range: \$545 million to \$818 million/year**

## **Step 5: \$ Value of 1% Share of Treated Patients**

A 1% share of treated patients corresponds to 1% of the total eligible patient population (29,000 patients) = **290 patients/year**.

**Value of 1% Share by Geography** (using midpoint pricing):

- **US:** 80 patients \* \$165,000 = **\$13.2 million/year**
- **EU5:** 100 patients \* \$105,000 = **\$10.5 million/year**
- **China:** 85 patients \* \$40,000 = **\$3.4 million/year**
- **Japan:** 25 patients \* \$105,000 = **\$2.6 million/year**
- **Total Value of 1% Share:** \$13.2M + \$10.5M + \$3.4M + \$2.6M = **~\$29.7 million/year**

## **Final Answer:**

- **Potential Peak Sales for Enhertu** in unresectable or metastatic HER2-low breast cancer (20%-30% market share) across the US, EU5, China, and Japan: **\$545 million to \$818 million per year**.
- **\$ Value of 1% Share of Treated Patients** across these geographies: **~\$29.7 million per year**.

## **Notes:**

1. These estimates are based on assumptions about patient numbers, pricing, and market penetration. Real-world data may differ due to competition (e.g., other HER2-targeted therapies), reimbursement challenges, or changes in treatment paradigms.
2. Peak sales could be higher if Enhertu gains broader adoption or if pricing increases; conversely, they could be lower if access is restricted in markets like China.
3. The analysis assumes a steady-state eligible population and does not account for growth in incidence or changes in treatment duration over time.