

To estimate the **Potential Peak Sales** for fam-trastuzumab deruxtecan-nxki (Enhertu) in the indication of locally advanced or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma in the US, EU5 (Germany, France, Italy, Spain, UK), China, and Japan, as well as the **\$ value of a 1% share of treated patients** in these geographies, we need to follow a structured approach. Since specific data such as exact patient numbers, pricing, and penetration rates may not be fully available, I will outline the methodology, use reasonable assumptions based on available data, and provide a framework for the calculation. If you have specific data points (e.g., exact patient numbers or pricing), they can be incorporated for more precision.

## **Step 1: Define Key Parameters**

1. **Target Patient Population:** Estimate the number of eligible patients with locally advanced or metastatic HER2-positive gastric or GEJ adenocarcinoma who have received a prior trastuzumab-based regimen.
2. **Market Share:** Assume a 20% to 30% share of treated patients as given in the query.
3. **Pricing:** Estimate the annual cost of treatment per patient for Enhertu in each geography (pricing varies by region due to healthcare systems and negotiations).
4. **Peak Sales:** Calculate potential peak sales based on patient population, market share, and pricing.
5. **Value of 1% Share:** Calculate the monetary value of treating 1% of the eligible patient population.

## **Step 2: Estimate Eligible Patient Population**

HER2-positive gastric or GEJ adenocarcinoma accounts for approximately 15-20% of all gastric cancer cases. Additionally, we are focusing on locally advanced or metastatic patients who have progressed on a trastuzumab-based regimen (second-line or later).

#### Incidence and Prevalence Data (Approximate Annual Eligible Patients):

### **- US:**

- Gastric cancer incidence: ~27,000 new cases/year.
- HER2-positive: ~20% (5,400 patients).
- Metastatic/advanced at diagnosis or progression: ~60% (3,240 patients).
- Post-trastuzumab (2L+): ~50% of advanced cases (1,620 patients).

### **- EU5 (Germany, France, Italy, Spain, UK):**

- Gastric cancer incidence: ~60,000 new cases/year.
- HER2-positive: ~20% (12,000 patients).
- Metastatic/advanced: ~60% (7,200 patients).
- Post-trastuzumab (2L+): ~50% (3,600 patients).

### **- China:**

- Gastric cancer incidence: ~400,000 new cases/year (highest globally).
- HER2-positive: ~15-20% (60,000-80,000 patients).

- Metastatic/advanced: ~60% (36,000-48,000 patients).
- Post-trastuzumab (2L+): ~30% (lower access to trastuzumab; ~10,800-14,400 patients).
- **Japan:**
  - Gastric cancer incidence: ~130,000 new cases/year.
  - HER2-positive: ~20% (26,000 patients).
  - Metastatic/advanced: ~60% (15,600 patients).
  - Post-trastuzumab (2L+): ~50% (7,800 patients).

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

- US: 1,620
- EU5: 3,600
- China: 12,600 (midpoint of 10,800-14,400)
- Japan: 7,800
- **Total:** ~25,620 patients annually across all geographies.

### **Step 3: Estimate Pricing per Patient per Year**

Pricing for Enhertu varies by region due to differences in healthcare systems, reimbursement policies, and negotiations. Based on publicly available data and analyst reports:

- **US:** ~\$150,000–\$180,000 per patient per year (list price; net price after discounts may be lower).
- **EU5:** ~\$100,000–\$120,000 per patient per year (varies by country due to negotiations).
- **China:** ~\$50,000–\$70,000 per patient per year (lower due to pricing controls and potential inclusion in NRDL with discounts).
- **Japan:** ~\$100,000–\$130,000 per patient per year (similar to EU due to advanced healthcare system).

#### **Assumed Average Annual Cost per Patient (midpoint):**

- US: \$165,000
- EU5: \$110,000
- China: \$60,000
- Japan: \$115,000

### **Step 4: Calculate Potential Peak Sales (20%-30% Market Share)**

Peak sales are calculated as:

**Peak Sales = Eligible Patients × Market Share × Annual Cost per Patient**

#### At 20% Market Share:

- **US:**  $1,620 \times 20\% \times \$165,000 = \$53.5 \text{ million}$

- **EU5:**  $3,600 \times 20\% \times \$110,000 = \$79.2 \text{ million}$
- **China:**  $12,600 \times 20\% \times \$60,000 = \$151.2 \text{ million}$
- **Japan:**  $7,800 \times 20\% \times \$115,000 = \$179.4 \text{ million}$
- **Total Peak Sales (20% share):**  $\$53.5\text{M} + \$79.2\text{M} + \$151.2\text{M} + \$179.4\text{M} = \$463.3 \text{ million}$

#### At 30% Market Share:

- **US:**  $1,620 \times 30\% \times \$165,000 = \$80.2 \text{ million}$
- **EU5:**  $3,600 \times 30\% \times \$110,000 = \$118.8 \text{ million}$
- **China:**  $12,600 \times 30\% \times \$60,000 = \$226.8 \text{ million}$
- **Japan:**  $7,800 \times 30\% \times \$115,000 = \$269.1 \text{ million}$
- **Total Peak Sales (30% share):**  $\$80.2\text{M} + \$118.8\text{M} + \$226.8\text{M} + \$269.1\text{M} = \$694.9 \text{ million}$

**Potential Peak Sales Range: \$463 million to \$695 million annually** across the US, EU5, China, and Japan for this indication.

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

The value of a 1% share is calculated as:

**Value of 1% Share = Eligible Patients  $\times$  1%  $\times$  Annual Cost per Patient**

- **US:**  $1,620 \times 1\% \times \$165,000 = \$2.67 \text{ million}$
- **EU5:**  $3,600 \times 1\% \times \$110,000 = \$3.96 \text{ million}$
- **China:**  $12,600 \times 1\% \times \$60,000 = \$7.56 \text{ million}$
- **Japan:**  $7,800 \times 1\% \times \$115,000 = \$8.97 \text{ million}$
- **Total Value of 1% Share:**  $\$2.67\text{M} + \$3.96\text{M} + \$7.56\text{M} + \$8.97\text{M} = \$23.16 \text{ million}$

## **Final Answer:**

**1. Potential Peak Sales for fam-trastuzumab deruxtecan-nxki (Enhertu)** in the indication of locally advanced or metastatic HER2-positive gastric or GEJ adenocarcinoma (assuming 20%-30% market share):

- **US, EU5, China, Japan Combined: \$463 million to \$695 million annually**
- Breakdown by region (20%-30% range):
- US: \$53.5M–\$80.2M
- EU5: \$79.2M–\$118.8M
- China: \$151.2M–\$226.8M
- Japan: \$179.4M–\$269.1M

## **2. \$ Value of 1% Share of Treated Patients:**

**- US, EU5, China, Japan Combined: \$23.16 million**

- Breakdown by region:

- US: \$2.67M

- EU5: \$3.96M

- China: \$7.56M

- Japan: \$8.97M

## **Notes and Caveats:**

- These estimates are based on assumptions for patient numbers, pricing, and market share. Actual figures may vary based on real-world data, competition (e.g., other HER2-targeted therapies), reimbursement decisions, and market access.

- China and Japan contribute significantly due to high gastric cancer incidence, though access to expensive biologics like Enhertu may be limited in China.

- Peak sales may take several years to achieve post-launch, depending on adoption rates and regulatory approvals (Enhertu is already approved in the US for this indication as of January 2021; approvals in other regions may vary).

- If you have specific data on patient numbers, pricing, or market dynamics, these estimates can be refined further.