

To estimate the **Potential Peak Sales** for fam-trastuzumab deruxtecan-nxki (Enhertu) in the indication of unresectable or metastatic non-small cell lung cancer (NSCLC) with HER2 mutations 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. Since specific sales data or patient numbers for this drug in this indication are not provided, we will make reasonable assumptions based on epidemiology, market dynamics, and publicly available information about NSCLC and HER2 mutations. Here's the step-by-step methodology and estimation:

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

- **Indication:** Unresectable or metastatic NSCLC with activating HER2 (ERBB2) mutations, post-prior systemic therapy.

- **Epidemiology of NSCLC:**

- NSCLC accounts for ~85% of all lung cancer cases.

- HER2 mutations occur in approximately 2-4% of NSCLC cases (based on literature and studies like those published in *\*Nature Reviews Cancer\** and *\*Journal of Thoracic Oncology\**).

- We will assume an average of **3% prevalence of HER2 mutations** in NSCLC for this analysis.

- **Annual Incidence of NSCLC** (estimated new cases per year, rounded for simplicity):

- US: ~200,000 new lung cancer cases, of which ~170,000 are NSCLC.

- EU5: ~250,000 new NSCLC cases (combined across France, Germany, Italy, Spain, UK).

- China: ~700,000 new NSCLC cases (due to high smoking rates and population size).

- Japan: ~100,000 new NSCLC cases.

- **HER2-Mutant NSCLC Population** (3% of NSCLC cases):

- US:  $170,000 * 0.03 = \sim 5,100$  patients.

- EU5:  $250,000 * 0.03 = \sim 7,500$  patients.

- China:  $700,000 * 0.03 = \sim 21,000$  patients.

- Japan:  $100,000 * 0.03 = \sim 3,000$  patients.

- **Total across geographies:** ~36,600 patients annually.

- **Eligible Patients (post-prior systemic therapy):**

- Assume ~50% of HER2-mutant NSCLC patients are in advanced stages (unresectable/metastatic) and have received prior systemic therapy.

- Eligible population:

- US:  $5,100 * 0.5 = \sim 2,550$  patients.

- EU5:  $7,500 * 0.5 = \sim 3,750$  patients.

- China:  $21,000 * 0.5 = \sim 10,500$  patients.

- Japan:  $3,000 * 0.5 = \sim 1,500$  patients.

- **Total eligible patients:** ~18,300 patients.

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

- Given Enhertu is the **first approved drug** for HER2-mutant NSCLC, it may achieve a significant market share, especially in a niche population with high unmet need.

- Assume a **peak market share of 20%-30% of eligible treated patients** (midpoint of 25% for calculations).

### **Treated Patients at Peak Share (25%):**

- US:  $2,550 * 0.25 = \sim 640$  patients.
- EU5:  $3,750 * 0.25 = \sim 940$  patients.
- China:  $10,500 * 0.25 = \sim 2,625$  patients.
- Japan:  $1,500 * 0.25 = \sim 375$  patients.
- **Total treated patients at peak:** ~4,580 patients.

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## **Step 3: Pricing and Annual Cost per Patient**

- Enhertu is a high-cost targeted therapy (antibody-drug conjugate). Based on its pricing in other indications (e.g., HER2-positive breast cancer), the annual cost per patient is estimated as follows (in USD):

- US: ~\$150,000 per year (based on typical oncology drug pricing).
- EU5: ~\$100,000 per year (lower due to pricing negotiations and healthcare systems).
- China: ~\$50,000 per year (significant discounts due to market access challenges and local pricing policies).
- Japan: ~\$120,000 per year (slightly lower than the US but higher than EU5 due to reimbursement policies).
- These are rough estimates and may vary based on treatment duration, dosing, and local market dynamics.

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

Peak sales are calculated as the number of treated patients at peak share multiplied by the annual cost per patient in each geography.

### **US:**

- $640 \text{ patients} * \$150,000 = \text{\$96 million}.$

- **EU5:**

- 940 patients \* \$100,000 = **\$94 million.**

- **China:**

- 2,625 patients \* \$50,000 = **\$131.25 million.**

- **Japan:**

- 375 patients \* \$120,000 = **\$45 million.**

- **Total Potential Peak Sales:**

- \$96M (US) + \$94M (EU5) + \$131.25M (China) + \$45M (Japan) = **\$366.25 million annually.**

**Range for Peak Sales (based on 20%-30% share):**

- At 20% share: ~\$293 million.

- At 30% share: ~\$439.5 million.

- **Midpoint (25% share): \$366.25 million.**

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

A 1% share of treated patients corresponds to 1% of the eligible patient population in each geography, multiplied by the annual cost per patient.

- **Eligible Patients (1% share):**

- US: 2,550 \* 0.01 = 25.5 patients.

- EU5: 3,750 \* 0.01 = 37.5 patients.

- China: 10,500 \* 0.01 = 105 patients.

- Japan: 1,500 \* 0.01 = 15 patients.

- **\$ Value of 1% Share:**

- US: 25.5 \* \$150,000 = **\$3.825 million.**

- EU5: 37.5 \* \$100,000 = **\$3.75 million.**

- China: 105 \* \$50,000 = **\$5.25 million.**

- Japan: 15 \* \$120,000 = **\$1.8 million.**

- **Total \$ Value of 1% Share Across Geographies:**

- \$3.825M (US) + \$3.75M (EU5) + \$5.25M (China) + \$1.8M (Japan) = **\$14.625 million.**

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## **Final Answer**

1. **Potential Peak Sales for Fam-trastuzumab deruxtecan-nxki** in HER2-mutant NSCLC (assuming 20%-30% market share):

- **Range:** \$293 million to \$439.5 million annually.
- **Midpoint (25% share): \$366.25 million annually.**
- Breakdown by geography (at 25% share):
- US: \$96 million.
- EU5: \$94 million.
- China: \$131.25 million.
- Japan: \$45 million.

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

- US: \$3.825 million.
- EU5: \$3.75 million.
- China: \$5.25 million.
- Japan: \$1.8 million.
- **Total across geographies: \$14.625 million.**

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## **Notes and Caveats**

- These estimates are based on assumptions about epidemiology, pricing, and market penetration. Real-world data may differ due to factors like competition, reimbursement, patient access, and treatment duration.
- Pricing in China is highly variable due to government negotiations and volume-based procurement policies.
- Peak sales may take several years to achieve post-launch as awareness, diagnosis rates (HER2 testing), and adoption increase.
- The analysis assumes annual incidence rather than prevalence; if patients are treated over multiple years, the eligible population and sales potential could be higher.