

To estimate the **Potential Peak Sales** for the drug combination of **trastuzumab and capecitabine** (along with TUKYSA, as per the FDA approval) in the indication of advanced unresectable or metastatic HER2-positive breast cancer 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 market penetration may not be fully available, I will outline the methodology and provide a reasonable estimate based on publicly available information, assumptions, and industry benchmarks.

Step 1: Define the Target Patient Population

The indication is for **advanced unresectable or metastatic HER2-positive breast cancer**, including patients with brain metastases, who have received one or more prior anti-HER2-based regimens. HER2-positive breast cancer accounts for approximately **15-20% of all breast cancer cases**.

Estimated Incidence and Prevalence of HER2-Positive Metastatic Breast Cancer

- **US**: ~3.2 million breast cancer patients (prevalence); ~40,000-50,000 new metastatic cases annually, of which ~15-20% are HER2-positive (~6,000-10,000 new cases). Prevalence of metastatic HER2-positive patients is estimated at ~20,000-30,000.
- **EU5**: Combined population is roughly similar to the US (~330 million). Prevalence of metastatic HER2-positive breast cancer is estimated at ~20,000-30,000.
- **China**: Larger population (~1.4 billion), but lower diagnosis rates and access to treatment. Prevalence of metastatic HER2-positive breast cancer is estimated at ~30,000-50,000.
- **Japan**: Smaller population (~125 million), but high diagnosis rates. Prevalence of metastatic HER2-positive breast cancer is estimated at ~5,000-10,000.

Since the indication specifies patients who have received **prior anti-HER2 regimens**, we can assume this is a **second-line or later treatment setting**, reducing the eligible patient population by ~50-60% (as many patients may not progress to second-line or may not be eligible due to other factors). Thus, the eligible population is roughly:

- US: ~10,000-15,000
- EU5: ~10,000-15,000
- China: ~15,000-25,000
- Japan: ~2,500-5,000
- **Total**: ~37,500-60,000 patients.

Treated Patient Share

Assuming a **20-30% market share** of treated patients for this combination therapy (considering competition from other anti-HER2 therapies like pertuzumab, ado-trastuzumab emtansine (T-DM1), and emerging therapies), the number of treated patients with this combination is:

- US: ~2,000-4,500
- EU5: ~2,000-4,500

- China: ~3,000-7,500
- Japan: ~500-1,500
- **Total:** ~7,500-18,000 patients.

Step 2: Estimate Annual Treatment Cost

The cost of therapy varies by geography due to differences in pricing, healthcare systems, and reimbursement. The combination includes **TUKYSA (tucatinib)**, **trastuzumab**, and **capecitabine**. Below are rough estimates of annual costs per patient (based on publicly available data and assumptions):

- **TUKYSA (tucatinib):** ~\$100,000-\$150,000 per year in the US (based on pricing for novel targeted therapies).
- **Trastuzumab (Herceptin or biosimilars):** ~\$50,000-\$70,000 per year in the US (lower in EU5, China, and Japan due to biosimilars and pricing controls).
- **Capecitabine (generic):** ~\$5,000-\$10,000 per year in the US (lower in other regions).

Total Annual Cost per Patient (Combination Therapy):

- US: ~\$155,000-\$230,000
- EU5: ~\$80,000-\$120,000 (lower due to pricing negotiations and biosimilars)
- China: ~\$40,000-\$60,000 (lower access and pricing)
- Japan: ~\$100,000-\$150,000 (similar to US but slightly lower due to pricing controls)

Step 3: Calculate Potential Peak Sales

Peak sales are calculated by multiplying the number of treated patients by the annual cost per patient in each geography.

US:

- Treated patients: 2,000-4,500
- Annual cost: \$155,000-\$230,000
- **Peak Sales:** \$310M - \$1,035M

EU5:

- Treated patients: 2,000-4,500
- Annual cost: \$80,000-\$120,000
- **Peak Sales:** \$160M - \$540M

China:

- Treated patients: 3,000-7,500
- Annual cost: \$40,000-\$60,000
- **Peak Sales:** \$120M - \$450M

Japan:

- Treated patients: 500-1,500
- Annual cost: \$100,000-\$150,000
- **Peak Sales:** \$50M - \$225M

Total Potential Peak Sales:

- **Low End:** \$310M (US) + \$160M (EU5) + \$120M (China) + \$50M (Japan) = **\$640M**
- **High End:** \$1,035M (US) + \$540M (EU5) + \$450M (China) + \$225M (Japan) = **\$2,250M**

Potential Peak Sales Range: \$640M - \$2,250M annually across the specified geographies, assuming a 20-30% share of treated patients.

Step 4: Calculate \$ Value of 1% Share of Treated Patients

A 1% share of treated patients corresponds to 1% of the eligible treated population (based on the 20-30% share assumption, we scale to the total eligible population and calculate for 1%).

Total Eligible Population (from Step 1):

- US: 10,000-15,000 → 1% = 100-150 patients
- EU5: 10,000-15,000 → 1% = 100-150 patients
- China: 15,000-25,000 → 1% = 150-250 patients
- Japan: 2,500-5,000 → 1% = 25-50 patients

\$ Value of 1% Share (Annual Cost per Patient x Number of Patients):

- **US:** 100-150 patients x \$155,000-\$230,000 = **\$15.5M - \$34.5M**
- **EU5:** 100-150 patients x \$80,000-\$120,000 = **\$8M - \$18M**
- **China:** 150-250 patients x \$40,000-\$60,000 = **\$6M - \$15M**
- **Japan:** 25-50 patients x \$100,000-\$150,000 = **\$2.5M - \$7.5M**

Total \$ Value of 1% Share Across Geographies:

- **Low End:** \$15.5M (US) + \$8M (EU5) + \$6M (China) + \$2.5M (Japan) = **\$32M**
- **High End:** \$34.5M (US) + \$18M (EU5) + \$15M (China) + \$7.5M (Japan) = **\$75M**

\$ Value of 1% Share of Treated Patients: \$32M - \$75M annually across the specified geographies.

Summary

1. **Potential Peak Sales (20-30% Share of Treated Patients): \$640M - \$2,250M annually** across the US, EU5, China, and Japan.

2. **\$ Value of 1% Share of Treated Patients: \$32M - \$75M annually** across the same geographies.

Caveats and Assumptions

- Patient population estimates are based on general epidemiology data for HER2-positive metastatic breast cancer and may vary.

- Pricing assumptions are approximate and depend on reimbursement, biosimilar competition, and regional pricing policies.

- Market share (20-30%) assumes competition from other therapies (e.g., T-DM1, pertuzumab, neratinib) and potential new entrants.

- Peak sales assume steady-state adoption and do not account for patent expiry or generic/biosimilar erosion.

If you have specific data (e.g., exact patient numbers, pricing, or market share projections), I can refine these calculations further.