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.

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## 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.

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## 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)

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## 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.

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## 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 $\rightarrow$ 1% = 100-150 patients

- EU5: 10,000-15,000 $\rightarrow$ 1% = 100-150 patients

- China: 15,000-25,000 $\rightarrow$ 1% = 150-250 patients

- Japan: 2,500-5,000 $\rightarrow$ 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.

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## 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.