

To estimate the **Potential Peak Sales** for zanidatamab-hrii (Ziihera) in the indication of previously treated, unresectable or metastatic HER2-positive (IHC 3+) biliary tract cancer (BTC) 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 based on available data and reasonable assumptions. Since specific data on zanidatamab-hrii's pricing, market penetration, and exact patient numbers may not be publicly available, I will outline the methodology and use realistic estimates based on epidemiology, market dynamics, and analogous drugs.

Step 1: Define Key Parameters

1. **Target Population:** Estimate the number of eligible patients with previously treated, unresectable or metastatic HER2-positive (IHC 3+) BTC in each geography.
2. **Market Share:** Use the provided range of 20% to 30% share of treated patients.
3. **Pricing:** Estimate the annual cost of treatment per patient based on analogous drugs for rare cancers or HER2-targeted therapies.
4. **Peak Sales:** Calculate peak sales by multiplying the treated patient population by the annual cost of treatment.
5. **1% Share Value:** Calculate the revenue associated with a 1% share of treated patients.

Step 2: Epidemiology of BTC and HER2-Positive Subset

- **Biliary Tract Cancer (BTC)** incidence varies by region. BTC includes cholangiocarcinoma and gallbladder cancer, and it is a rare cancer with poor prognosis.
- **HER2-Positive (IHC 3+):** Approximately 5-10% of BTC patients are HER2-positive (IHC 3+), based on literature for cholangiocarcinoma and gallbladder cancer.
- **Previously Treated, Unresectable or Metastatic:** This subset represents patients who have progressed after first-line therapy (often gemcitabine-based regimens). We assume ~50-60% of BTC patients progress to second-line therapy.

Estimated Annual Incidence of BTC (New Cases per Year):

- **US:** ~12,000-15,000 cases (source: American Cancer Society and literature).
- **EU5:** ~20,000-25,000 cases (scaled based on population and incidence rates similar to US).
- **China:** ~50,000-60,000 cases (higher incidence in East Asia due to risk factors like liver fluke infections).
- **Japan:** ~20,000-25,000 cases (high incidence in East Asia).

Eligible Patient Population (HER2+ and Second-Line):

- Assuming 7.5% of BTC patients are HER2-positive (IHC 3+) and 55% progress to second-line therapy:

- **US:** 12,000 cases x 7.5% x 55% = ~500 patients.
- **EU5:** 22,500 cases x 7.5% x 55% = ~930 patients.
- **China:** 55,000 cases x 7.5% x 55% = ~2,270 patients.
- **Japan:** 22,500 cases x 7.5% x 55% = ~930 patients.
- **Total Eligible Patients Across Geographies:** ~4,630 patients annually.

Step 3: Pricing Assumptions

- Zanidatamab-hrii is a bispecific HER2-directed antibody for a rare cancer indication. Pricing for similar targeted therapies (e.g., trastuzumab, trastuzumab deruxtecan) in oncology is high, especially for rare diseases.

- **Annual Cost per Patient:** Estimated at \$150,000 in the US (based on pricing of similar drugs like Enhertu or Kadcyla for HER2-positive cancers). Adjust for other regions based on healthcare system differences:

- **EU5:** ~\$100,000 (lower due to pricing negotiations and reimbursement policies).
- **China:** ~\$50,000 (significant discounts due to market access challenges and local pricing policies).
- **Japan:** ~\$120,000 (closer to US pricing but slightly lower).

Step 4: Potential Peak Sales Calculation (20%-30% Market Share)

Peak sales are calculated as:

Peak Sales = Eligible Patients x Market Share x Annual Cost per Patient

At 20% Market Share:

- **US:** 500 patients x 20% x \$150,000 = **\$15 million**
- **EU5:** 930 patients x 20% x \$100,000 = **\$18.6 million**
- **China:** 2,270 patients x 20% x \$50,000 = **\$22.7 million**
- **Japan:** 930 patients x 20% x \$120,000 = **\$22.3 million**
- **Total Peak Sales (20% share):** \$15M + \$18.6M + \$22.7M + \$22.3M = **\$78.9 million**

At 30% Market Share:

- **US:** 500 patients x 30% x \$150,000 = **\$22.5 million**
- **EU5:** 930 patients x 30% x \$100,000 = **\$27.9 million**
- **China:** 2,270 patients x 30% x \$50,000 = **\$34.1 million**
- **Japan:** 930 patients x 30% x \$120,000 = **\$33.5 million**

- **Total Peak Sales (30% share):** \$22.5M + \$27.9M + \$34.1M + \$33.5M = **\$118 million**

Range of Potential Peak Sales:

- **\$78.9 million to \$118 million annually** across the US, EU5, China, and Japan, assuming 20%-30% market share.

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

Value of 1% share is calculated as:

Value of 1% Share = Eligible Patients x 1% x Annual Cost per Patient

- **US:** 500 patients x 1% x \$150,000 = **\$0.75 million (\$750,000)**

- **EU5:** 930 patients x 1% x \$100,000 = **\$0.93 million (\$930,000)**

- **China:** 2,270 patients x 1% x \$50,000 = **\$1.14 million (\$1,135,000)**

- **Japan:** 930 patients x 1% x \$120,000 = **\$1.12 million (\$1,116,000)**

- **Total Value of 1% Share Across Geographies:** \$0.75M + \$0.93M + \$1.14M + \$1.12M = **\$3.94 million**

Final Answer

1. **Potential Peak Sales for zanidatamab-hrri** in previously treated, unresectable or metastatic HER2-positive BTC (assuming 20%-30% market share):

- **US, EU5, China, and Japan combined: \$78.9 million to \$118 million annually.**

- Breakdown by region (20%-30% share):

- **US:** \$15M - \$22.5M

- **EU5:** \$18.6M - \$27.9M

- **China:** \$22.7M - \$34.1M

- **Japan:** \$22.3M - \$33.5M

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

- **US:** \$750,000

- **EU5:** \$930,000

- **China:** \$1,135,000

- **Japan:** \$1,116,000

- **Total Across Geographies: \$3.94 million**

Notes and Caveats

- These estimates are based on assumptions about epidemiology, HER2-positivity rates, progression to second-line therapy, pricing, and market penetration. Actual numbers may vary based on real-world data, competition (e.g., other HER2-targeted therapies), reimbursement policies, and uptake rates.
- BTC is a rare cancer, and the eligible patient pool is small, which limits peak sales potential despite high pricing.
- Pricing in China is particularly uncertain due to government-driven price negotiations and inclusion in the National Reimbursement Drug List (NRDL).
- Peak sales may take several years to achieve post-launch as market penetration builds.