

To estimate the **Potential Peak Sales** for zanubrutinib (Brukinsa) in the indication of relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy 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 (e.g., exact patient numbers, pricing, or penetration rates) are not provided, I will use reasonable assumptions based on publicly available information, market research trends, and oncology drug sales patterns. I'll also outline the methodology so you can adjust the numbers based on more precise data if available.

Step 1: Key Assumptions and Methodology

1. **Indication:** Relapsed or refractory follicular lymphoma (FL) after ≥ 2 lines of therapy. This is a niche patient population within non-Hodgkin lymphoma (NHL), as FL is an indolent (slow-growing) cancer, and many patients may not progress to third-line treatment.

2. **Patient Population:**

- FL accounts for ~20-30% of NHL cases.
- Relapsed/refractory patients after ≥ 2 lines of therapy represent a smaller subset (estimated ~10-20% of FL patients).
- Total NHL incidence and prevalence data will be used to estimate the FL patient pool in each geography.

3. **Market Share:** Assuming zanubrutinib captures 20-30% of treated patients in this indication.

4. **Pricing:** Zanubrutinib's annual cost of therapy will be estimated based on typical BTK inhibitor pricing in oncology (e.g., ibrutinib, acalabrutinib). Pricing varies by region due to healthcare systems and negotiations.

5. **Treatment Duration:** Assuming an average treatment duration of 1-2 years for relapsed/refractory FL patients, as many patients may discontinue due to progression or toxicity.

6. **Peak Sales:** Peak sales are typically achieved 5-7 years after launch in a specific indication, assuming full market penetration.

Step 2: Estimate Treated Patient Population

Below are rough estimates of the eligible patient population for third-line or later FL treatment in each geography. These are based on NHL incidence/prevalence, FL proportion, and progression to ≥ 3 rd line therapy.

- **US:**

- NHL prevalence: ~800,000 (American Cancer Society).
- FL proportion: ~25% \rightarrow ~200,000 FL patients.
- Relapsed/refractory ≥ 3 rd line: ~15% \rightarrow ~30,000 eligible patients.

- Treated patients: Assuming 80% receive treatment → ~24,000 patients.
- **EU5** (Germany, France, Italy, Spain, UK):
- NHL prevalence: ~600,000 (combined, based on population and incidence rates).
- FL proportion: ~25% → ~150,000 FL patients.
- Relapsed/refractory ≥3rd line: ~15% → ~22,500 eligible patients.
- Treated patients: Assuming 75% receive treatment → ~17,000 patients.
- **China:**
- NHL prevalence: ~400,000 (adjusted for population and lower diagnosis rates).
- FL proportion: ~20% (slightly lower than Western countries) → ~80,000 FL patients.
- Relapsed/refractory ≥3rd line: ~10% (lower access to multiple lines) → ~8,000 eligible patients.
- Treated patients: Assuming 50% receive treatment → ~4,000 patients.
- **Japan:**
- NHL prevalence: ~100,000 (based on population and incidence).
- FL proportion: ~25% → ~25,000 FL patients.
- Relapsed/refractory ≥3rd line: ~15% → ~3,750 eligible patients.
- Treated patients: Assuming 80% receive treatment → ~3,000 patients.

Total Treated Patients Across Geographies: ~24,000 (US) + 17,000 (EU5) + 4,000 (China) + 3,000 (Japan) = **48,000 patients**.

Step 3: Estimate Market Share for Zanubrutinib

- Assuming a **20-30% market share** of treated patients for zanubrutinib:
- At 20%: ~9,600 patients treated with zanubrutinib.
- At 30%: ~14,400 patients treated with zanubrutinib.

Step 4: Estimate Pricing and Annual Cost of Therapy

Zanubrutinib pricing varies by region due to healthcare systems, negotiations, and access programs. Below are approximate annual costs per patient (based on BTK inhibitor benchmarks like ibrutinib, which costs ~\$100,000-\$150,000/year in the US):

- **US:** ~\$120,000/year.
- **EU5:** ~\$80,000/year (lower due to price controls and negotiations).
- **China:** ~\$30,000/year (significant discounts and local manufacturing by BeiGene).

- **Japan:** ~\$90,000/year (similar to EU5 but slightly higher due to smaller market).

Step 5: Calculate Potential Peak Sales

Peak sales are calculated by multiplying the number of treated patients (at 20% and 30% market share) by the annual cost per patient in each geography.

At 20% Market Share (~9,600 patients):

- **US:** 24,000 treated patients × 20% = 4,800 patients × \$120,000 = **\$576 million.**
- **EU5:** 17,000 treated patients × 20% = 3,400 patients × \$80,000 = **\$272 million.**
- **China:** 4,000 treated patients × 20% = 800 patients × \$30,000 = **\$24 million.**
- **Japan:** 3,000 treated patients × 20% = 600 patients × \$90,000 = **\$54 million.**
- **Total Peak Sales at 20%:** \$576M + \$272M + \$24M + \$54M = **\$926 million.**

At 30% Market Share (~14,400 patients):

- **US:** 24,000 treated patients × 30% = 7,200 patients × \$120,000 = **\$864 million.**
- **EU5:** 17,000 treated patients × 30% = 5,100 patients × \$80,000 = **\$408 million.**
- **China:** 4,000 treated patients × 30% = 1,200 patients × \$30,000 = **\$36 million.**
- **Japan:** 3,000 treated patients × 30% = 900 patients × \$90,000 = **\$81 million.**
- **Total Peak Sales at 30%:** \$864M + \$408M + \$36M + \$81M = **\$1,389 million (or ~\$1.4 billion).**

Potential Peak Sales Range: \$926 million to \$1.4 billion annually for this indication across the specified geographies.

Step 6: Calculate \$ Value of 1% Share of Treated Patients

A 1% share of treated patients corresponds to 1% of the total treated patient pool (48,000 patients) = **480 patients**. The \$ value is calculated by multiplying the number of patients by the annual cost per patient in each geography.

- **US:** 24,000 treated patients × 1% = 240 patients × \$120,000 = **\$28.8 million.**
- **EU5:** 17,000 treated patients × 1% = 170 patients × \$80,000 = **\$13.6 million.**
- **China:** 4,000 treated patients × 1% = 40 patients × \$30,000 = **\$1.2 million.**
- **Japan:** 3,000 treated patients × 1% = 30 patients × \$90,000 = **\$2.7 million.**
- **Total \$ Value of 1% Share:** \$28.8M + \$13.6M + \$1.2M + \$2.7M = **\$46.3 million.**

\$ Value of 1% Share of Treated Patients: \$46.3 million annually across the specified geographies.

Final Answer

- **Potential Peak Sales for Zanubrutinib** in relapsed/refractory FL (≥ 3 rd line) at 20-30% market share:
- **\$926 million to \$1.4 billion** annually across the US, EU5, China, and Japan.
- **\$ Value of 1% Share of Treated Patients:**
- **\$46.3 million** annually across the US, EU5, China, and Japan.

Notes and Caveats

1. These estimates are based on assumptions about patient populations, market share, and pricing. Actual figures may differ based on real-world data, competition (e.g., other BTK inhibitors like ibrutinib or acalabrutinib), and market access.
2. Zanubrutinib is approved in combination with obinutuzumab, so the cost of obinutuzumab may also impact total treatment costs, though I've focused on zanubrutinib alone for simplicity.
3. Peak sales could be influenced by additional indications for zanubrutinib (e.g., mantle cell lymphoma, chronic lymphocytic leukemia), which are not included here.
4. If you have access to more precise data (e.g., exact patient numbers, pricing, or market research), the calculations can be refined accordingly.