

To estimate the **Potential Peak Sales** for zanubrutinib (Brukinsa) in the indication of relapsed or refractory marginal zone lymphoma (R/R MZL) 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 on patient numbers, pricing, and market penetration may not be publicly available in full detail, I will outline the methodology and make reasonable assumptions based on available information and typical market dynamics for oncology drugs. Please note that these are illustrative calculations and should be validated with real-world data from sources like company reports, market research (e.g., EvaluatePharma, GlobalData), or clinical trial data.

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## **Step 1: Define the Target Population (R/R MZL Patients)**

Marginal Zone Lymphoma (MZL) is a rare subtype of non-Hodgkin lymphoma (NHL), accounting for about 5-10% of NHL cases. R/R MZL refers to patients who have relapsed or are refractory after at least one prior therapy (e.g., anti-CD20-based regimen like rituximab). The target population is the number of R/R MZL patients eligible for treatment with zanubrutinib in the specified geographies.

#### Estimated Incidence and Prevalence:

- **US:** NHL incidence is ~70,000 cases/year. Assuming 7% are MZL (~5,000 new cases/year), and ~30-40% become R/R after first-line therapy, we estimate ~1,500-2,000 R/R MZL patients annually.
- **EU5:** NHL incidence is ~90,000 cases/year. Assuming 7% are MZL (~6,300 new cases/year), and ~30-40% R/R, we estimate ~1,900-2,500 R/R MZL patients annually.
- **China:** NHL incidence is ~90,000-100,000 cases/year. Assuming 7% are MZL (~6,300-7,000 new cases/year), and ~30-40% R/R, we estimate ~1,900-2,800 R/R MZL patients annually.
- **Japan:** NHL incidence is ~30,000 cases/year. Assuming 7% are MZL (~2,100 new cases/year), and ~30-40% R/R, we estimate ~600-800 R/R MZL patients annually.

Total estimated R/R MZL patients across geographies: ~5,900-8,100 annually.

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

The problem assumes zanubrutinib captures **20%-30% of treated R/R MZL patients**. Not all patients may be treated with zanubrutinib due to competition (e.g., other BTK inhibitors like ibrutinib, acalabrutinib, or other therapies), physician preference, or access issues. For simplicity, we assume all eligible R/R MZL patients are treated, and zanubrutinib captures 20%-30% of them.

- **Low-end (20%):**  $5,900 * 0.2 = \sim 1,180$  patients treated with zanubrutinib.
- **High-end (30%):**  $8,100 * 0.3 = \sim 2,430$  patients treated with zanubrutinib.

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## **Step 3: Pricing of Zanubrutinib**

Zanubrutinib pricing varies by geography due to differences in healthcare systems, reimbursement policies, and market access. Based on available data and comparisons with other BTK inhibitors (e.g., ibrutinib, which costs ~\$150,000-\$180,000 per year in the US), we assume the following annual treatment costs per patient (hypothetical but realistic):

- **US:** \$150,000/year (high due to lack of price controls).
- **EU5:** \$80,000/year (lower due to negotiated pricing and reimbursement).
- **China:** \$30,000/year (significantly lower due to pricing policies and BeiGene's local presence).
- **Japan:** \$100,000/year (moderate pricing with reimbursement constraints).

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

Peak sales are calculated by multiplying the number of treated patients (20%-30% share) by the annual cost per patient in each geography. We'll use the midpoint of patient estimates for simplicity.

#### US:

- Patients treated (20%-30%): 300-600 (based on 1,500-2,000 total R/R MZL patients).
- Annual cost: \$150,000.
- Peak Sales:
- 20% share:  $300 * \$150,000 = \text{\$45M}$ .
- 30% share:  $600 * \$150,000 = \text{\$90M}$ .

#### EU5:

- Patients treated (20%-30%): 380-750 (based on 1,900-2,500 total R/R MZL patients).
- Annual cost: \$80,000.
- Peak Sales:
- 20% share:  $380 * \$80,000 = \text{\$30.4M}$ .
- 30% share:  $750 * \$80,000 = \text{\$60M}$ .

#### China:

- Patients treated (20%-30%): 380-840 (based on 1,900-2,800 total R/R MZL patients).
- Annual cost: \$30,000.
- Peak Sales:
- 20% share:  $380 * \$30,000 = \text{\$11.4M}$ .
- 30% share:  $840 * \$30,000 = \text{\$25.2M}$ .

#### Japan:

- Patients treated (20%-30%): 120-240 (based on 600-800 total R/R MZL patients).
- Annual cost: \$100,000.
- Peak Sales:
- 20% share:  $120 * \$100,000 = \$12\text{M}$ .
- 30% share:  $240 * \$100,000 = \$24\text{M}$ .

#### Total Peak Sales Across Geographies:

- **20% share:** \$45M (US) + \$30.4M (EU5) + \$11.4M (China) + \$12M (Japan) = **\$98.8M**.
- **30% share:** \$90M (US) + \$60M (EU5) + \$25.2M (China) + \$24M (Japan) = **\$199.2M**.

Thus, the **Potential Peak Sales** for zanubrutinib in R/R MZL across the US, EU5, China, and Japan range from **\$98.8M to \$199.2M annually**, depending on the market share (20%-30%).

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

A 1% share corresponds to 1% of the total estimated R/R MZL patients across geographies (5,900-8,100 patients), which is ~59-81 patients. Using the same pricing per geography, we calculate the revenue for 1% share.

#### US:

- Patients (1%): 15-20.
- Annual cost: \$150,000.
- Revenue:  $15 * \$150,000$  to  $20 * \$150,000 = \$2.25\text{M to } \$3\text{M}$ .

#### EU5:

- Patients (1%): 19-25.
- Annual cost: \$80,000.
- Revenue:  $19 * \$80,000$  to  $25 * \$80,000 = \$1.52\text{M to } \$2\text{M}$ .

#### China:

- Patients (1%): 19-28.
- Annual cost: \$30,000.
- Revenue:  $19 * \$30,000$  to  $28 * \$30,000 = \$0.57\text{M to } \$0.84\text{M}$ .

#### Japan:

- Patients (1%): 6-8.
- Annual cost: \$100,000.
- Revenue:  $6 * \$100,000$  to  $8 * \$100,000 = \$0.6\text{M to } \$0.8\text{M}$ .

#### Total \$ Value of 1% Share:

- Low end: \$2.25M (US) + \$1.52M (EU5) + \$0.57M (China) + \$0.6M (Japan) = **\$4.94M**.

- High end: \$3M (US) + \$2M (EU5) + \$0.84M (China) + \$0.8M (Japan) = **\$6.64M**.

Thus, the **\$ value of a 1% share of treated patients** across the US, EU5, China, and Japan ranges from **\$4.94M to \$6.64M annually**.

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## **Summary of Results**

### **1. Potential Peak Sales for Zanubrutinib in R/R MZL (20%-30% share):**

- US: \$45M to \$90M.

- EU5: \$30.4M to \$60M.

- China: \$11.4M to \$25.2M.

- Japan: \$12M to \$24M.

- **Total: \$98.8M to \$199.2M annually.**

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

- US: \$2.25M to \$3M.

- EU5: \$1.52M to \$2M.

- China: \$0.57M to \$0.84M.

- Japan: \$0.6M to \$0.8M.

- **Total: \$4.94M to \$6.64M annually.**

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## **Caveats and Notes**

- These estimates are based on assumptions about patient numbers, pricing, and market share. Real-world data may differ due to competition, reimbursement challenges, and patient access.

- Zanubrutinib is approved for other indications (e.g., mantle cell lymphoma, chronic lymphocytic leukemia), which could contribute to higher overall sales but are not included here as the focus is on R/R MZL.

- Pricing in China may be lower due to BeiGene's strategy to penetrate the local market, while EU5 pricing reflects typical discounts in Europe.

- Peak sales may take several years to achieve post-approval and depend on market penetration rates and duration of therapy.

For more accurate figures, consult market research reports, BeiGene's financial disclosures, or epidemiology data specific to R/R MZL.