

To estimate the **Potential Peak Sales** for zolbetuximab-clzb (Vyloy) in the specified indication (first-line treatment of adults with locally advanced unresectable or metastatic HER2-negative gastric or gastroesophageal junction (GEJ) adenocarcinoma that is CLDN18.2 positive) 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, assumptions, and market analysis. Since exact figures may not be publicly available, I will outline the methodology and provide reasonable estimates based on epidemiology, pricing, and market penetration assumptions.

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## **Step 1: Define the Target Patient Population**

The target indication is first-line treatment for locally advanced unresectable or metastatic HER2-negative gastric/GEJ adenocarcinoma that is CLDN18.2 positive.

### **1. Epidemiology of Gastric/GEJ Cancer:**

- **US:** Approximately 26,500 new cases of gastric cancer annually (American Cancer Society, 2023). About 60-70% are advanced or metastatic at diagnosis, and ~80% are HER2-negative. Of these, ~38-40% are estimated to be CLDN18.2 positive (based on clinical trial data for zolbetuximab).
- Target population:  $\sim 26,500 * 0.65 \text{ (advanced)} * 0.8 \text{ (HER2-negative)} * 0.4 \text{ (CLDN18.2+)} \approx \mathbf{5,500 \text{ patients}}$ .
- **EU5:** Combined incidence of gastric cancer is ~60,000 annually. Using similar proportions:
  - Target population:  $\sim 60,000 * 0.65 * 0.8 * 0.4 \approx \mathbf{12,500 \text{ patients}}$ .
- **Japan:** Incidence of gastric cancer is ~130,000 annually (one of the highest globally). Using similar proportions:
  - Target population:  $\sim 130,000 * 0.65 * 0.8 * 0.4 \approx \mathbf{27,000 \text{ patients}}$ .
- **China:** Incidence of gastric cancer is ~400,000 annually (highest globally). Using similar proportions:
  - Target population:  $\sim 400,000 * 0.65 * 0.8 * 0.4 \approx \mathbf{83,000 \text{ patients}}$ .

Total target population across all geographies:

- US: 5,500
- EU5: 12,500
- Japan: 27,000
- China: 83,000
- **Total: ~128,000 patients annually.**

**2. First-Line Treatment Eligible Patients:** Since zolbetuximab is for first-line treatment, we assume all of these patients are eligible for first-line therapy.

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

The problem assumes a 20%-30% share of treated patients for zolbetuximab. This reflects the competitive landscape, physician adoption, and payer access.

- **Low-end (20%):**

- US:  $5,500 * 0.2 = 1,100$  patients
- EU5:  $12,500 * 0.2 = 2,500$  patients
- Japan:  $27,000 * 0.2 = 5,400$  patients
- China:  $83,000 * 0.2 = 16,600$  patients
- Total: ~25,600 patients

- **High-end (30%):**

- US:  $5,500 * 0.3 = 1,650$  patients
- EU5:  $12,500 * 0.3 = 3,750$  patients
- Japan:  $27,000 * 0.3 = 8,100$  patients
- China:  $83,000 * 0.3 = 24,900$  patients
- Total: ~38,400 patients

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### **Step 3: Pricing Assumptions**

Zolbetuximab is a novel targeted therapy, and pricing for such drugs in oncology is typically high, especially in the US and Japan, with lower prices in China due to market dynamics and pricing controls.

- **US:** Annual cost per patient ~\$150,000 (based on pricing for similar biologics like trastuzumab or pembrolizumab in oncology).
- **EU5:** Annual cost per patient ~\$100,000 (discounted due to payer negotiations and health technology assessments).
- **Japan:** Annual cost per patient ~\$120,000 (slightly lower than the US but higher than EU due to high gastric cancer burden and favorable reimbursement).
- **China:** Annual cost per patient ~\$50,000 (significantly lower due to pricing controls and local competition).

**Note:** These costs are rough estimates and assume a full year of treatment. Actual treatment duration may vary based on progression-free survival (PFS) data from trials (e.g., SPOTLIGHT and GLOW trials for zolbetuximab showed median PFS of ~8-10 months, so costs could be adjusted downward).

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

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

#### Low-end (20% Share)

- **US:** 1,100 patients \* \$150,000 = **\$165 million**
- **EU5:** 2,500 patients \* \$100,000 = **\$250 million**
- **Japan:** 5,400 patients \* \$120,000 = **\$648 million**
- **China:** 16,600 patients \* \$50,000 = **\$830 million**
- **Total Peak Sales (20% share):** \$165M + \$250M + \$648M + \$830M = **\$1.893 billion**

#### High-end (30% Share)

- **US:** 1,650 patients \* \$150,000 = **\$247.5 million**
- **EU5:** 3,750 patients \* \$100,000 = **\$375 million**
- **Japan:** 8,100 patients \* \$120,000 = **\$972 million**
- **China:** 24,900 patients \* \$50,000 = **\$1.245 billion**
- **Total Peak Sales (30% share):** \$247.5M + \$375M + \$972M + \$1.245B = **\$2.84 billion**

Thus, **Potential Peak Sales** for zolbetuximab-clzb in this indication across the US, EU5, Japan, and China range from **\$1.9 billion to \$2.8 billion annually**, assuming a 20%-30% market share.

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

A 1% share of treated patients corresponds to 1% of the total target population in each geography. We calculate the number of patients and multiply by the annual cost per patient.

- **US:** 5,500 patients \* 0.01 = 55 patients \* \$150,000 = **\$8.25 million**
- **EU5:** 12,500 patients \* 0.01 = 125 patients \* \$100,000 = **\$12.5 million**
- **Japan:** 27,000 patients \* 0.01 = 270 patients \* \$120,000 = **\$32.4 million**
- **China:** 83,000 patients \* 0.01 = 830 patients \* \$50,000 = **\$41.5 million**
- **Total \$ Value of 1% Share:** \$8.25M + \$12.5M + \$32.4M + \$41.5M = **\$94.65 million**

Thus, the **\$ value of a 1% share of treated patients** across these geographies is approximately **\$94.7 million**.

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## **Summary**

1. **Potential Peak Sales for zolbetuximab-clzb (20%-30% market share):**

- Range: **\$1.9 billion to \$2.8 billion annually**

- Breakdown by geography (at 20% share):

- US: \$165M

- EU5: \$250M

- Japan: \$648M

- China: \$830M

- Breakdown by geography (at 30% share):

- US: \$247.5M

- EU5: \$375M

- Japan: \$972M

- China: \$1,245M

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

- Total: **\$94.7 million**

- Breakdown by geography:

- US: \$8.25M

- EU5: \$12.5M

- Japan: \$32.4M

- China: \$41.5M

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## **Caveats and Assumptions**

- **Epidemiology:** Incidence and prevalence data are approximate and may vary based on updated sources or regional differences.

- **CLDN18.2 Positivity:** Assumed at 40% based on trial data; real-world testing and eligibility may differ.

- **Pricing:** Pricing is estimated based on comparable oncology drugs; actual pricing for zolbetuximab may differ by market.

- **Market Penetration:** 20%-30% is an assumption; actual uptake depends on competition (e.g., other therapies for gastric cancer), reimbursement, and physician adoption.

- **Treatment Duration:** Assumed full-year cost; actual duration may be shorter based on PFS or overall survival (OS) data.

If more specific data (e.g., exact pricing, trial results, or market access details) becomes available, these estimates can be refined. For now, these figures provide a reasonable range for planning and analysis purposes.