

To estimate the **Potential Peak Sales** for ripretinib (QINLOCK) in the indication of advanced gastrointestinal stromal tumor (GIST) 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 exact figures (e.g., patient population, pricing, or market penetration) are not provided, I will outline the methodology and use illustrative numbers based on industry standards and publicly available information on GIST and ripretinib. You can refine these numbers with specific data if available.

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## **Step 1: Define Key Parameters**

1. **Indication:** Ripretinib is approved for adult patients with advanced GIST who have received prior treatment with 3 or more kinase inhibitors, including imatinib. This is a specific, late-line treatment population (4th line or beyond).
2. **Target Geographies:** US, EU5 (Germany, France, Italy, Spain, UK), China, Japan.
3. **Market Share Assumption:** 20% to 30% of treated patients in this indication.
4. **Peak Sales:** The maximum annual revenue a drug achieves at the height of its market penetration, typically a few years after launch, before generics or competition erode sales.
5. **Pricing and Treatment Duration:** Ripretinib's pricing and duration of therapy will vary by region due to differences in healthcare systems and reimbursement policies.

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## **Step 2: Estimate the Eligible Patient Population**

GIST is a rare cancer, and the subset of patients who progress to 4th-line treatment after failing 3 or more kinase inhibitors (including imatinib) is even smaller. Below are rough estimates of the eligible population based on epidemiology data and treatment progression rates:

### **- US:**

- Annual GIST incidence: ~4,000–6,000 new cases.
- Advanced GIST requiring systemic treatment: ~50% of cases.
- Patients progressing to 4th-line therapy: ~10–15% of advanced cases (due to high attrition after earlier lines of therapy).
- Eligible population: ~200–450 patients annually.

### **- EU5:**

- Combined population is roughly similar to the US in terms of GIST incidence per capita.
- Eligible population: ~250–500 patients annually.

### **- China:**

- Much larger population, but lower diagnosis rates and access to advanced therapies.
- Annual GIST incidence: ~20,000–30,000 new cases.

- Eligible population (4th-line, considering access barriers): ~500–1,000 patients annually.

- **Japan:**

- Smaller population, but high diagnosis and treatment rates.

- Eligible population: ~100–200 patients annually.

**Total Eligible Population (across all geographies):** ~1,050–2,150 patients annually.

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### **Step 3: Estimate Pricing and Treatment Duration**

Ripretinib is a specialty oncology drug, and pricing for such therapies is high, especially in the US. Treatment duration for advanced GIST patients in late-line settings is often limited by disease progression or tolerability, typically ranging from 6–12 months.

- **US Pricing:** Ripretinib's annual cost is approximately \$250,000–\$300,000 per patient (based on reported figures for QINLOCK, ~\$32,000/month for a 150 mg daily dose).

- **EU5 Pricing:** Typically 30–50% lower than the US due to price controls and negotiations. Estimated annual cost: \$125,000–\$150,000 per patient.

- **China Pricing:** Significantly lower due to affordability and market access programs. Estimated annual cost: \$50,000–\$75,000 per patient.

- **Japan Pricing:** Similar to EU5, ~\$125,000–\$150,000 per patient.

**Average Treatment Duration:** Assume 8 months of therapy on average (based on progression-free survival data from the INVICTUS trial, which showed a median PFS of ~6.3 months for ripretinib).

**Annual Cost per Patient (Adjusted for Duration):**

- US: ~\$166,000–\$200,000 (8/12 of annual cost).

- EU5: ~\$83,000–\$100,000.

- China: ~\$33,000–\$50,000.

- Japan: ~\$83,000–\$100,000.

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### **Step 4: Calculate Potential Peak Sales (20%–30% Market Share)**

Assuming ripretinib captures 20%–30% of the eligible treated population in each geography, we calculate peak sales as follows:

#### US

- Eligible patients: 200–450.

- Treated patients (20%–30% share): 40–135.

- Annual cost per patient: \$166,000–\$200,000.
- Peak Sales:  $(40 \times \$166,000)$  to  $(135 \times \$200,000) = \mathbf{\$6.6M-\$27M}$ .

#### #### EU5

- Eligible patients: 250–500.
- Treated patients (20%–30% share): 50–150.
- Annual cost per patient: \$83,000–\$100,000.
- Peak Sales:  $(50 \times \$83,000)$  to  $(150 \times \$100,000) = \mathbf{\$4.2M-\$15M}$ .

#### #### China

- Eligible patients: 500–1,000.
- Treated patients (20%–30% share): 100–300.
- Annual cost per patient: \$33,000–\$50,000.
- Peak Sales:  $(100 \times \$33,000)$  to  $(300 \times \$50,000) = \mathbf{\$3.3M-\$15M}$ .

#### #### Japan

- Eligible patients: 100–200.
- Treated patients (20%–30% share): 20–60.
- Annual cost per patient: \$83,000–\$100,000.
- Peak Sales:  $(20 \times \$83,000)$  to  $(60 \times \$100,000) = \mathbf{\$1.7M-\$6M}$ .

#### **Total Peak Sales Across Geographies:**

- Low end: \$6.6M (US) + \$4.2M (EU5) + \$3.3M (China) + \$1.7M (Japan) = **\$15.8M**.
- High end: \$27M (US) + \$15M (EU5) + \$15M (China) + \$6M (Japan) = **\$63M**.

**Potential Peak Sales Range: \$16M–\$63M annually.**

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

A 1% share of treated patients corresponds to 1% of the eligible population being treated with ripretinib. Using the same patient numbers and cost per patient:

#### #### US

- Eligible patients: 200–450.
- 1% share: 2–4.5 patients.
- Annual cost per patient: \$166,000–\$200,000.
- Value of 1% share:  $(2 \times \$166,000)$  to  $(4.5 \times \$200,000) = \mathbf{\$332,000-\$900,000}$ .

#### #### EU5

- Eligible patients: 250–500.
- 1% share: 2.5–5 patients.
- Annual cost per patient: \$83,000–\$100,000.
- Value of 1% share:  $(2.5 \times \$83,000)$  to  $(5 \times \$100,000) = \mathbf{\$207,500\text{--}\$500,000}$ .

#### #### China

- Eligible patients: 500–1,000.
- 1% share: 5–10 patients.
- Annual cost per patient: \$33,000–\$50,000.
- Value of 1% share:  $(5 \times \$33,000)$  to  $(10 \times \$50,000) = \mathbf{\$165,000\text{--}\$500,000}$ .

#### #### Japan

- Eligible patients: 100–200.
- 1% share: 1–2 patients.
- Annual cost per patient: \$83,000–\$100,000.
- Value of 1% share:  $(1 \times \$83,000)$  to  $(2 \times \$100,000) = \mathbf{\$83,000\text{--}\$200,000}$ .

#### **Total Value of 1% Share Across Geographies:**

- Low end: \$332K (US) + \$207.5K (EU5) + \$165K (China) + \$83K (Japan) = **\$787,500**.
- High end: \$900K (US) + \$500K (EU5) + \$500K (China) + \$200K (Japan) = **\$2.1M**.

**\$ Value of 1% Share Range: \$0.8M–\$2.1M annually.**

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### **Final Answer**

#### **1. Potential Peak Sales for Ripretinib (assuming 20%–30% market share):**

- **US, EU5, China, Japan Combined: \$16M–\$63M annually.**

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

- **US, EU5, China, Japan Combined: \$0.8M–\$2.1M annually.**

### **Caveats and Notes**

- These estimates are based on rough approximations of patient populations, pricing, and treatment duration. Actual figures may vary due to differences in market access, reimbursement, competition, and real-world treatment patterns.

- Ripretinib's peak sales could be influenced by label expansions, additional indications, or competition from other therapies in GIST.
- If you have access to specific data (e.g., exact patient numbers, pricing in each region, or market share projections), these estimates can be refined further.