

To estimate the **Potential Peak Sales** for avapritinib (Ayvakit) in the indication of unresectable or metastatic gastrointestinal stromal tumor (GIST) with PDGFRA exon 18 mutations (including D842V mutations) 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 exact patient numbers, pricing, and market penetration data are not provided, I will use reasonable assumptions based on publicly available information, epidemiology data, and standard industry practices. The calculations will be approximate and should be validated with more precise data if available.

Step 1: Define the Target Patient Population

GIST is a rare cancer, and PDGFRA exon 18 mutations (including D842V) represent a small subset of GIST cases. According to literature:

- The incidence of GIST is approximately **1-1.5 per 100,000** people annually.
- About **10-15% of GIST cases** have PDGFRA mutations, and of these, **~60-70%** are D842V or related exon 18 mutations.
- Thus, PDGFRA exon 18 mutations account for roughly **6-10% of all GIST cases**.

We will estimate the prevalent population of unresectable or metastatic GIST patients with PDGFRA exon 18 mutations in each geography using population data and these proportions.

Population Estimates (2023):

- **US:** 330 million
- **EU5:** 260 million (Germany: 84M, France: 65M, Italy: 60M, Spain: 47M, UK: 67M, adjusted for overlap)
- **China:** 1,410 million
- **Japan:** 125 million

Annual GIST Incidence and Target Population:

- Incidence of GIST: ~1.2 per 100,000 (midpoint of 1-1.5)
- Proportion with PDGFRA exon 18 mutations: ~8% (midpoint of 6-10%)
- Proportion of GIST cases that are unresectable/metastatic: ~30-40% (assumed 35%)

Annual Incident Cases of GIST with PDGFRA Exon 18 Mutations (Unresectable/Metastatic):

- US: $330M * 1.2/100,000 * 8% * 35% = \sim 1,100$ patients
- EU5: $260M * 1.2/100,000 * 8% * 35% = \sim 870$ patients
- China: $1,410M * 1.2/100,000 * 8% * 35% = \sim 4,740$ patients
- Japan: $125M * 1.2/100,000 * 8% * 35% = \sim 420$ patients

Prevalent Population (Assuming 2-3 years of treatment duration for metastatic GIST):

Using a multiplier of 2.5 years for prevalence:

- US: $1,100 * 2.5 = \sim 2,750$ patients
- EU5: $870 * 2.5 = \sim 2,175$ patients
- China: $4,740 * 2.5 = \sim 11,850$ patients
- Japan: $420 * 2.5 = \sim 1,050$ patients

Total Prevalent Patients Across Geographies: $\sim 17,825$ patients

Step 2: Estimate Market Share and Treated Patients

The problem assumes a **20-30% share of treated patients**. This likely refers to the proportion of eligible patients who receive avapritinib. We will use the midpoint of **25%** for calculations.

Treated Patients (25% of Prevalent Population):

- US: $2,750 * 25\% = \sim 690$ patients
- EU5: $2,175 * 25\% = \sim 545$ patients
- China: $11,850 * 25\% = \sim 2,965$ patients
- Japan: $1,050 * 25\% = \sim 265$ patients
- **Total Treated Patients:** $\sim 4,465$ patients

Step 3: Estimate Drug Pricing

Avapritinib is a targeted therapy for a rare indication, so pricing is high. Based on available data:

- **US:** Annual cost of avapritinib is approximately **\$384,000** per patient (based on list price of $\sim \$32,000/\text{month}$ as per initial launch data).
- **EU5:** Pricing is typically 60-70% of US price due to negotiations and healthcare systems. Assume **\$250,000** per patient annually.
- **Japan:** Pricing is often similar to EU, assume **\$250,000** per patient annually.
- **China:** Pricing is significantly lower due to market access challenges and local policies. Assume **\$100,000** per patient annually.

Step 4: Calculate Potential Peak Sales

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

- **US:** $690 \text{ patients} * \$384,000 = \text{\$265 million}$
- **EU5:** $545 \text{ patients} * \$250,000 = \text{\$136 million}$
- **China:** $2,965 \text{ patients} * \$100,000 = \text{\$297 million}$
- **Japan:** $265 \text{ patients} * \$250,000 = \text{\$66 million}$
- **Total Potential Peak Sales:** $\text{\$265M} + \text{\$136M} + \text{\$297M} + \text{\$66M} = \text{\$764 million}$

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

A 1% share of treated patients refers to 1% of the total prevalent population being treated with avapritinib.

1% of Prevalent Population:

- US: $2,750 * 1\% = 27.5$ patients
- EU5: $2,175 * 1\% = 21.75$ patients
- China: $11,850 * 1\% = 118.5$ patients
- Japan: $1,050 * 1\% = 10.5$ patients

Revenue from 1% Share:

- US: $27.5 * \$384,000 = \10.6 million
- EU5: $21.75 * \$250,000 = \5.4 million
- China: $118.5 * \$100,000 = \11.9 million
- Japan: $10.5 * \$250,000 = \2.6 million
- **Total Value of 1% Share:** $\$10.6M + \$5.4M + \$11.9M + \$2.6M = \$30.5$ million

Final Answer:

1. Potential Peak Sales for Avapritinib (at 20-30% share, calculated at 25%):

- US: \$265 million
- EU5: \$136 million
- China: \$297 million
- Japan: \$66 million
- **Total: \$764 million**

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

- US: \$10.6 million
- EU5: \$5.4 million
- China: \$11.9 million
- Japan: \$2.6 million
- **Total: \$30.5 million**

Notes:

- These estimates are based on assumptions for epidemiology, pricing, and market penetration. Real-world data may vary due to factors like competition, reimbursement, and patient access.

- Peak sales could be influenced by additional indications, patent life, or generic entry.
- Pricing in China is particularly uncertain due to ongoing reforms in drug pricing and access.
- If more precise data on patient numbers, pricing, or market share is available, these figures can be refined.