

To estimate the **Potential Peak Sales** for adagrasib (Krazati) in combination with cetuximab for KRAS G12C-mutated locally advanced or metastatic colorectal cancer (CRC) 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 data may not be publicly available, I will provide a framework based on reasonable assumptions, epidemiology data, and market dynamics. You can adjust the numbers based on more specific data if available.

Step 1: Define the Target Patient Population

Adagrasib targets **KRAS G12C-mutated locally advanced or metastatic colorectal cancer (CRC)** in patients who have received prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy (i.e., second-line or later treatment).

- **KRAS G12C Mutation Prevalence:** Approximately 3-4% of CRC patients harbor the KRAS G12C mutation.
- **CRC Incidence and Prevalence:** We will use estimated incidence rates and focus on advanced/metastatic CRC patients eligible for second-line or later therapies.
- **Geographic Focus:** US, EU5, China, and Japan.

Estimated CRC Incidence and Metastatic CRC Population

Using general epidemiology data (e.g., from WHO, GLOBOCAN, or published literature):

- **US:** ~150,000 new CRC cases annually; ~50% are metastatic or locally advanced (~75,000). Of these, ~50% progress to second-line or later (~37,500). KRAS G12C mutation (~3-4%) = ~1,125-1,500 patients.
- **EU5:** ~350,000 new CRC cases annually; ~50% metastatic (~175,000); ~50% second-line or later (~87,500); KRAS G12C (~3-4%) = ~2,625-3,500 patients.
- **China:** ~550,000 new CRC cases annually; ~50% metastatic (~275,000); ~50% second-line or later (~137,500); KRAS G12C (~3-4%) = ~4,125-5,500 patients.
- **Japan:** ~150,000 new CRC cases annually; ~50% metastatic (~75,000); ~50% second-line or later (~37,500); KRAS G12C (~3-4%) = ~1,125-1,500 patients.

Total Target Population (KRAS G12C-Mutated, Second-Line or Later)

- US: ~1,300 patients (midpoint)
- EU5: ~3,000 patients (midpoint)
- China: ~4,800 patients (midpoint)
- Japan: ~1,300 patients (midpoint)
- **Total:** ~10,400 patients annually across these geographies.

Step 2: Estimate Market Share of Treated Patients

The question assumes a **20% to 30% share of treated patients** for adagrasib. This accounts for competition, physician adoption, access, pricing, and reimbursement dynamics.

- **Low-end (20%):** 20% of 10,400 = ~2,080 patients treated annually.

- **High-end (30%):** 30% of 10,400 = ~3,120 patients treated annually.

Breakdown by Geography (Proportional Distribution):

- US: 1,300 / 10,400 = ~12.5% of total patients.

- EU5: 3,000 / 10,400 = ~28.8% of total patients.

- China: 4,800 / 10,400 = ~46.2% of total patients.

- Japan: 1,300 / 10,400 = ~12.5% of total patients.

Treated Patients by Geography (20%-30% Range):

- US: 260-390 patients

- EU5: 600-900 patients

- China: 960-1,440 patients

- Japan: 260-390 patients

Step 3: Estimate Pricing for Adagrasib + Cetuximab

Adagrasib is a targeted therapy, and cetuximab is a monoclonal antibody (anti-EGFR). Pricing will vary by geography due to healthcare systems and purchasing power.

- **US:** Adagrasib annual cost ~\$200,000-\$250,000 per patient (based on similar targeted therapies like sotorasib). Cetuximab ~\$50,000-\$100,000 annually. Combined cost: ~\$300,000 per patient per year.

- **EU5:** Pricing is typically 50-70% of US prices due to negotiations. Combined cost: ~\$150,000-\$210,000 per patient per year.

- **Japan:** Similar to EU5, ~\$150,000-\$210,000 per patient per year.

- **China:** Pricing is significantly lower due to market access programs and generics. Combined cost: ~\$50,000-\$70,000 per patient per year.

For simplicity, assume **average annual treatment cost per patient** (midpoint):

- US: \$300,000

- EU5: \$180,000

- Japan: \$180,000

- China: \$60,000

Step 4: Calculate Potential Peak Sales

Peak sales are calculated by multiplying the number of treated patients by the average annual treatment cost per patient.

Low-End (20% Market Share)

- **US:** 260 patients * \$300,000 = **\$78 million**
- **EU5:** 600 patients * \$180,000 = **\$108 million**
- **China:** 960 patients * \$60,000 = **\$57.6 million**
- **Japan:** 260 patients * \$180,000 = **\$46.8 million**
- **Total Peak Sales (20%): \$290.4 million**

High-End (30% Market Share)

- **US:** 390 patients * \$300,000 = **\$117 million**
- **EU5:** 900 patients * \$180,000 = **\$162 million**
- **China:** 1,440 patients * \$60,000 = **\$86.4 million**
- **Japan:** 390 patients * \$180,000 = **\$70.2 million**
- **Total Peak Sales (30%): \$435.6 million**

Summary of Potential Peak Sales

- **Range: \$290 million to \$436 million annually** across the US, EU5, China, and Japan.

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

A 1% share of treated patients corresponds to 1% of the total target population (10,400 patients) = **104 patients**.

Breakdown by Geography:

- **US:** 12.5% of 104 = ~13 patients
- **EU5:** 28.8% of 104 = ~30 patients
- **China:** 46.2% of 104 = ~48 patients
- **Japan:** 12.5% of 104 = ~13 patients

Revenue for 1% Share:

- **US:** 13 patients * \$300,000 = **\$3.9 million**
- **EU5:** 30 patients * \$180,000 = **\$5.4 million**
- **China:** 48 patients * \$60,000 = **\$2.9 million**

- **Japan:** 13 patients * \$180,000 = **\$2.3 million**
- **Total \$ Value of 1% Share:** **\$14.5 million**

Final Answer

1. Potential Peak Sales for Adagrasib in KRAS G12C-Mutated CRC (20%-30% Market Share):

- US: \$78 million to \$117 million
- EU5: \$108 million to \$162 million
- China: \$57.6 million to \$86.4 million
- Japan: \$46.8 million to \$70.2 million
- **Total: \$290 million to \$436 million annually**

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

- US: \$3.9 million
- EU5: \$5.4 million
- China: \$2.9 million
- Japan: \$2.3 million
- **Total: \$14.5 million**

Notes and Assumptions

- These estimates are based on rough epidemiology data and assumptions about pricing and market share. Actual numbers may vary based on real-world adoption, competition (e.g., sotorasib or other KRAS inhibitors), reimbursement policies, and treatment duration.
- Peak sales assume steady-state market penetration, which may take several years post-launch.
- The treatment cost includes both adagrasib and cetuximab, though actual costs may differ based on dosing schedules and combination discounts.
- If you have access to more precise data (e.g., exact patient numbers, pricing, or market research), the calculations can be refined accordingly.