To estimate the **Potential Peak Sales** for the drug combination "avutometinib capsules; defactinib tablets" (Avmapki Fakzynja Co-pack) in the indication of KRAS-mutated recurrent low-grade serous ovarian cancer (LGSOC) in the US, EU5 (Germany, France, Italy, Spain, UK), China, and Japan, as well as the **$ value of 1% share of treated patients** in these geographies, we need to follow a structured approach. Since specific data on patient populations, pricing, and market penetration may not be fully available, I will outline the methodology, make reasonable assumptions based on publicly available information, and provide a framework for the calculation. The final numbers are estimates and should be validated with more precise data.

Step 1: Indication and Patient Population

The drug is approved for adult patients with **KRAS-mutated recurrent low-grade serous ovarian cancer (LGSOC)** who have received prior systemic therapy. LGSOC is a rare subtype of ovarian cancer, accounting for approximately 5-10% of all epithelial ovarian cancers. Additionally, KRAS mutations are present in about 30-50% of LGSOC cases.

Key Assumptions for Patient Population:

- **Prevalence of LGSOC**: LGSOC represents ~5-10% of ovarian cancer cases. Using an average of 7.5%, we can estimate the number of LGSOC patients from total ovarian cancer incidence.

- **KRAS Mutation Rate**: Approximately 40% of LGSOC patients have KRAS mutations (based on literature).

- **Recurrent and Previously Treated Patients**: We assume ~50% of LGSOC patients are recurrent and have received prior systemic therapy (a common criterion for second-line or later treatments).

- **Geographical Incidence of Ovarian Cancer**: Using data from sources like the World Health Organization (WHO) or GLOBOCAN, we estimate ovarian cancer incidence in each region.

Estimated Ovarian Cancer Incidence (2020 data from GLOBOCAN or similar sources):

- **US**: ~22,000 new cases per year

- **EU5 (combined)**: ~45,000 new cases per year

- **China**: ~55,000 new cases per year

- **Japan**: ~13,000 new cases per year

Calculation of Eligible Patient Population:
1. **LGSOC Patients (7.5% of ovarian cancer cases):**

- US: 22,000 * 0.075 = 1,650

- EU5: 45,000 * 0.075 = 3,375

- China: 55,000 * 0.075 = 4,125

- Japan: 13,000 * 0.075 = 975

2. **KRAS-Mutated LGSOC (40% of LGSOC):**

- US: 1,650 * 0.4 = 660

- EU5: 3,375 * 0.4 = 1,350

- China: 4,125 * 0.4 = 1,650

- Japan: 975 * 0.4 = 390

3. **Recurrent and Previously Treated (50% of KRAS-mutated LGSOC):**

- US: 660 * 0.5 = 330

- EU5: 1,350 * 0.5 = 675

- China: 1,650 * 0.5 = 825

- Japan: 390 * 0.5 = 195

Total Eligible Patients Across Geographies: 330 (US) + 675 (EU5) + 825 (China) + 195 (Japan) = **2,025 patients per year**.

Step 2: Market Share and Treated Patients

The problem assumes a **20% to 30% share of treated patients**. We will calculate for both ends of the range to provide a range for peak sales.

- **20% Market Share**:

- US: 330 * 0.2 = 66 patients

- EU5: 675 * 0.2 = 135 patients

- China: 825 * 0.2 = 165 patients

- Japan: 195 * 0.2 = 39 patients

- **Total Treated Patients (20%)**: 66 + 135 + 165 + 39 = **405 patients**

- **30% Market Share**:

- US: 330 * 0.3 = 99 patients

- EU5: 675 * 0.3 = 203 patients

- China: 825 * 0.3 = 248 patients

- Japan: 195 * 0.3 = 59 patients

- **Total Treated Patients (30%)**: 99 + 203 + 248 + 59 = **609 patients**

Step 3: Pricing per Patient

Pricing for oncology drugs varies significantly by region due to differences in healthcare systems, reimbursement policies, and purchasing power. Since "Avmapki Fakzynja Co-pack" is a novel targeted therapy, we assume pricing similar to other targeted therapies for rare cancers (e.g.,

$100,000–$200,000 per year in the US).

Assumed Annual Cost per Patient:

- **US**: $150,000 (mid-range for targeted oncology therapies)

- **EU5**: $100,000 (lower due to price negotiations and reimbursement caps)

- **China**: $50,000 (lower due to pricing controls and generics competition)

- **Japan**: $120,000 (similar to US but slightly lower due to national pricing regulations)

Step 4: Potential Peak Sales Calculation

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

Peak Sales at 20% Market Share:

- **US**: 66 patients * $150,000 = $9.9 million

- **EU5**: 135 patients * $100,000 = $13.5 million

- **China**: 165 patients * $50,000 = $8.25 million

- **Japan**: 39 patients * $120,000 = $4.68 million

- **Total Peak Sales (20%)**: $9.9M + $13.5M + $8.25M + $4.68M = **$36.33 million**

Peak Sales at 30% Market Share:

- **US**: 99 patients * $150,000 = $14.85 million

- **EU5**: 203 patients * $100,000 = $20.3 million

- **China**: 248 patients * $50,000 = $12.4 million

- **Japan**: 59 patients * $120,000 = $7.08 million

- **Total Peak Sales (30%)**: $14.85M + $20.3M + $12.4M + $7.08M = **$54.63 million**

Potential Peak Sales Range: **$36.33 million to $54.63 million** annually across the US, EU5, China, and Japan.

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

To calculate the value of a 1% share of treated patients, we use the total eligible patient population (2,025 patients) and calculate 1% of that, then multiply by the respective regional pricing.

- **1% of Total Eligible Patients**: 2,025 * 0.01 = 20.25 patients

- US: 330 * 0.01 = 3.3 patients

- EU5: 675 * 0.01 = 6.75 patients

- China: 825 * 0.01 = 8.25 patients

- Japan: 195 * 0.01 = 1.95 patients

Revenue for 1% Share:

- **US**: 3.3 patients * $150,000 = $0.495 million ($495,000)

- **EU5**: 6.75 patients * $100,000 = $0.675 million ($675,000)

- **China**: 8.25 patients * $50,000 = $0.4125 million ($412,500)

- **Japan**: 1.95 patients * $120,000 = $0.234 million ($234,000)

- **Total Value of 1% Share**: $0.495M + $0.675M + $0.4125M + $0.234M = **$1.8165 million ($1,816,500)**

Final Answers

1. **Potential Peak Sales** for "avutometinib capsules; defactinib tablets" in KRAS-mutated recurrent LGSOC (20% to 30% market share):

- **Range**: **$36.33 million to $54.63 million annually** across the US, EU5, China, and Japan.

- Breakdown by region:

- US: $9.9M to $14.85M

- EU5: $13.5M to $20.3M

- China: $8.25M to $12.4M

- Japan: $4.68M to $7.08M

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

- **Total**: **$1.8165 million ($1,816,500)**

- Breakdown by region:

- US: $495,000

- EU5: $675,000

- China: $412,500

- Japan: $234,000

Notes and Caveats

- These estimates are based on assumptions about patient populations, mutation rates, recurrence rates, market share, and pricing. Real-world data may differ.

- Peak sales could be influenced by factors like competition, reimbursement policies, and market access timelines.

- Pricing assumptions are indicative and may vary based on negotiations with payers or government policies (especially in China and EU5).

- The patient population is based on incidence data; prevalence (existing patients) could increase the pool if patients remain on therapy for multiple years.

- Additional costs like diagnostics for KRAS mutations or combination therapies could impact adoption rates.

If more specific data (e.g., exact pricing, trial data on efficacy, or market research) is available, these estimates can be refined further.