To estimate the **Potential Peak Sales** for tovorafenib (Ojemda) in the indication of relapsed or refractory pediatric low-grade glioma (LGG) with specific BRAF alterations 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 on patient numbers, pricing, and penetration rates are not provided, I will make reasonable assumptions based on available information and industry standards. I will also outline the methodology for clarity.

Step 1: Define the Target Patient Population

- **Indication**: Relapsed or refractory pediatric low-grade glioma (LGG) with BRAF fusion, rearrangement, or V600 mutation.

- **Age Group**: Patients aged 6 months and older.

- **Geographies**: US, EU5, China, Japan.

Pediatric LGG is the most common brain tumor in children, accounting for approximately 30-40% of all childhood brain tumors. BRAF alterations (fusions, rearrangements, or V600 mutations) are present in a significant subset of LGG cases, estimated at 60-70% of cases based on literature.

Epidemiology Assumptions:

- Annual incidence of pediatric LGG:

- US: ~1,200-1,500 new cases per year (based on ~3-4 per 100,000 children and a pediatric population of ~40 million).

- EU5: ~1,000-1,200 new cases per year (similar incidence rate, pediatric population ~30 million).

- China: ~2,500-3,000 new cases per year (larger population, ~200 million children, adjusted for lower diagnosis rates).

- Japan: ~300-400 new cases per year (pediatric population ~15 million).

- Relapsed/Refractory Cases: Approximately 30-50% of LGG patients relapse or become refractory to first-line treatments (surgery, chemotherapy).

- BRAF Alteration Prevalence: ~60-70% of LGG cases have BRAF alterations eligible for tovorafenib.

Estimated Eligible Patients (Annual Incident Cases):

Using the midpoint of ranges and applying percentages:

- US: 1,350 cases x 40% relapsed/refractory x 65% BRAF = ~350 eligible patients/year.

- EU5: 1,100 cases x 40% x 65% = ~285 eligible patients/year.

- China: 2,750 cases x 40% x 65% = ~715 eligible patients/year.

- Japan: 350 cases x 40% x 65% = ~90 eligible patients/year.

- **Total Annual Eligible Patients**: ~1,440 patients across these geographies.

Since tovorafenib targets relapsed/refractory patients, we also consider a **prevalent pool** of existing patients (e.g., those diagnosed in prior years who are still eligible). Assuming a 5-year prevalence for

pediatric LGG (given survival rates are high), the prevalent pool could be 3-5 times the annual incidence. For simplicity, let's assume a **total addressable prevalent population of 4x the annual incidence**:

- US: 350 x 4 = 1,400 patients.

- EU5: 285 x 4 = 1,140 patients.

- China: 715 x 4 = 2,860 patients.

- Japan: 90 x 4 = 360 patients.

- **Total Prevalent Eligible Patients**: ~5,760 patients.

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

The problem states that tovorafenib is assumed to capture **20%-30% of treated patients**. Since LGG treatment often involves surgery as first-line, and only relapsed/refractory patients are eligible, we assume most eligible patients are treated with systemic therapies upon relapse. Thus, the share of treated patients approximates the share of the eligible population.

- At 20% penetration:

- US: 1,400 x 20% = 280 patients.

- EU5: 1,140 x 20% = 228 patients.

- China: 2,860 x 20% = 572 patients.

- Japan: 360 x 20% = 72 patients.

- **Total**: 1,152 patients.

- At 30% penetration:

- US: 1,400 x 30% = 420 patients.

- EU5: 1,140 x 30% = 342 patients.

- China: 2,860 x 30% = 858 patients.

- Japan: 360 x 30% = 108 patients.

- **Total**: 1,728 patients.

Step 3: Pricing Assumptions

Tovorafenib is a targeted oncology drug for a rare pediatric indication, so pricing is expected to be high, in line with other orphan drugs or targeted therapies (e.g., $150,000-$300,000 per patient per year in the US). Pricing in other regions is typically lower due to healthcare system differences:

- **US**: $250,000 per patient/year.

- **EU5**: $150,000 per patient/year (lower due to pricing negotiations).

- **Japan**: $180,000 per patient/year (similar to EU5 but with premium for innovative drugs).

- **China**: $80,000 per patient/year (significantly lower due to market access challenges and pricing controls).

Step 4: Potential Peak Sales Calculation

Peak sales are calculated as the number of treated patients multiplied by the annual cost per patient. We assume peak sales occur when the drug reaches maximum penetration (20%-30%) across the prevalent pool, with annual sales sustained by incident cases thereafter. For simplicity, we calculate based on the prevalent pool being treated over a few years, annualized.

At 20% Penetration:

- **US**: 280 patients x $250,000 = $70 million.

- **EU5**: 228 patients x $150,000 = $34.2 million.

- **China**: 572 patients x $80,000 = $45.8 million.

- **Japan**: 72 patients x $180,000 = $13 million.

- **Total Peak Sales (20%)**: $163 million.

At 30% Penetration:

- **US**: 420 patients x $250,000 = $105 million.

- **EU5**: 342 patients x $150,000 = $51.3 million.

- **China**: 858 patients x $80,000 = $68.6 million.

- **Japan**: 108 patients x $180,000 = $19.4 million.

- **Total Peak Sales (30%)**: $244.3 million.

Thus, **Potential Peak Sales** for tovorafenib in this indication across the specified geographies range from **$163 million to $244 million annually**, depending on penetration rate.

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

A 1% share of treated patients corresponds to 1% of the total eligible prevalent population being treated with tovorafenib.

- **Total Eligible Prevalent Patients**: 5,760.

- **1% of Eligible Patients**: 5,760 x 1% = 57.6 patients.

Breakdown by geography (based on proportional distribution of eligible patients):

- **US**: 1,400 / 5,760 = ~24.3% of total → 57.6 x 24.3% ≈ 14 patients.

- **EU5**: 1,140 / 5,760 = ~19.8% → 57.6 x 19.8% ≈ 11.4 patients.

- **China**: 2,860 / 5,760 = ~49.7% → 57.6 x 49.7% ≈ 28.6 patients.

- **Japan**: 360 / 5,760 = ~6.3% → 57.6 x 6.3% ≈ 3.6 patients.

Now, calculate revenue for 1% share:

- **US**: 14 patients x $250,000 = $3.5 million.

- **EU5**: 11.4 patients x $150,000 = $1.71 million.

- **China**: 28.6 patients x $80,000 = $2.29 million.

- **Japan**: 3.6 patients x $180,000 = $0.65 million.

- **Total $ Value of 1% Share**: $3.5M + $1.71M + $2.29M + $0.65M = **$8.15 million**.

Final Answers

1. **Potential Peak Sales for tovorafenib** in relapsed/refractory pediatric LGG with BRAF alterations:

- At 20% penetration: **$163 million annually**.

- At 30% penetration: **$244 million annually**.

- Range: **$163M - $244M annually** across US, EU5, China, and Japan.

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

- **$8.15 million** across US, EU5, China, and Japan.

Notes and Caveats

- These estimates are based on assumptions for patient numbers, BRAF prevalence, relapse rates, market penetration, and pricing. Actual numbers may vary depending on real-world data, competition (e.g., other BRAF inhibitors), market access, and reimbursement policies.

- Peak sales may be higher initially if the prevalent pool is treated quickly, then stabilize based on incident cases.

- Pricing in China and other markets may be lower or higher depending on negotiations and local policies.

- If more precise data (e.g., exact patient numbers or pricing) is available, these calculations can be refined.