To estimate the **Potential Peak Sales** for alpelisib (Vijoice) in the indication of PIK3CA-related overgrowth spectrum (PROS) 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 specific data on PROS prevalence, patient population, and pricing may not be fully available in the public domain, I will outline the methodology and use reasonable assumptions based on available information for rare diseases, drug pricing, and market dynamics. If you have specific data (e.g., prevalence, pricing, or penetration rates), I can refine the calculations.

Step 1: Background on Alpelisib and PROS

- **Alpelisib (Vijoice)** is a PI3K inhibitor approved by the FDA in April 2022 for the treatment of PROS, a group of rare disorders caused by PIK3CA gene mutations leading to overgrowth of tissues.

- PROS is an ultra-rare condition, and there are limited epidemiological data on its prevalence. Estimates suggest a prevalence of less than 1 in 1 million for some PROS-related conditions, though exact numbers vary.

- The drug targets a small, niche patient population but is priced at a premium due to its orphan drug status and lack of alternative therapies.

Step 2: Methodology for Estimating Potential Peak Sales

To calculate **Potential Peak Sales**, we need:

1. **Total Addressable Patient Population (TAPP):** Number of patients with PROS eligible for treatment in each geography.

2. **Market Penetration Rate:** Percentage of patients likely to be treated with alpelisib (assumed 20% to 30% as per your query).

3. **Annual Cost of Therapy (ACOT):** Price of alpelisib per patient per year.

4. **Peak Sales Calculation:** Multiply TAPP by penetration rate and ACOT.

To calculate the **$ value of 1% share of treated patients**, we divide the total peak sales by the penetration rate and then calculate the value for 1%.

Step 3: Assumptions

Since exact data for PROS prevalence and pricing are not publicly available in full detail, I will make the following assumptions:

1. **Prevalence of PROS:**

- PROS is ultra-rare, with an estimated prevalence of ~1 in 1 million to 1 in 10 million. For simplicity, I'll assume a midpoint prevalence of **1 in 5 million** across geographies unless specific data is available.

- Population estimates (2023):

- US: 330 million

- EU5: 260 million (Germany: 84M, France: 65M, Italy: 59M, Spain: 47M, UK: 67M)

- China: 1,410 million

- Japan: 125 million

- Based on 1 in 5 million prevalence:

- US: ~66 patients

- EU5: ~52 patients

- China: ~282 patients

- Japan: ~25 patients

- **Total Patients Across Geographies:** ~425 patients

- Note: This is a rough estimate. Some sources suggest PROS may have a slightly higher prevalence (e.g., 1 in 1 million for certain subtypes), but I'll use conservative numbers.

2. **Diagnosed and Treatable Population:**

- Not all patients may be diagnosed or eligible for systemic therapy. Assuming a diagnosis rate of 50% and eligibility of 80% of diagnosed patients:

- US: 66 * 0.5 * 0.8 = ~26 treatable patients

- EU5: 52 * 0.5 * 0.8 = ~21 treatable patients

- China: 282 * 0.5 * 0.8 = ~113 treatable patients

- Japan: 25 * 0.5 * 0.8 = ~10 treatable patients

- **Total Treatable Patients:** ~170 patients

3. **Annual Cost of Therapy (ACOT):**

- Alpelisib is an orphan drug for a rare disease, and pricing for such drugs typically ranges from $100,000 to $500,000 per year per patient in the US. For this analysis, I'll assume an annual cost of **$300,000** in the US.

- Pricing in other regions is typically lower due to healthcare system differences:

- EU5: ~70% of US price = $210,000/year

- Japan: ~80% of US price = $240,000/year

- China: ~50% of US price = $150,000/year (lower due to pricing controls and access challenges).

4. **Market Penetration Rate:**

- As per your query, we assume a penetration rate of **20% to 30%** of treatable patients. I'll calculate for both ends of the range.

Step 4: Peak Sales Calculation

Peak sales are calculated as:

Peak Sales = Treatable Patients * Penetration Rate * Annual Cost of Therapy

US:

- Treatable Patients: 26

- Penetration Rate: 20% = 5.2 patients; 30% = 7.8 patients

- ACOT: $300,000

- Peak Sales at 20%: 5.2 * 300,000 = **$1.56 million**

- Peak Sales at 30%: 7.8 * 300,000 = **$2.34 million**

EU5:

- Treatable Patients: 21

- Penetration Rate: 20% = 4.2 patients; 30% = 6.3 patients

- ACOT: $210,000

- Peak Sales at 20%: 4.2 * 210,000 = **$0.88 million**

- Peak Sales at 30%: 6.3 * 210,000 = **$1.32 million**

China:

- Treatable Patients: 113

- Penetration Rate: 20% = 22.6 patients; 30% = 33.9 patients

- ACOT: $150,000

- Peak Sales at 20%: 22.6 * 150,000 = **$3.39 million**

- Peak Sales at 30%: 33.9 * 150,000 = **$5.09 million**

Japan:

- Treatable Patients: 10

- Penetration Rate: 20% = 2 patients; 30% = 3 patients

- ACOT: $240,000

- Peak Sales at 20%: 2 * 240,000 = **$0.48 million**

- Peak Sales at 30%: 3 * 240,000 = **$0.72 million**

Total Peak Sales Across Geographies:

- At 20% Penetration: $1.56M (US) + $0.88M (EU5) + $3.39M (China) + $0.48M (Japan) = **$6.31 million**

- At 30% Penetration: $2.34M (US) + $1.32M (EU5) + $5.09M (China) + $0.72M (Japan) = **$9.47 million**

Potential Peak Sales Range: $6.31 million to $9.47 million annually

---

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

To calculate the value of a 1% share of treated patients, we divide the total peak sales by the penetration rate (since penetration rate represents the percentage of treated patients) to get the value for 100% of treatable patients, then calculate for 1%.

Since 1% of treatable patients corresponds to a proportional share of sales:

- At 20% penetration, total sales = $6.31M for 20% of patients → 1% of patients = $6.31M / 20 = **$0.316 million** (or $316,000)

- At 30% penetration, total sales = $9.47M for 30% of patients → 1% of patients = $9.47M / 30 = **$0.316 million** (or $316,000)

Interestingly, the value per 1% is consistent because sales scale linearly with penetration rate.

$ Value of 1% Share of Treated Patients Across Geographies: $316,000

Breakdown by Geography (at 20% penetration for reference):

- US: 1% of 26 patients = 0.26 patients * $300,000 = **$78,000**

- EU5: 1% of 21 patients = 0.21 patients * $210,000 = **$44,100**

- China: 1% of 113 patients = 1.13 patients * $150,000 = **$169,500**

- Japan: 1% of 10 patients = 0.1 patients * $240,000 = **$24,000**

- Total: $78,000 + $44,100 + $169,500 + $24,000 = **$315,600** (approx. $316,000)

Final Answer

1. **Potential Peak Sales for Alpelisib in PROS Indication (US, EU5, China, Japan):**

- At 20% penetration: **$6.31 million annually**

- At 30% penetration: **$9.47 million annually**

- Range: **$6.31M to $9.47M annually**

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

- Approximately **$316,000**

Caveats and Notes

- **Prevalence Uncertainty:** PROS prevalence data is limited, and the actual number of patients may differ. If you have specific prevalence or incidence data, the calculations can be updated.

- **Pricing Variability:** Drug pricing can vary significantly by country due to negotiations, reimbursement policies, and access programs.

- **Penetration Rate:** The 20-30% penetration rate is an assumption. Real-world uptake depends on diagnosis rates, physician awareness, and payer coverage.

- **Market Dynamics:** Peak sales may take years to achieve due to slow diagnosis and adoption in rare diseases.

- **Competition:** Currently, alpelisib is one of the few targeted therapies for PROS, but future competition could impact market share.

If you have additional data or specific inputs (e.g., exact patient numbers, pricing, or penetration rates), I can refine these estimates further.