To calculate the **Potential Peak Sales** for pembrolizumab (Keytruda) in the indication of unresectable or metastatic tumor mutational burden-high (TMB-H) solid tumors and the **$ value of a 1% share of treated patients** in the US, EU5 (Germany, France, Italy, Spain, UK), China, and Japan, we need to follow a structured approach. Since specific data on patient numbers, pricing, and market penetration may not be publicly available in real-time, I will outline the methodology using reasonable assumptions based on publicly available data, oncology market trends, and pembrolizumab's pricing and market performance. If you have access to specific data (e.g., exact patient numbers or pricing), I can refine the calculations.

Step 1: Define the Indication and Patient Population

Pembrolizumab has been approved for TMB-H solid tumors (≥10 mutations/megabase) in patients with unresectable or metastatic disease who have progressed after prior treatment and have no alternative options. This is a niche indication, as TMB-H is not universally common across all cancers, and the approval applies to a second-line or later setting.

- **TMB-H Prevalence**: Studies suggest that approximately 5-15% of solid tumors may have high TMB (≥10 mut/Mb), with higher prevalence in cancers like non-small cell lung cancer (NSCLC), melanoma, and bladder cancer.

- **Target Population**: This includes patients with advanced solid tumors across multiple cancer types in a relapsed/refractory setting. The total addressable population is a subset of all cancer patients.

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

Step 2: Estimate the Addressable Patient Population

We will estimate the number of eligible patients for pembrolizumab in this indication. Given the lack of exact data, we use cancer incidence and prevalence data, adjusting for TMB-H prevalence and second-line eligibility.

Approximate Cancer Incidence (New Cases per Year) and Prevalence (Existing Cases):

- **US**: ~1.9 million new cancer cases annually (American Cancer Society). Prevalence of advanced solid tumors in second-line or later is roughly 20-30% of incidence, i.e., ~400,000-500,000 patients. Assuming 10% are TMB-H, this is ~40,000-50,000 patients.

- **EU5**: ~1.5 million new cases annually (ECIS - European Cancer Information System). Prevalence of advanced solid tumors in second-line or later is ~300,000-450,000. Assuming 10% TMB-H, this is ~30,000-45,000 patients.

- **China**: ~4.5 million new cases annually (GLOBOCAN). Prevalence of advanced solid tumors in second-line or later is ~900,000-1,350,000. Assuming 10% TMB-H, this is ~90,000-135,000 patients.

- **Japan**: ~1 million new cases annually (GLOBOCAN). Prevalence of advanced solid tumors in second-line or later is ~200,000-300,000. Assuming 10% TMB-H, this is ~20,000-30,000 patients.

Total Addressable Patients (TMB-H, second-line or later):

- US: ~40,000-50,000

- EU5: ~30,000-45,000

- China: ~90,000-135,000

- Japan: ~20,000-30,000

- **Total**: ~180,000-260,000 patients across these geographies.

Step 3: Estimate Market Penetration (20%-30% Share of Treated Patients)

Assuming pembrolizumab captures **20%-30%** of the eligible TMB-H patient population (due to competition from other immunotherapies, alternative treatments, or access barriers):

- **US**: 20%-30% of 40,000-50,000 = 8,000-15,000 patients.

- **EU5**: 20%-30% of 30,000-45,000 = 6,000-13,500 patients.

- **China**: 20%-30% of 90,000-135,000 = 18,000-40,500 patients.

- **Japan**: 20%-30% of 20,000-30,000 = 4,000-9,000 patients.

- **Total Treated Patients**: 36,000-78,000 patients.

Step 4: Estimate Annual Treatment Cost per Patient

Pembrolizumab's pricing varies by region due to differences in healthcare systems, negotiations, and discounts. Approximate annual costs (based on historical data and reports) for a full course of treatment (often ~1 year or until progression) are:

- **US**: ~$150,000-$180,000 per patient per year (based on list price; actual net price may be lower due to discounts).

- **EU5**: ~$100,000-$130,000 per patient per year (varies by country due to pricing negotiations).

- **China**: ~$80,000-$100,000 per patient per year (lower due to market access programs and pricing controls; may be subsidized in some cases).

- **Japan**: ~$120,000-$150,000 per patient per year (aligned with developed markets but subject to reimbursement policies).

Using mid-range values for simplicity:

- US: $165,000

- EU5: $115,000

- China: $90,000

- Japan: $135,000

Step 5: Calculate Potential Peak Sales

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

Peak Sales at 20% Market Share:

- **US**: 8,000 patients × $165,000 = **$1.32 billion**

- **EU5**: 6,000 patients × $115,000 = **$0.69 billion**

- **China**: 18,000 patients × $90,000 = **$1.62 billion**

- **Japan**: 4,000 patients × $135,000 = **$0.54 billion**

- **Total (20% share)**: $1.32B + $0.69B + $1.62B + $0.54B = **$4.17 billion**

Peak Sales at 30% Market Share:

- **US**: 15,000 patients × $165,000 = **$2.48 billion**

- **EU5**: 13,500 patients × $115,000 = **$1.55 billion**

- **China**: 40,500 patients × $90,000 = **$3.65 billion**

- **Japan**: 9,000 patients × $135,000 = **$1.22 billion**

- **Total (30% share)**: $2.48B + $1.55B + $3.65B + $1.22B = **$8.90 billion**

Potential Peak Sales Range: **$4.17 billion to $8.90 billion** annually across the US, EU5, China, and Japan for this indication.

Step 6: Calculate $ Value of 1% Share of Treated Patients

A 1% share corresponds to 1% of the total addressable patient population in each region.

- **US**: 1% of 40,000-50,000 = 400-500 patients × $165,000 = **$66 million to $82.5 million**

- **EU5**: 1% of 30,000-45,000 = 300-450 patients × $115,000 = **$34.5 million to $51.8 million**

- **China**: 1% of 90,000-135,000 = 900-1,350 patients × $90,000 = **$81 million to $121.5 million**

- **Japan**: 1% of 20,000-30,000 = 200-300 patients × $135,000 = **$27 million to $40.5 million**

- **Total $ Value of 1% Share**: $66M-$82.5M (US) + $34.5M-$51.8M (EU5) + $81M-$121.5M (China) + $27M-$40.5M (Japan) = **$208.5 million to $296.3 million**

Final Answer:

1. **Potential Peak Sales for Pembrolizumab in TMB-H Solid Tumors (20%-30% Market Share):**

- **Range**: $4.17 billion to $8.90 billion annually across the US, EU5, China, and Japan.

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

- **Range**: $208.5 million to $296.3 million annually across the US, EU5, China, and Japan.

Notes and Caveats:

- These estimates are based on assumptions about patient populations, TMB-H prevalence, market penetration, and pricing. Real-world numbers may differ due to competition (e.g., other PD-1/PD-L1 inhibitors like nivolumab), access barriers, reimbursement policies, and evolving treatment paradigms.

- Peak sales may take several years to achieve post-approval as market uptake ramps up.

- Pricing in China may be lower due to inclusion in the National Reimbursement Drug List (NRDL) or volume-based procurement.

- If you have access to more precise data (e.g., exact patient numbers from market research reports or specific pricing), these calculations can be refined further.