To estimate the **Potential Peak Sales** for dabrafenib (Tafinlar) in combination with trametinib (Mekinist) for the treatment of unresectable or metastatic solid tumors with BRAF V600E mutation 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 such as exact patient numbers, pricing, or market penetration rates are not provided, I will outline the methodology and make reasonable assumptions based on publicly available information and industry standards. The final numbers are illustrative and would need validation with real-world data.

Step 1: Define the Target Indication and Patient Population

- **Indication**: Unresectable or metastatic solid tumors with BRAF V600E mutation in adult and pediatric patients ≥ 6 years who have progressed following prior treatment and have no satisfactory alternative treatment options. Excludes colorectal cancer and wild-type BRAF tumors.

- **BRAF V600E Mutation Prevalence**: BRAF V600E mutations are found in various cancers, including melanoma (most common), thyroid cancer, non-small cell lung cancer (NSCLC), and others. The prevalence varies by cancer type:

- Melanoma: ~40-50% of cases.

- NSCLC: ~1-2% of cases.

- Thyroid cancer: ~30-50% of papillary thyroid cancer.

- Other solid tumors: Lower prevalence (1-5%).

- **Target Population**: Focus on unresectable/metastatic patients who have progressed on prior therapy. This is a smaller subset of the total cancer population, estimated at ~10-20% of BRAF V600E-positive patients across tumor types.

Step 2: Estimate Eligible Patient Population

Since exact numbers are not available, we use approximate incidence rates for key cancers with BRAF V600E mutations and adjust for the metastatic/unresectable and post-progression subset. Below are rough estimates for annual new cases (incidence) of relevant cancers in each geography, followed by adjustments for BRAF V600E mutation and eligibility criteria.

- **US**:

- Melanoma: ~100,000 new cases/year; ~40% BRAF V600E = 40,000.

- NSCLC: ~230,000 new cases/year; ~1.5% BRAF V600E = 3,450.

- Thyroid cancer: ~44,000 new cases/year; ~40% BRAF V600E = 17,600.

- Other solid tumors: ~5,000 (conservative estimate).

- Total BRAF V600E: ~66,050.

- Unresectable/metastatic and post-progression (~15%): ~9,900 patients.

- **EU5** (combined):

- Melanoma: ~80,000 new cases/year; ~40% BRAF V600E = 32,000.

- NSCLC: ~200,000 new cases/year; ~1.5% BRAF V600E = 3,000.

- Thyroid cancer: ~35,000 new cases/year; ~40% BRAF V600E = 14,000.

- Other solid tumors: ~4,000.

- Total BRAF V600E: ~53,000.

- Unresectable/metastatic and post-progression (~15%): ~7,950 patients.

- **China**:

- Melanoma: ~20,000 new cases/year; ~40% BRAF V600E = 8,000.

- NSCLC: ~800,000 new cases/year; ~1.5% BRAF V600E = 12,000.

- Thyroid cancer: ~90,000 new cases/year; ~40% BRAF V600E = 36,000.

- Other solid tumors: ~10,000.

- Total BRAF V600E: ~66,000.

- Unresectable/metastatic and post-progression (~15%): ~9,900 patients.

- **Japan**:

- Melanoma: ~5,000 new cases/year; ~40% BRAF V600E = 2,000.

- NSCLC: ~120,000 new cases/year; ~1.5% BRAF V600E = 1,800.

- Thyroid cancer: ~15,000 new cases/year; ~40% BRAF V600E = 6,000.

- Other solid tumors: ~2,000.

- Total BRAF V600E: ~11,800.

- Unresectable/metastatic and post-progression (~15%): ~1,770 patients.

Total Eligible Patients Across Geographies: ~9,900 (US) + 7,950 (EU5) + 9,900 (China) + 1,770 (Japan) = **29,520 patients/year**.

Step 3: Estimate Treated Patient Share

- The problem assumes a **20% to 30% share of treated patients** for dabrafenib + trametinib.

- This accounts for competition (e.g., other BRAF/MEK inhibitors like vemurafenib + cobimetinib or encorafenib + binimetinib), access issues, and physician/patient preferences.

- **Treated Patients**:

- At 20% share: 29,520 * 0.2 = **5,904 patients**.

- At 30% share: 29,520 * 0.3 = **8,856 patients**.

Step 4: Estimate Annual Treatment Cost per Patient

- Dabrafenib (Tafinlar) and trametinib (Mekinist) are premium-priced targeted therapies.

- **US Pricing**: Annual cost of combination therapy is ~$200,000–$250,000 per patient (based on historical data for BRAF/MEK inhibitors).

- **EU5 Pricing**: Typically 50-70% of US pricing due to negotiations and health systems; assume ~$120,000–$150,000 per patient.

- **China Pricing**: Lower due to pricing controls and generics; assume ~$50,000–$70,000 per patient.

- **Japan Pricing**: Similar to EU5; assume ~$120,000–$150,000 per patient.

- For simplicity, use midpoint estimates:

- US: $225,000/patient.

- EU5: $135,000/patient.

- China: $60,000/patient.

- Japan: $135,000/patient.

Step 5: Calculate Potential Peak Sales

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

- **US**:

- Eligible patients: 9,900.

- At 20% share: 1,980 patients * $225,000 = **$445.5 million**.

- At 30% share: 2,970 patients * $225,000 = **$668.3 million**.

- **EU5**:

- Eligible patients: 7,950.

- At 20% share: 1,590 patients * $135,000 = **$214.7 million**.

- At 30% share: 2,385 patients * $135,000 = **$322.0 million**.

- **China**:

- Eligible patients: 9,900.

- At 20% share: 1,980 patients * $60,000 = **$118.8 million**.

- At 30% share: 2,970 patients * $60,000 = **$178.2 million**.

- **Japan**:

- Eligible patients: 1,770.

- At 20% share: 354 patients * $135,000 = **$47.8 million**.

- At 30% share: 531 patients * $135,000 = **$71.7 million**.

Total Potential Peak Sales:

- At 20% share: $445.5M (US) + $214.7M (EU5) + $118.8M (China) + $47.8M (Japan) = **$826.8 million**.

- At 30% share: $668.3M (US) + $322.0M (EU5) + $178.2M (China) + $71.7M (Japan) = **$1,240.2 million**.

Range of Potential Peak Sales: **$827 million to $1.24 billion annually**.

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

- **1% of eligible patients** = 29,520 * 0.01 = **295 patients**.

- Breakdown by geography:

- US: 9,900 * 0.01 = 99 patients * $225,000 = **$22.3 million**.

- EU5: 7,950 * 0.01 = 80 patients * $135,000 = **$10.8 million**.

- China: 9,900 * 0.01 = 99 patients * $60,000 = **$5.9 million**.

- Japan: 1,770 * 0.01 = 18 patients * $135,000 = **$2.4 million**.

- **Total $ Value of 1% Share**: $22.3M + $10.8M + $5.9M + $2.4M = **$41.4 million**.

Final Answer

- **Potential Peak Sales for Dabrafenib + Trametinib** in the specified indication across the US, EU5, China, and Japan (assuming 20% to 30% share of treated patients): **$827 million to $1.24 billion annually**.

- **$ Value of 1% Share of Treated Patients** in these geographies: **$41.4 million**.

Caveats

- These estimates are based on assumptions for patient numbers, pricing, and market share. Real-world data (e.g., exact incidence, mutation testing rates, reimbursement, and competition) could significantly alter these figures.

- The indication is broad ("solid tumors with BRAF V600E"), but uptake may vary by tumor type due to differences in standard of care and clinical evidence.

- Pricing in China and other markets may be lower due to local policies or generic competition over time.