To estimate the **Potential Peak Sales** for mirdametinib in the indication of neurofibromatosis type 1 (NF1) with symptomatic plexiform neurofibromas (PN) 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 pricing, patient population, and market penetration for mirdametinib may not be fully available, I will outline a methodology using reasonable assumptions based on publicly available data, rare disease market trends, and typical pricing for orphan drugs. Please note that these are illustrative calculations and would need to be refined with actual data on pricing, patient numbers, and market dynamics.

Step 1: Define the Target Patient Population

Neurofibromatosis type 1 (NF1) is a rare genetic disorder with a prevalence of approximately **1 in 2,500 to 3,000 individuals** worldwide. Plexiform neurofibromas (PN) occur in about **30-50% of NF1 patients**, and a subset of these are symptomatic and inoperable, making them eligible for mirdametinib treatment. Let's estimate the eligible patient population in each geography.

Prevalence and Eligible Population Estimates

- **US**: Population ~330 million; NF1 prevalence ~1 in 3,000 = ~110,000 patients. PN in 40% = ~44,000; symptomatic/inoperable (assume 50%) = ~22,000 patients.

- **EU5**: Combined population ~260 million; NF1 prevalence ~1 in 3,000 = ~87,000 patients. PN in 40% = ~35,000; symptomatic/inoperable (50%) = ~17,500 patients.

- **China**: Population ~1.4 billion; NF1 prevalence ~1 in 3,000 = ~467,000 patients. PN in 40% = ~187,000; symptomatic/inoperable (50%) = ~93,500 patients.

- **Japan**: Population ~125 million; NF1 prevalence ~1 in 3,000 = ~42,000 patients. PN in 40% = ~17,000; symptomatic/inoperable (50%) = ~8,500 patients.

Total Eligible Patients Across Geographies: ~22,000 (US) + 17,500 (EU5) + 93,500 (China) + 8,500 (Japan) = **141,500 patients**.

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

Assuming mirdametinib captures **20-30% of the eligible treated patient population**, we calculate the number of treated patients:

- **Low End (20%)**: 141,500 * 0.20 = **28,300 patients**.

- **High End (30%)**: 141,500 * 0.30 = **42,450 patients**.

Breakdown by Geography:

- **US**: 22,000 * 20-30% = 4,400 to 6,600 patients.

- **EU5**: 17,500 * 20-30% = 3,500 to 5,250 patients.

- **China**: 93,500 * 20-30% = 18,700 to 28,050 patients.

- **Japan**: 8,500 * 20-30% = 1,700 to 2,550 patients.

Step 3: Estimate Annual Drug Cost per Patient

Mirdametinib is an orphan drug for a rare disease, and pricing for such drugs is typically high in Western markets (US, EU5, Japan) and lower in emerging markets like China due to pricing regulations and affordability. Based on comparable drugs (e.g., Koselugo, another MEK inhibitor for NF1), we assume the following annual costs per patient:

- **US**: $150,000/year (high pricing for rare disease drugs).

- **EU5**: $100,000/year (slight discount due to pricing negotiations).

- **Japan**: $120,000/year (similar to EU but adjusted for market dynamics).

- **China**: $30,000/year (significantly lower due to pricing controls and affordability).

Step 4: Calculate Potential Peak Sales

Peak sales are calculated as **Number of Treated Patients * Annual Cost per Patient** for each geography, summed across regions.

Low End (20% Market Share):

- **US**: 4,400 patients * $150,000 = **$660 million**.

- **EU5**: 3,500 patients * $100,000 = **$350 million**.

- **China**: 18,700 patients * $30,000 = **$561 million**.

- **Japan**: 1,700 patients * $120,000 = **$204 million**.

- **Total Peak Sales (20%)**: $660M + $350M + $561M + $204M = **$1,775 million (~$1.78 billion)**.

High End (30% Market Share):

- **US**: 6,600 patients * $150,000 = **$990 million**.

- **EU5**: 5,250 patients * $100,000 = **$525 million**.

- **China**: 28,050 patients * $30,000 = **$841.5 million**.

- **Japan**: 2,550 patients * $120,000 = **$306 million**.

- **Total Peak Sales (30%)**: $990M + $525M + $841.5M + $306M = **$2,662.5 million (~$2.66 billion)**.

Potential Peak Sales Range: **$1.78 billion to $2.66 billion annually**.

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

A 1% share of the eligible patient population (141,500) is **1,415 patients**. Using the same annual cost per patient by geography, we calculate the revenue for 1% share.

Breakdown by Geography:

- **US**: 1% of 22,000 = 220 patients * $150,000 = **$33 million**.

- **EU5**: 1% of 17,500 = 175 patients * $100,000 = **$17.5 million**.

- **China**: 1% of 93,500 = 935 patients * $30,000 = **$28.05 million**.

- **Japan**: 1% of 8,500 = 85 patients * $120,000 = **$10.2 million**.

- **Total Value of 1% Share**: $33M + $17.5M + $28.05M + $10.2M = **$88.75 million**.

$ Value of 1% Share of Treated Patients: **$88.75 million annually**.

Summary of Results

1. **Potential Peak Sales for Mirdametinib** (20-30% market share):

- Range: **$1.78 billion to $2.66 billion annually** across the US, EU5, China, and Japan.

- Breakdown:

- US: $660M to $990M

- EU5: $350M to $525M

- China: $561M to $841.5M

- Japan: $204M to $306M

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

- Total: **$88.75 million annually** across all geographies.

- Breakdown:

- US: $33M

- EU5: $17.5M

- China: $28.05M

- Japan: $10.2M

Key Assumptions and Caveats

- **Patient Population**: Based on general prevalence estimates for NF1 and assumptions about PN and eligibility for treatment. Actual numbers may vary based on diagnosis rates and access to healthcare.

- **Market Penetration**: 20-30% is a reasonable range for a rare disease drug, but competition (e.g., Koselugo) and payer dynamics could impact this.

- **Pricing**: Estimated based on comparable orphan drugs. Actual pricing for mirdametinib may differ by region, especially in China, where pricing reforms could lower costs further.

- **Adoption and Access**: Assumes uniform access across geographies, which may not hold true due to reimbursement policies, especially in China and parts of the EU5.

For more precise estimates, detailed market research, actual pricing data, and real-world uptake rates for mirdametinib would be required.