

To estimate the **Potential Peak Sales** for pralsetinib (GAVRETO) in the indication of advanced or metastatic RET-mutant medullary thyroid cancer (MTC) and RET fusion-positive thyroid cancer in the US, EU5 (France, Germany, 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 such as exact patient numbers, treatment costs, and market penetration rates are not provided, I will outline the methodology and use reasonable assumptions based on publicly available information and typical market dynamics for rare cancer indications. The final numbers will be illustrative, and real-world data would be needed for precision.

Step 1: Define the Target Patient Population

Pralsetinib is approved for a niche indication: RET-mutant MTC and RET fusion-positive thyroid cancer in patients requiring systemic therapy (and radioactive iodine-refractory for the latter). These are rare subsets of thyroid cancer.

- **Medullary Thyroid Cancer (MTC):** Accounts for ~1-2% of thyroid cancers. Of these, ~25% have RET mutations (hereditary MTC) and ~40-50% of sporadic MTC cases have somatic RET mutations. Thus, roughly 50-60% of MTC patients may have RET mutations.

- **RET Fusion-Positive Thyroid Cancer:** RET fusions occur in ~10-20% of papillary thyroid cancer (PTC), which is the most common type of thyroid cancer (~80% of cases), though the actionable population is smaller due to the radioactive iodine-refractory requirement.

- **Total Thyroid Cancer Incidence:** Using global cancer statistics (e.g., GLOBOCAN), thyroid cancer incidence is ~586,000 cases/year globally, with the US, EU5, China, and Japan accounting for a significant portion due to population size and diagnosis rates.

Estimated Incidence of Thyroid Cancer (Annual New Cases)

- **US:** ~44,000 cases/year
- **EU5:** ~53,000 cases/year (combined)
- **China:** ~220,000 cases/year (highest incidence globally due to population size)
- **Japan:** ~18,000 cases/year

Proportion Eligible for Pralsetinib

- MTC is ~1-2% of thyroid cancers: ~2% used for calculation.
- RET-mutant MTC: ~50% of MTC cases.
- RET fusion-positive PTC (actionable): ~5% of non-MTC thyroid cancers (accounting for refractory cases).
- Total eligible population: ~3-5% of all thyroid cancer cases (combining MTC and PTC subsets).

Eligible Incident Patients (Annual New Cases)

- **US:** ~1,320-2,200 (3-5% of 44,000)
- **EU5:** ~1,590-2,650 (3-5% of 53,000)
- **China:** ~6,600-11,000 (3-5% of 220,000)
- **Japan:** ~540-900 (3-5% of 18,000)

Prevalent Patients (Living with Disease)

Since thyroid cancer has a relatively high survival rate (especially PTC), prevalence is higher than incidence. For rare indications like RET-driven cancers requiring systemic therapy, we assume a prevalence-to-incidence ratio of ~5:1 (5 years of treatment eligibility on average).

- **US:** ~6,600-11,000
- **EU5:** ~7,950-13,250
- **China:** ~33,000-55,000
- **Japan:** ~2,700-4,500

Step 2: Treated Patient Share

The problem assumes a **20-30% share of treated patients** for pralsetinib. This accounts for market penetration, competition (e.g., selpercatinib, another RET inhibitor), and access barriers (cost, diagnosis rates, etc.).

Treated Patients (Peak Penetration at 20-30% of Prevalent Eligible Patients)

- **US:** 1,320-3,300 (20-30% of 6,600-11,000)
- **EU5:** 1,590-3,975 (20-30% of 7,950-13,250)
- **China:** 6,600-16,500 (20-30% of 33,000-55,000)
- **Japan:** 540-1,350 (20-30% of 2,700-4,500)

Step 3: Annual Treatment Cost

Pralsetinib is a targeted therapy for a rare cancer, so pricing is high. Based on similar drugs (e.g., selpercatinib):

- **US:** ~\$250,000/year per patient (list price before discounts)
- **EU5:** ~\$150,000/year (lower due to pricing negotiations)
- **China:** ~\$50,000/year (significant price reductions due to market access programs and generics)
- **Japan:** ~\$200,000/year (similar to US but slightly lower)

Step 4: Calculate Potential Peak Sales

Peak sales = (Number of treated patients) × (Annual cost per patient). Using midpoints of ranges for simplicity:

- **US:** 2,310 patients (midpoint of 1,320-3,300) × \$250,000 = **\$577.5 million**
- **EU5:** 2,782 patients (midpoint of 1,590-3,975) × \$150,000 = **\$417.3 million**
- **China:** 11,550 patients (midpoint of 6,600-16,500) × \$50,000 = **\$577.5 million**
- **Japan:** 945 patients (midpoint of 540-1,350) × \$200,000 = **\$189.0 million**

Total Potential Peak Sales Across Geographies

- Total = \$577.5M (US) + \$417.3M (EU5) + \$577.5M (China) + \$189.0M (Japan) = **~\$1.76 billion**

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

A 1% share corresponds to 1% of the eligible prevalent patients being treated with pralsetinib.

- **US:** 1% of 8,800 (midpoint of 6,600-11,000) = 88 patients × \$250,000 = **\$22.0 million**

- **EU5:** 1% of 10,600 (midpoint of 7,950-13,250) = 106 patients × \$150,000 = **\$15.9 million**

- **China:** 1% of 44,000 (midpoint of 33,000-55,000) = 440 patients × \$50,000 = **\$22.0 million**

- **Japan:** 1% of 3,600 (midpoint of 2,700-4,500) = 36 patients × \$200,000 = **\$7.2 million**

Total \$ Value of 1% Share Across Geographies

- Total = \$22.0M (US) + \$15.9M (EU5) + \$22.0M (China) + \$7.2M (Japan) = **~\$67.1 million**

Final Answer

- **Potential Peak Sales for Pralsetinib** (20-30% treated patient share) in the US, EU5, China, and Japan: **~\$1.76 billion annually** (based on midpoint estimates).

- **\$ Value of 1% Share of Treated Patients** in these geographies: **~\$67.1 million annually**.

Notes and Caveats

1. These estimates are based on assumptions for patient populations, pricing, and market penetration. Real-world data (e.g., exact RET mutation testing rates, competitor dynamics, and reimbursement policies) could significantly alter these figures.

2. Pricing in China is highly variable due to government negotiations and volume-based procurement policies.

3. Peak sales may take years to achieve due to diagnostic and market access challenges for rare diseases.

4. The analysis assumes a steady-state prevalence and does not account for potential label expansions or off-label use.

If you have access to specific data (e.g., exact patient numbers or pricing), I can refine these calculations further.