

To estimate the **Potential Peak Sales** for belzutifan (Welireg) in the indication of locally advanced, unresectable, or metastatic pheochromocytoma or paraganglioma (PPGL) 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, pricing, and penetration rates are not publicly available in full detail, I will outline the methodology and make reasonable assumptions based on available information about rare diseases, pricing of oncology drugs, and market dynamics.

## **Step 1: Key Assumptions and Methodology**

### **1. Indication and Patient Population:**

- Pheochromocytoma and paraganglioma (PPGL) are rare neuroendocrine tumors with an estimated incidence of 0.8 to 1.6 per million people per year. Of these, approximately 10-20% are metastatic or unresectable.
- We will focus on the eligible patient population (locally advanced, unresectable, or metastatic PPGL) for belzutifan.
- Population estimates for each geography will be used to calculate the approximate number of eligible patients.

### **2. Market Share:**

- The problem assumes a 20-30% share of treated patients for belzutifan. We will use the midpoint (25%) for peak sales calculations.
- This share accounts for competition, treatment adoption, and access to therapy.

### **3. Pricing:**

- Belzutifan is an oral targeted therapy for a rare cancer indication. Pricing for such drugs in the US is typically high, often in the range of \$150,000–\$200,000 per patient per year. For other regions, pricing is generally lower due to healthcare system negotiations (e.g., 50-70% of US pricing in EU5 and Japan, and even lower in China).
- Assumed annual cost per patient:
  - US: \$180,000
  - EU5: \$100,000 (average across countries)
  - Japan: \$120,000
  - China: \$50,000 (due to lower pricing and access programs)

### **4. Peak Sales:**

- Peak sales are typically reached 5-7 years after launch as adoption grows.
- We assume all eligible patients in the 25% market share are treated for one year annually.

### **5. Geographic Population and Incidence:**

- Total population (2023 estimates):
  - US: 330 million

- EU5: 270 million
- China: 1,400 million
- Japan: 125 million
- Incidence of PPGL: ~1 per million per year (average).
- Prevalence (eligible patients): Since PPGL is chronic in metastatic cases, we assume a prevalence of ~5-10 years of incidence for metastatic/unresectable cases (10-20% of total cases). We'll use a conservative estimate of 0.2 per million as the annual treatable population.

## **Step 2: Estimate Eligible Patient Population**

Using the incidence and prevalence assumptions:

- Annual incidence of PPGL: 1 per million.
- Proportion metastatic/unresectable: 15% (midpoint of 10-20%).
- Annual treatable population: 1 per million \* 15% = 0.15 per million.
- However, since patients may be treated for multiple years, we estimate a **prevalent treatable population** by multiplying annual incidence by an average treatment duration of 5 years for metastatic cases.
- Therefore, prevalent treatable population = 1 per million \* 0.15 \* 5 = 0.75 per million.

Now calculate for each geography:

- US: 330 million \* 0.75 per million = 248 patients
- EU5: 270 million \* 0.75 per million = 203 patients
- China: 1,400 million \* 0.75 per million = 1,050 patients
- Japan: 125 million \* 0.75 per million = 94 patients
- **Total treatable patients across geographies:** 248 + 203 + 1,050 + 94 = **1,595 patients**

## **Step 3: Estimate Treated Patients with 20-30% Market Share**

Using the midpoint of 25% market share:

- US: 248 \* 25% = 62 patients
- EU5: 203 \* 25% = 51 patients
- China: 1,050 \* 25% = 263 patients
- Japan: 94 \* 25% = 24 patients
- **Total treated patients:** 62 + 51 + 263 + 24 = **400 patients**

## **Step 4: Estimate Potential Peak Sales**

Using the pricing assumptions per geography:

- US: 62 patients \* \$180,000 = **\$11.2 million**
- EU5: 51 patients \* \$100,000 = **\$5.1 million**
- China: 263 patients \* \$50,000 = **\$13.2 million**
- Japan: 24 patients \* \$120,000 = **\$2.9 million**
- **Total Peak Sales:** \$11.2M + \$5.1M + \$13.2M + \$2.9M = **\$32.4 million**

### **Step 5: Estimate \$ Value of 1% Share of Treated Patients**

A 1% share corresponds to 1% of the total treatable patients in each geography:

- US: 248 patients \* 1% = 2.48 patients \* \$180,000 = **\$0.45 million** (~\$450,000)
- EU5: 203 patients \* 1% = 2.03 patients \* \$100,000 = **\$0.20 million** (~\$200,000)
- China: 1,050 patients \* 1% = 10.5 patients \* \$50,000 = **\$0.53 million** (~\$530,000)
- Japan: 94 patients \* 1% = 0.94 patients \* \$120,000 = **\$0.11 million** (~\$110,000)
- **Total \$ Value for 1% Share:** \$0.45M + \$0.20M + \$0.53M + \$0.11M = **\$1.29 million**

### **Final Answer**

- **Potential Peak Sales for Belzutifan (25% market share)** in the US, EU5, China, and Japan for the PPGL indication: **\$32.4 million**

- **\$ Value of 1% Share of Treated Patients** across these geographies: **\$1.29 million**

### **Caveats and Notes**

1. These estimates are highly sensitive to assumptions about incidence, prevalence, pricing, and market share. Real-world data may differ based on actual diagnosis rates, access to treatment, and competition.
2. PPGL is a rare disease, and patient numbers are small, leading to relatively modest peak sales compared to more common indications.
3. Pricing in China and EU5 may vary significantly due to local reimbursement policies and negotiations.
4. If additional data (e.g., exact patient numbers or pricing) becomes available, these estimates can be refined.