

To estimate the **Potential Peak Sales** for tisagenlecleucel (Kymriah) in the indication of relapsed or refractory follicular lymphoma (FL) 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 exact data on patient populations, pricing, and penetration rates may not be publicly available, I will outline the methodology and make reasonable assumptions based on available information and industry standards.

Key Steps for Estimation:

1. **Define the Target Patient Population:** Estimate the number of patients with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy in each geography.
2. **Estimate Market Share:** Use the provided range of 20% to 30% share of treated patients.
3. **Determine Pricing:** Estimate the cost of tisagenlecleucel per patient in each region.
4. **Calculate Potential Peak Sales:** Multiply the treated patient population by the price per patient.
5. **Calculate Value of 1% Share:** Determine the monetary value of treating 1% of the eligible patient population.

Step 1: Estimate Target Patient Population

Follicular lymphoma (FL) is a subtype of non-Hodgkin lymphoma (NHL). Relapsed or refractory FL after two or more lines of therapy represents a smaller subset of the total FL population. We will estimate the eligible patient population based on epidemiology data and treatment patterns.

Incidence and Prevalence of FL:

- **US:** Approximately 74,000 new cases of NHL annually, with FL accounting for ~20-25% (14,800-18,500 cases). Of these, ~20-30% become relapsed/refractory after 2+ lines of therapy (~3,000-5,500 patients annually).
- **EU5:** Combined NHL incidence is ~100,000 annually. FL accounts for ~20-25% (20,000-25,000 cases). Relapsed/refractory after 2+ lines: ~4,000-7,500 patients annually.
- **China:** NHL incidence is ~90,000 annually. FL proportion is lower (~10-15%) due to higher prevalence of aggressive lymphomas (9,000-13,500 cases). Relapsed/refractory after 2+ lines: ~1,800-4,000 patients annually.
- **Japan:** NHL incidence is ~30,000 annually. FL accounts for ~20-25% (6,000-7,500 cases). Relapsed/refractory after 2+ lines: ~1,200-2,250 patients annually.

Total estimated eligible patients (relapsed/refractory FL after 2+ lines):

- US: ~4,250 (midpoint of 3,000-5,500)
- EU5: ~5,750 (midpoint of 4,000-7,500)
- China: ~2,900 (midpoint of 1,800-4,000)
- Japan: ~1,725 (midpoint of 1,200-2,250)
- **Total across geographies:** ~14,625 patients annually.

Step 2: Estimate Market Share

The problem assumes a 20% to 30% share of treated patients. We will calculate peak sales for both ends of this range and use the midpoint (25%) for a single-point estimate where needed.

- **20% share:** $14,625 * 0.20 = 2,925$ patients treated annually.
- **30% share:** $14,625 * 0.30 = 4,388$ patients treated annually.
- **25% share (midpoint):** $14,625 * 0.25 = 3,656$ patients treated annually.

Breakdown by geography (using 25% share for simplicity):

- US: $4,250 * 0.25 = 1,063$ patients
- EU5: $5,750 * 0.25 = 1,438$ patients
- China: $2,900 * 0.25 = 725$ patients
- Japan: $1,725 * 0.25 = 431$ patients

Step 3: Estimate Pricing per Patient

Tisagenlecleucel (Kymriah) is a CAR-T cell therapy with high pricing due to its personalized nature and manufacturing costs. Pricing varies by region due to healthcare systems and reimbursement structures:

- **US:** Kymriah is priced at ~\$475,000 per patient for other indications (e.g., DLBCL). We assume a similar price for FL.
- **EU5:** Pricing is typically lower due to negotiations with health authorities. Assume ~\$350,000 per patient.
- **China:** Pricing is significantly lower due to cost sensitivities and local policies. Assume ~\$200,000 per patient (if approved and reimbursed).
- **Japan:** Pricing is closer to EU levels due to advanced healthcare system. Assume ~\$350,000 per patient.

Step 4: Calculate Potential Peak Sales

Peak sales are calculated as: (Number of treated patients) * (Price per patient). We will calculate for 20%, 25%, and 30% market shares.

At 20% Market Share (2,925 treated patients):

- US: $850 \text{ patients } (4,250 * 0.20) * \$475,000 = \text{\$403.8 million}$

- EU5: 1,150 patients $(5,750 * 0.20) * \$350,000 = \text{\$402.5 million}$
- China: 580 patients $(2,900 * 0.20) * \$200,000 = \text{\$116.0 million}$
- Japan: 345 patients $(1,725 * 0.20) * \$350,000 = \text{\$120.8 million}$
- **Total Peak Sales (20%):** $\$403.8\text{M} + \$402.5\text{M} + \$116.0\text{M} + \$120.8\text{M} = \text{\$1,043.1 million (~\$1.04 billion)}$

At 25% Market Share (3,656 treated patients):

- US: 1,063 patients $* \$475,000 = \text{\$504.9 million}$
- EU5: 1,438 patients $* \$350,000 = \text{\$503.3 million}$
- China: 725 patients $* \$200,000 = \text{\$145.0 million}$
- Japan: 431 patients $* \$350,000 = \text{\$150.9 million}$
- **Total Peak Sales (25%):** $\$504.9\text{M} + \$503.3\text{M} + \$145.0\text{M} + \$150.9\text{M} = \text{\$1,304.1 million (~\$1.30 billion)}$

At 30% Market Share (4,388 treated patients):

- US: 1,275 patients $(4,250 * 0.30) * \$475,000 = \text{\$605.6 million}$
- EU5: 1,725 patients $(5,750 * 0.30) * \$350,000 = \text{\$603.8 million}$
- China: 870 patients $(2,900 * 0.30) * \$200,000 = \text{\$174.0 million}$
- Japan: 518 patients $(1,725 * 0.30) * \$350,000 = \text{\$181.3 million}$
- **Total Peak Sales (30%):** $\$605.6\text{M} + \$603.8\text{M} + \$174.0\text{M} + \$181.3\text{M} = \text{\$1,564.7 million (~\$1.56 billion)}$

Potential Peak Sales Range: \$1.04 billion to \$1.56 billion, with a midpoint of **\$1.30 billion** at 25% market share.

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

A 1% share corresponds to 1% of the total eligible patient population (14,625 patients) = 146 patients annually.

- US: $4,250 * 0.01 = 42.5 \text{ patients} * \$475,000 = \text{\$20.2 million}$
- EU5: $5,750 * 0.01 = 57.5 \text{ patients} * \$350,000 = \text{\$20.1 million}$
- China: $2,900 * 0.01 = 29 \text{ patients} * \$200,000 = \text{\$5.8 million}$
- Japan: $1,725 * 0.01 = 17.25 \text{ patients} * \$350,000 = \text{\$6.0 million}$
- **Total \$ Value of 1% Share:** $\$20.2\text{M} + \$20.1\text{M} + \$5.8\text{M} + \$6.0\text{M} = \text{\$52.1 million}$

Final Answer:

1. **Potential Peak Sales for Tisagenlecleucel in Relapsed/Refractory FL** (20% to 30% market share):

- Range: **\$1.04 billion to \$1.56 billion**
- Midpoint (25% share): **\$1.30 billion**

Breakdown by geography (at 25% share):

- US: **\$504.9 million**
- EU5: **\$503.3 million**
- China: **\$145.0 million**
- Japan: **\$150.9 million**

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

- Total: **\$52.1 million**
- Breakdown by geography:
- US: **\$20.2 million**
- EU5: **\$20.1 million**
- China: **\$5.8 million**
- Japan: **\$6.0 million**

Notes and Assumptions:

- Patient population estimates are based on general NHL and FL epidemiology data and may vary with more precise data.
- Pricing assumptions are based on Kymriah's pricing in other indications and adjusted for regional differences.
- Market share of 20-30% assumes competition from other therapies (e.g., other CAR-T therapies, bispecific antibodies).
- These calculations assume full market access and reimbursement in all regions, which may not yet be the case (especially in China).
- Peak sales are annual figures at steady-state market penetration, typically 5-7 years post-launch in each region.

If you have access to more specific data (e.g., exact patient numbers or pricing), these estimates can be refined further.