

To estimate the **Potential Peak Sales** for **nadofaragene firadenovec-vncg (Adstiladrin)** in the indication of high-risk BCG-unresponsive non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) in the US, EU5 (France, Germany, 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 on pricing, patient population, and market penetration might not be fully available or up-to-date, I will outline the methodology, make reasonable assumptions based on publicly available information, and provide an estimated range. If you have access to specific data (e.g., exact pricing or epidemiology), the calculations can be refined further.

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## **Step 1: Define the Target Patient Population**

**Indication:** High-risk BCG-unresponsive NMIBC with CIS (with or without papillary tumors).

### **- Epidemiology of NMIBC:**

- Bladder cancer is one of the most common cancers globally, with NMIBC accounting for ~70-75% of cases at diagnosis.

- High-risk NMIBC patients often receive BCG therapy as the standard of care. However, ~30-50% of patients become BCG-unresponsive.

- Among BCG-unresponsive patients, a subset have CIS, which is the specific target for nadofaragene firadenovec-vncg.

### **- Estimated Patient Population** (based on literature and approximations):

- **US:** ~80,000 new bladder cancer cases annually; ~75% are NMIBC (~60,000); ~30% are high-risk (~18,000); ~40% of high-risk become BCG-unresponsive (~7,200); ~50% of these have CIS (~3,600 patients annually).

- **EU5:** ~120,000 new cases annually; ~75% NMIBC (~90,000); ~30% high-risk (~27,000); ~40% BCG-unresponsive (~10,800); ~50% with CIS (~5,400 patients annually).

- **Japan:** ~20,000 new cases annually; ~75% NMIBC (~15,000); ~30% high-risk (~4,500); ~40% BCG-unresponsive (~1,800); ~50% with CIS (~900 patients annually).

- **China:** ~80,000 new cases annually; ~75% NMIBC (~60,000); ~30% high-risk (~18,000); ~40% BCG-unresponsive (~7,200); ~50% with CIS (~3,600 patients annually).

Total target incident patients annually:

- US: ~3,600

- EU5: ~5,400

- Japan: ~900

- China: ~3,600

- **Total across geographies:** ~13,500 incident patients annually.

Since NMIBC patients may require ongoing treatment, the **prevalent population** (existing patients eligible for treatment) could be 2-3x higher, depending on recurrence rates and survival. For simplicity, we'll focus on incident patients and assume peak sales are based on a steady annual treatment

population.

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

- The problem assumes a **20-30% share of treated patients** for nadofaragene firadenovec-vncg.
- Not all eligible patients may receive treatment due to cost, access, or physician/patient preference. We'll assume ~80% of eligible patients are treated with some form of therapy in these markets.

Treated patient population (80% of eligible):

- US:  $3,600 * 0.8 = \sim 2,880$
- EU5:  $5,400 * 0.8 = \sim 4,320$
- Japan:  $900 * 0.8 = \sim 720$
- China:  $3,600 * 0.8 = \sim 2,880$
- **Total treated patients:**  $\sim 10,800$

**Market share for nadofaragene firadenovec-vncg (20-30%):**

- At 20% share:  $\sim 2,160$  patients annually
- At 30% share:  $\sim 3,240$  patients annually

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## **Step 3: Pricing Assumptions**

- **Nadofaragene firadenovec-vncg (Adstiladrin)** is a gene therapy administered intravesically. Pricing for such innovative therapies in rare or niche indications is typically high.

- In the US, the list price for Adstiladrin is reportedly  $\sim \$160,500$  per treatment (based on available data as of 2023; subject to change). Assuming one treatment course per year per patient for peak sales estimation.

- Pricing in other markets is typically lower due to healthcare system negotiations and pricing controls:
- EU5:  $\sim 50\text{-}70\%$  of US price ( $\sim \$80,000\text{-}\$112,000$  per treatment; assume midpoint of  $\$96,000$ )
- Japan:  $\sim 60\text{-}80\%$  of US price ( $\sim \$96,000\text{-}\$128,000$ ; assume midpoint of  $\$112,000$ )
- China:  $\sim 30\text{-}50\%$  of US price ( $\sim \$48,000\text{-}\$80,000$ ; assume midpoint of  $\$64,000$ )

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

Peak sales are calculated as: **(Number of treated patients at 20-30% share) x (Price per treatment)** for each geography.

#### At 20% Market Share:

- **US:**  $(2,880 * 0.2) * \$160,500 = 576 \text{ patients} * \$160,500 = \sim\$92.4 \text{ million}$
- **EU5:**  $(4,320 * 0.2) * \$96,000 = 864 \text{ patients} * \$96,000 = \sim\$82.9 \text{ million}$
- **Japan:**  $(720 * 0.2) * \$112,000 = 144 \text{ patients} * \$112,000 = \sim\$16.1 \text{ million}$
- **China:**  $(2,880 * 0.2) * \$64,000 = 576 \text{ patients} * \$64,000 = \sim\$36.9 \text{ million}$
- **Total Peak Sales at 20% share:**  $\sim\$228.3 \text{ million annually}$

#### At 30% Market Share:

- **US:**  $(2,880 * 0.3) * \$160,500 = 864 \text{ patients} * \$160,500 = \sim\$138.7 \text{ million}$
- **EU5:**  $(4,320 * 0.3) * \$96,000 = 1,296 \text{ patients} * \$96,000 = \sim\$124.4 \text{ million}$
- **Japan:**  $(720 * 0.3) * \$112,000 = 216 \text{ patients} * \$112,000 = \sim\$24.2 \text{ million}$
- **China:**  $(2,880 * 0.3) * \$64,000 = 864 \text{ patients} * \$64,000 = \sim\$55.3 \text{ million}$
- **Total Peak Sales at 30% share:**  $\sim\$342.6 \text{ million annually}$

**Potential Peak Sales Range: \$228 million to \$343 million annually** across the US, EU5, Japan, and China, assuming 20-30% market share.

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

1% share of treated patients corresponds to 1% of the total treated patient population ( $\sim 10,800$  patients) =  $\sim 108$  patients annually.

- **US:**  $(2,880 * 0.01) * \$160,500 = 28.8 \text{ patients} * \$160,500 = \sim\$4.62 \text{ million}$
- **EU5:**  $(4,320 * 0.01) * \$96,000 = 43.2 \text{ patients} * \$96,000 = \sim\$4.15 \text{ million}$
- **Japan:**  $(720 * 0.01) * \$112,000 = 7.2 \text{ patients} * \$112,000 = \sim\$0.81 \text{ million}$
- **China:**  $(2,880 * 0.01) * \$64,000 = 28.8 \text{ patients} * \$64,000 = \sim\$1.84 \text{ million}$
- **Total \$ Value of 1% Share:**  $\sim\$11.42 \text{ million annually}$

**\$ Value of 1% Share of Treated Patients:**  $\sim\$11.4 \text{ million annually}$  across the specified geographies.

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## **Final Answer:**

1. **Potential Peak Sales for nadofaragene firadenovec-vncg** (assuming 20-30% market share):

- **US, EU5, Japan, China combined:**  $\sim\$228 \text{ million to } \$343 \text{ million annually}$ .

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

-  $\sim\$11.4 \text{ million annually}$  across the US, EU5, Japan, and China.

**Note:** These estimates are based on assumptions regarding epidemiology, pricing, and market access. Actual figures may vary based on real-world pricing, reimbursement, competition (e.g., pembrolizumab in BCG-unresponsive NMIBC), and regulatory approvals in each geography (e.g., Adstiladrin's approval status in China and Japan may not be confirmed as of now). If you have additional data or specific inputs, the analysis can be refined further.