Adstiladrin® (nadofaragene firadenovec-vncg) – New drug approval

- On December 16, 2022, the FDA announced the approval of Ferring Pharmaceuticals' Adstiladrin (nadofaragene firadenovec-vncg), for the treatment of adult patients with high-risk Bacillus Calmette-Guérin (BCG)-unresponsive non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors.

- Most newly diagnosed bladder cancers (75% to 80%) are classified as NMIBC – a type of cancer that has grown through the lining of the bladder but hasn't yet invaded the muscle layer. This type of cancer is associated with high rates of recurrence (between 30 to 80%) and the risk of progression to invasive and metastatic cancer. Treatment and care of patients with high-risk NMIBC often involves removing the tumor and the use of BCG to reduce the risk that the cancer will recur. Few effective treatment options exist for patients who develop BCG-unresponsive disease.

    - About 57,000 men and 18,000 women are diagnosed with bladder cancer annually, and roughly 12,000 men and 4,700 women die from the disease each year in the U.S.

- Adstiladrin is a non-replicating adenoviral vector-based gene therapy designed to deliver a copy of a gene encoding a human interferon-alfa 2b (IFNα2b) to the bladder urothelium. Intravesical instillation of Adstiladrin results in cell transduction and transient local expression of the IFNα2b protein that is anticipated to have anti-tumor effects.

- The efficacy of Adstiladrin was established in a CS-003, an open-label, single-arm study in 103 adults with BCG-unresponsive, high-risk, NMIBC with CIS with or without papillary tumors following transurethral resection, of whom 98 were considered evaluable for response. Patients received Adstiladrin once every 3 months for up to 12 months (4 doses) or until unacceptable toxicity or recurrent high-grade NMIBC. The major outcome measures were complete response (CR) at any time (as defined by negative results for cystoscopy and urine cytology) and duration of response (DOR).

    - The CR rate was 51% (95% CI: 41, 61).
    - The median DOR was 9.7 months (range: 3, 52+).

- Warnings and precautions for Adstiladrin include risk of muscle invasive or metastatic bladder cancer with delayed cystectomy and risk of disseminated adenovirus infection.

- The most common (> 10%) adverse reactions, including laboratory abnormalities (> 15%), with Adstiladrin use were increased glucose, instillation site discharge, increased triglycerides, fatigue, bladder spasm, micturition (urination urgency), increased creatinine, hematuria (blood in urine), decreased phosphate, chills, pyrexia (fever), and dysuria (painful urination).

- The recommended dose of Adstiladrin is 75 mL at a concentration of 3×10^{11} viral particles (vp)/mL instilled once every 3 months into the bladder via a urinary catheter.

    - Adstiladrin should be administered by intravesical instillation only.
    - Adstiladrin should be left in the bladder for 1 hour following instillation.

- Ferring Pharmaceuticals plans to launch Adstiladrin in the second half of 2023. Adstiladrin will be available as a vial with a nominal concentration of 3 x 10^{11} vp/mL. Each vial of Adstiladrin contains an extractable volume of not less than 20 mL.