PRESS RELEASE 2022

Ferring Receives Approval from U.S. FDA for Adstiladrin for High-Risk, BCG-Unresponsive Non-Muscle Invasive Bladder Cancer

- *Ferring's novel adenovirus vector-based gene therapy Adstiladrin® (nadofaragene firadenovec-vncg) is the first gene therapy approved for bladder cancer*
- *Efficacy and safety of Adstiladrin supported by Phase 3 results demonstrating that more than half of patients (51% of CIS ± Ta/T1 cohort) achieved a complete response (CR) at three months and of these, 46% continued to remain free of high-grade recurrence at 12 months*
- *Bladder cancer is the sixth most common cancer in the U.S.; Adstiladrin provides NMIBC patients a valuable alternative compared to an invasive bladder removal surgery*

Saint-Prex, Switzerland– 16 December 2022 – Ferring Pharmaceuticals today announced the U.S. Food and Drug Administration (FDA) approved Adstiladrin® (nadofaragene firadenovec-vncg), a novel adenovirus vector-based gene therapy, 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.

“Patients with BCG-unresponsive NMIBC have historically had limited treatment options other than bladder removal surgery,” said Steven A. Boorjian, M.D., Carl Rosen Professor and Chair of the Department of Urology at Mayo Clinic, and lead investigator on the recent clinical trial of Adstiladrin. “The approval of Adstiladrin is therefore a significant advance in the current treatment landscape and provides a novel treatment option for patients.”

Bladder cancer is the sixth most common cancer in the U.S., with NMIBC representing approximately 75% of all new bladder cancer cases.[1,2] BCG remains the first-line standard of care for people living with high-grade NMIBC. However, more than 50% of patients who receive initial treatment with BCG will experience disease recurrence and progression within one year, with many developing BCG-unresponsive disease.[3]

Adstiladrin, an intravesical therapy administered every three months, targets the patient’s own bladder wall cells to enhance the body’s natural defenses to fight cancer. The FDA approval was based on results of the Phase 3 clinical trial, which met its primary endpoint with more than half (51%, n=50 of 98; 95% CI 41 to 61) of patients with carcinoma in situ with or without concomitant high-grade Ta or T1 disease (CIS ± Ta/T1) achieving a complete response (CR) by three months. Of the patients who achieved an initial CR, 46% (n=23 of 50) continued to remain free of high-grade recurrence at 12 months.

“The approval of Adstiladrin showcases the power of private industry-academia partnerships in bringing novel treatments to market,” said Colin

Dinney, M.D., Chairman, Department of Urology, Division of Surgery, University of Texas MD Anderson Cancer Center. “The Society of Urologic Oncology Clinical Trials Consortium (SUO-CTC) defined the clinical trial design required to address this patient population and has been a proud collaborator in the research of Adstiladrin, and we are delighted that such a transformative treatment is now approved by the FDA.”

“Ferring has been working diligently to realize the potential of gene therapy for bladder cancer patients, where there has long been a critical unmet need for additional treatment options,” said Armin Metzger, Executive Vice President and Chief Science Officer, Ferring Pharmaceuticals. “We are proud to have achieved this critical milestone towards fulfilling the potential of Adstiladrin, a first-of-its-kind therapy, for bladder cancer patients. Adstiladrin is the culmination of a complex research, development, and production process, and we are grateful to the teams, physicians and patients who have helped us reach this approval.”

Ferring expects that Adstiladrin will be commercially available in the United States in the second half of 2023, following manufacturing capacity expansion which will see the company pioneering commercial scale vector production for oncology.

For full prescribing information, please visit: https://www.ferringusa.com/wp-content/uploads/sites/12/2022/12/ADSTILADRIN_pi.pdf

About ADSTILADRIN

Adstiladrin® (nadofaragene firadenovec-vncg) is a gene therapy developed as a treatment for adult patients with BCG-unresponsive NMIBC. It is a non-replicating adenovirus vector-based gene therapy containing the gene interferon alfa-2b, administered by catheter into the bladder once every three months. The vector enters the cells of the bladder wall, releasing the active

gene to do its work. The internal gene/DNA machinery of the cells “picks up” the gene and translates its DNA sequence, resulting in the cells secreting high quantities of interferon alfa-2b protein, a naturally occurring protein the body uses to fight cancer. This novel gene therapy approach thereby turns the patient’s own bladder wall cells into interferon microfactories, enhancing the body’s natural defenses against the cancer. Nadofaragene firadenovec-vncg has been studied in a clinical trial program that includes 221 patients with high-grade, BCG-unresponsive NMIBC who had been treated with adequate BCG previously and did not see benefit from additional BCG treatment (full inclusion criteria published on clinicaltrials.gov: NCT02773849)[6].

About Non-Muscle Invasive Bladder Cancer (NMIBC)

NMIBC is a form of bladder cancer which is present in the superficial layer of the bladder and has not invaded deeper into the bladder or spread to other parts of the body.[3] Bladder cancer is the sixth most common cancer in the U.S., and it is estimated that there were approximately 81,180 new cases of bladder cancer in the U.S. in 2022[4], 75% of which present as NMIBC.[2] In patients with high-risk NMIBC, intravesical BCG remains the first-line standard of care. However, more than 50% of patients who receive initial treatment with BCG will experience disease recurrence and progression within one year, with many developing BCG-unresponsive disease.[3] Current treatment options for BCG-unresponsive patients are very limited, and often result in a highly invasive life-changing procedure of radical cystectomy (complete removal of the bladder).[5]

About the Phase 3 Study

The Phase 3 study of nadofaragene firadenovec-vncg in 157 patients from 33 U.S. sites met its primary endpoint with more than half (51%) of the 98 patients (95% CI 41 to 61) with carcinoma in situ with or without concomitant

high-grade Ta or T1 disease (CIS ± Ta/T1) achieving a complete response (CR), all by three months. Of the patients who achieved an initial CR, 46% (n=23 of 50) continued to remain free of high-grade recurrence at 12 months. In the study, nadofaragene firadenovec-vncg was administered directly into the patient's bladder by instillation once every three months by a healthcare professional.

The most common adverse events (AEs) observed in the study that occurred in patients in order of decreasing frequency were: instillation site discharge (33%), fatigue (24%), bladder spasm (20%), micturition urgency (19%), and hematuria (17%). The discontinuation rate due to AEs was 1.9%.

The long-term follow-up phase of the four-year study is ongoing, and patients are continuing to be monitored for a total of five years.

IMPORTANT SAFETY INFORMATION

- Administer ADSTILADRIN by intravesical instillation only.
- ADSTILADRIN is not for intravenous use, topical use, or oral administration.

CONTRAINDICATIONS

ADSTILADRIN is contraindicated in patients with hypersensitivity to interferon alfa or any component of the product.

WARNINGS AND PRECAUTIONS

- Delaying cystectomy could lead to the development of metastatic bladder cancer, which can be lethal.
- Risk of disseminated adenovirus infection: Persons who are immunocompromised or immunodeficient may be at risk for disseminated infection from ADSTILADRIN due to low levels of

replication-competent adenovirus. Avoid ADSTILADRIN exposure to immunocompromised or immunodeficient individuals.

ADVERSE REACTIONS

The most common (>10%) adverse reactions, including laboratory abnormalities (>15%), were glucose increased (38%), instillation site discharge (33%), triglycerides increased (30%), fatigue (24%), bladder spasm (20%), micturition (urination urgency) (19%), creatinine increased (17%), hematuria (blood in urine) (17%), phosphate decreased (16%), chills (16%), pyrexia (fever) (15%), and dysuria (painful urination) (16%).

To report SUSPECTED ADVERSE REACTIONS, contact Ferring Pharmaceuticals at 1 888 337-7464 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS

Immunocompromise/immunodeficiency: Avoid in patients with immunocompromise or immunodeficiency.

About Ferring Pharmaceuticals

Ferring Pharmaceuticals is a research-driven, specialty biopharmaceutical group committed to helping people around the world build families and live better lives. Headquartered in Saint-Prex, Switzerland, Ferring is a leader in reproductive medicine and women’s health, and in specialty areas within gastroenterology and urology. Ferring has been developing treatments for mothers and babies for over 50 years and has a portfolio covering treatments from conception to birth. Founded in 1950, privately owned Ferring now employs around 6,000 people worldwide, has its own operating subsidiaries in more than 50 countries, and markets its products in 110 countries.

Learn more at www.ferring.com, or connect with us on Twitter, Facebook, Instagram, LinkedIn, and YouTube.

References:

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4. American Cancer Society. Key Statistics for Bladder Cancer. https://www.cancer.org/cancer/bladder-cancer/about/key-statistics.html. Updated January 12,2022. Accessed November 22, 2022.
5. NCCN Guideline Insights. Bladder Cancer, Version 2.2022. *J Natl Compr Canc Netw.* 2022;20(8):866–878
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