ABLE-32: A randomized, controlled, phase 3b clinical trial of nadofaragene firadenovec-vncg versus observation in patients with intermediate-risk non–muscle-invasive bladder cancer.

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Background: There is currently no Food and Drug Administration (FDA)-approved treatment for intermediate-risk non–muscle-invasive bladder cancer (IR NMIBC), defined by the AUA as recurrence of low-grade (LG) Ta within 1 year, solitary LG Ta >3 cm, multifocal LG Ta, high-grade (HG) Ta (≤3 cm), and/or LG T1. Nadofaragene firadenovec-vncg is the first FDA-approved intravesical nonreplicating gene therapy for the treatment of adult patients with high-risk Bacillus Calmette Guérin (BCG)-unresponsive NMIBC with carcinoma in situ (CIS) with or without papillary tumors. In a nonrandomized, multicenter, open-label, repeat-dose, phase 3 study, 53.4% of participants (55/103) with CIS ± HG Ta/T1 achieved complete response 3 months after the first instillation. Nadofaragene firadenovec was well tolerated, with no grade 4/5 study drug-related AEs. Because maintenance treatment with nadofaragene firadenovec following tumor resection may improve clinical outcomes in patients with IR NMIBC, the ABLE-32 open-label randomized study is being conducted to evaluate the efficacy of nadofaragene firadenovec administered every 3 months versus observation in participants with IR NMIBC. **Methods:** This phase 3 study includes approximately 100 global sites with 454 anticipated participants. Adults diagnosed with new or recurrent IR NMIBC and having undergone transurethral resection of bladder tumor within 60 days prior to randomization are eligible. Participants will be randomly assigned 1:1 to receive nadofaragene firadenovec or continue observation. The nadofaragene firadenovec group will receive quarterly doses unless disease recurs or progresses. The observation group will be followed quarterly and may receive nadofaragene firadenovec if IR NMIBC recurs within 24 months. All participants will be evaluated for recurrence and progression using cytology, cystoscopy, and for-cause biopsy for up to 5 years. The primary endpoint is recurrence-free survival (RFS), from randomization to first documented recurrence, progression, or death. Secondary endpoints include RFS at 12 and 24 months and safety. Exploratory endpoints include effect on potential biomarkers and health-related quality of life. Final results are expected in 2031. Clinical trial information: NCT06510374. Research Sponsor: Ferring Pharmaceuticals Inc.