LEGEND Phase 2 study design

Phase 1: Completed

Phase 2: Ongoing

BCG-unresponsive NMIBC with CIS* (n≈100)

- Persistent/recurrent high-grade disease (Ta, T1, or TIS) within 12 months of receiving ≥1 course of intravesical BCG (≥5 of 6 induction), and ≥2 maintenance or re-induction doses
- **PIVOTAL COHORT**

BCG-naïve NMIBC with CIS* (n=70)

- No prior treatment with BCG or treatment with intravesical BCG >5 years prior to enrollment, but may have previously been treated with at least 1 dose of intravesical chemotherapy following TURBT

BCG-exposed NMIBC with CIS* (n=30)

- **Incomplete** BCG treatment (≥ 1 dose and less than the (5+2) doses required for adequate dosing per Cohort 1)

BCG-unresponsive HG Ta/T1 papillary disease without CIS (n=90)

- NMIBC HG Ta/T1 tumor(s) with persistent disease within 12 months of treatment or a recurrence within 6 months of completion of adequate BCG therapy (as noted for Cohort 1)

Key eligibility criteria

- Persons ≥18 years of age
- ECOG Performance Status 0, 1, 2
- Ineligible for, or electing not to undergo, cystectomy
- Adequate bladder function with ability to retain study drug for ≥60 minutes

Treatment

Detalimogene 0.8 mg/mL in 50 mL solution instilled intravesically via a catheter (retention time 60 minutes) delivered over four 12-week cycles on Weeks 1, 2, 5 & 6 per cycle

Cycle 1 → IF CR / Non-CR → **Cycle 2** → IF CR → **Cycle 3** → IF CR → **Cycle 4**

Treatment evaluation

Response will be assessed by cystoscopy, urine cytology, biopsy:

- At end of Cycle 1, if CR, or non-CR due to persistent CIS or recurrent high grade Ta disease, continue with Cycle 2. Discontinue if progressive disease
- After Cycle 2, only patients with a CR will continue for up to 2 more cycles, discontinuation will occur if there is persistent, recurrent or progressive disease
- If CR at end of Cycle 4, continue to maintenance treatment

Endpoints:

- **Primary:** Efficacy (CR at 48 weeks), safety
- **Secondary:** PFS, RFS, CR at end of each cycle and overall treatment, investigator assessed CR (at 48 weeks), DOR, cystectomy-free survival, HRQOL
- **Exploratory:** ADA, PK, biomarkers

Maintenance treatment Follow-up

- If CR at end of Cycle 4, continue with detalimogene intravesically on Weeks 1, 2 of each 12-week cycle, up to 4 additional cycles
- If CR at Cycle 8, either continue for up to 4 additional cycles or enter follow-up

Post-treatment:

- Duration of response
- Subsequent treatment/cystectomy

LEGEND
ClinicalTrials.gov
NCT04752722

*NMIBC with CIS with or without coexisting papillary (Ta/T1 tumors), protocol requires re-resection of T1 tumors prior to enrollment

ADA, anti-drug antibodies; BCG, bacillus Calmette-Guérin; CIS, carcinoma *in situ*; CR, complete response; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; HRQOL, health-related quality of life; NMIBC, non-muscle-invasive bladder cancer; PFS, progression-free survival; PK, pharmacokinetics; RFS, recurrence-free survival; TURBT, transurethral resection of bladder tumor