

Preliminary results from LEGEND: a Phase 2 study of detalimogene voraplasamid (EG-70), a novel, non-viral intravesical gene therapy for patients with BCG-unresponsive non-muscle invasive bladder cancer (NMIBC) with carcinoma *in situ* (CIS)

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Background: Detalimogene voraplasamid is a novel, investigational, non-integrating, non-viral gene therapy specifically engineered for intravesical administration to elicit local activation of anti-tumor immune responses in the bladder and drive durable efficacy in patients with high-risk NMIBC, including BCG-unresponsive disease, while mitigating the risk of systemic toxicities from immune stimulation. Preclinically, detalimogene voraplasamid remodels the tumor microenvironment, activating both innate and adaptive anti-tumor immune responses. Results from the Phase 1 portion of LEGEND (NCT04752722) demonstrated a promising safety/tolerability profile and an overall CR of 73% in patients with NMIBC with CIS. The pivotal Phase 2 portion is ongoing, and the preliminary outcomes will be reported herein.

Methods: Patient eligibility criteria: age ≥18 years; ECOG PS 0–2; BCG-unresponsive NMIBC with CIS ± Ta/T1 disease, ineligible for, or elected not to undergo, cystectomy; satisfactory bladder function with ability to retain study drug for ≥60 minutes. Based on the Phase 1 portion of the study, a dose concentration of 0.8 mg/mL was administered at a

four-dose 50 mL instillation schedule at study weeks 1, 2, 5 and 6 of a 12-week cycle. After completing the initial 12-week cycle, patients without progressive disease remained on detolimogene voraplasmid for up to three additional 12-week cycles. Primary endpoint: Week 48 CR rate; secondary endpoint: safety and tolerability. Efficacy data on BCG-unresponsive patients with CIS (n=26; Cohort 1) and safety data on all patients dosed (N=42) are reported.

Results: Twenty-six patients (20 males/6 females; median age 74 (range 47–92) years have been enrolled in Cohort 1. Treatment-related adverse events (TRAEs; any grade) were reported in 20 (47.6%) patients and were all Grade 1/2 in severity. The most common TRAEs were dysuria in 9 (21.4%) patients, bladder spasm in 8 (19.0%); pollakiuria in 5 (11.9%), and fatigue in 5 (11.9%) patients. In the efficacy-evaluable population for Cohort 1, the overall CR rate was 71% (15/21), with a CR rate of 67% (14/21) at 3 months, and 47% (8/17) at 6 months. The Kaplan-Meier estimate of the 6-month CR is 51%.

Conclusions: Preliminary data from the pivotal Phase 2 portion of the LEGEND study suggest a promising safety/tolerability profile, with TRAEs that were largely consistent with instrumentation/intravesical administration. Overall, 71% of patients dosed with detolimogene voraplasmid achieved a CR, with 67% achieving a CR at 3 months and 47% achieving a CR at 6 months. Cohort 1 (BCG-refractory patients with CIS) continues to enroll, with a target accrual of 100 patients.

Source of Funding: enGene Inc.