

LEGEND: A phase 1/2 study of detolimogene voraplasamid (EG-70), an intravesical monotherapy for patients with high-risk non-muscle-invasive bladder cancer (NMIBC).

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Background: High-risk NMIBC is generally treated with adjuvant intravesical Bacille Calmette-Guérin (BCG). However, ~50% of patients experience recurrence and/or progression afterwards and are considered unresponsive. Detolimogene voraplasamid (EG-70) is an investigational, non-viral, non-integrating, intravesically administered gene therapy designed to elicit local stimulation of anti-tumor immune responses in the bladder and drive durable efficacy in NMIBC, while mitigating the risk of systemic toxicities from immune stimulation. The Phase 1 (dose-escalation) portion of the first-in-human Phase 1/2, open-label, multicenter study (LEGEND; NCT04752722) of detolimogene voraplasamid is complete. The Phase 2 dose was identified, treatment was generally well tolerated, with an overall complete response (CR) rate of 73% [Kalota S, et al. AUA 2024]. Herein, we describe the ongoing Phase 2 portion of the study, which opened to enrollment in May 2023, which recently added a new cohort of BCG-unresponsive HG Ta/T1 papillary only (no carcinoma *in situ* [CIS]) disease. **Methods:** Eligibility criteria: age ≥ 18 years; ECOG PS 0–2; NMIBC, with/without resected coexisting papillary tumors, ineligible for, or elected not to undergo, cystectomy; satisfactory bladder function. Patients receive detolimogene voraplasamid 0.8 mg/mL in 50 mL (intravesical administration, Weeks 1, 2, 5 & 6, 12-week cycle) for 4 cycles, and patients with CR at the end of the 4th cycle will enter maintenance treatment to receive 2 instillations per cycle (at Weeks 1 and 2) for up to another 8 cycles: BCG-unresponsive with CIS (Cohort 1); BCG-naïve with CIS (Cohort 2A) or BCG-exposed with CIS (Cohort 2B); BCG-unresponsive NMIBC with high-grade papillary disease without CIS (Cohort 3). Phase 2 primary endpoints: efficacy (CR rate at Week 48); safety. Secondary endpoints: progression-free survival; CR rate at Weeks 12, 24, 36, and 48; duration of response. The study is being conducted in accordance with the ethical principles of the Declaration of Helsinki and is consistent with ICH/GCP. All patients provide written informed consent. The Phase 2 portion of the study is enrolling and will recruit approximately 300 patients across all cohorts, from sites in the USA, Canada, Europe, and the Asia-Pacific region. Clinical trial information: NCT04752722. Research Sponsor: enGene Inc.