

Preliminary results from LEGEND: a Phase 2 study of detalimogene voraplasmid (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)

John Taylor,¹ Shreyas Joshi,² Raj Satkunasivam,³ Rian Dickstein,⁴ Amirali Salmasi,⁵ Yair Lotan,⁶ Scott Johnson,⁷ Raj Pruthi,⁸ Christine Tosone,⁸ Anne Schuckman,⁹ Ashish M. Kamat,¹⁰ Jen-Jane Liu¹¹

¹University of Kansas Cancer Center, Kansas City, KS; ²Emory University School of Medicine, Atlanta, GA; ³Houston Methodist-Weill Cornell Medical College, Houston, TX; ⁴Chesapeake Urology, Hanover, MD; ⁵University of California San Diego, San Diego, CA; ⁶University of Texas Southwestern Medical Center, Dallas, TX; ⁷Medical College of Wisconsin, Milwaukee, WI; ⁸enGene Inc., Waltham, MA; ⁹University of Southern California, Los Angeles, CA; ¹⁰University of Texas MD Anderson Cancer Center, Houston, TX; ¹¹Oregon Health & Science University, Portland, OR

Introduction

- Bladder-sparing therapies for high-risk non-muscle invasive bladder cancer (NMIBC) address an important unmet need (**Figure 1**).¹⁻⁴
- Detalimogene voraplasmid is a novel, investigational, non-integrating, non-viral, genetic medicine-based immunotherapy carrying a plasmid that simultaneously expresses IL-12 and regulators of RIG-I (**Figure 2**):
 - Stimulates innate and adaptive immunity.
 - Promising efficacy demonstrated in high-risk NMIBC, while minimizing the risk of systemic toxicities.
 - Lyophilized powder easily reconstituted in clinic with sterile water—no special handling and no ultra-cold chain storage required.
 - Intravesical administration via a catheter.
- The ongoing Phase 1/2 LEGEND study (ClinicalTrials.gov: NCT04752722) continues to investigate the safety and efficacy of detalimogene voraplasmid in patients with high-risk NMIBC:
 - Phase 1 is now complete; treatment with detalimogene voraplasmid resulted in a 73% complete response rate at any time and a promising safety and tolerability profile.^{5,6}
 - Here we describe the ongoing Phase 2 portion of the study.

Figure 1: Bladder-sparing therapies for high-risk NMIBC address an important unmet need

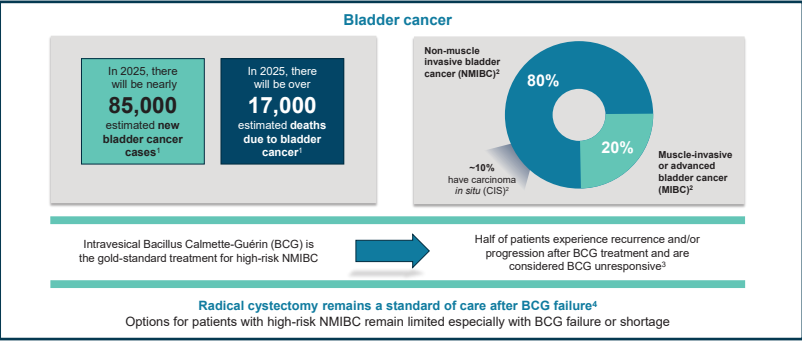
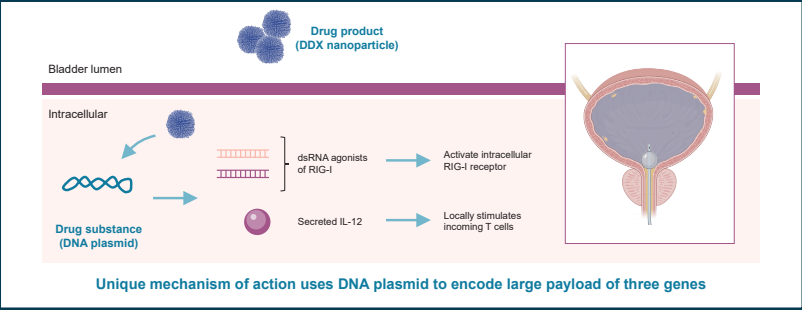


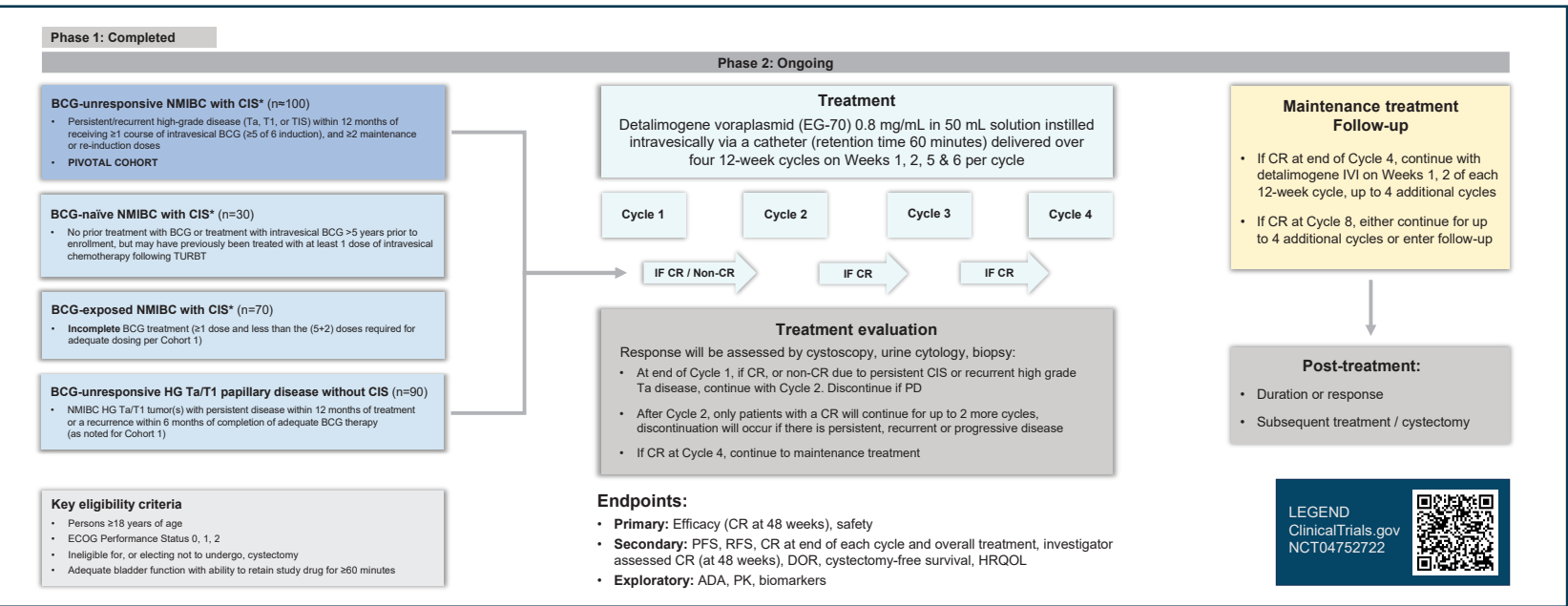
Figure 2: Detalimogene voraplasmid (EG-70): non-viral activation of both innate and adaptive immunity



LEGEND Phase 1/2 clinical study

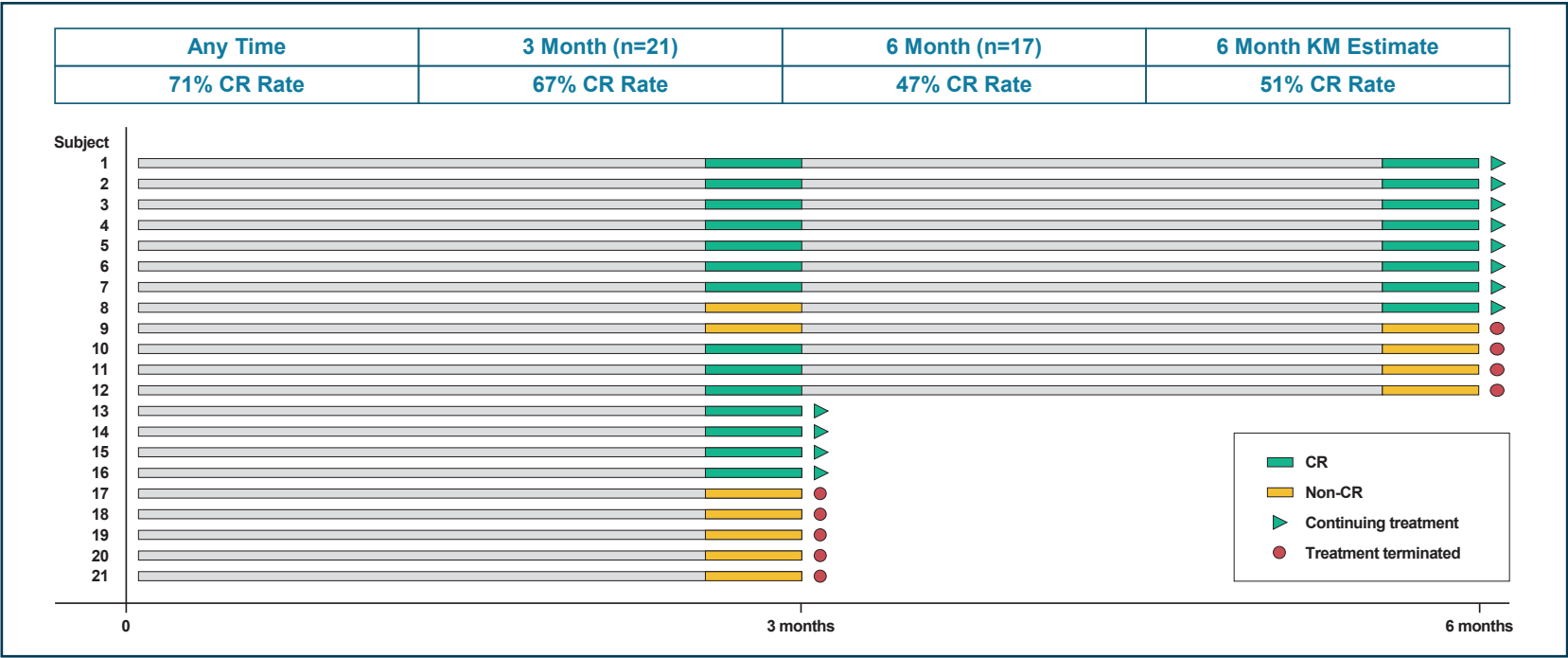
- Phase 1 of the pivotal LEGEND study (NCT04752722) evaluated the safety and efficacy of detalimogene voraplasmid in patients with high-risk NMIBC:
 - Phase 1 patient population: BCG-unresponsive NMIBC with CIS (n=24).
 - Detalimogene voraplasmid dosing: 2 or 4 doses over a 12-week cycle at three different dose levels.
 - Primary endpoint: safety; secondary endpoint: efficacy at 3 months.
 - Phase 1 is now complete; the recommended Phase 2 dose is 0.8 mg/mL via intravesical instillation, 4 doses/12-week cycle.
- Treatment resulted in a **73% complete response rate at any time** and a promising safety and tolerability profile.^{5,6}
- This poster presents preliminary outcomes from Cohort 1 (BCG-unresponsive with CIS) of the Phase 2 pivotal portion of the LEGEND trial (Figure 3), which opened to enrollment in May 2023.**

Figure 3: LEGEND Phase 2 study design



*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; DFS, disease-free survival; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; HRQOL, health-related quality of life; IVI, intravesical instillation; NMIBC, non-muscle invasive bladder cancer; PD, progressive disease; PFS, progression-free survival; PK, pharmacokinetics; RFS, recurrence-free survival; SD, stable disease; TURBT, transurethral resection of bladder tumor

Figure 4: LEGEND Phase 2 Cohort 1 (BCG-unresponsive NMIBC with CIS): Preliminary efficacy results



Data relate to 3m and 6m efficacy-evaluable patients available as of September 13, 2024; *BCG-unresponsive with CIS
KM, Kaplan-Meier analysis; CR, complete response

Table 1. LEGEND Phase 2 Cohort 1 (BCG-unresponsive NMIBC with CIS): Patient demographics

Baseline characteristic	n=21
Sex, n (%)	
Male	15 (71.4)
Female	6 (28.6)
Age, years	
Mean (SD)	72.7 (9.4)
Median (range)	74 (59–92)
Age categories, n (%)	
≤65	6 (28.6)
>65	15 (71.4)
Ethnicity/race, n (%)	
White	20 (95)
Black	1 (5)
Non-Hispanic	21 (100)
ECOG, n (%)	
0	19 (90.5)
1	2 (9.5)
BCG doses	
Median	11
Range	8–33
Tumor stage, n (%)	
T1 + CIS	3 (14.3)
Ta + CIS	3 (14.3)
CIS	15 (71.4)

Demographic data relate to 3m and 6m efficacy-evaluable patients available as of September 13, 2024

Table 2. Phase 2 treatment-related adverse events

(N=42*)	Any Grade	Grade 1	Grade 2	Grade 3	Grade 4/5
Patients with ≥1 TRAE	20 (47.6%)	17 (40.5%)	9 (21.4%)	0 (0)	0 (0)
TRAE reported in >10% patients:					
Bladder spasm	8 (19.0%)	4 (9.5%)	4 (9.5%)	0 (0)	0 (0)
Dysuria	9 (21.4%)	8 (19.0%)	1 (2.4%)	0 (0)	0 (0)
Fatigue	5 (11.9%)	3 (7.1%)	2 (4.8%)	0 (0)	0 (0)
Poliakiuria	5 (11.9%)	5 (11.9%)	0 (0)	0 (0)	0 (0)

TRAE, treatment-related adverse event
*Across all dosed patients in all LEGEND Phase 2 cohorts as of September 13, 2024 data cut-off

- No Grade 3 or Grade 4 treatment-related adverse events (TRAEs)**
- No patient discontinuations due to TRAEs**
- Promising safety and tolerability profile**
- TRAEs were reversible and largely consistent with catheterization**

Conclusions

- Preliminary data from the ongoing pivotal Phase 2 portion of the LEGEND study (n=42) suggest a promising safety/tolerability profile, with TRAEs that were largely consistent with instrumentation/intravesical administration.
- 71% of patients dosed with detalimogene achieved a CR at any time:**
 - 67% achieving a CR at 3 months**
 - 47% achieving a CR at 6 months**
- The LEGEND trial (ClinicalTrials.gov: NCT04752722) is now enrolling patients in multiple cohorts with a target accrual of ~300 patients.



References

- Siegel RL, et al. CA Cancer J Clin 2025;75:10–45.
- Nielsen ME, et al. Cancer 2014;120:86–95.
- Babjuk M, et al. Eur Urol 2022;81:75–94.
- Broughton EI, et al. Curr Urol 2022;16:147–153.
- Steinberg G, et al. SUO Annual Meeting, Washington, DC, November 28–December 1, 2023.
- Kalota S, et al. AUA Annual Meeting, San Antonio, Texas, May 3–6, 2024.

Acknowledgements

- The authors would like to thank the patients, their caregivers, and all site staff and investigators for participating in the LEGEND study.
- This work was funded by the study sponsor (enGene Inc.).