AUA 2024 San Antonio MAY 3-6

LEGEND: a Phase 1/2 study of EG-70 (detalimogene voraplasmid), a novel, non-viral intravesical gene therapy for patients with BCG-unresponsive non-muscle invasive bladder cancer with carcinoma *in situ* (CIS)

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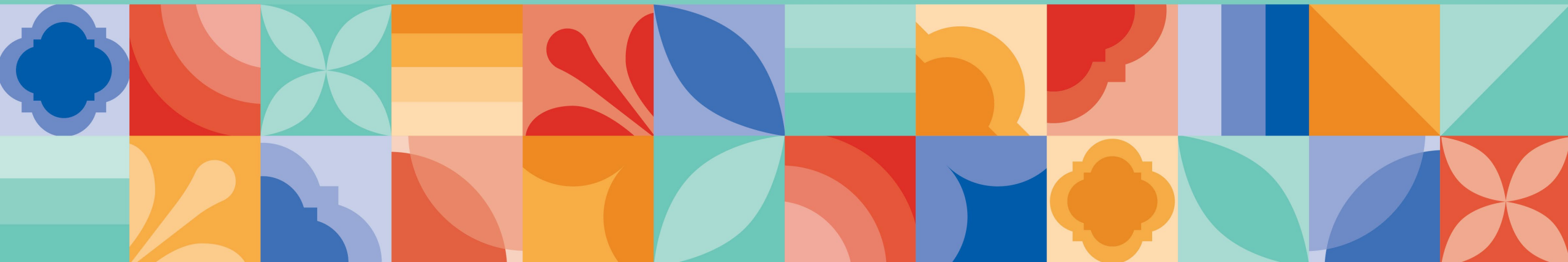

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Disclosures: Gordon Brown D.O., FACOS

Affiliations

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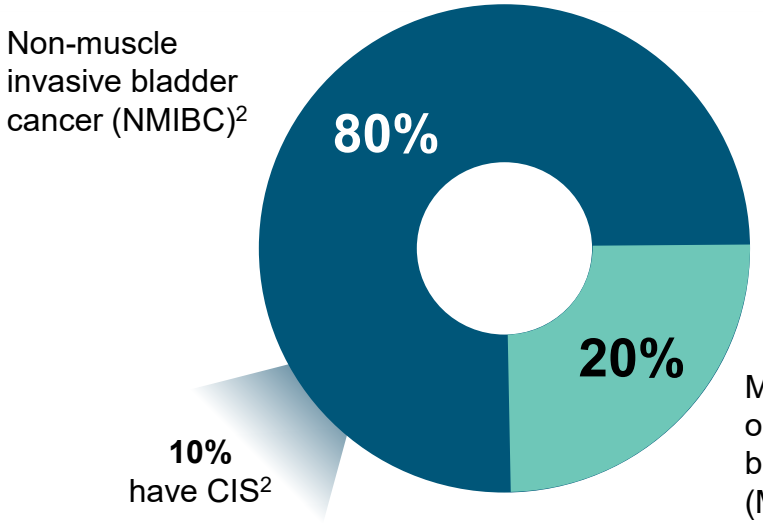
Bladder-sparing therapies for BCG-unresponsive NMIBC address an important unmet need

Bladder cancer

In 2023, there were more than **82,000** estimated **new bladder cancer cases**[1]

In 2023, there were over **16,000** estimated **deaths due to bladder cancer**[1]



Intravesical bacillus Calmette-Guérin (BCG) is the gold-standard treatment for high-risk NMIBC

Half of patients experience recurrence and/or progression after BCG treatment and are considered BCG unresponsive[3]

Radical cystectomy remains standard of care to prevent muscle invasion after BCG failure due to lack of alternative options[4]

1. SEER 2023. https://seer.cancer.gov/statfacts/html/urinb.html (Accessed March 19, 2024); 2. Nielsen ME, et al. Cancer 2014;120:86–95
3. Babjuk M, et al. Eur Urol 2022;81:75−94; 4. Broughton EI, et al. Curr Urol 2022;16:147−153

What is EG-70 (detalimogene voraplasmid)?

A novel, investigational, non-integrating, non-viral gene therapy designed for ease of use in any urology clinic

Simplified preparation & administration

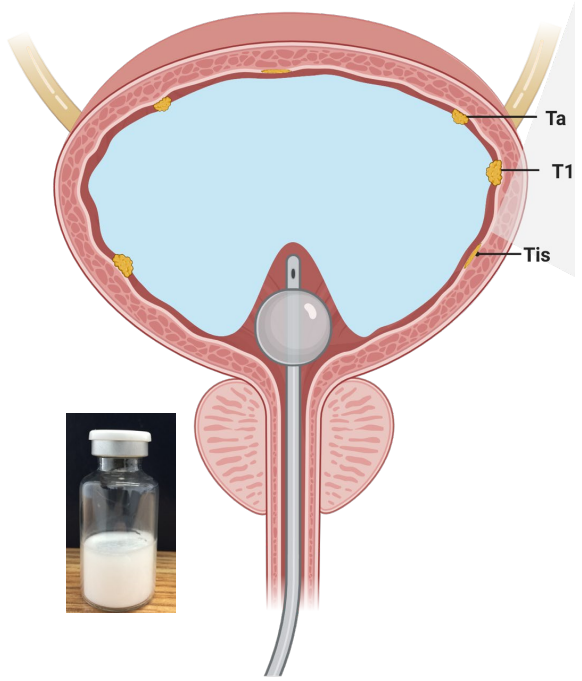
No extended vial thaw; no pre-medication required	✓
Simple IVI administration of 50 mL volume; 60 minutes bladder dwell time; no detergent or bladder wash steps	✓
Universal biosafety precautions not required for preparation or use	✓

No specialized storage & handling requirements

Supplied as lyophilized powder; reconstitution in sterile water; with stability at room temperature	✓
Common storage conditions in standard freezers; no –80°C requirement	✓
No infectious or potentially immunogenic virus contained in product	✓

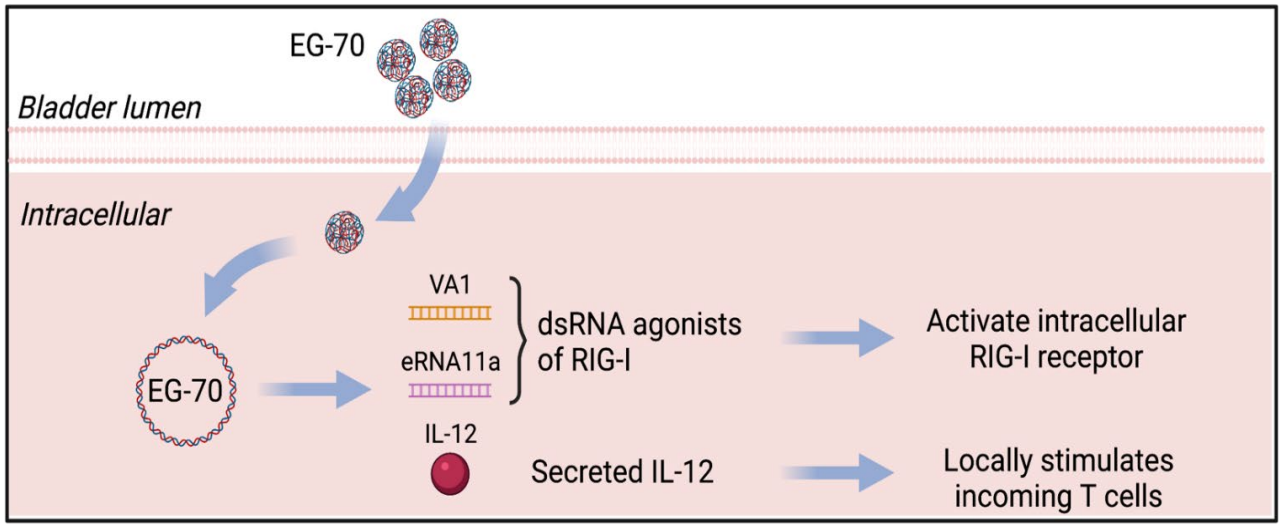
Reduced patient & clinic burden

In contrast to viral vectors, there are no isolation, urine bleaching, or contact-avoidance protocols for patients	✓
Avoids infection risk commonly attributed to use of indwelling devices	✓



EG-70: Designed to bring genetic medicine to any urology clinic

EG-70 is designed to eradicate tumors via synergistic stimulation of specific innate and adaptive immune responses localized to the bladder



Innate immune system activation: dual RIG-I agonists

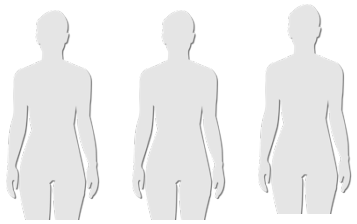
- Combination of NK cell stimulation and suppressor cell attenuation promotes tumor killing
- Stimulates T-cell recruitment and neo-antigen presentation

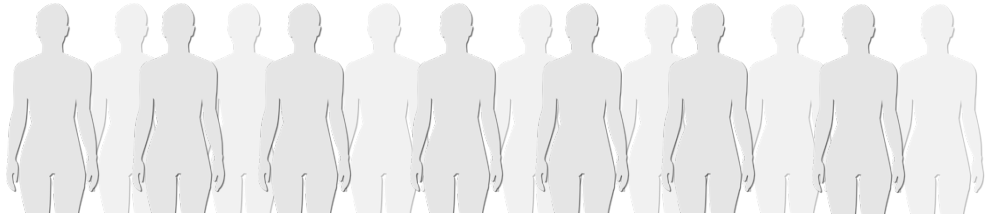
Adaptive immune system activation: secreted IL-12

- T-cell dependent cytokine response promotes tumor killing, immune memory
- Bladder-restricted production has potential to drive strong therapeutic effect while reducing potential for systemic adverse events

Schematic created using BioRender.com
IL-12, interleukin 12; NK, natural killer; RIG-I, retinoic acid-inducible gene I

LEGEND (NCT04752722): Phase 1/2 study





Phase 1: Primary, secondary endpoints – completed
N = 24

Phase 2: Interim data – mid 2024
N = ~100

Patients: High-risk NMIBC failed BCG, with CIS

EG-70 dosing: 2 or 4 doses over 12-week cycle

Cohorts: 3+3 dose escalation: 3 dose levels (0.25 mg/mL, 0.8 mg/mL, 2.5 mg/mL); 2 schedules (2 doses/12-week cycle versus 4 doses/12-week cycle)

Endpoints: 1° – Safety; 2° – Efficacy at 3 months

Patients: BCG-unresponsive NMIBC with CIS*

EG-70 dosing: 4 x 0.8 mg/mL at weeks 1, 2, 5, & 6 of 12-week cycles

Cohorts: Single-arm, open label

Endpoints: 1° – Complete response rate at 12 months; 2° – Safety and durability

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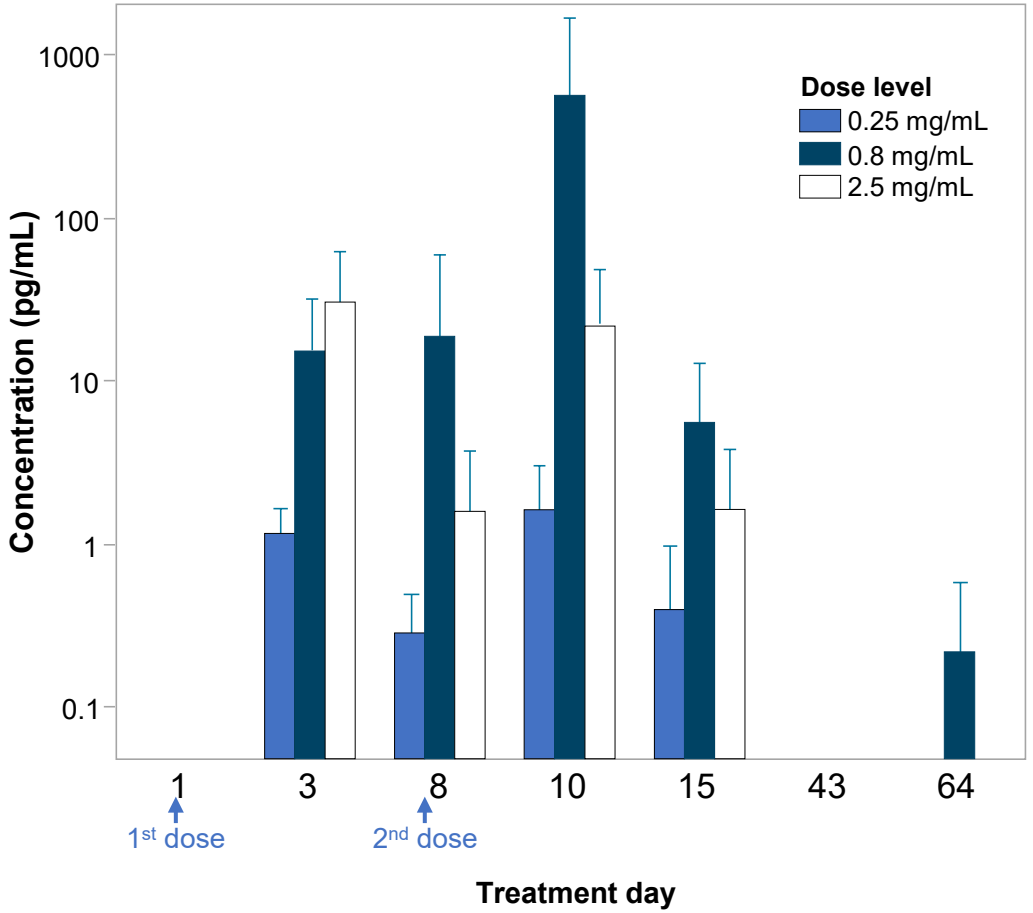
ClinicalTrials.gov
NCT04752722

*A second cohort investigates patients with NMIBC with CIS who are BCG-naïve or BCG-intolerant or inadequately treated with BCG

Phase 1: IL-12 detected in the urine

- **Transgene IL-12 protein detected in a dose–responsive manner in the urine of every patient**
  - Urine IL-12 levels at Dose level 2 (0.8 mg/mL) were an order of magnitude higher than Dose level 1 (0.25 mg/mL)
  - No further increases in IL-12 production were observed at Dose level 3 (2.5 mg/mL)
- **No clinically significant IL-12 detected in plasma**

Concentration of IL-12 protein in patient urine during treatment



Phase 1: Status and patient demographics

Status*

- 24 patients had received ≥1 dose of EG-70 by intravesical administration and are evaluable for safety
- 22 patients are in the efficacy dataset

Treatment

- Dose level 1 (0.25 mg/mL): n=3
  - Two instillations per 12-week cycle
- Dose level 2 (0.8 mg/mL): n=16
  - Two instillations per 12-week cycle: n=6
  - Four instillations per 12-week cycle: n=10
- Dose level 3 (2.5 mg/mL): n=3
  - Two instillations per 12-week cycle

Baseline demographics/disease characteristics (safety population)

Baseline characteristic	N=24
Gender, n (%)	
Male	18 (75)
Female	6 (25)
Age, years	
Mean (SD)	74.4 (9.9)
Median (range)	74 (53, 91)
Age categories, n (%)	
≤65	4 (16.7)
>65	20 (83.3)
ECOG, n (%)	
0	21 (87.5)
1	3 (12.5)

*LEGEND phase 1 now closed for enrollment; Data cut 08.22.2023

Phase 1: Treatment-related adverse events (TRAEs)

All TRAEs

Patients with TRAEs n (%)	N=24
Any	13 (54.2)
Grade 1	11 (45.8)
Grade 2	7 (29.2)
Grade 3	1 (4.2)
Grade 4/5	0 (0.0)

- **Promising safety and tolerability profile**
- **Reversible and largely consistent with catheterization**

Patients with TRAEs, n (%)	Grade 1 (Mild)	Grade 2 (Moderate)	Grade 3 (Severe)	Grades 4 or 5 (life-threatening or death)
Hematuria	3 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)
Urinary tract infection	0 (0.0)	3 (12.5)	0 (0.0)	0 (0.0)
Micturition urgency	2 (8.3)	1 (4.2)	0 (0.0)	0 (0.0)
Dysuria	3 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)
Fatigue	2 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)
Nocturia	2 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)
Pyrexia	2 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)
Renal failure*	0 (0.0)	0 (0.0)	1 (4.2)	0 (0.0)

*Patient had a history of renal failure and recurrent obstructive uropathy with presence of bilateral hydroureteronephrosis at screening – enrollment criteria later modified and excludes patients with a history of unresolved vesicoureteral reflux, indwelling urinary catheter or unresolved hydronephrosis due to ureteral obstruction

LEGEND: Phase 1 efficacy

Complete Response	% (n/N)*	
	All doses (n=22)	Selected Phase 2 dose (n=10)
Any time	73% (16/22)	70% (7/10)
3 months	68% (15/22)	70% (7/10)
6 months	45% (10/22)	60% (6/10)
Duration of response		
≥3 months	11/15 (73%)	6/7 (86%)
≥6 months	6/10 (60%)	3/4 (75%)

*The efficacy evaluable population consisted of 22 patients who received intravesical EG-70 with at least 3-month response assessment available: One patient was dosed but not included in the efficacy evaluable population as they did not meet inclusion criteria. A second patient withdrew consent after a single instillation of EG-70

Complete Response was defined per FDA guidance on BCG-unresponsive NMIBC [February 2018]

LEGEND study: Conclusions

- EG-70 is an investigational, non-viral, non-integrating, intravesically administered immunotherapy undergoing evaluation for the treatment of patients with NMIBC with CIS
- Interim data from the phase 1 portion of the LEGEND study suggest a promising safety, tolerability and efficacy profile:
  - **73% of patients achieved a CR at any time. At the dose selected for phase 2, CR rates were 70% at 3 months and 60% at 6 months**
  - Reported TRAEs to date are mostly Grade 1/2 and consistent with catheterization/intravesical administration
- As a non-viral, non-infective gene therapy, there are no special handling precautions, patient restrictions post-treatment, or ultra cold chain logistics considerations
- The global LEGEND study is currently enrolling into the pivotal phase 2 portion for patients with BCG-unresponsive NMIBC with CIS

LEGEND
ClinicalTrials.gov
NCT04752722

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