

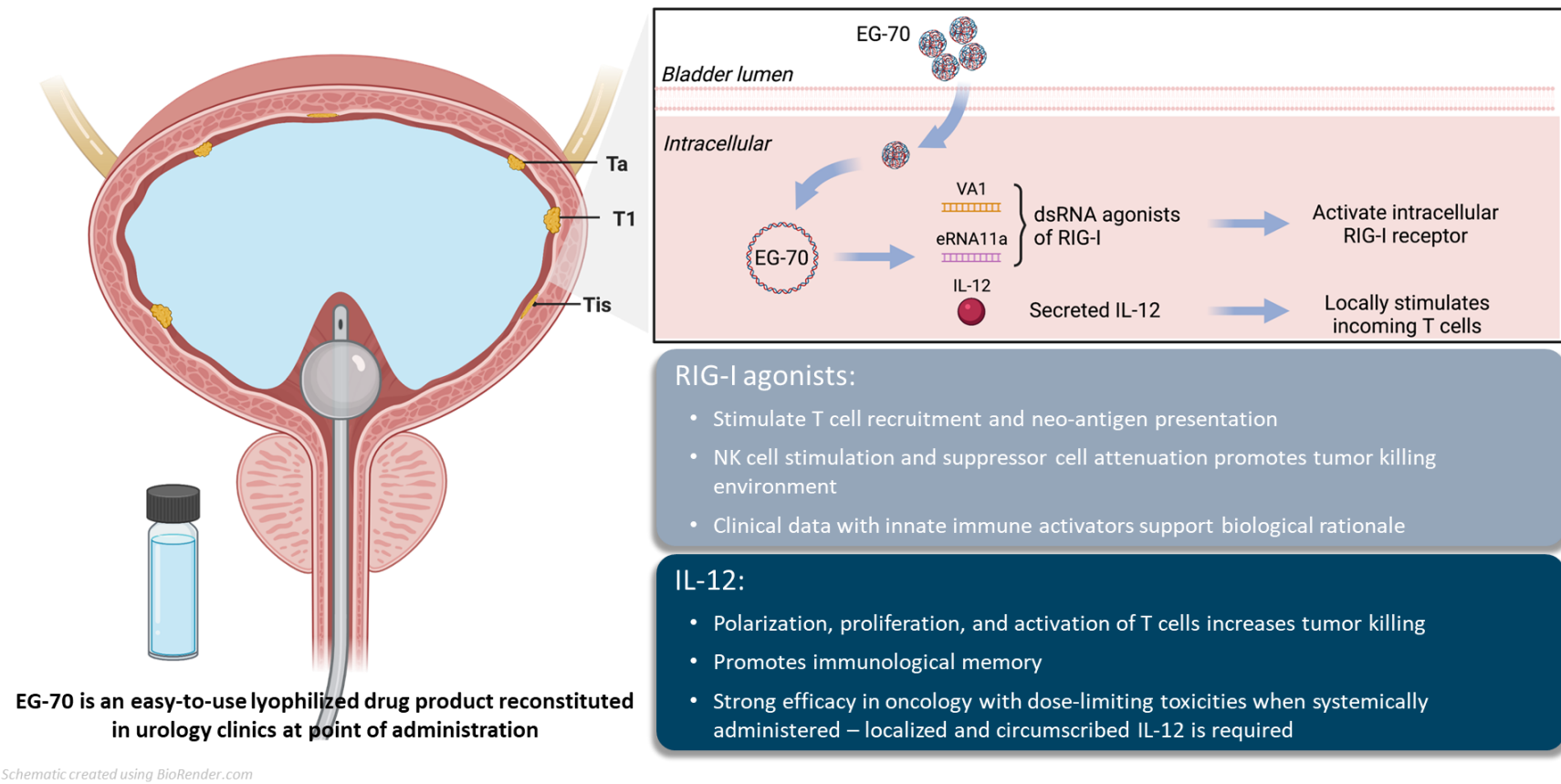
512: Clinical results of a Phase 1 study of intravesical EG-70 in patients with BCG-unresponsive NMIBC

Gary D. Steinberg¹, Susan J. Kalota², Yair Lotan³, Loraine Warner⁴, Shauna Dauphinee⁴, Rosemary Mazanet⁴

¹ NYU Dept of Urology, Perlmutter Cancer Center, New York, NY; ² Urological Associates of Southern Arizona, Tuscon, AZ; ³ UT Southwestern Medical Center, Dallas, TX; ⁴ enGene Inc, Montreal, QC & Boston, MA

BACKGROUND:

enGene is developing a non-viral gene therapy platform to deliver plasmid DNA to mucosal tissues, such as bladder urothelium. EG-70 (detalimogene voraplasmid) is a nanoparticle formulation comprising a plasmid that expresses three genes that simultaneously activate the innate and adaptive immune responses within the bladder. The plasmid encodes both IL-12 and dsRNA that activate the intracellular receptor, RIG-I. EG-70 is administered intravesically to elicit bladder-localized, robust anti-tumor immune responses providing efficacy in high grade non-muscle invasive bladder cancer (NMIBC) while avoiding systemic toxicities. EG-70 does not have the safety risks associated with viral-based gene therapy and it is designed to fit into the clinical practice of community urologists without the need for biosafety containment and ultra-low temperature storage.



METHODS:

In the ongoing Phase 1/2 study (LEGEND; NCT04752722), escalating doses of EG-70 were administered intravesically to patients with high risk BCG-unresponsive Carcinoma in situ (Cis) NMIBC on weeks 1 and 2 or weeks 1, 2, 5, and 6 of a 12-week treatment cycle. At the week 12 assessment, patients with stable disease (SD) or complete response (CR), as assessed by urine cytology, cystoscopy, and bladder biopsy, were allowed electively to remain on EG-70 for up to 3 additional 12-week cycles. The study was conducted in accordance with the ICH for Good Clinical Practice guidelines and with the principles of the Declaration of Helsinki.

RESULTS: PATIENT DEMOGRAPHICS

At time of the data cut, 20 subjects had received at least 1 dose of EG-70. Most were white (95%) and male (80%), with an average age ($\pm$ SD) of 72 $\pm$ 8.9 years and a BMI of 28.4 $\pm$ 5.24. On average, patients had previously received 11 $\pm$ 3.5 doses of BCG, with an average of 15 $\pm$ 13.6 months between their last BCG dose and their first EG-70 dose.

EG-70 is a novel, non-viral immuno-oncology gene therapy for NMIBC

Complete response (CR) rate of 71% in Phase 1 LEGEND Study in high risk BCG –unresponsive patients

Take a photo of the QR code for more information on the LEGEND Study

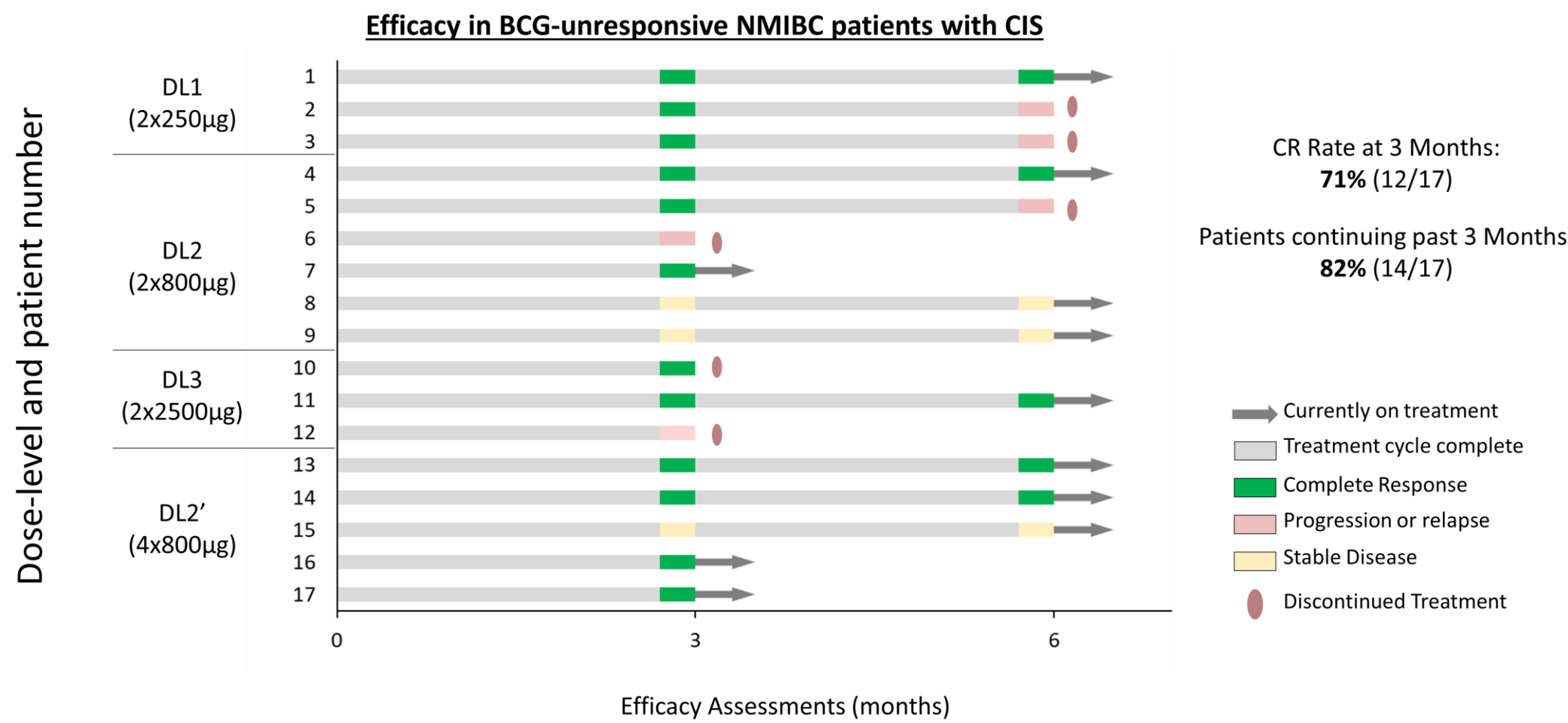


RESULTS: SAFETY

EG-70 was generally safe and well tolerated. Adverse events have been largely consistent with urinary tract instrumentation and were not dose related.

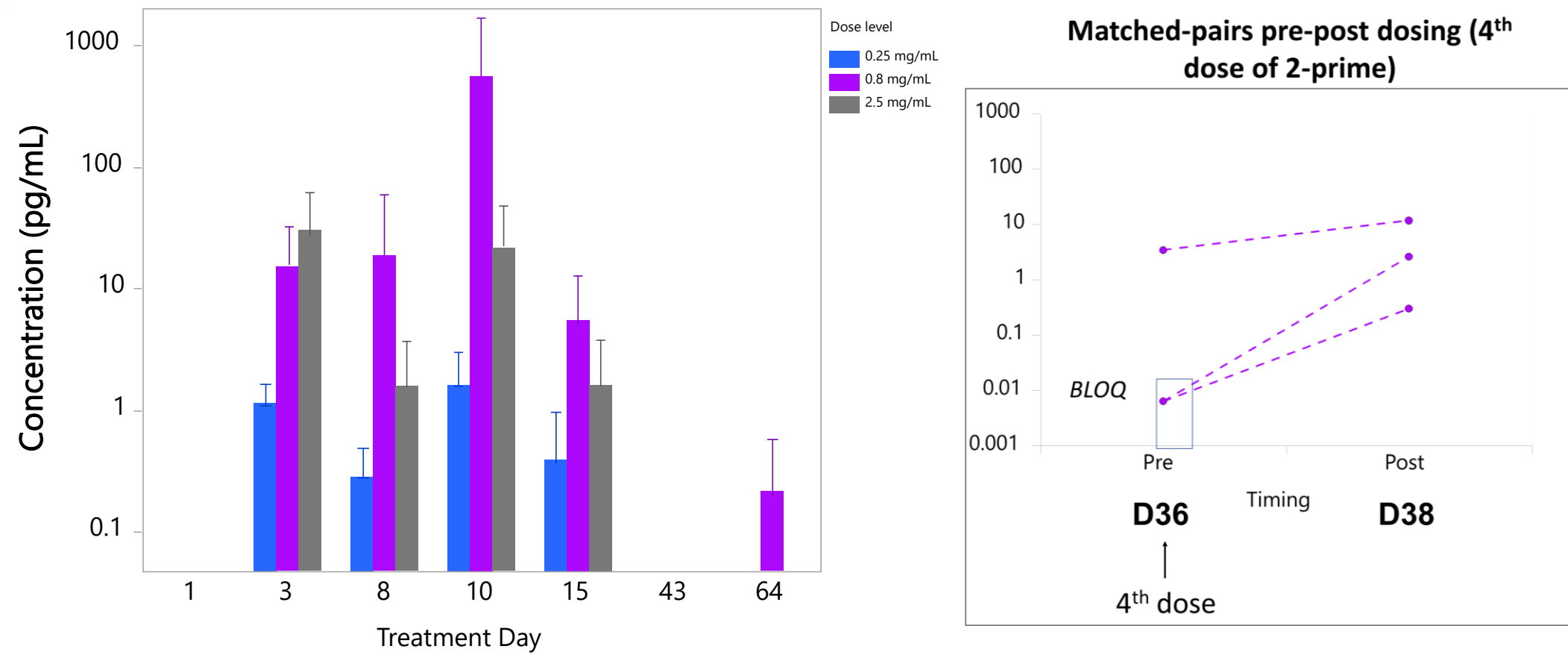
	Total (N=20) n (%)	0.25 mg/mL 2 Doses (N=3) n (%)	0.8 mg/mL 2 Doses (N=6) n (%)	0.8 mg/mL 4 Doses (N=8) n (%)	2.5 mg/mL 2 Doses (N=3) n (%)
Adverse Events (AEs)					
Any AEs	18 (90.0)	3 (100.0)	5 (83.3)	7 (87.5)	3 (100.0)
Any TEAEs	18 (90.0)	3 (100.0)	5 (83.3)	7 (87.5)	3 (100.0)
Serious TEAEs	1 (5.0)	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)
CTCAE Grade 3/4/5 TEAEs	1 (5.0)	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)
Study Drug-Related TEAEs					
Any TEAEs	13 (65.0)	2 (66.7)	2 (33.3)	6 (75.0)	3 (100.0)
Serious TEAEs	1 (5.0)	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)
CTCAE Grade 3/4/5 TEAEs	1 (5.0)	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)
Discont' Study Drug Due to					
Any TEAEs	1 (5.0)	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)
Study Drug-Related TEAEs	1 (5.0)	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)

RESULTS: EFFICACY AND BIOMARKERS



3 patients were dosed and included in the Safety Database yet not included in this modified Intent-to-Treat cohort: 1 patient was dosed but has not yet reached the Month 3 efficacy visit. A second was dosed but later deemed ineligible. A third did not receive the full regimen and voluntarily withdrew consent.

EG-70 resulted in strong efficacy (based on cytology, cystoscopy, and biopsy) in all doses tested (above). The therapeutic transgene IL-12 protein was detected in a dose-responsive manner in the urine of every patient, demonstrating transfection, and was still induced through 4 instillations (below).



FUTURE DIRECTIONS, PHASE 2:

- Preliminary data demonstrate:
 - A high level of efficacy, that is
 - driven by demonstrated expression of therapeutic gene cargos, with a safe and tolerable adverse event profile
- Based on the promise of these data, the Phase 2 portion of the trial is scheduled to begin in the first half of 2023