

A Non-Viral Intravesical Gene Therapy for BCG-Unresponsive NMIBC With CIS, With or Without Papillary Disease: Pivotal Phase 2 Interim Results of Detalimogene Voraplasamid

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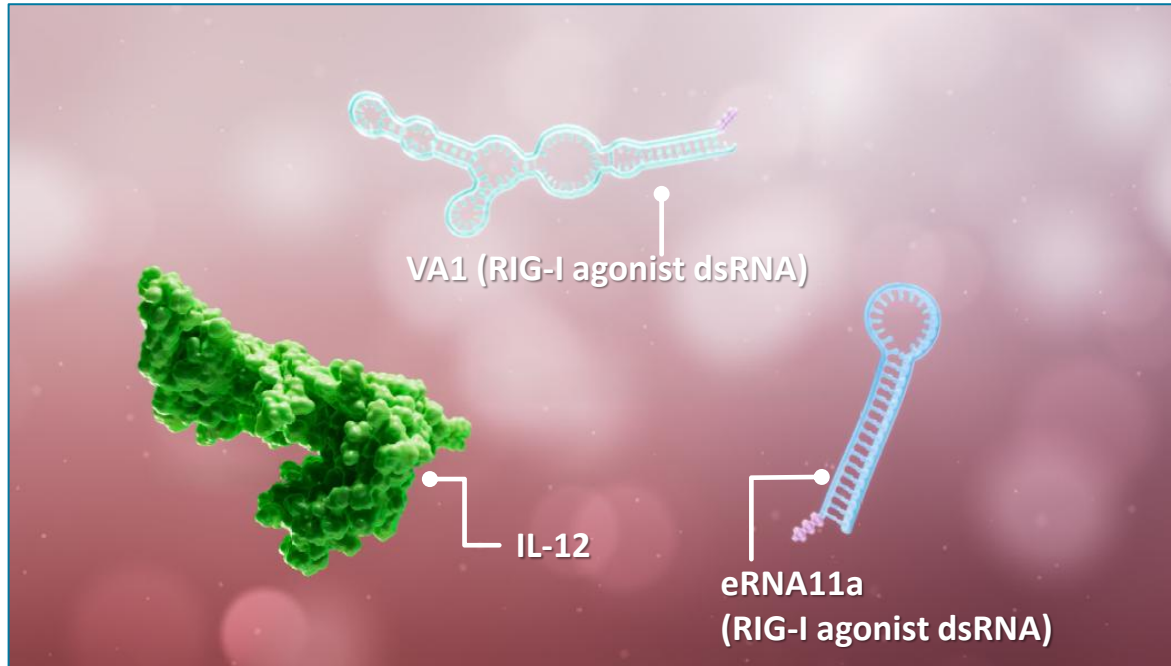
Patients With BCG-Unresponsive NMIBC Have a Persistent Need for Novel Bladder-Sparing Treatment Options

- **Global burden:** ~656,000 new bladder cancer cases worldwide in 2025, including ~87,000 in the United States^{1,2}
- **Despite recent approvals, there is still a significant need for novel therapies that address key limitations³⁻⁶ :**
 - **Patient burden:** toxicity, frequent visits and procedures, and post-treatment precautions^{3-6, 7}
 - **Practice burden:** complex administration, storage, and biosafety handling requirements^{3-6, 8}
 - **Limited durability:** ~60%-80% of patients are not in response within 1 year of treatment^{3-6, 9-12}

BCG, Bacillus Calmette-Guérin; CIS, carcinoma in situ; NMIBC, non-muscle invasive bladder cancer.

1. International Agency for Research on Cancer WHO Global. Accessed March 14, 2026. https://gco.iarc.fr/tomorrow/en/dataviz/isotype?cancers=30&single_unit=50000&years=2025. 2. International Agency for Research on Cancer WHO United States. Accessed March 14, 2026. https://gco.iarc.fr/tomorrow/en/dataviz/isotype?cancers=30&single_unit=500&years=2025&sexes=0&populations=840. 3. Inlexzo. Prescribing Information. Johnson & Johnson; 2025. Accessed March 14, 2026. <https://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/INLEXZO-pi.pdf>. 4. Anktiva. Prescribing Information. ImmunityBio; 2024. Accessed March 14, 2026. <https://anktiva.com/wp-content/uploads/ANKTIVA-Annotated-Approved-Label-Clean.pdf>. 5. Adstiladrin. Prescribing Information. Ferring Pharmaceuticals, Inc. Accessed March 14, 2026. <http://ferringusa.com/pi/adstiladrin>. 6. Keytruda. Prescribing Information. Merck Sharp & Dohme LLC. Accessed March 14, 2026. 7. Gribsch et al. *Oncol Ther*. 2025;13:895-918. 8. Marx et al. *Infect Control Hosp Epidemiol*. 2024;45(4):520-525. https://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_pi.pdf. 9. Boorjian et al. *Lancet Oncol*. 2021;22(1):107-117. 10. Daneshmand et al. *J Clin Oncol*. 2025;43:3578-3588. 11. Chamie et al. *NEJM Evid*. 2022;215:44-56. 12. Balar et al. *Lancet Oncol*. 2021;22(7):919-930.

As a Non-Viral Gene Therapy, Investigational Detalimogene Is Easy to Administer and Overcomes Several Limitations of Viral Therapies



Detalimogene simultaneously activates innate immune signaling and adaptive immune responses by delivering 3 genes to bladder urothelium

PATIENTS



PRACTICE



Fewer doses per 12-week cycle



Storage in a standard freezer



No thaw or pre-wash steps



Administered by medical assistants or nurses in exam rooms



No urine bleaching or close contact precautions with family/caregivers



No decontamination and no special PPE requirements

BCG, Bacillus Calmette-Guérin; PPE, personal protective equipment.

1. Gao et al, inventors; enGene, Inc., assignee. US patent WO 2013/138930 A1. September 26, 2013. 2. Joshi et al. Presented at: 2025 ASCO GU Cancers Symposium; February 13-15, 2025; San Francisco, CA. Abstract TPS886. 3. Narayan et al. Poster presented at: 2025 ASCO GU Cancers Symposium; February 13-15, 2025; San Francisco, CA. Abstract 826. 4. Taylor et al. Presented at: 2025 ASCO GU Cancers Symposium; February 13-15, 2025; San Francisco, CA. Abstract 802. 5. Steinberg et al. Presented at: 2023 SUO; November 28-December 1, 2023; Washington, DC. Abstract 112. 6. American Urological Association. Accessed May 7, 2026. <https://www.auanet.org/about-us/aua-statements/intravesical-administration-of-therapeutic-medication>.

LEGEND: A Single-Arm, Open-Label Study of Detalimogene In High-Risk NMIBC

PHASE 2: ONGOING

Pivotal Cohort

BCG-unresponsive NMIBC with CIS^a
(n=125)

- CIS ± HG Ta/T1 with persistent or recurrent disease within 12 months of adequate BCG

Key Eligibility Criteria

- Age ≥18 years
- ECOG PS of 0, 1, or 2
- Ineligible for or not electing cystectomy
- Adequate bladder function and can retain study drug for ≥60 minutes

Other Cohorts

BCG-naïve NMIBC with CIS^a (n=30)
BCG-exposed NMIBC with CIS^a (n≈70)
BCG-unresponsive HG Ta/T1 papillary disease without CIS (n≈90)
BCG-unresponsive with CIS^a utilizing a bladder rinse

Treatment Schedule

Detalimogene 0.8 mg/mL (50 mL) IVE via catheter with 60-min dwell time^b

Year 1 (induction) (Q12W)												Re-induction at month 6 (persistent/ recurrent disease)	Years 2-3 (maintenance) (Q12W)											
Week	1	2	3	4	5	6	7	8	9	10	11		12	1	2	3	4	5	6	7	8	9	10	11

Endpoints

Primary

- Complete response (CR) rate at any time

Key Secondary

- Duration of response ≥ 12 months
- CR at landmark timepoints
- Safety
- PFS

LEGEND



ClinicalTrials.gov
NCT04752722

^aNMIBC with CIS with or without co-existing papillary (Ta/T1 tumors), protocol requires re-resection of T1 tumors prior to enrollment.
^bInvestigational intravesical therapy.
BCG, Bacillus Calmette-Guérin; CIS, carcinoma in situ; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; HG, high grade; IVE, intravesical instillation; NMIBC, non-muscle invasive bladder cancer; PFS, progression-free survival; Q12W, every 12 weeks.

LEGEND Phase 2 Cohort 1:

Baseline Demographics and High-Risk Disease Characteristics^a

Characteristics	Pivotal cohort 1 (N=125)
Age, years	
Median (range)	71.0 (35.0-90.0)
Sex, n (%)	
Female	24 (19.2%)
Male	101 (80.8%)
Race n (%)	
White	114 (91.2%)
Asian	4 (3.2%)
Black or African American	2 (1.6%)
Not Reported	5 (4.0%)
ECOG PS, n (%)	
0	119 (95.2%)
1	6 (4.8%)

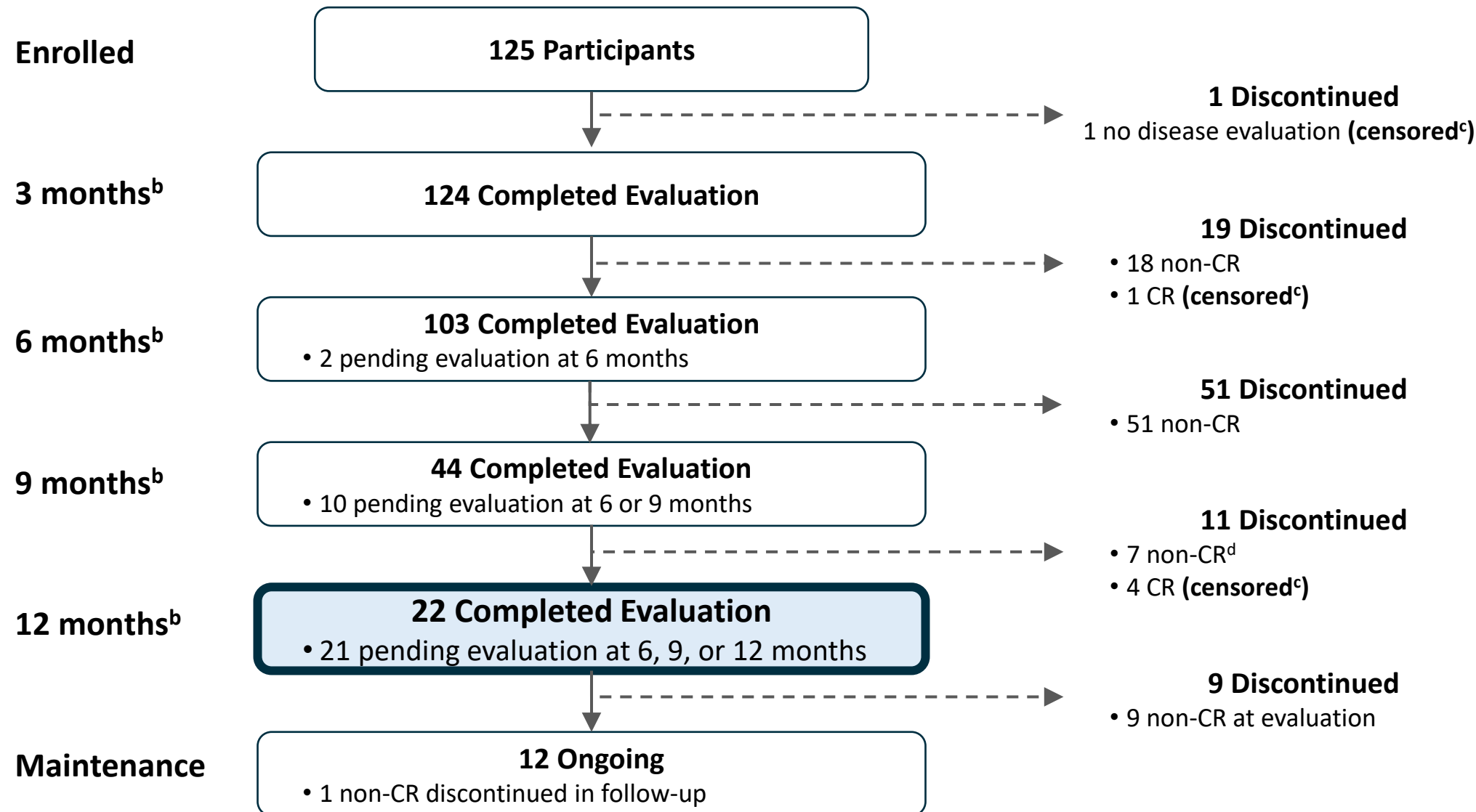
Characteristics	Pivotal cohort 1 (N=125)
Tumor stage, n (%)	
CIS with Ta/T1 disease	49 (39.2%)
CIS only	76 (60.8%)
Reason for no cystectomy, n (%)	
Ineligible	9 (7.2%)
Declined	116 (92.8%)
Prior BCG doses, No.	
Median (range)	12 (6-50)
Prior therapy other than BCG^b, (n %)	
Total	31 (24.8%)
Intravesical chemotherapy	21 (16.8%)
Systemic immunotherapy	8 (6.4%)
Viral gene therapy	5 (4.0%)
Other	4 (3.2%)
Prior NMIBC recurrence(s)	
Median (range)	2 (0-11)

^aData as of April 21, 2026. Data collection and cleaning is ongoing.

^bDefined as serial administration for treatment of NMIBC.

BCG, Bacillus Calmette-Guérin; CIS, carcinoma in situ; ECOG PS, Eastern Cooperative Oncology Group performance status; NMIBC, non-muscle invasive bladder cancer.

LEGEND Phase 2 Cohort 1: CONSORT Diagram^a



^aData as of April 21, 2026. Data collection and cleaning is ongoing.

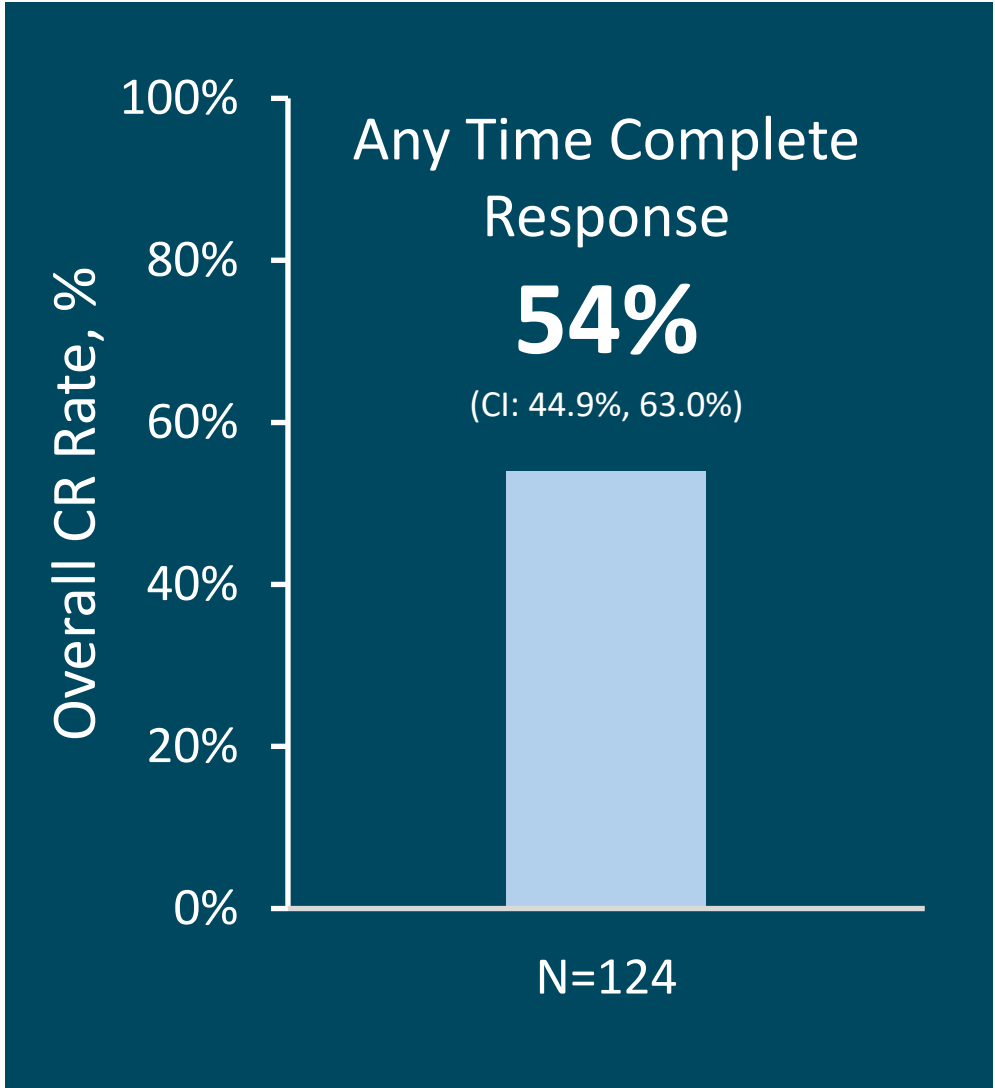
^b3-month interval equals 12-week cycle.

^cParticipants who discontinued without any disease evaluation or who discontinued after a CR are excluded from subsequent landmark response analysis.

^dOne participant is displayed as non-complete response at 9 months based on April 21, 2026, data analysis, and initiated cycle 4. This participant has since been updated to complete response after data analysis.

CR, complete response.

LEGEND Phase 2 Cohort 1: Complete Response Rates^a



CR Landmark	CR Rate, % (95% CI)	CR by KM (Est %)
6 month (n=121)	43.0% (CI: 34.0%, 52.3%)	39.4%
12 month (n=98)	13.3% (CI: 7.3%, 21.6%)	24.5%

- Median follow-up was 5.5 months (range, 1.0-25.8 months)
- **91.0% of CRs occurred at first assessment**
- Median time to onset of CR was 2.1 months (range, 1.5-6.2 months)
- Re-induction success rate was 14.0%^b
- **96.8% were free from progression to ≥T2 disease^c**
- 90.4% of participants remain free from cystectomy^c

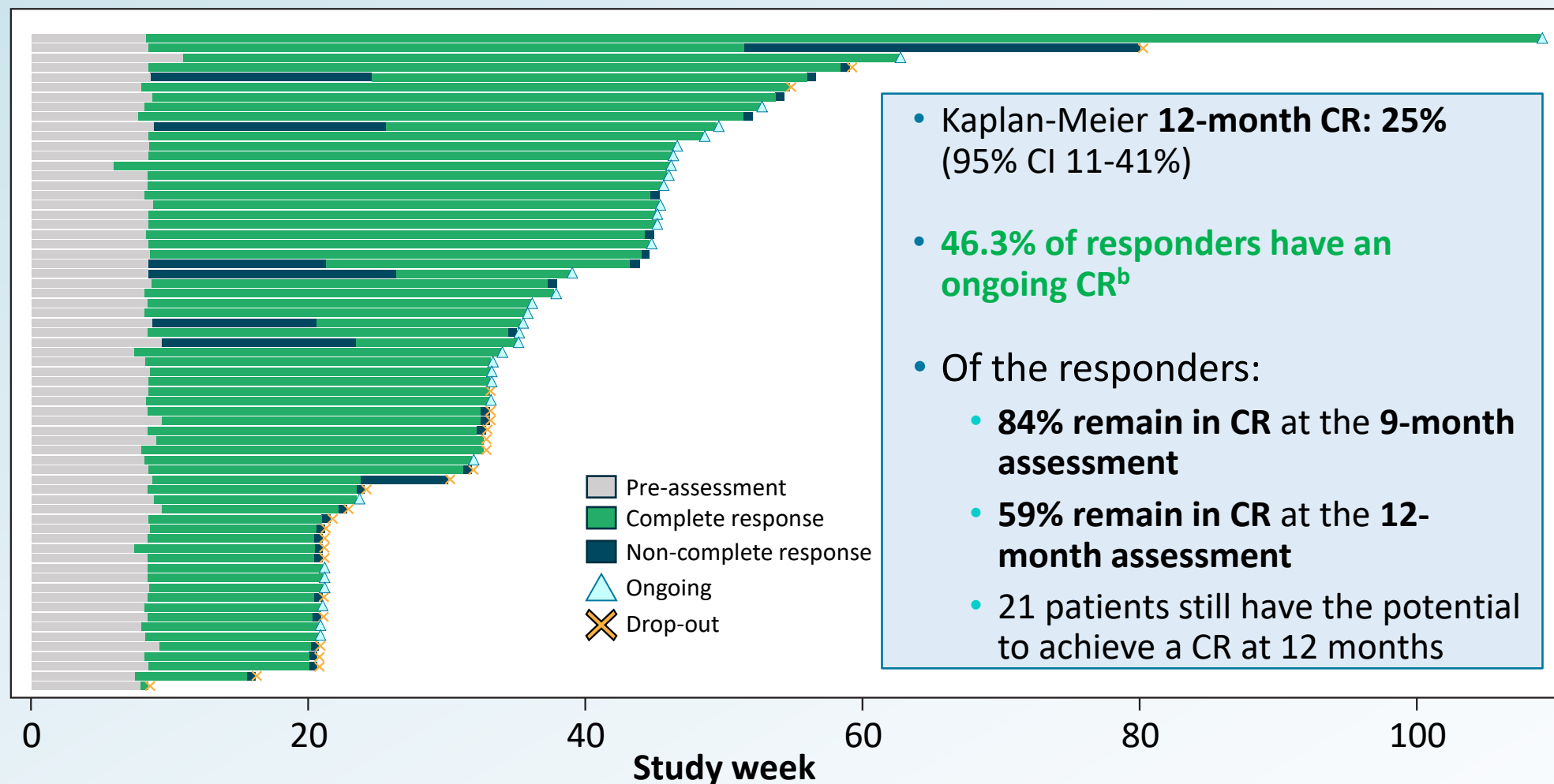
^aData as of April 21, 2026; Data collection and cleaning is ongoing.

^bIncludes all participants who completed re-induction and who were evaluable at cycle 2.

^cDescriptive analysis.

CR, complete response; defined as negative cystoscopy and negative urine cytology, or positive cystoscopy/cytology with negative bladder biopsy; KM, Kaplan-Meier.

LEGEND Phase 2 Cohort 1: Preliminary Durability in Complete Responders^a



^aData as of April 21, 2026. Data collection and cleaning is ongoing. Cycle 3 and cycle 4 correspond approximately to the 9- and 12-month disease assessments, respectively.

^bOne participant is displayed as non-CR in cycle 3 based on April 21, 2026 data cutoff. This participant has since been updated to CR after data cut.
CR, complete response.

Detalimogene Demonstrates Favorable Safety and Tolerability Profile

TRAEs Were Generally Mild and Reversible, Consistent With Catheterization^a

Participants with events, (%)	Pivotal cohort 1 (N=125)
≥ 1 Treatment-related adverse event	55.2%
Most frequent TRAEs (≥10%)	
Fatigue	21.6%
Dysuria	13.6%
Micturition urgency	12.0%
Pollakiuria	12.0%
Bladder spasm	11.2%

Most treatment-related adverse events (TRAEs) were localized, brief, low-grade events

- **69 patients (55.2%)** had **any grade TRAEs**
- Of those with TRAEs, **91.3% had grades 1-2**
- TRAEs resolved after a median of 8 days
- Only 6 patients (4.8%) had grade ≥3 TRAEs^{b,c}
- 2 patients (1.6%) each had 1 “serious TRAE”, both of which resolved and did not lead to discontinuation
- No grade 5 TRAEs were reported

TRAEs leading to dose interruption or discontinuation were rare

- Dose interruption in **3 patients (2.4%)**
- Discontinuation in **3 patients (2.4%)**

ALT, alanine aminotransferase; TRAE, treatment-related adverse event.

^aData as of April 21, 2026. Data collection and cleaning is ongoing.

^bSix participants had grade ≥3 TRAEs of which 5 have resolved. The 1 participant with a grade 4 TRAE (elevated ALT) has resolved.

^cOne participant had a treatment-related pyelonephritis/sepsis that led to a dose interruption. No grade ≥3 TRAEs led to discontinuation.

Conclusions^a

Detalimogene is a next-generation non-viral gene therapy in development for HR NMIBC, designed to:

- **Reduce patient burden** (fewer visits, procedures, pre- or post-treatment precautions)
- **Simplify urologist workflow** (administration, storage, handling)

Detalimogene was safe and very well tolerated

- Most TRAEs were brief, low-grade, lower urinary tract symptoms
- Serious TRAEs (1.6%) and grade ≥ 3 TRAEs (4.8%) were highly infrequent
- TRAEs leading to dose interruption (2.4%) or discontinuation (2.4%) were rare

Detalimogene showed encouraging activity in heavily pre-treated participants with BCG-unresponsive NMIBC

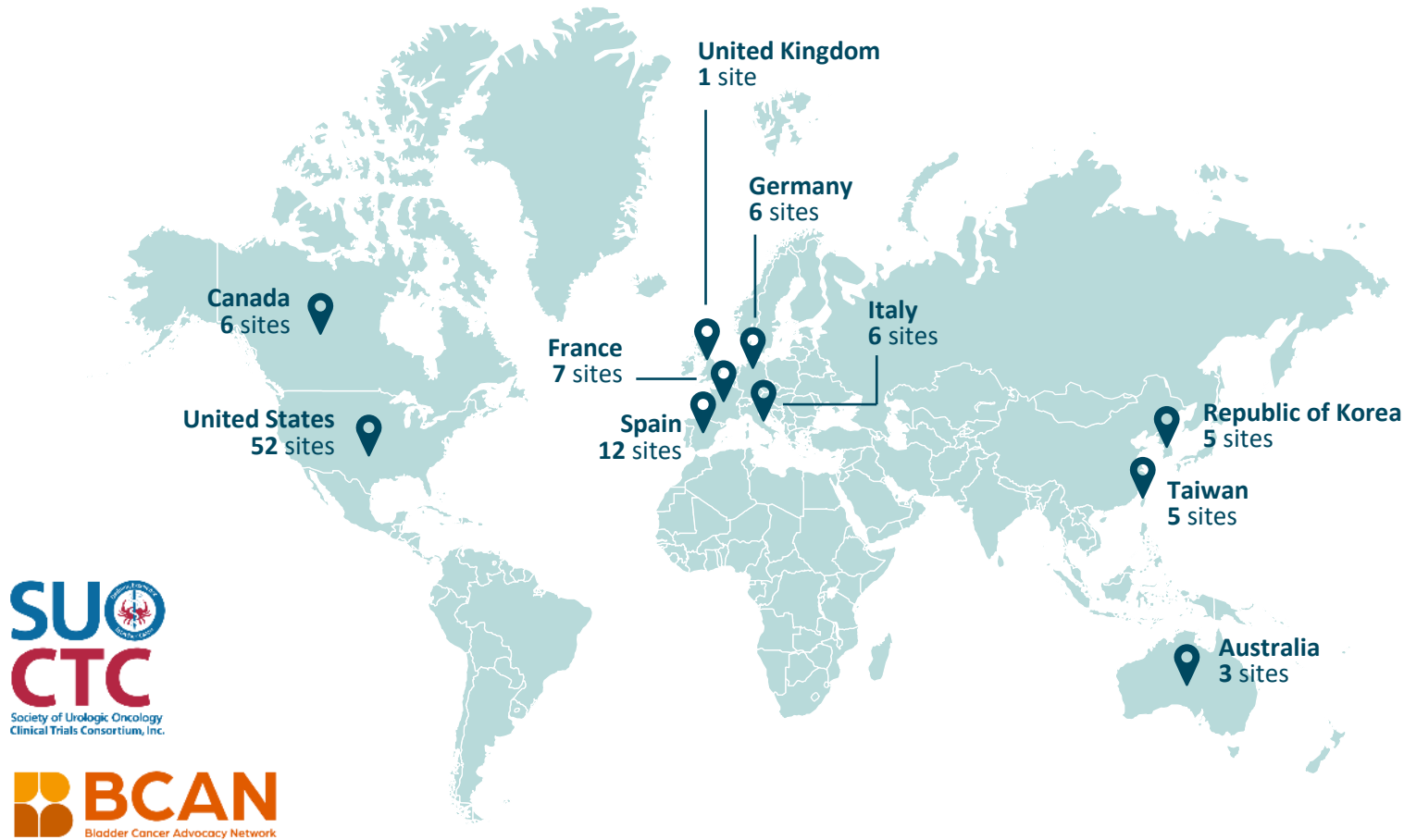
- **CR rate of 54.0% at any time**
- Durability data is preliminary (N=104) and continues to evolve
- **96.8% free from progression to $\geq T2$ disease**

Primary analysis with longer follow-up expected 2H 2026

FDA discussion planned in 2H 2026

2H, second half; BCG, Bacillus Calmette-Guérin; CR, complete response; FDA, United States Food and Drug Administration; HR, high risk; NMIBC, non-muscle invasive bladder cancer; TRAE, treatment-related adverse event.

^aData as of April 21, 2026. Data collection and cleaning is ongoing.



Ongoing phase 2 targets enrollment of n≈350 patients across all cohorts from sites in the USA, Canada, Europe, and the Asia-Pacific Region

ClinicalTrials.gov NCT04752722



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