A0652 CORE-008 Cohort B: Evaluating Intravesical Cretostimogene Grenadenorepvec in Patients with High-Risk, BCG-Exposed Non-Muscle Invasive Bladder Cancer

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BACKGROUND

- **Patients with HR NMIBC whose disease trajectory falls outside the strict FDA guidance of BCG-UR represent a significant unmet need, often lacking access to clinical trials or evidence-based treatment options**.
- **Cretostimogene is an oncolytic immunotherapy with dual mechanisms of action; it selectively replicates in and lyses cancer cells while simultaneously amplifying the immune response against bladder tumors.**
- **BOND-003 evaluating cretostimogene in HR BCG-UR NMIBC with CIS population showed a 75.5% CR at anytime and median DoR of 27.9 months, with 0% ≥ Grade 3 TRAEs- consistent with previous findings.[1-5]**
- **Granted US FDA Fast Track and Breakthrough Therapy Designations in HR BCG-UR NMIBC CIS +/- Ta/T1**

CORE-008 is a phase 2, multi-arm, multi-cohort, open-label trial to evaluate the safety and efficacy of cretostimogene across HR NMIBC:

- **Cohort A**: BCG-Naïve NMIBC
- **Cohort B**: BCG-Exposed NMIBC
- **Cohort CX**: Combination with intravesical gemcitabine in BCG-UR or BCG-Exposed NMIBC

Abbreviations: BCAN= Bladder Cancer Advocacy Network; CR = complete response; DoR= duration of response; GEM= gemcitabine; HG= high-grade; HR= high-risk; EFS = event-free survival NMIBC = non-muscle invasive bladder cancer; SUO-CTC= Society of Urologic Oncology Clinical Trials Consortium; TRAE = treatment-related adverse event; UR = unresponsive

References: **1** Burke, *J Urol*; 2012, **2** Packiam, *Urol Oncol*; 2018, **3** Li, AUA Meeting; 2022, **4** Li, *Nat Med*; 2024, **5** Tyson, SUO Meeting, 2025

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SUO CTC Society of Urologic Oncology Clinical Trials Consortium, Inc.

CORE-008 COHORT B

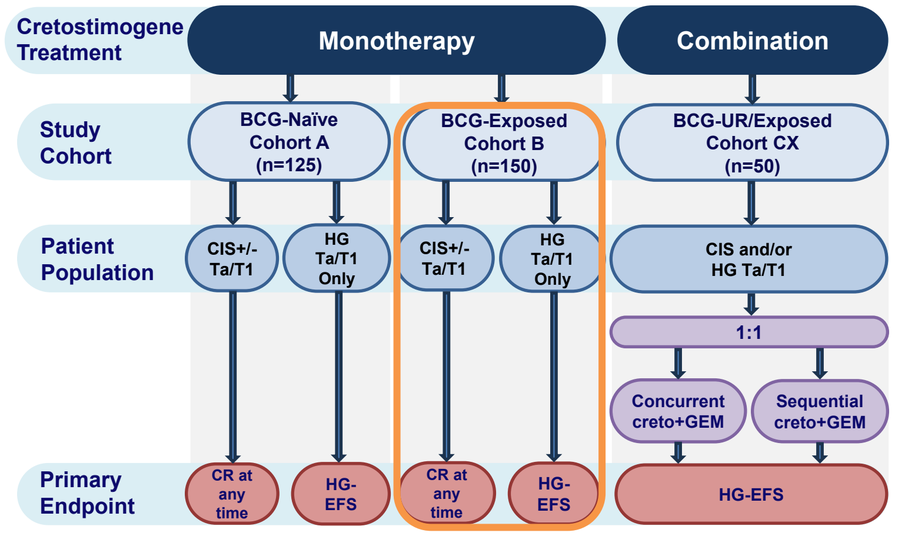
BCAN 20 Years of Impact

Trial in Progress

First Patients Enrolled

BCG-Exposed CIS or Papillary Only

SUO-CTC Collaboration

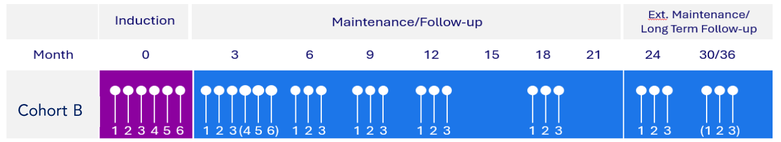


METHODS

- **HR eligibility per AUA/SUO NMIBC guideline criteria**
- **Primary endpoint for CIS is CR at any time and HG-EFS for HG Ta/T1 (papillary-only)**
- **Response Assessments include cystoscopy, biopsy as indicated & cytology every 3 months for first 2 years and every 6 months starting Year 3**
- **Key trial features: Broad & inclusive population, mandatory biopsy at week 51, central pathology review**

BCG-Exposed NMIBC:
BCG-Resistant: Persistent or recurrent HG Ta or CIS at the first evaluation that follows at least 5 of 6 doses of induction BCG, **OR**
Delayed Relapse after Adequate BCG: HG recurrence outside of the BCG-UR window (>6 mo for Ta/T1 and >12 mo for CIS) but within 24 mo after the last dose of adequate BCG, **OR**
Delayed Relapse After Inadequate BCG: HG recurrence within 24 mo after the final dose of inadequate BCG (3–6 doses)

Additional Endpoints:
Duration of Response
CR/HG-EFS at 12 mo
All-Cause EFS
Bladder Cancer Specific Survival
Cystectomy-Free Survival
Progression-Free Survival
Safety
Exploratory: Overall Survival, Patient-Reported Outcomes, Molecular response



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Penn Medicine

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PENN UROLOGY

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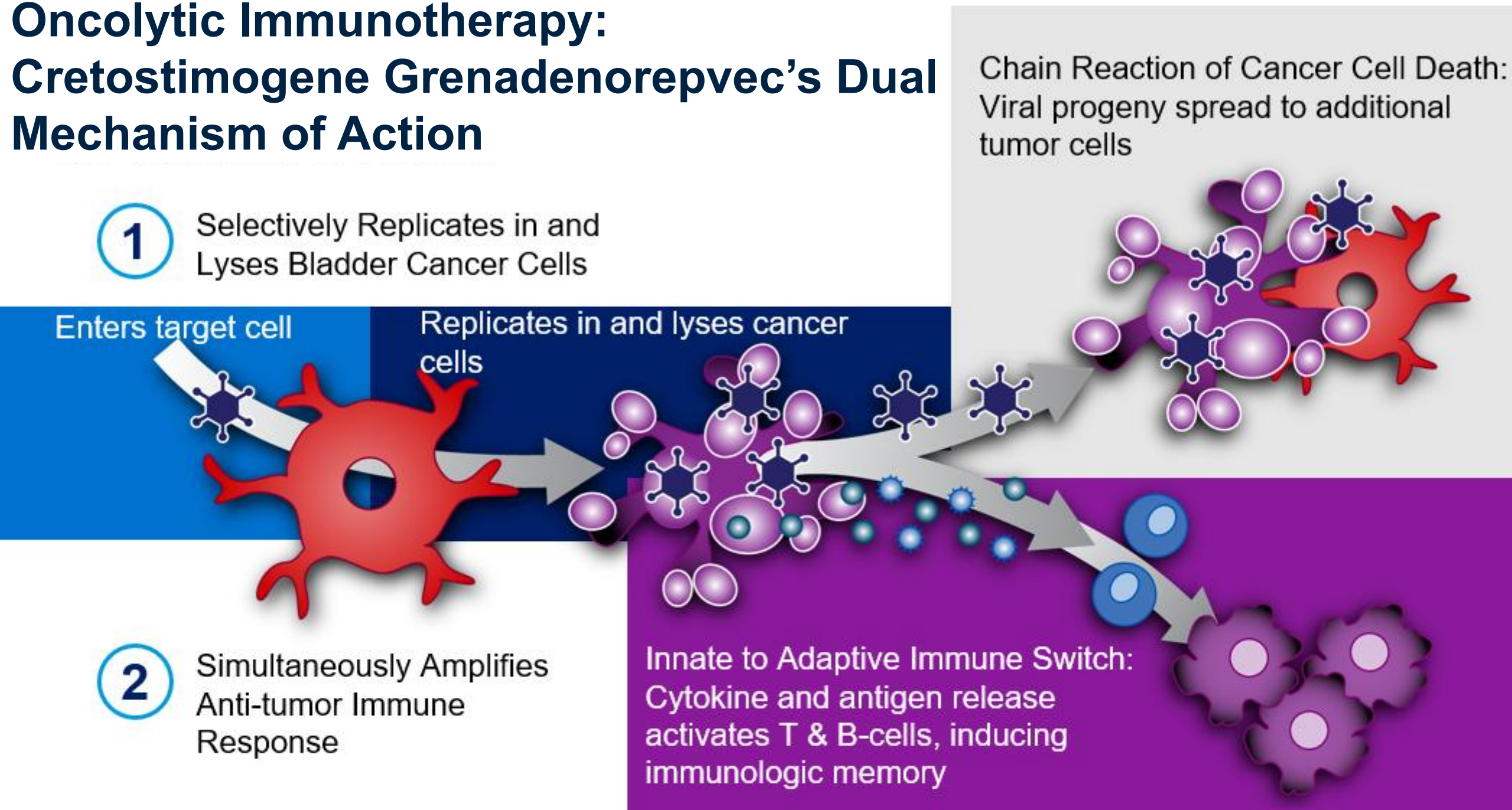
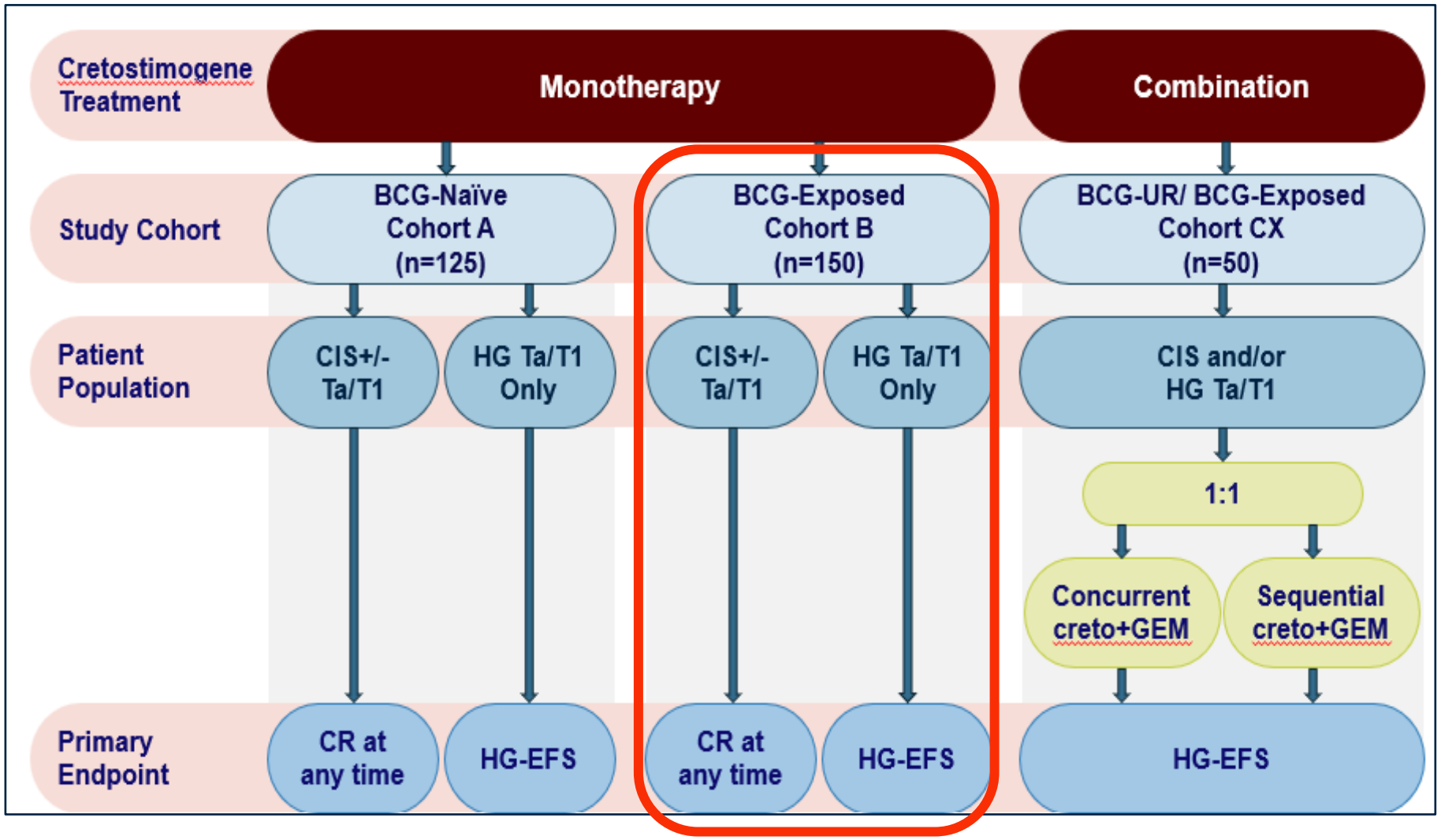
- Grants: NIH SBIR, DOD, RO1, AUA Care Foundation (mentor).
- Clinical trials: CG Oncology, Ferring Pharmaceuticals.
- Scientific Advisory Board: Urogen, CG Oncology, Pfizer.
- Co-Founder: OncoSTING LLC (www.OncoSTING.com).

Oncolytic Immunotherapy: Cretostimogene Grenadenorepvec's Dual Mechanism of Action



CORE-008: Phase 2, Multi-Cohort Trial in HR NMIBC



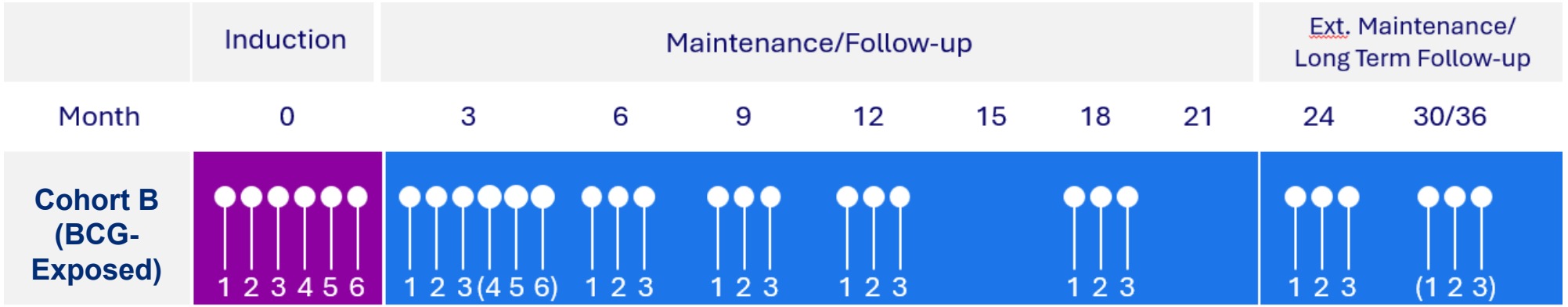
BCG-Exposed NMIBC

BCG-resistant-
Persistent or recurrent HG Ta or CIS at the first evaluation following 5 of 6 induction BCG

Delayed relapse after adequate BCG-
HG recurrence outside of BCG-UR but within 24 mo after last dose of adequate BCG (5+2 doses)

Delayed relapse after inadequate BCG-
HG recurrence within 24 mo after initial dose of inadequate BCG (3-6 doses)

Treatment and Assessment Schedule



- Re-induction allowed for patients with HG Ta and/or CIS at Month 3
- Cystoscopy & Cytology every 3 months with mandatory mapping biopsies at 12 Mo
- CT/MRU every 6 months
- Treatment is optional in Year 3

CORE-008 Cohort B Trial in Progress

- Patients with HR NMIBC whose disease trajectory falls outside the strict FDA guidance of BCG-UR represent a significant unmet need, often lacking access to clinical trials or evidence-based treatment options.
- CORE-008 Cohort B evaluates intravesical cretostimogene in a **broad, inclusive HR BCG-Exposed NMIBC** with CIS or HG Ta/T1 population
- Trial in **collaboration with SUO-CTC with first patients enrolled**

Thank You

All Bladder Cancer Patients and Their Families

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