Updates to the CORE-008 Trial Protocol: A Phase 2 Multi-Arm, Multi-Cohort Study to Evaluate Intravesical Cretostimogene Grenadenorepvec in Patients with High-risk Non-Muscle Invasive Bladder Cancer

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BACKGROUND

- **High-Risk NMIBC challenges: considerable recurrence and progression risk; ongoing BCG shortage [1-2]**
- **Cretostimogene grenadenorepvec is an oncolytic immunotherapy with a dual mechanism of action; it selectively replicates in and lyses cancer cells while simultaneously amplifying the immune response against bladder tumors**
- **BOND-003 evaluating cretostimogene in BCG-UR NMIBC with CIS population showed a 75% CR and median DoR of 27.9 months, with 0% ≥ Grade 3 TRAEs—consistent with previous findings [3-7]**
- **Granted US FDA Fast Track and Breakthrough Therapy Designations in HR BCG-UR NMIBC CIS +/- Ta/T1**

CORE-008 is evaluating creotostimogene as a monotherapy, and in rational combinations, in a broad High-Risk NMIBC population:

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

Abbreviations: CR = complete response; EFS = event-free survival NMIBC = non-muscle invasive bladder cancer; TRAE = treatment-related adverse event; UR = unresponsive

References: **1** NCCN Bladder Cancer Guidelines; 2025 **2** AUA/SUO NMIBC Guidelines; 2024 **3** Burke, J Urol; 2012, **4** Packiam, Urol Oncol; 2018, **5** Li, AUA Meeting; 2022, **6** Li, *Nat Med*; 2024, **7** Tyson, AUA Meeting, 2025

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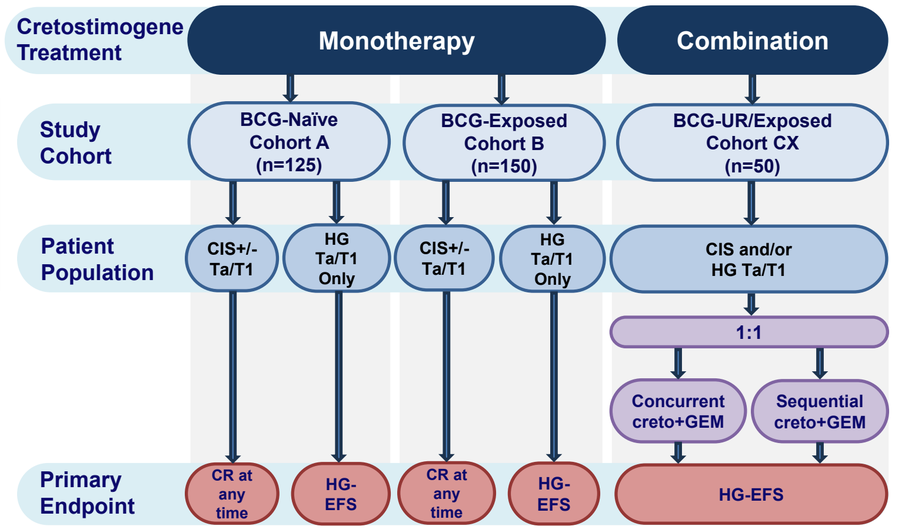
Trial in Progress

Cohort A First Results 2H2025

Cohort B Planned with SUO-CTC

Cohort CX Enrollment Complete

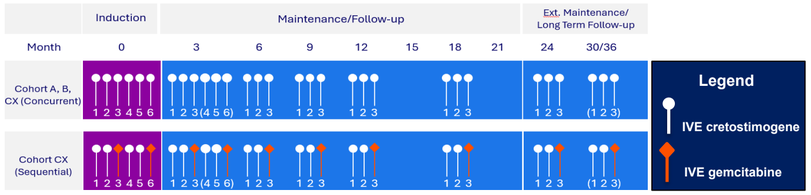


METHOD

- **CORE-008 is a phase 2, multi-arm, multi-cohort, open-label trial to evaluate the safety and efficacy of Cretostimogene in patients with high-risk NMIBC**
- **High-Risk eligibility per AUA/SUO guideline criteria**
- **Primary endpoint for CIS is CR at any time and HG-EFS for papillary-only**
- **Response Assessments include cystoscopy, biopsy as indicated & cytology every 3 months for first 2 years and every 6 months starting Year 3**

Study Population
BCG-Naïve- no prior BCG, BCG >24 mo ago, or 1-2 doses within past 24 mo
BCG-Exposed- received prior BCG and recurred either immediately at the first evaluation or at a delayed timepoint, after adequate or inadequate BCG
BCG-Unresponsive- must receive adequate BCG and present with recurrence at specified timepoints

Key Secondary Endpoints
Duration of Response
All-Cause Event Free Survival
Bladder Cancer Specific Survival
Cystectomy-Free Survival
Progression-Free Survival
Safety



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