



Penn Medicine

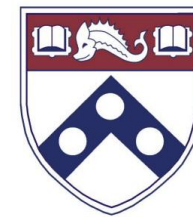
# **Updates to the CORE-008 Trial Protocol: A Phase 2 Multi-Arm, Multi-Cohort Study to Evaluate Intravesical Cretostimogene Grenadenorepvec in Patients with High- Risk Non-Muscle Invasive Bladder Cancer**

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Trinity J. Bivalacqua, MD, PhD

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UROLOGY

# Disclosures

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

# Oncolytic Immunotherapy: Cretostimogene Grenadenorepvec's Dual Mechanism of Action

- 1 Selectively Replicates in and Lyses Bladder Cancer Cells

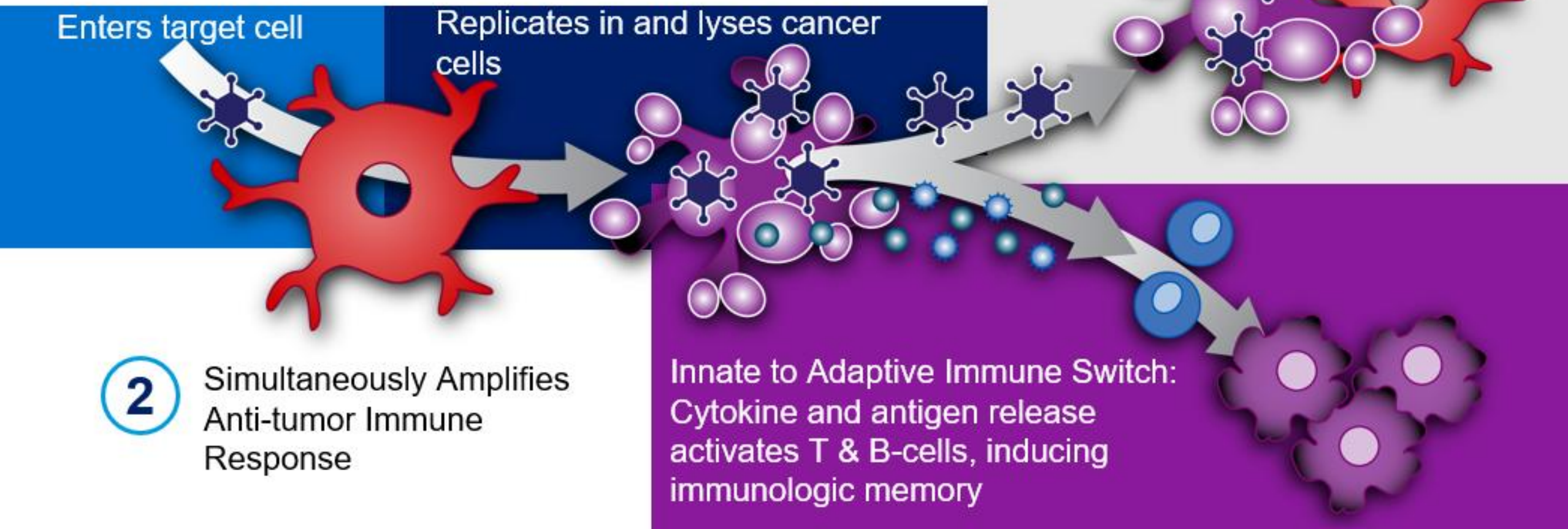
Enters target cell

Replicates in and lyses cancer cells

Chain Reaction of Cancer Cell Death:  
Viral progeny spread to additional  
tumor cells

- 2 Simultaneously Amplifies Anti-tumor Immune Response

Innate to Adaptive Immune Switch:  
Cytokine and antigen release  
activates T & B-cells, inducing  
immunologic memory



# Considerable Unmet Needs in High-Risk NMIBC

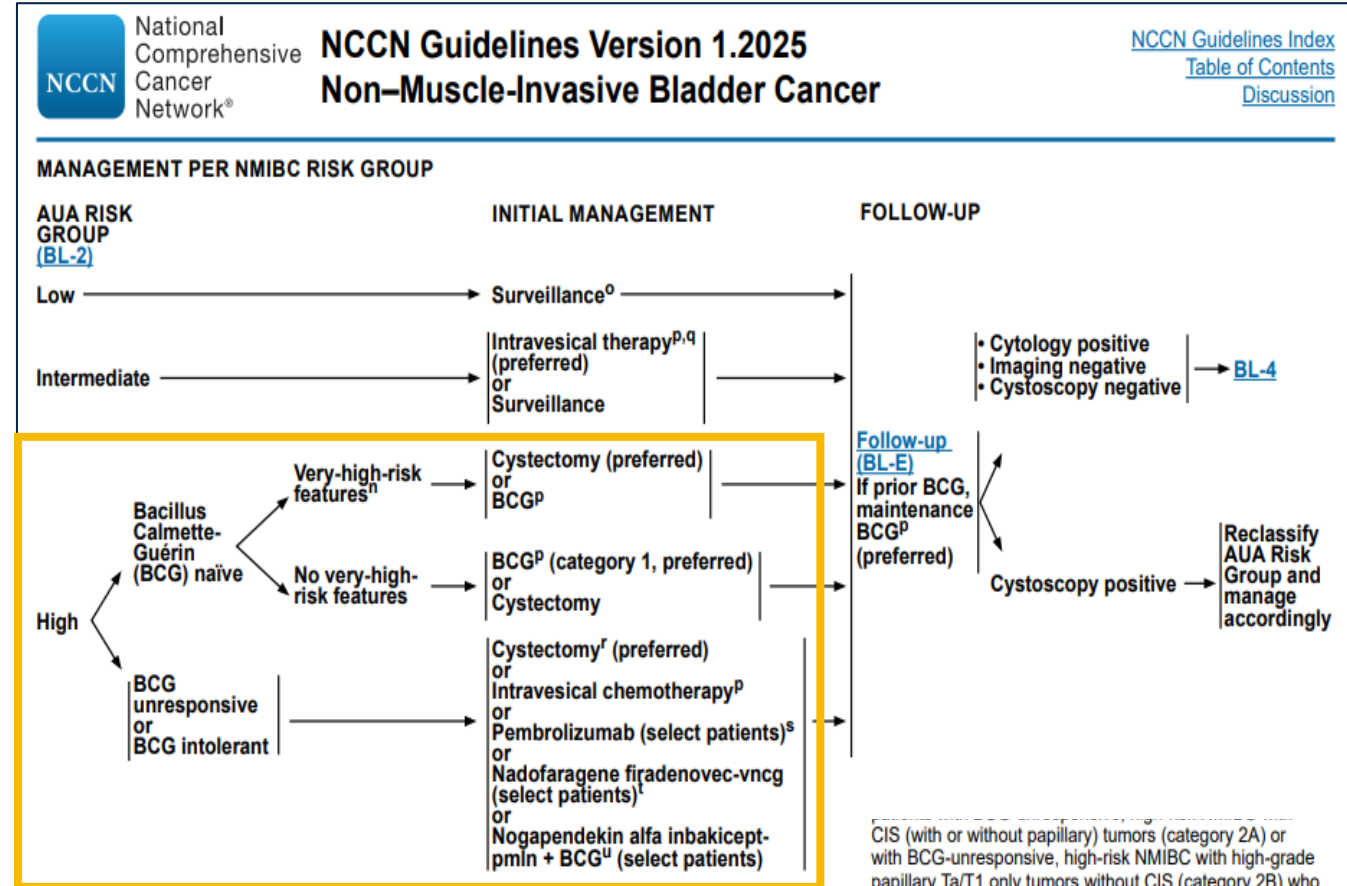
- ▶ Guidelines currently recommend IVE BCG or radical cystectomy

## ▶ Challenges with BCG

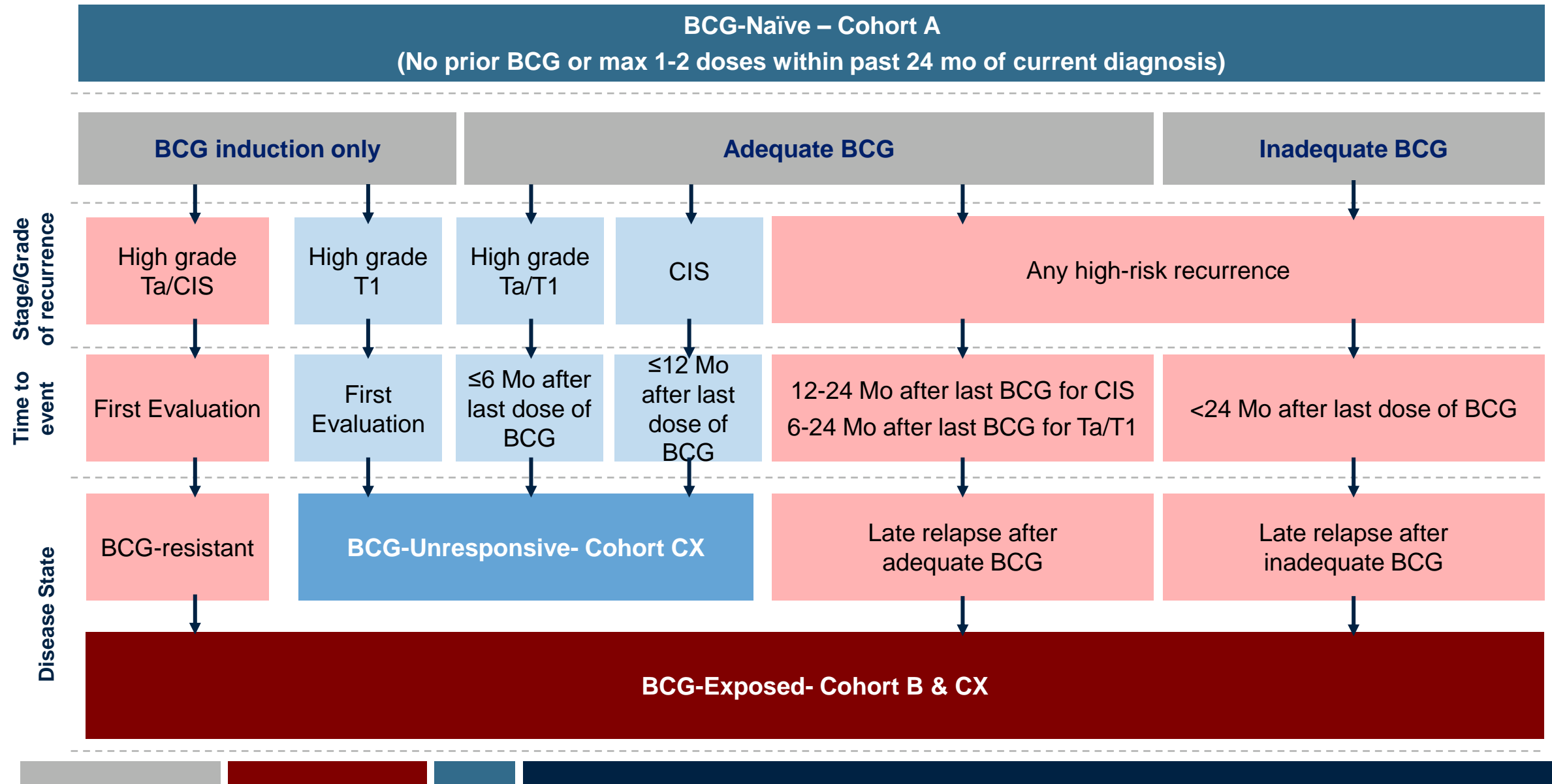
- Despite high initial response rates, over 50% of patients will recur<sup>1</sup>
- 20-40% are at risk for progression<sup>2,3</sup>
- Ongoing BCG shortages<sup>4</sup>

## ▶ Risks with radical cystectomy

- Post-operative complications<sup>5,6</sup>
- Impact on quality of life<sup>6</sup>

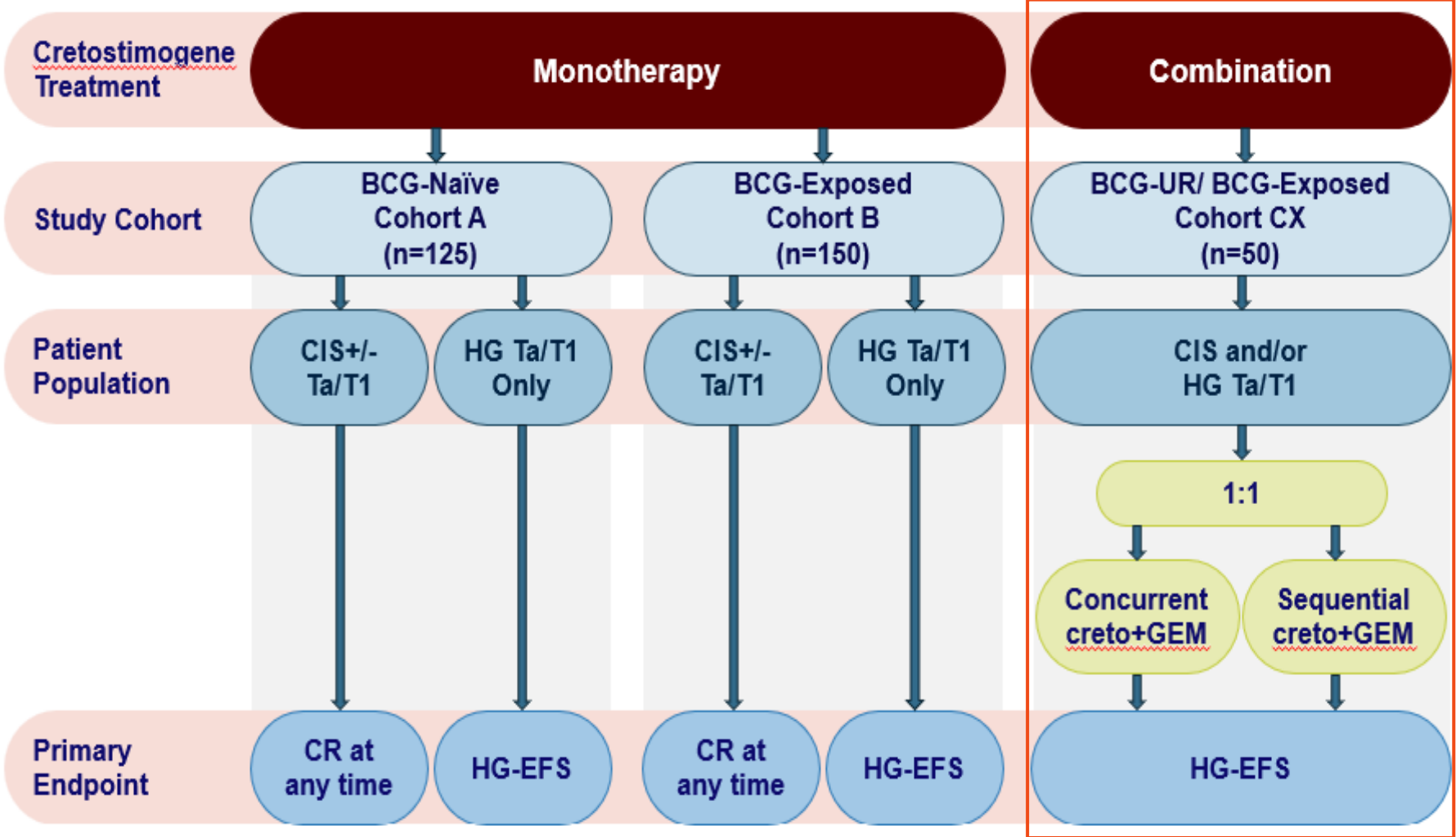


# CORE-008 Study Population





# Phase 2, Multi-Cohort, Open-Label Study of Cretostimogene Grenadenorepvec in High-Risk NMIBC



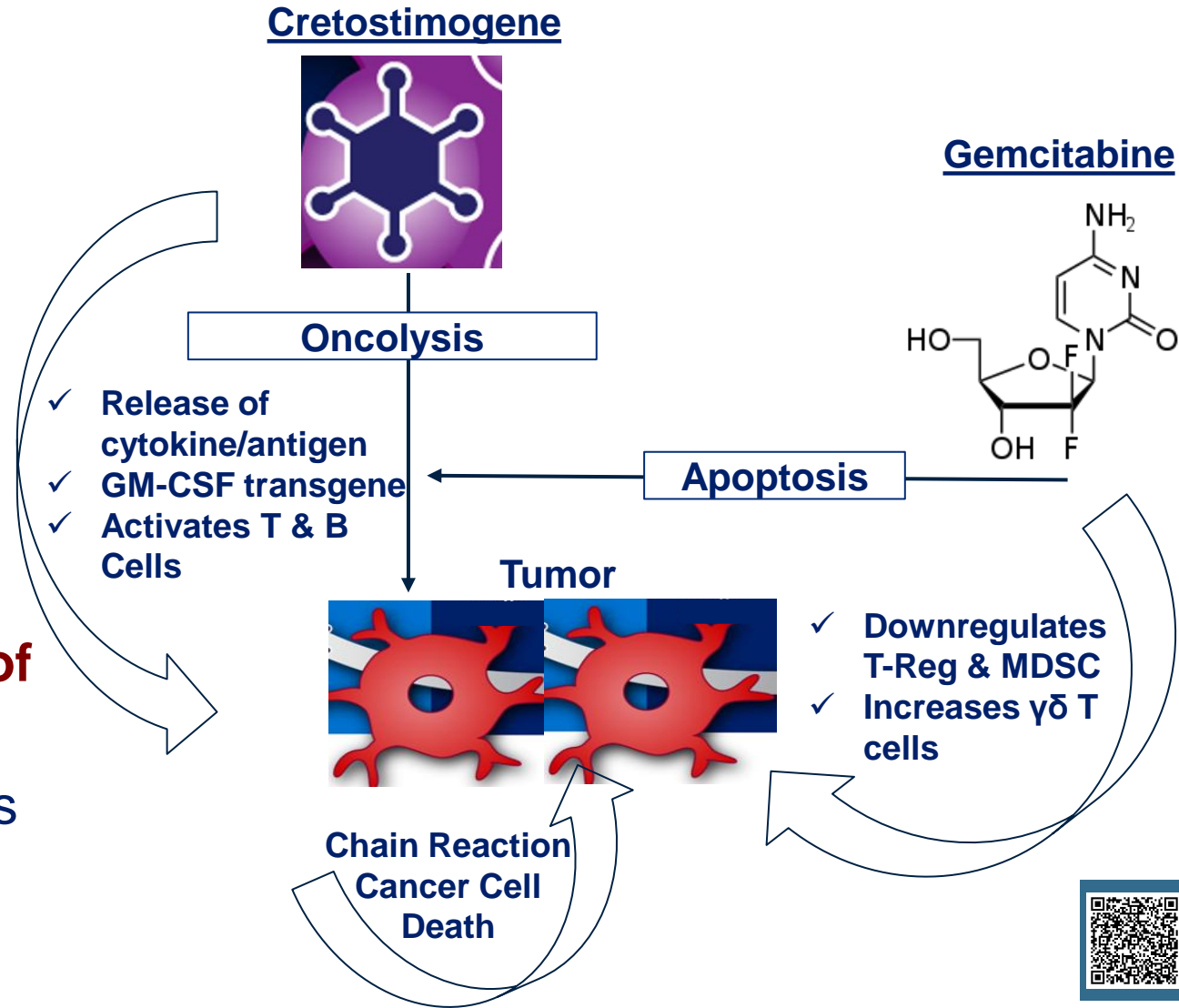
- ### Key Secondary Endpoints
- Duration of Response
  - All-Cause Event Free Survival
  - Bladder Cancer Specific Survival
  - Cystectomy-Free Survival
  - Safety
  - Tolerability



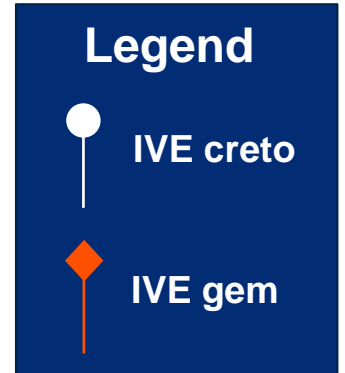
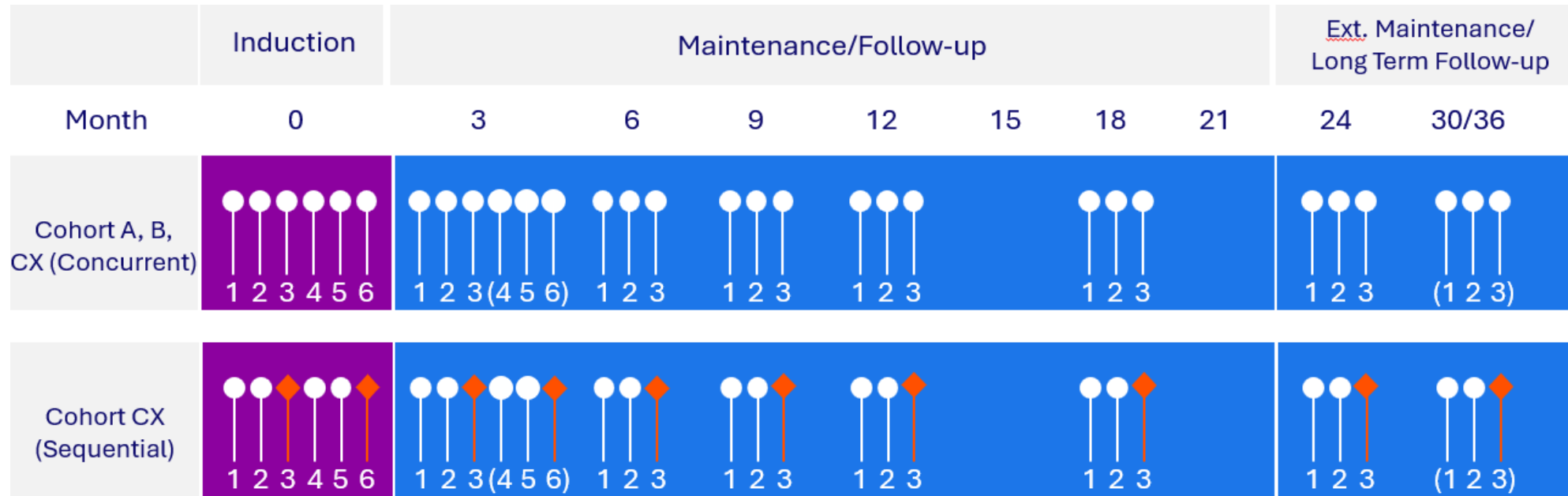
\* BCG-naïve includes no prior treatment with BCG, no BCG within past 24 mo prior to current diagnosis, or maximum 1-2 doses of BCG within past 24 mo prior to current diagnosis  
\*\* BCG exposed includes BCG resistant and delayed relapse after adequate and inadequate BCG  
BCG-Bacillus Calmette-Guerin, CIS- Carcinoma in Situ, CR- Complete Response, HG-EFS- High-Grade Event-free survival, GEM- intravesical gemcitabine  
NCT06567743

# Cohort CX: Possible Synergism Between Cretostimogene & Gemcitabine

- ▶ Efficacy, safety, and tolerability demonstrated as monotherapy and in combination
- ▶ Pre-clinical synergy with gem and oncolytic immunotherapy in other tumor types
- ▶ Prior phase 1-3 studies of gem+ immunotherapy in high-risk NMIBC
- ▶ **Proposed complementary mechanisms of action**
  - Direct oncolytic and pro-apoptotic effects
  - Potential immune modulating synergy



# Treatment & Assessment Schedule



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





# Key Eligibility Criteria

## Inclusion Criteria

- HR NMIBC, AUA definition
- BCG-naïve (**Cohort A**)
- BCG-exposed (**Cohort B**)
- BCG-exposed & BCG-unresponsive (**Cohort CX**)
- Complete TURBT within 90 days
- Adult, ECOG 0-2
- Willing to use contraception, comply with procedures
- Adequate organ function

## Exclusion Criteria

- MIBC, Nodal or Metastatic UC
- UC in upper tract or urethra within 24 months
- Any history of T3 or higher in upper tract/T2 within 4 years
- Prior systemic treatment, radiation, or surgery (beyond TURBT) for bladder cancer
- Intravesical therapy within 90 days  
For Cohort CX- systemic or IVE gemcitabine within 2 yrs except single perioperative instillations
- Antiplatelet/anticoagulation, antiviral or immunosuppressive meds that can't be held
- Transplant, AIDS, active Hep B/C, malignancy, active infection
- Live vaccine, within 30 days
- Not recovered from AE's, condition that contraindicates study, pregnant/breastfeeding (or planning to), can't tolerate study procedures

# CORE-008 is Currently Ongoing & Actively Enrolling

## ► As of April 2025:

- **Cohort A (BCG-Naïve)**
  - **CIS containing arms have completed enrollment**
  - **HG Ta/T1 arm planned**
- Cohort B (BCG-Exposed) is planned and received collaborative SUO-CTC support
- **Cohort CX (BCG-Exposed & BCG-UR)- Open as of April 21**



## ► First results Cohort A 2H2025





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# Thank You

All Bladder Cancer Patients and Their Families  
Key Investigators, Study Coordinators, Nurses

## Key Collaborators

Gary Steinberg, Rush University, IL  
Siamak Daneshmand, USC, CA  
Neal Shore, CURC, SC  
Shreyas Joshi, Emory, GA  
Colin P.N. Dinney, MDACC, TX

## CG Oncology

Rebecca Tregunna  
Daytriona Clemons  
Jee-Hyun Kim  
Kristen Scholz  
Pat Keegan  
Shelja Patel  
Vijay Kasturi