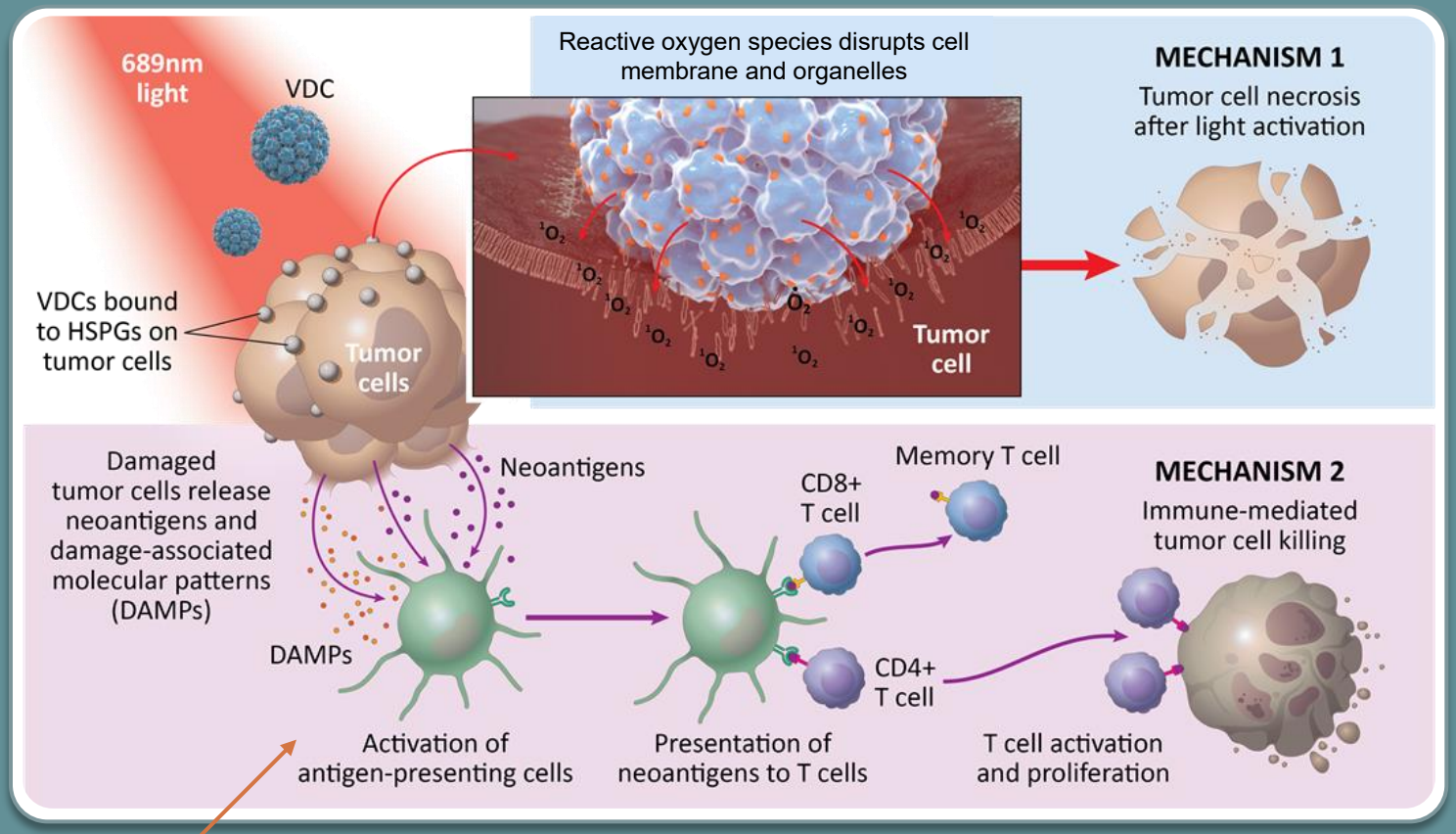
SIU 2025 Trial in Motion:
Safety and Efficacy of AU-011, a Virus-Like Drug Conjugate, in Participants with NMIBC

Piyush Agarwal, M.D., Sabine D. Brookman-May, M.D., Joseph W. McQuaid, M.D., Jennifer Linehan, M.D., Xianne Penny, PhD, Max Kates, M.D., Joseph Jacob, M.D., Gary D. Steinberg, M.D., Neal D. Shore, M.D., Seth P. Lerner, M.D.

AU-011 has a novel dual mechanism of action

Disruption of the tumor cell membrane and pro-immunogenic cell death by necrosis leads to T cell activation and immune-mediated tumor cell killing

VLPs bind to macrophages, B cells, dendritic cells and neutrophils and are capable of **stimulating antigen-presenting cells** through TLR-4 engagement and NFk-β production



Release of **DAMPs** induces **anti-tumor immunity**

AU-011 treatment is designed to be cytopathic to resident suppressor cells, reducing the immune-suppressive microenvironment and contributing to **anti-tumor immunity**

Kines RC, et al. *Int J Cancer*. 2016;138(4):901–11. Kines RC, et al. *Mol Cancer Ther*. 2018;17(2):565–74. Kines RC, et al. *Cancer Immunol Res*. 2021;9:693–706.
DAMPs, damage-associated molecular patterns; **HSPG**, heparan sulfate proteoglycan.
Bel-sar (AU-011) is an investigational product candidate. The effectiveness and safety of bel-sar have not been established, and bel-sar is not approved for use in any jurisdiction.

Bel-sar has an innovative dual MoA

Bel-sar is designed to reduce recurrence and treatment burden with potential to increase bladder preservation

Immune ablation offers an effective front-line therapy, leveraging the immune system to fight cancer at an early stage

1

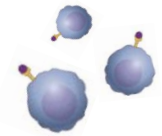
Robust targeted cytotoxicity

designed to rapidly destroy cancer cells

+

2

Long-term anti-tumor immune memory



has the potential to provide immune surveillance, urothelial field effect, and prevent recurrence

- **Focal administration** treats the tumor, not the entire urothelium
- **No need for general anesthesia** – administration is aligned with current urology office practice
- **Procedure is brief (<15 min for both injection and activation) and familiar to urologists,** using standard cystoscopy needles and common technique for laser application

MoA, mechanism of action.

Phase 1

Safety, Feasibility, Efficacy, Immune Response Assessment

aura

Phase 1 safety and feasibility study:
Bel-sar administered before scheduled biopsy and SoC TURBT

Treatment phase: Feasibility and mechanism of action

Day 1

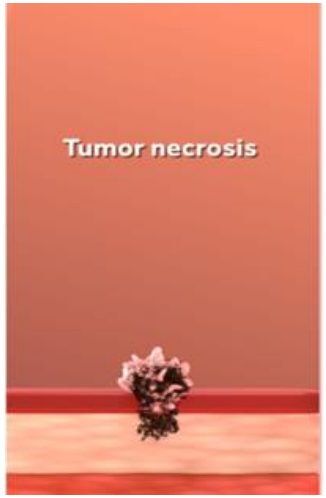
Cystoscopy + biopsy
Bel-sar injection

Pathology specimen

Day 2

Cystoscopy
Laser light activation

Day 9 ± 1 (Cohort A)
Day 14+7 (Cohort B+C)



Final cystoscopy

SoC TURBT
Pathology specimen

Final efficacy evaluation

Follow-up phase: Safety

Day 56 ± 7

Final safety evaluation

End of follow-up

Clinical response data up to 21 days; safety data up to 56 days

Bel-sar, belzupacap sarotalocan; **SoC**, standard-of-care; **TURBT**, transurethral resection of bladder tumor.
Clinicaltrials.gov identifier: NCT05483868; AU-011-102.

Single dose of bel-sar produced **clinical complete responses** in intermediate- and high-risk NMIBC

Intermediate risk (n=5)

- **4/5 treated tumors achieved cCR**, while the fifth treated tumor showed visual tumor shrinkage
- **3/5** participants demonstrated **cCR** in at least one **untreated tumor**
- **Visual changes** on cystoscopy identified in **4/5** participants
- **100%** of treated and untreated tumors demonstrated **immune response**[a]

High risk (n=5)

- **3/5** treated tumors demonstrated **visual tumor shrinkage**
- **1/5** participants achieved **cCR** in both the **treated tumor and an untreated tumor**
- **Visual changes** on cystoscopy identified in **4/5** participants
- **100%** of treated and untreated tumors demonstrated **immune response**[a]

Favorable safety profile observed (n=17)[b]

- <10% of participants experienced Grade 1 TEAEs related to study drug
- No Grade 2/3 TEAEs related to study drug
- No SAEs or DLTs

For purposes of this analysis, cCR is defined as absence of tumor cells on histopathologic evaluation. [a] Immune response defined by immunocyte infiltration on post-treatment histopathology. [b] Safety data includes all completed light-activated cohorts (A, B, and C), including two participants treated but not efficacy evaluable (n=12), plus the drug-only cohort that received no light activation (n=5). Safety data cutoff July 28, 2025.
Bel-sar, belzupacap sarotalocan; **cCR**, clinical complete response; **DLT**, dose-limiting toxicity; **NMIBC**, non-muscle invasive bladder cancer; **SAE**, serious adverse event; **TEAE**, treatment-emergent adverse event.
Clinicaltrials.gov identifier: NCT05483868; AU-011-102. Data cutoff March 3, 2025.

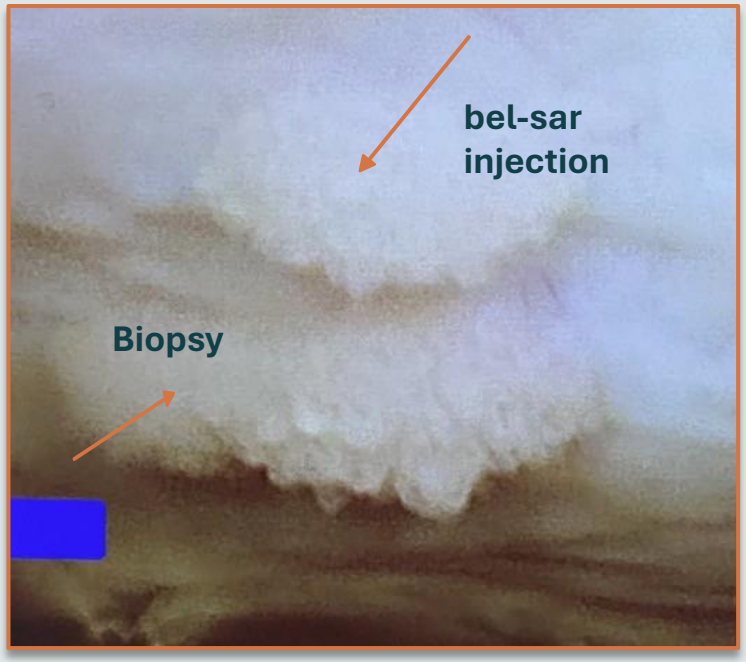
Case study: Clinical complete response confirmed in a participant with highly recurrent disease

Cohort A:
72-year-old male

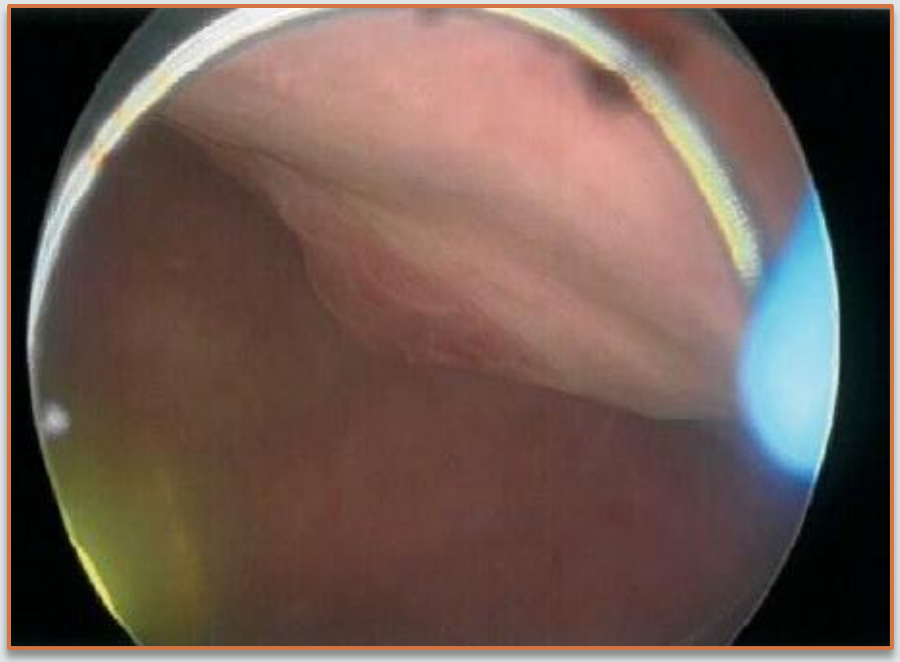
Single dose bel-sar + light activation

- Multiple Ta low-grade tumors, intermediate risk (no CIS)
- History of Ta high-grade (<3cm), intermediate risk
- Multiple prior TURBT surgery (x6)
- Prior BCG induction and maintenance

Clinical complete response visualized at time of TURBT[a]



Tumor pre-injection/pre-biopsy

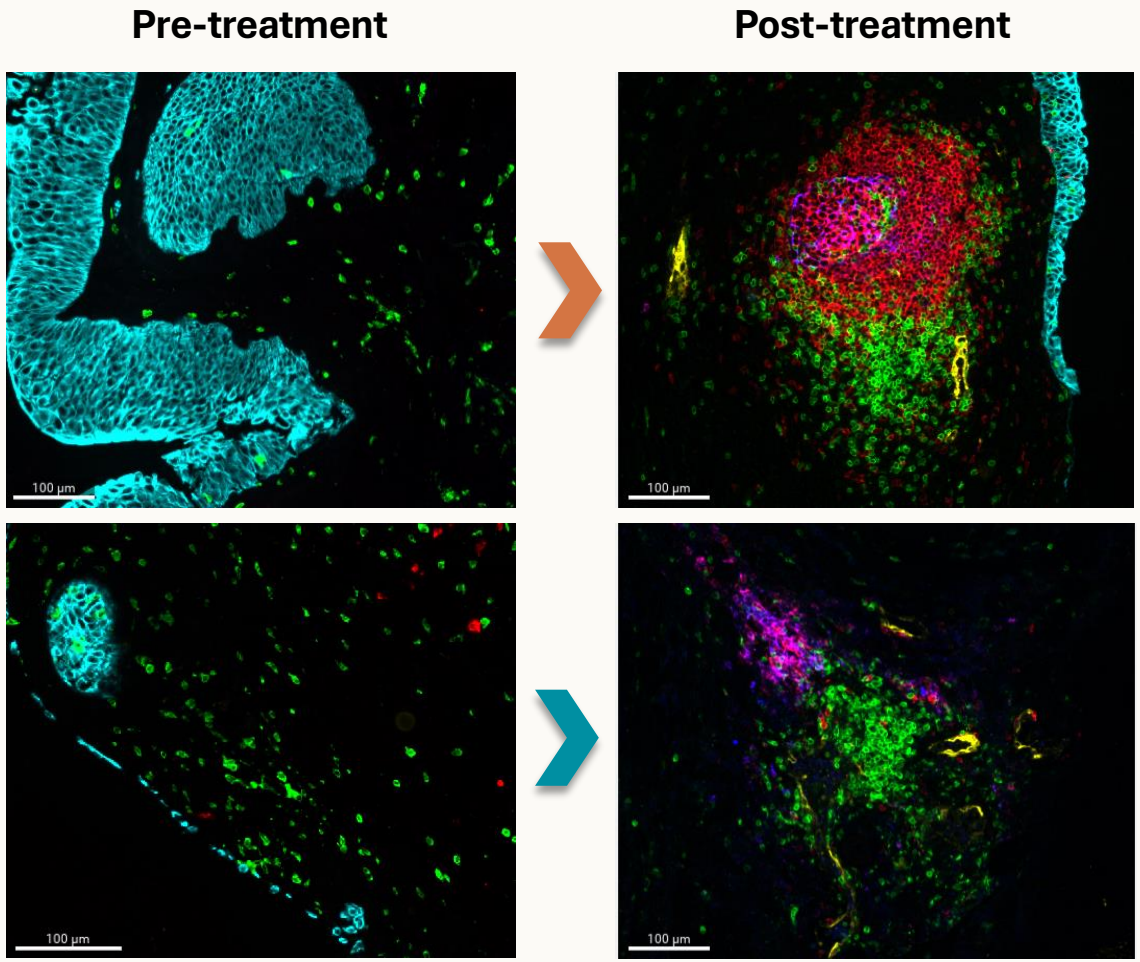


Post-injection edema and ecchymosis at injection site

[a] Confirmed with histopathologic evaluation. **BCG**, Bacillus Calmette-Guerin; **bel-sar**, belzupacap sarotalocan; **CIS**, carcinoma in situ; **TURBT**, transurethral resection of bladder tumor.
Clinicaltrials.gov identifier: NCT05483868; AU-011-102. Data cutoff March 3, 2025.

Multiplex Immune Fluorescence in 5 participants with cCR or visually smaller tumors

Tumor Microenvironment Profiling and Activation



Bel-sar induced **adaptive immune memory** through generation of *de novo* mature tertiary lymphoid structures (TLS)

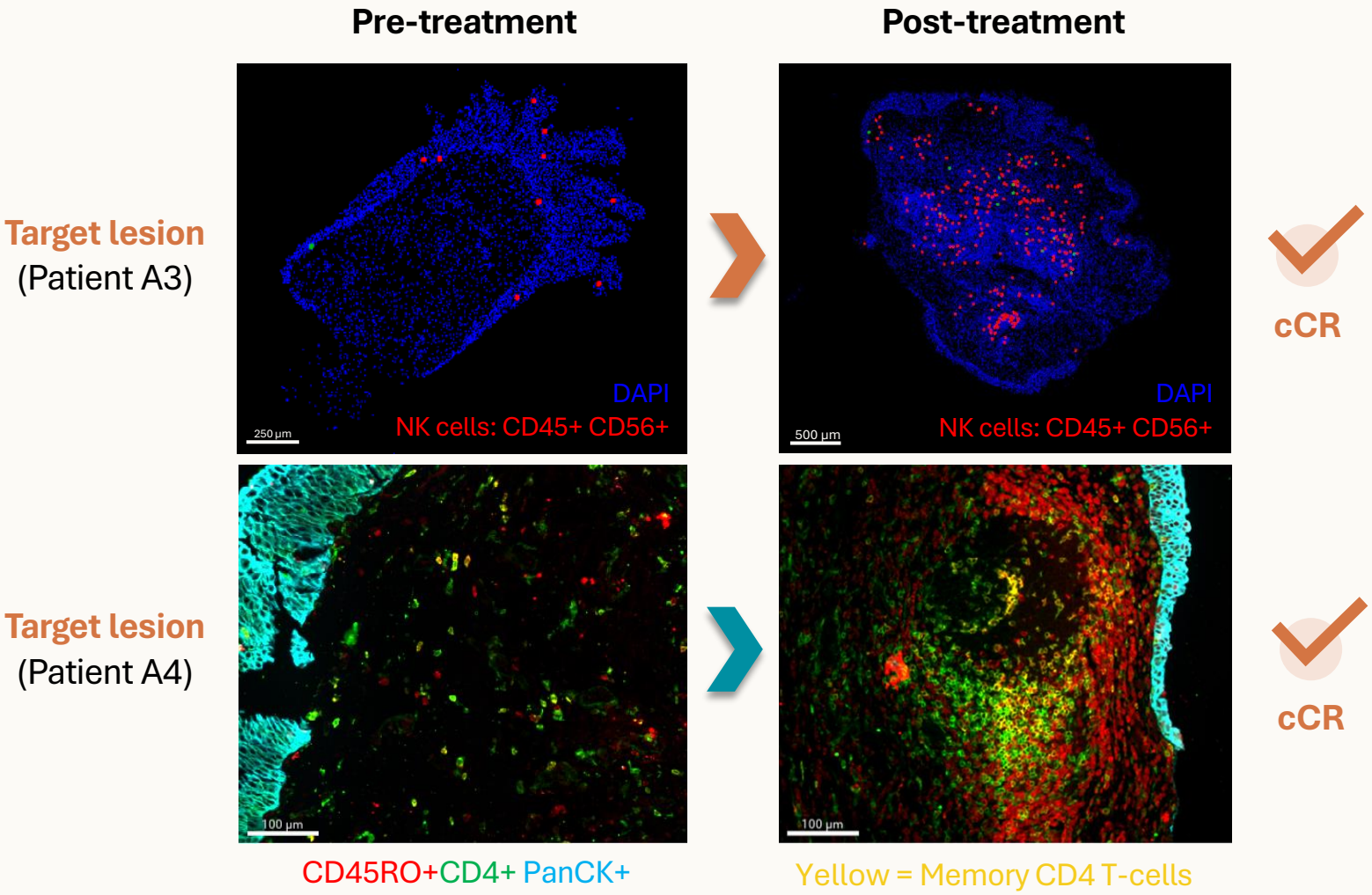
In **5/5** participants, **mature TLS** were present in **target lesions** (3 formed TLS *de novo*)

In **2/5** participants, mature TLS were also present in **non-target lesions**, supporting potential for a **urothelial field effect**

Multiplex immunofluorescence images from participant A4.
Bel-sar, belzupacap sarotalocan; **cCR**, clinical complete response; **TLS**, tertiary lymphoid structures.
Clinicaltrials.gov identifier: NCT05483868; AU-011-102.

Multiplex Immune Fluorescence in 5 participants with cCR or visually smaller tumors

Tumor Microenvironment Profiling and Activation



- Bel-sar generated **innate and adaptive effectors** regardless of immune environment
- Converted **"cold"** TME to **"hot"**, and reversed dysfunction in exhausted tumors

In treated lesions:

- **Natural killer cell** density increased up to **40x**
- **CD4+ cytolytic T cell** density increased up to **7x**

In **5/5** participants, **CD4+ and CD8+ memory T cells** were observed after bel-sar treatment

Multiplex immune fluorescence images from participants A3 and A4. Pre-treatment specimens available in 4/5 participants.
Bel-sar, belzupacap sarotalocan; **cCR**, clinical complete response; **NK**, natural killer.
Clinicaltrials.gov identifier: NCT05483868; AU-011-102.

Phase 1b/2 Study:

Efficacy, safety and immune activation

Advancing bel-sar in NMIBC: **Phase 1b/2 trial overview**

Goal: Evaluate potential of bel-sar across the disease spectrum, and determine dose levels to advance clinical development in bladder cancer

Potential use across disease spectrum

~26 participants with NMIBC

Intermediate-risk

High-risk

Two front-line treatment approaches

Immune-ablative

OR

Multimodal neoadjuvant (bel-sar followed by TURBT)

Dose escalation and multiple doses

Higher-dose bel-sar

Up to 3 tumors per treatment

Two treatment cycles

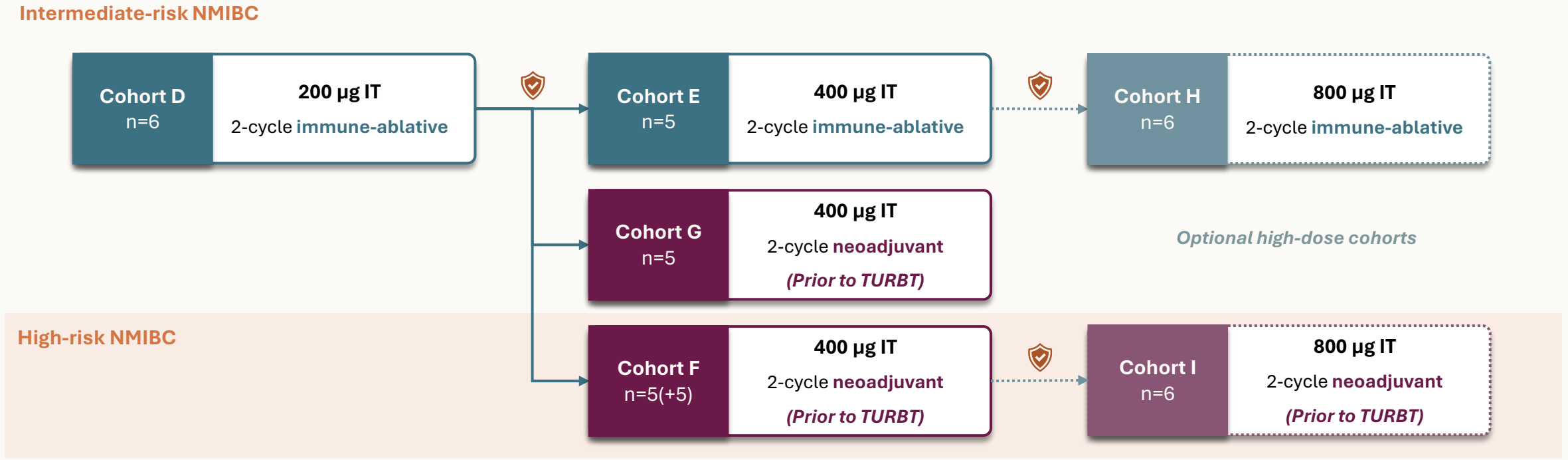
Assessments and Key Endpoints: participants assessed by cystoscopy ± biopsy and urine cytology at 3, 6, 9, and 12 months to evaluate:

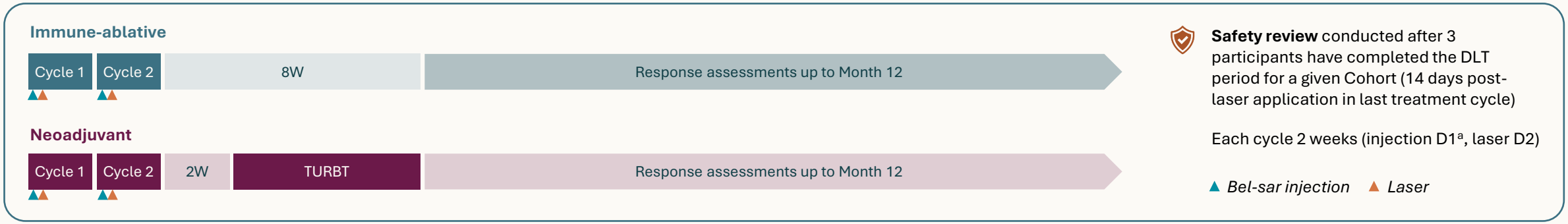
Primary – Safety and tolerability (AEs, SAEs, DLTS)

Key Secondary - Complete response rate (3 mo and TURBT), duration and durability of response (6-12 mo) (immune ablative cohorts), recurrence-free survival (neoadjuvant cohorts), and immune response

Bel-sar, belzupacap sarotalocan; **NMIBC**, non-muscle-invasive bladder cancer; **TURBT**, transurethral resection of bladder tumor.
Clinicaltrials.gov identifier: NCT05483868; AU-011-102.

Advancing bel-sar in NMIBC: **Phase 1b/2 study design**





Dose per tumor, per treatment. Up to three tumors treated per visit. [a]+2-day window for injection in 2nd treatment cycle.
Bel-sar, belzupacap sarotalocan; **D**, day; **DLT**, dose-limiting toxicity; **IT**, intratumoral; **NMIBC**, non-muscle-invasive bladder cancer; **TURBT**, transurethral resection of bladder tumor; **W**, week.
Clinicaltrials.gov identifier: NCT05483868; AU-011-102.

Conclusions from Phase 1 Study of Bel-sar in NMIBC

Efficacy

- In both IR and HR NMIBC participants, focal administration of a single, low-dose of bel-sar induced clinical complete responses through rapid tumor necrosis, effector cell infiltration, localized immune memory, and a urothelial field effect.

Safety

- Only grade 1 drug-related adverse events.

Immune Response

- Bel-sar induced adaptive immune memory through generation of *de novo* mature tertiary lymphoid structures (TLS) in 3/5 participants.
- Bel-sar generated innate and adaptive effectors regardless of immune environment; converted “cold” TME to “hot”, and reversed dysfunction in exhausted tumors.

Ongoing Ph1b/2 Study

- Objective: Evaluation of additional bel-sar doses and cycles in participants with NMIBC

Bel-sar (AU-011) is an investigational product candidate. The effectiveness and safety of bel-sar have not been established, and bel-sar is not approved for use in any jurisdiction.
Pre-treatment innate and adaptive effectors evaluated in 4/5 participants with pre-treatment specimens.
Bel-sar, belzupacap sarotalocan; **TME**, tumor microenvironment; **TLS**, tertiary lymphoid structure; **IR**, intermediate risk; **HR**, high risk; **NMIBC**, non-muscle invasive bladder cancer.
Clinicaltrials.gov identifier: NCT05483868; AU-011-102.

Discussion