CLINICAL TRIAL PROTOCOL

A Phase 1, Open-label trial of Belzupacap Sarotalocan (AU-011) to Determine the Feasibility and Safety of Intratumoral Injection with or without Intramural Injection in Subjects with Bladder Cancer

Protocol Number: AU-011-102

Inclusion Criteria:

Participants must:

1. Be at least 18 years of age.
2. Have been informed about the investigative nature and requirements of the trial, voluntarily agreed to participate in the trial and have documented their consent by signing and dating the Informed Consent Form before participating in any trial-related activities.
3. Meet the following histopathologic requirements for urothelial carcinoma:

   Note: For **Cohorts 4d, 4e, 4g and 4h**, a diagnosis of LG IR NMIBC (according to AUA risk classification guidelines) is required, specifically:

   - Multifocal LG Ta; OR
   - Solitary LG Ta >3 cm; OR
   - Low-grade Ta with prior recurrence(s) within 1 year.

   In addition, participants:

   - Must have a current lesion that clinically appears to be NMIBC (per the

Investigator's judgement based on cystoscopy).

- Must have histopathologic confirmation of LG NMIBC based on TURBT or biopsy within the last 24 months of screening visit for recurrent disease and within the last 6 months of screening visit for first time disease.
- Must have papillary lesions or broader sessile lesions indicative of bladder cancer identified at Screening and appropriate for bel-sar injection.
- On screening cytology, must not have positive or suspicious of HG urothelial carcinoma. If subsequent diagnostic work-up did not confirm HG NMIBC and there is no evidence remaining for HG NMIBC, the participant can be considered for enrollment in Cohort 4d, 4e, 4g, or 4h.

Note: Risk classification may be updated based on pre-treatment biopsy results obtained prior to or at the time of injection. Participants initially enrolled into an IR cohort may be reassigned to a HR cohort if pathology supports a HR classification. If reassignment occurs, the participant will be replaced in the original cohort.

Note: For **Cohorts 4f and 4i**, a diagnosis of HR NMIBC (according to AUA risk classification guidelines) is required, specifically:

- Ta HG papillary disease with or without CIS; OR
- T1 papillary disease with or without CIS
    - Participants may be BCG-naïve or may have received prior treatment with BCG for HR or IR NMIBC (BCG-exposed, BCG-failed, BCG-intolerant)
    - BCG-refractory participants are excluded. BCG-refractory is defined by the following:
        - Persistent HG disease at 6 months following adequate BCG (defined as ≥5/6 induction instillations and ≥2 additional doses, either from re-induction or maintenance), OR
        - High-grade T1 disease at first evaluation (3 months) after BCG, OR
        - Persistent CIS that remains despite a second BCG course, OR
        - Disease progression in stage or grade during BCG therapy, including maintenance.

In addition, participants:

- Must have a current lesion that clinically appears to be NMIBC (per the Investigator's judgement based on cystoscopy).
- Must have histopathologic confirmation of HR NMIBC based on TURBT or biopsy within the last 24 months of screening visit for recurrent disease and within the last 6 months of screening visit for first time disease.

- Must have papillary lesion or broader sessile lesions indicative of bladder cancer with or without flat lesions indicative of CIS identified at Screening appropriate for bel-sar injection.
- If screening cytology shows HG urothelial carcinoma, a baseline CT or MRU should be completed within 3 months of enrollment to assess oncologic status of the upper tracts as per international guidelines (EEU 2025; Coleman 2023).

For **Cohorts 4d-i** there is no restriction on the number of lesions in the bladder at Screening for trial eligibility. A maximum of 3 lesions (the largest 3) may be injected (starting with the largest) at each treatment cycle (these need not be the same tumors treated in a previous cycle). Tumors of any size are eligible for treatment with bel-sar.

4. Have no evidence of current or prior metastatic urothelial carcinoma.

   Note: Only bladder tumors may be treated with bel-sar. Upper tract or prostatic urethra lesions may be present, but cannot be the lesion injected (i.e., Investigator can treat upper tract or prostatic urethra per SoC as long as this treatment will not interfere with the local bel-sar injection of the trial tumor).

5. If female and capable of becoming pregnant, agree to have pregnancy testing performed at screening (must be negative) and if required within 24 hours of bel-sar injection (must be negative); must agree to use highly effective method of contraception from the date of the screening pregnancy test; and must agree to continue using such precautions for 90 days after the final dose of bel-sar. Women considered capable of becoming pregnant include all females who have experienced menarche and have not experienced menopause (as defined by amenorrhea for greater than 12 consecutive months) or have not undergone successful surgical sterilization (hysterectomy, bilateral tubal ligation, or bilateral oophorectomy).
6. If male, must be of non-reproductive potential (i.e., have azoospermia either from a vasectomy or from an underlying medical condition) or must use a highly effective method of contraception defined as one that results in a low failure rate (i.e., less than 1% per year) when used consistently and correctly. Males with sexual partners of childbearing potential must agree to use a highly effective form of barrier birth control as outlined in the protocol or abstain from sexual intercourse during the trial and for 90 days after a bel-sar injection. Males should not donate sperm until 90 days after injection of bel-sar.
7. Be able and willing to avoid all prohibited medications (Section 5.8) for the appropriate washout period and during trial follow-up.

   Note: participants may receive continuous anticoagulation or antiplatelet therapy as medically required (temporary discontinuation is permitted as long as bel-sar injections and laser application procedures can be safely administered and following discussion with the clinical trial's Medical Monitor).

8. Adequate bone marrow, renal, and hepatic function as defined by:

Adequate Organ Function Definitions

System	Laboratory Values
Hematologic	
Absolute Neutrophil Count	>1200 cells/μL
Hemoglobin	>9 g/dL
Platelets	>75,000/μL
Hepatic	
ALT and AST	≤3.0 × ULN
Total bilirubin	≤1.5 × ULN unless the participant has documented/suspected Gilbert's, then ≤3 × ULN
Albumin	≥3.0 g/dL (30 g/L)
Renal	
Glomerular Filtration Rate	≥30 mL/min

ALT: alanine aminotransferase; AST: aspartate aminotransferase ULN: upper limit of normal.

Exclusion Criteria:

Participants:

1. Must not have evidence of current or prior metastatic urothelial carcinoma.
2. Must not have any additional malignancy that requires active treatment, unless deemed appropriate after discussion by the Investigator with the trial's Medical Monitor.
3. Must not have any contraindication to general or spinal anesthesia.
4. Is unable to undergo flexible or rigid cystoscopy.
5. Must not be pregnant or lactating.
6. Must not have used an investigational drug or medical device within 30 days or 5 half-lives (whichever is longer) of Visit 1 or concurrent enrollment in another investigational clinical trial.
7. Must not have known contraindications or sensitivities to phthalocyanine-based dye, bel-sar, the capsid component, or prior treatment with laser.
8. Must not have active autoimmune disease, chronic inflammatory condition, or other conditions (like solid organ transplant or bone marrow allograft) requiring concurrent use of any systemic immunosuppressants or steroids.
9. Must not have a known active immune-deficiency state(s) or infection state – including but not limited to active human immunodeficiency virus, chronic active Hepatitis B or C, myelodysplastic disorders, marrow failures, history of solid organ transplant, or bone marrow allograft.
10. Must not have received any systemic anticancer therapy not otherwise mentioned above within the last 28 days.
11. Must not have active bacterial, fungal, or viral infections – all prior infections must have resolved following optimal therapy and participants must be off all systemic anti-infective agents.

12. Must not have a history of coagulopathy resulting in uncontrolled bleeding, e.g., hemophilia, von Willebrand's disease, etc.
13. Cardiac Exclusions:
    a. New York Heart Association Class 3 or 4 congestive heart failure.
    b. Uncontrolled hypertension.
    c. Unstable angina pectoris.
    d. Clinically important cardiac arrhythmia (e.g., requiring anti-arrhythmic drugs like sotalol).
    e. Mean QT interval corrected for heart rate (QTc) $\geq$470 ms calculated from an electrocardiogram (ECG) using Fredericia's Correction by manual read.
14. Must not have any other condition or previous surgery that, in the opinion of the Investigator (with Sponsor input as needed), would interfere with trial participation, evaluation of the IP, interpretation of trial results, or put the participant at any unnecessary risk.