A Combined Phase I/II Study of BT8009 a Novel *Bicycle*® Toxin Conjugate with MMAE in Patients with Advanced Malignancies with Nectin-4

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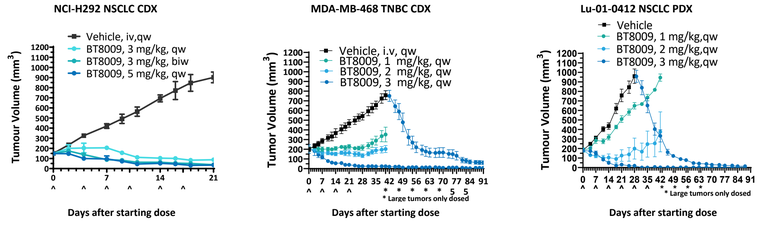
Background:

- BT8009 is a *Bicycle*® Toxin Conjugate (BTC) in which a Nectin-4 binding *Bicycle* (bicyclic peptide) is conjugated through an inert sarcosine spacer chain and a cleavable linker to the antimitotic toxin MMAE.
- Nectin-4 is expressed in bladder, NSCLC, esophageal, pancreatic, ovarian, head and neck, gastric, and breast cancers[1-5].
- Overexpression of Nectin-4 in tumor tissue is a marker for poor prognosis[1-4].
- BT8009 is designed to have rapid tumor penetration and a short terminal plasma half-life, associated with rapid release and prolonged retention of MMAE in tumor thereby reducing toxin exposure to other tissues.
- BT8009 exhibited a satisfactory preclinical profile supporting the initiation of a FIH study to investigate safety and efficacy in indications with evidence of Nectin-4 expression.

BT8009 in Xenograft Tumor Models



Enrollment Criteria:

Part A (Dose Escalation) Specific Inclusion Criteria

- Tumor types:
  - Urothelial carcinoma
  - Tumor with confirmed Nectin-4 expression on tissue
  - Solid tumors known to frequently express Nectin-4 (pancreatic, breast, NSCLC, gastric, esophageal, head and neck, or ovarian)

Part B Patients

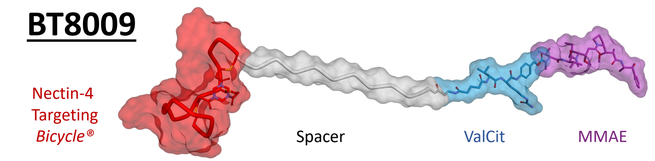
- Confirmed Nectin-4 expression on fresh biopsy or archived tissue

Part C Patients

- Renal insufficiency

First-in-Human Study with a *Bicycle*® Toxin Conjugate targeting Nectin-4 with an MMAE cytotoxic payload. Patient enrollment ongoing.

BT8009



Primary objectives

- Dose escalation
  - -Safety and tolerability of BT8009 as monotherapy and in combination with nivolumab or in patients with renal insufficiency (Part C).
  - -MTD and RP2D of BT8009 as monotherapy and in combination with nivolumab
- Dose expansion
  - -Clinical activity of BT8009 as monotherapy and in combination with nivolumab

Secondary objectives

- Dose escalation
  - -Preliminary signals of activity of BT8009 as monotherapy and in combination with nivolumab or in patients having renal insufficiency (Part C).
  - -PK parameters of BT8009 and MMAE
  - -Incidence of anti-drug antibody (ADA) development
- Dose expansion
  - -Safety and tolerability of BT8009 as monotherapy and in combination with nivolumab
  - -PK parameters of BT8009 and MMAE
  - -Incidence of ADA development

Study Design

- Phase I/II, first-in-human, open-label dose-escalation study of BT8009 given as a single agent or in combination with nivolumab.
- Up to 146 patients (up to 66 in Phase I and 80 in Phase II) are expected to be enrolled in this study at approximately 20 sites globally.
- Three parts to this study:
  - -Phase I: dose escalation
    - Part A-1: BT8009 monotherapy dose escalation (34 patients)
    - Part A-2: BT8009 plus nivolumab dose escalation (20 patients)
  - -Phase II: dose expansion
    - Part B-1: BT8009 monotherapy dose expansion (40 patients)
    - Part B-2: BT8009 plus nivolumab dose expansion (40 patients)
  - -Phase I: patients with renal insufficiency (12 patients)

References

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