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 and breast cancers1,4. Overexpression of Nectin-4 in tumor tissue is a marker for poor prognosis1,4. BT8009 is designed to have rapid tumor penetration, release and prolonged retention of MMAE in tumor and short terminal plasma half-life to reduce exposure to tissues outside of tumor. 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.

**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 and breast cancers1,4.
- Overexpression of Nectin-4 in tumor tissue is a marker for poor prognosis1,4.
- BT8009 is designed to have rapid tumor penetration, release and prolonged retention of MMAE in tumor and short terminal plasma half-life to reduce exposure to tissues outside of tumor.
- 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
  - Urothelial carcinoma naïve to Nectin-4-directed therapies; or confirmed Nectin-4 expression on fresh biopsy or archived tissue (<12 months) without intervening anti-cancer therapies or solid tumors known to frequently express Nectin-4 (pancreatic, TNBC, NSCLC, gastric, esophageal or ovarian.)
- Part B Patients
  - Confirmed Nectin-4 expression on fresh biopsy or archived tissue (<12 months) without intervening anti-cancer therapies
- Part C Patients
  - Renal insufficiency

**Primary objectives**
- **Dose escalation**
  - Safety and tolerability of BT8009 as monotherapy and in combination with nivolumab in patients having renal insufficiency.
  - 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 in patients having renal insufficiency.
  - 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

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

**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 in 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 escalation
    - 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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For additional information, please contact Dr. McKean at mmckean@tnonc.com

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