Background:
- BT5528 is a Bicycle® Toxin Conjugate (BTC), a novel class of chemically synthesized molecules, comprising a bicyclic peptide targeting EphA2 tumor antigen, linked to cytotoxin (monomethyl auristatin E [MMAE]) via a cleavable linker.
- EphA2 is overexpressed in a range of solid tumors, contributes to oncogenesis, tumor-associated angiogenesis and metastasis. Intracellular EphA2 signaling converges on pathways that are integral to cell growth, proliferation, migration and invasion.
- Increased EphA2 identified as a TKI resistance mechanism
- BT5528 mechanism of action is dependent on tumor penetration, target binding and release of MMAE payload.
- BT5528 exhibited a favorable preclinical profile with no bleeding or coagulopathy, unlike MedImmune’s MEDI-547 (Annunziata, et al. Invest New Drugs 2013).
- Advantages over ADC exhibiting rapid penetration of dense tumors and decreased extra-tumor exposure.

First-in-Human (FIH) Study with a Bicycle® Toxin Conjugate (BTC) targeting EphA2 with an MMAE cytotoxic payload.
Patient enrollment ongoing.

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TPS3655: BT5528-100 Phase I/II Study; Safety, Pharmacokinetics & Preliminary Clinical Activity of BT5528 in Patients with Advanced Malignancies Associated with EphA2 Expression (ASCO 2020)

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First-in-Human (FIH) Study with a Bicycle® Toxin Conjugate (BTC) targeting EphA2 with an MMAE cytotoxic payload.
Patient enrollment ongoing.

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BT5528-100 (NCT04180371). Ph I/II FIH study: Escalation Phase 1
- To evaluate safety & tolerability of weekly BT5528 alone and in combination with q4w nivolumab (provided by Sponsor), and determination of RP2D
- Patients with advanced solid tumors associated with EphA2 expression after exhausting SOC options (i.e. NSCLC, TNBC, pancreatic, ovarian, gastric/upper GI, and urothelial cancers)
- At baseline must have available tumor tissue, acceptable hematologic and organ function
- Excluded if uncontrolled brain metastasis, thrombotic/bleeding disorders, uncontrolled hypertension, CYP3A4 inhibitors; and, autoimmune disease for nivolumab cohorts
- PK serial collections on D1 and D15
- Radiologic tumor assessments q8w for response per RECIST

EphA2 expression in patient samples by IHC to be presented at AACR 2020, see abstract #3302

Expansion Phase 2a (part B-1 and B-2):
- Expansion cohorts to investigate efficacy (ORR and DOR) & safety of BT5528 in EphA2-enriched or -selected NSCLC populations with or without nivolumab.