**Phase 1/2 study of novel HER2-targeting, TLR7/8 immune-stimulating antibody conjugate (ISAC) BDC-1001 as a single agent and in combination with an immune checkpoint inhibitor in patients with advanced HER2-expressing solid tumors**

**Objectives**

- **Primary Objectives**
  - The dose-escalation phase will define safety and tolerability and determine the recommended phase 2 dose of BDC-1001 as monotherapy and in combination with an immune checkpoint inhibitor.
  - The dose-escalation portion of the trial will evaluate preliminary antitumor activity of BDC-1001 alone and in combination with an immune checkpoint inhibitor.

- **Secondary Objectives**
  - Secondary objectives will evaluate pharmacokinetic (PK) parameters and pharmacodynamic (PD) biomarkers in tumor tissue and in peripheral blood associated with drug exposure.
  - EXPLORATORY OBJECTIVES
    - Evaluate exploratory pharmacodynamic biomarkers and potential biomarkers associated with biological activity.

**Background**

**Traditional Immunotherapies Focus on an Adaptive Immune System**

**Traditional** dysfunctional immune response

1. **T cell Targeted Therapies**
   - Not elicit significant T cell immune response
   - Risk of T cell exhaustion.
   - Some approaches require complex manufacturing processes.

2. **Myeloid biology contributes to productive cancer immunity cycle**
   - Myeloid cells help immature dendritic cells to acquire new antitumor immune responses.
   - Myeloid cells can promote antitumor T cell response.
   - Converse "cancer" tumors to "host" response in preclinical models.

**Boltbody ISACs Act at Different Stages of the Cancer Immunity Cycle**

**Boltbody ISACs initiate new immune response**

- **Boltbody ISACs combine:**
  - Precise antibody targeting.
  - Activation of innate immune.
  - Triggering adaptive immune response.

- **Boltbody ISACs initiate an entirely new immune response.**
  - Boltbody ISACs combine:
    - Precise antibody targeting.
    - Activation of innate immune.
    - Triggering adaptive immune response.
  - All within a single therapeutic.

**Boltbody ISACs enhance the antigen presentation and immune response of immunosuppressed APCs, driving a robust tumor-specific antitumor immune response that can recognize additional neoantigens.**

**Study Design**

**Monotherapy - Parts 1 and 3**

- **Safety, PK, Efficacy, PD Biomarkers**
- **Combination Therapy with Checkpoint Inhibitor - Parts 2 and 4**

**Endpoints**

- **Parts 1 and 3**
  - Incidence of adverse events and serious adverse events graded according to National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) v5.0.
  - Incidence and nature of dose-limiting toxicities within a D+3 design.
  - Changes from baseline in clinical safety laboratory values and vital signs. Incidence of potential immune-related toxicities.
  - The maximum tolerated dose (MTD) or a tolerated dose below MTD (MTD not reached)
  - PK parameters (eg, Cmax, AUC, MRT, CL, Vz/F, t1/2)
  - Incidence of anti-drug antibodies (ADAs)

- **Additional Endpoints for Parts 2 and 4**
  - Overall response rate using RECIST v1.1 and iRECIST. Disease control rate of confirmed complete response, partial response, lasting 4 or more weeks following the initiation of BDC-1001, duration of response, progression-free survival, and overall survival.
  - Antitumor activity in tumors with different levels of HER2 and PD-L1 expression.

**Study Status**

- **Phase 1/2 Trial Initiated Q1 2020:** Currently in Dose Escalation
  - Enrollment in monotherapy dose-escalation phase is proceeding well.
  - Status: Phase 1/2 Trial Initiated Q1 2020; Currently in Dose Escalation
  - Expected Upcoming Milestones:
    - Complete phase 1/2 dose escalation portion in Q1 2021.
    - Initiate phase 2 dose expansions in Q2 2021.
  - Phase 1/2 data anticipated to provide clinical proof of concept.

**References**