**Background**

BDC-1001 has a Targeted IO Approach to Stimulate and Bridge the Innate and Adaptive Immune Systems

**Study Objectives**

- **Primary Objectives**
  - Define safety and tolerability and determine the recommended phase 2 dose (RP2D) of BDC-1001 as monotherapy and in combination with immune checkpoint inhibitor
  - Evaluate preliminary anti-tumor activity of BDC-1001 alone and in combination with an immune checkpoint inhibitor

- **Secondary & Exploratory Objectives**
  - Evaluate pharmacokinetic (PK) parameters and pharmacodynamic biomarkers associated with anti-tumor activity
  - Changes in TLR7/8 pathway activation, myeloid, and T cell content, and activation status in baseline biomarkers
  - Study PK parameters in Patients with HER2-Expressing Tumors
  - Robust single-agent anti-tumor activity and elimination of HER2-expressing tumors

**Study Design**

- **Off-the-Grid Protocol**
  - Potential for the patient’s own immune system to determine the relevant neoantigen-specific T cells to eliminate tumor destruction to achieve a personalized therapeutic outcome

**Key Inclusion Criteria**

- Patients with advanced/metastatic solid tumors
- Treatment with BDC-1001 is safe and well tolerated
- Adequate hematologic, renal, and hepatic function as defined in Part 1 study protocol
- No symptomatic or progressive disease by RECIST 1.1
- Adequate baseline laboratory values

**Patient Safety Summary**

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<th>Treatment Duration (Weeks)</th>
<th>All-grade TEs</th>
<th>Grade 3 TEs</th>
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**Safety and Response**

- **Overall Safety Summary**
  - No DLTs observed to date, and the MTD has not been reached
  - The single Grade 3 treatment-related event was anemia (patient had Grade 2 anemia at screening)
  - No Grade 5 treatment-related events
  - Treatment-emergent adverse events (AEs) that led to treatment discontinuation included 1 patient with a treatment-related event (TRE) of grade 3 anemia that went on to stop study drug after the event
  - Of the treatment-related AEs, a mild decrease in left-ventricular ejection fraction occurred in 1 patient, and no DLTs observed to date, and the MTD has not been reached
  - All AEs were grade 1 or 2 and did not require interruption to the infusion
  - Two additional severe adverse events (SAEs) occurred with immunosuppression and no further BIIs; the other 2 patients went off study prior to subsequent infusions

**Study Assessments**

- **Safety (primary clinical endpoint for dose escalation)**
  - Incidence of severe adverse events (SAEs), serious adverse events (SAEs), and dose-limiting toxicities (DLTs) using NCI-CTCAE criteria version v5.0
  - Incidence of potential immune-related toxicities
  - Maximum tolerated dose (MTD) or a tolerated dose below MTD (MTD is not reached)

- **Efficacy (primary clinical endpoint for dose expansion)**
  - Tumor assessments using RECIST V1.1

**Pharmacokinetics**

- PK parameters (eg, Cmax, AUC0–τ, Cl, Vz, t1/2)

**Immunological Analyses**

- Changes in TLR7 pathway activation, myeloid, and T cell content, and activation status in plasma and tumor tissues by means of cytokines and chemokines as well as gene expression profiling, and bone image analysis

**Overall Pharmacokinetics and Pharmacodynamics**

- **Preliminary Pharmacokinetics and Pharmacodynamics**
  - Early pharmacodynamic data demonstrate that Cmax levels are consistent with those predicted in non-human primate (NHP) models
  - Elevations in exploratory pharmacodynamic biomarkers were observed with a trend towards greater magnitude in patients with increasing dose level. These included biomarkers associated with TLR7 activation, myeloid cell activation and T cell activation (eg, TNFa, IP-10, MCP-1, IL-6, IL-15, TNF-alpha)
  - The plasma cytokines and chemokines data are consistent with predicable data and with the proposed mechanism of action of BDC-1001, including markers of myeloid and TLR activation

**Conclusions**

- The novel ISAC BDC-1001 has been well-tolerated to date (N=20, dosed cut-off date) with evidence of early clinical activity in advanced HER2-expressing solid tumors
- No DLTs or drug-related SAEs have been reported
- Mild infusion-related reactions were reported in 4 patients among the early cohort at the 5 mg/kg dose level, but no subsequent AEs have been seen in subsequent patients enrolled on the same dose
- Other TEAEs are consistent with those reported across phase 1 trials 1 Phase 1 trials in patients with advanced solid tumors
- The MTD has not been reached, and the study continues to enroll patients in the microtherapy dose-escalation phase
- Early pharmacodynamic data demonstrate that Cmax levels are consistent with that predicted in NHP models
- More details and data on pharmacodynamic biomarkers in blood and tumor are anticipated to be presented at upcoming conferences
- The checkpoint inhibitor combination and dose-expansion parts are planned to start after completion of microtherapy dose escalation later in 2021

**Acknowledgments**

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**References**