

platform technology, we are developing it to treat other solid tumors using different target tumor markers.

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**401 PHASE 1/2 STUDY OF NOVEL HER2-TARGETING, TLR7/8 IMMUNE-STIMULATING ANTIBODY CONJUGATE (ISAC) BDC-1001 WITH OR WITHOUT IMMUNE CHECKPOINT INHIBITOR IN PATIENTS WITH ADVANCED HER2-EXPRESSING SOLID TUMORS**

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**Background** In spite of advances made in the management of patients with HER2-expressing or -driven solid tumors, there remains a significant unmet need for novel approaches to improve patient outcomes. Intratumoral delivery of antitumor antibodies and immunostimulatory adjuvants such as toll-like receptor (TLR)7/8 agonists has been shown to activate tumor resident antigen-presenting cells (APCs), driving uptake, processing, and presentation of tumor neoantigens to T cells that mediate antitumor immunity. BDC-1001 is delivered systemically and has demonstrated superior preclinical biology. This novel ISAC consists of an investigational biosimilar of the humanized monoclonal antibody trastuzumab chemically conjugated to a TLR7/8 agonist with a non-cleavable linker. BDC-1001 activates human myeloid APCs in addition to retaining antibody-mediated effector functions such as antibody-dependent cellular cytotoxicity/phagocytosis (ADCC/ADCP). Studies in trastuzumab-resistant xenograft models and syngeneic tumor models indicate that HER2-targeted ISACs elicit potent and durable immune-mediated antitumor efficacy, leading to complete tumor regression in a TLR- and Fc receptor-dependent manner.<sup>1-2</sup> Importantly, BDC-1001 did not induce interstitial lung disease, cytokine release syndrome, or thrombocytopenia in non-human primate studies. A four-part phase 1/2, first-in-human study has been initiated that evaluates BDC-1001 with or without ( $\pm$ ) an immune checkpoint inhibitor targeting PD-1 in patients with HER2-expressing or HER2-amplified advanced/metastatic solid tumors.

**Methods** This dose-escalation and dose-expansion study is enrolling up to 390 patients with HER2-expressing (IHC2+ or 3+ protein, irrespective of gene amplification) or HER2-amplified (by in situ hybridization or next-generation sequencing) advanced solid tumors. Primary objectives of the dose-escalation phase are to define safety and tolerability and determine the recommended phase 2 dose of BDC-1001 as monotherapy (Part 1) and in combination with an immune

checkpoint inhibitor (Part 2). Part 2 is planned to start once BDC-1001 safety data are available. Primary endpoints include incidence of 1) adverse events and serious adverse events; 2) dose-limiting toxicities within a 3+3 design; and 3) potential immune-related toxicities. The dose-expansion portion of the trial will evaluate preliminary antitumor activity of BDC-1001 alone (Part 3) and in combination with an immune checkpoint inhibitor (Part 4). Secondary objectives will evaluate pharmacokinetic parameters and pharmacodynamic biomarkers in tumor tissue and in peripheral blood associated with drug exposure. These exploratory studies will help elucidate the mechanism of action and seek to identify biomarkers associated with BDC-1001 biological activity with or without immune checkpoint inhibitor. This global study is currently recruiting patients.

**Results** N/A

**Conclusions** N/A

**Trial Registration** ClinicalTrials.gov (NCT04278144).

**Ethics Approval** The study and the protocol were or will be approved by the Institutional Review Board or ethics committee at each site.

**Consent** N/A

**REFERENCES**

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**402 DRAGON: PHASE 1 TRIAL OF SRK-181, A LATENT TGF $\beta$ 1 INHIBITOR IN COMBINATION WITH ANTI-PD-(L)1 INHIBITORS FOR PATIENTS WITH SOLID TUMORS UNRESPONSIVE TO ANTI-PD-(L)1 THERAPY ALONE**

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**Background** TGF $\beta$ 1 is a key mediator of primary resistance to PD1 (programmed cell death protein 1) pathway blockade. SRK-181 is a high-affinity, fully humanized antibody that selectively binds to latent TGF $\beta$ 1 and inhibits its activation on suppressive immune cells as well as within tumor stroma. Pre-clinical data demonstrated that selective inhibition of latent TGF $\beta$ 1 with SRK-181 overcomes primary anti-PD-1 resistance and has an improved safety profile compared to broad inhibition of the TGF $\beta$  pathway.

**Methods** The DRAGON trial is a multi-center, open-label, Phase 1, first-in-human (FIH), dose-escalation, and dose expansion study to evaluate the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD), and efficacy of SRK-181 administered by IV infusion every 3 weeks (q3w) alone and in combination with an anti-PD-(L)-1 in adult patients with locally advanced or metastatic solid tumors. The study is divided into 3 parts: Part A1, a single agent dose escalation, will determine the maximum tolerated dose (MTD) or maximum administered dose (MAD) of SRK-181 as a single agent. Part A2, a combination dose escalation, will determine the MTD or MAD of SRK-181 in combination with anti-PD-(L)1 therapy and the RP2D of the combination treatment for use in Part B. Part B, the dose expansion, will enroll parallel cohorts of patients with non-small cell lung cancer, urothelial