Methods Eligible pts were aged ≥18 years with an Eastern Cooperative Oncology Group performance status of 0–1. The cSCC cohorts enrolled pts with histologically confirmed metastatic or locally advanced cSCC not amenable to local therapy. The NSCLC cohort enrolled previously untreated NSCLC pts with advanced disease and a PD-L1 tumor proportion score of at least 50%. Pts received a fixed dose of 800 mg cosibelimab administered intravenously every two weeks. Anti-tumor activity was assessed by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 and were conducted every 8 weeks for the initial 32 weeks on study, and every 12 weeks thereafter.

Results As of August 2020, 114 pts (73M/41F, median age 66 years) with diverse tumor types have been enrolled and treated with cosibelimab. Among these pts, 103 (90%) experienced ≥1 treatment-emergent adverse event (AE), 42 (37%) experienced a grade ≥3 AE, and 6 (5%) experienced a grade ≥3 drug-related AE. The most common AEs were fatigue (25%), anemia (21%), rash (18%) and nausea (16%) and the most common drug-related AEs were fatigue (15%) and rash (14%). In 42 cSCC pts evaluable for response, ORR based on investigator assessment of tumor response was 55% (95% confidence interval [CI]: 39, 70), including 5 (12%) complete responses, with 20/23 (87%) responses ongoing and 10 responses ≥6 months in duration as of data cutoff. In 25 NSCLC pts evaluable for response, ORR based on investigator assessment was 44% (95% CI: 24, 65), with 5/11 (45%) responses ongoing and 10 responses ≥6 months in duration.

Conclusions Cosibelimab has a predictable and manageable safety profile and demonstrated robust clinical activity in cSCC and NSCLC pts, including durable complete and partial responses. Updated results will be presented.

Trial Registration NCT03212404

Ethics Approval The study was approved by an appropriate ethics committee for each participating institution. Informed consent was obtained for all subjects.

Consent Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

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400 COUPLEDCARTM TECHNOLOGY FOR TREATING THYROID CANCER

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Background Chimeric antigen receptor modified T cells (CAR T) have demonstrated remarkable clinical efficacy in the treatment of B cell malignancies and multiple myeloma. Significant challenges restrict their application across solid tumors due to multiple obstacles, including the lack of robust in vivo CAR-T cell expansion and persistence, the immunosuppressive tumor microenvironment, and tumor escape due to heterogeneous tumor cell composition with a potential loss of the targeted tumor antigen.To address these difficulties, we generated CAR T cells using a novel CoupledCAR® technology. Specifically, we engineered CoupledCAR T cells with lentiviral vectors encoding an anti-thyroid stimulating hormone receptor (TSHR) CAR molecule. Immunohistochemistry (IHC) results showed that TSHR was highly expressed in thyroid cancer cells making it an ideal tumor-specific target antigen. In vitro co-culture experiments showed that TSHR CAR T cells specifically recognized and subsequently killed TSHR-positive tumor cells. Animal model experiments showed that TSHR CAR T cells inhibited the proliferation of TSHR-positive tumor cells.

Methods We designed a 'CoupledCAR' lentivirus vector containing a single-chain variable fragment (scFv) targeting human TSHR. The lentivirus was produced by transfecting HEK-293T cells with 'CoupledCAR' lentiviral vectors and viral packaging plasmids. Patient's CD3 T cells were cultured in X-VIVO medium containing 125U/mL 1interleukin-2 (IL-2), and transduced with 'CoupledCAR' lentivirus at certain MOI. Transduction efficiency and was evaluated at 7 to 9 days after 'CoupledCAR' lentivirus transduction, and quality controls for fungi, bacteria, mycoplasma, chlamydia, and endotoxin were performed. After infusion, serial peripheral blood samples were collected, and the expansion and the cytokine release of CART cells were detected by FACS and QPCR. The evaluation of response level for patients were performed at month 1,month 3,and month 6 by PET/CT.

Results To evaluate the clinical safety and efficacy of anti-TSHR CoupledCAR T cells on refractory or relapsed thyroid cancer, we treated refractory/relapsed post-thyroidectomy thyroid cancer patients according to an IRB approved protocol. We treated two patients using anti-TSHR CoupledCAR T cells and observed the rapid expansion of CAR T cells and enhanced the killing of tumor cells. One patient's best response was complete remission, and the other was near complete remission.Patient Profile:Patient 1 Male, 64Y, Papillary Thyroid Carcinoma. In May 2017, Thyroid cancer was diagnosed, bilateral total thyroidectomy, and right cervical lymph node functional dissection were performed in Jun 2018, followed by iodine 131 isotope therapy. In December 2018, bilateral multiple cervical lymph nodes were enlarged, especially on the right side. In February 2019, right neck lymphadenectomy was performed.Patient 2 Female, 60Y, Thyroid Carcinoma. In Aug 2013, a 'double lobectomy of the thyroid gland' was performed. From Oct 2013 to Jan 2014, she received iodine 131 isotope therapy. In Sep 2014, she was diagnosed with iodine - resistant thyroid cancer. From Sep to Jan 2016, 5 cycles of chemotherapy were performed. In Jun 2016, she enrolled in the Anlotinib experimental group. In Mar 2019, multiple metastases in both lungs and multiple enlarged lymph nodes in the mediastinum were observed. Observations and Results:Patient 1: One month after infusion (M1), the patient was evaluated as PR: lymph node metastasis became undetectable and the size of the thoracic paratracheal tumor nodules decreased significantly. Three months after infusion (M3), the patient was evaluated as CR, and the tumor tissue was substantially smaller than M1.Patient 2: M1, the patient was evaluated as PR (Partial Response): the tumor volume in the right lower lobe of the lung was reduced by approximately 67.51% (decreased from 65*55 mm to 42*39 mm). Three months after infusion (M3), compared with that before, the tumor volume was reduced by approximately 73.54% and SUV max value decreased from 14.9 to 2.8, therefore, the patient was evaluated as nCR (near complete remission).

Conclusions We show that TSHR is a good target for treating thyroid cancer, and our anti-TSHR CoupledCAR T cells are safe and effective for treating thyroid cancer. Recruitment is ongoing to evaluate the safety and efficacy of our CoupledCAR T cells. Further, since our CoupledCAR® technology is a

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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.[1 2] 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 (±) 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

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402 DRAGON: PHASE 1 TRIAL OF SRK-181, A LATENT TGFβ1 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 TGFβ1 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 TGFβ1 and inhibits its activation on suppressive immune cells as well as within tumor stroma. Preclinical data demonstrated that selective inhibition of latent TGFβ1 with SRK-181 overcomes primary anti-PD-1 resistance and has an improved safety profile compared to broad inhibition of the TGFβ 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

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