756 INCLINE-101, A PHASE 1/2, OPEN LABEL, DOSE ESCALATION AND EXPANSION STUDY OF TAC-001 (A TLR9 AGONIST CONJUGATED TO A CD22 ANTIBODY) IN PATIENTS WITH SELECT ADVANCED OR METASTATIC SOLID TUMORS

[1]Cesar Perez*, [2]Jason Henry, [3]Timothy Humphries, [4]Sunnie Kim, [5]Adi Diab, [6]Ons Harrabi, [6]Feng Jin, [6]Hong Wan, [6]Candy Bermingham, [7]Anthony El-Khoueiry. *[1]SCRI at Florida Cancer Specialists, Lake Nona, FL, USA; [2]SCRI at HealthONE, Denver, CO, USA; [3]Linear Clinical Research Ltd, Nedlands, WA, 6009, Australia; [4]University of Colorado Cancer Center, Aurora, CO, USA; [5]MD Anderson Cancer Center, Houston, TX, USA; [6]Tallac Therapeutics, Burlingame, CA, USA; [7]Norris Comprehensive Cancer Center, USC, Los Angeles, CA, USA*

Background Enrichment of memory B cells, plasma cells and tertiary lymphoid structure is a positive prognostic factor in patients with a variety of solid tumors.[1-3] Toll-like receptor 9 (TLR9) agonists generate both innate and adaptive immune responses. TLR9 activation in B cells has been shown to induce expression of co-stimulatory molecules, enhanced cross-presentation leading to T cell activation and proliferation, cytokine, chemokine and immunoglobulin secretion. Designed for systemic administration, TAC-001 is a Toll-like Receptor Agonist Antibody Conjugate (TRAAC) comprised of a potent and differentiated TLR9 agonist (T-CpG) conjugated to an antibody against CD22, a receptor restricted to B cells, including tumor-infiltrating B cells. In preclinical models, TAC-001 has demonstrated single agent anti-tumor activity in checkpoint inhibitor resistant and refractory tumor models, accompanied by increased B cell infiltration, T cell effector functions and modulation of suppressive myeloid cells within the tumor microenvironment.[4] INCLINE-101 is a Phase 1/2 study designed to evaluate the safety, efficacy, pharmacokinetics (PK) and biomarkers of TAC-001 in patients with select advanced or metastatic solid tumors.

Methods TAC-001 is being evaluated in an open-label, non-randomized, dose-escalation (Phase 1) study in patients with select advanced or metastatic solid tumors, and dose-expansion (Phase 2) in patients with select tumor types (NCT05399654). Eligible patients in Phase 1 must have histologically or cytologically-documented advanced, metastatic, unresectable or recurrent breast cancer, cervical squamous cell carcinoma, cholangiocarcinoma, colorectal carcinoma, cutaneous melanoma, endometrial carcinoma, gastro-esophageal adenocarcinoma, head and neck squamous cell carcinoma, hepatocellular carcinoma, Merkle cell carcinoma, non-small cell lung cancer, ovarian cancer, renal cell carcinoma, or urothelial carcinoma that have progressed on or are intolerant to standard therapy, including checkpoint inhibitor therapy if appropriate. Phase 1 study will explore ascending dose levels of TAC-001 monotherapy administrated intravenously every 2 weeks and utilize the Bayesian Optimal Interval (BOIN) design in order to identify the maximum tolerated dose (MTD) or maximum administered dose (MAD), and recommended Phase 2 dose (RP2D). Once RP2D is determined, the Phase 2 expansion in four specific tumor-type cohorts is planned. A 2-stage design will be utilized for Phase 2, and the Clopper-Pearson method to compute exact confidence limits for the response rates will be employed. The primary endpoints are safety and preliminary efficacy (overall response rate, duration of response, clinical benefit rate) per RECIST v1.1 and iRECIST. Additional endpoints include PK, immunogenicity, progression free survival, overall survival, and changes in relevant biomarkers. INCLINE-101 is enrolling in the USA and Australia.

Trial Registration NCT05399654

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Ethics Approval The study has received ethics approval from the WCG IRB (tracking number 20222058, study numbers 1334808 and 1334807) and Bellberry Human Research Ethics Committee (application number 2022-04-408).

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