AN OPEN LABEL PHASE IA/IB STUDY FOR SAFETY, PHARMACOKINETICS (PK), AND EFFICACY OF ONC 392 AS A SINGLE AGENT AND IN COMBINATION WITH PEMBROLIZUMAB IN ADVANCED SOLID TUMORS

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Background ONC-392 is a highly selective, humanized monoclonal IgG1 antibody against CTLA-4. The parental clone was identified through in vivo screening in a humanized CTLA-4 mouse model for high anti-tumor efficacy and low autoimmune toxicity. By preserving CTLA-4 on the cell surface, ONC 392 leaves a higher ligand density for better antibody-dependent cellular cytotoxicity (ADCC), resulting in more efficient in Treg depletion in the tumor microenvironment (TME) and more potent tumor rejection in pre-clinical models. Based on encouraging Phase I dose escalation study, a major revision of the protocol has been performed to expand clinical indications among patients with advanced solid tumors.

Methods This is a Phase IA/IB, open label, dose-escalation, and dose-expansion study of intravenous (IV) ONC 392 as a single agent and in combination with Pembrolizumab (anti PD-1, marketed as KEYTRUDA® by Merck) in patients with advanced/metastatic solid tumors. The study consists of three parts: (1) Part A (Figure 1) is a dose-finding rapid titration study of ONC-392 as a single agent in patients with advanced solid tumors of various histology to define the recommended Phase II dose for ONC-392 monotherapy (RP2D-M). (2) Part B (Figure 2 and 3) has Part B1 and Part B2 as dose-finding for combination therapy with either pembrolizumab or Osimertinib 80 mg orally once daily to define the recommended Phase II dose for ONC-392 in combination with either drug (3) Part C (Figure 4) Phase IB expansion cohorts of ONC-392 in monotherapy and in combination therapy with Pembrolizumab to determine safety and initial efficacy. A total of 8 cohorts encompassing monotherapy for pancreatic cancer and triple negative breast cancer and combination therapy of non-small cell lung carcinoma, melanoma and Merkel cell carcinoma. The primary endpoints for Part A and B are safety and tolerability to observe maximal tolerable dose and recommended doses for Phase II, while that for part C is efficacy as measured by overall response rates. The planned enrollment is 300 patients and the study duration is 18 months.

DLT=dose-limiting toxicity; Gr=Grade; Q3W=every 3 weeks; RECIST=Response Evaluation Criteria in Solid Tumors; RP2D-M=recommended Phase II dose for ONC-392 as monotherapy; TEAE=treatment-emergent adverse event.

Abstract 533 Figure 1 Diagram of ONC-392-001 study Part A

Abstract 533 Figure 2 Diagram of ONC-392-001 study Part B1

Abstract 533 Figure 3 Diagram of ONC-392-001 study Part B2

Abstract 533 Figure 4 Diagram of ONC-392-001 study Part C

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Ethics Approval The study obtained ethics approval from WIRB, study number 20193108. The participants gave informed consent before the enrollment and treatment.

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