736 A PHASE 1/2 OPEN-LABEL, DOSE-ESCALATION STUDY OF ST-067, A DECOY-RESISTANT IL-18 CYTOKINE, GIVEN AS A MONOTHERAPY AND WITH PEMBROLIZUMAB IN ADVANCED SOLID TUMOR MALIGNANCIES

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Background IL-18 is an inflammatory cytokine with immunostimulatory activities on both the innate and adaptive immune systems. However, tumors generate an IL-18 decoy receptor (IL-18 BP), which inactivates both endogenous and exogenously administered IL-18. A decoy-resistant variant of IL-18 (ST-067) has been developed which binds to IL-18Ra but not IL-18 BP. In murine colorectal and melanoma syngeneic tumor models, ST-067 monotherapy and in combination with an anti-PD1 antibody demonstrated significant tumor regression and prolonged survival with an acceptable safety profile. These preclinical data provide the rationale for the current study which will determine the tolerability of both monotherapy and combination therapy in patients with solid tumor malignancies who have disease progression following the standard of care therapy which will include prior immunotherapy (NCT04787042).

Methods This Phase 1 study is a multi-center, multi-dose dose-escalation trial to determine the maximum tolerated dose (MTD) and recommended Phase 2 dose (R2PD) of ST-067 monotherapy and combination therapy with pembrolizumab in subjects with advanced, solid tumor malignancies. Secondary endpoints of the trial include safety, characterization of pharmacokinetics, and immunogenicity. The dose-escalation phase will use a modified toxicity probability interval method to determine R2PD of ST-067 monotherapy and combination therapy with pembrolizumab. All subjects will receive ST-067 by the subcutaneous route once every 7 days. The RP2D for all ST-067 treatment arms will be based on the safety, tolerability, PK, and available preliminary anti-tumor activity. Key eligibility requirements include advanced, pre-treated solid tumor malignancy with adequate end-organ function and a PS of 0–1. All subjects will have pre- and on-treatment tumor biopsies which will be analyzed for PD biomarkers potentially predictive of response to therapy. Subjects will receive treatment until disease progression or unacceptable toxicity. Tumor assessments will be performed every 8 weeks and interpreted according to RECIST v1.1. Recruitment is ongoing in the US.

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Ethics Approval This study was approved by either centralized or local institutional review board committees. All enrolled subjects gave signed informed consent prior to taking part of this study.

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

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