A PHASE 1/2 DOSE ESCALATION/EXPANSION STUDY EVALUATING THE SAFETY, PHARMACOKINETICS, PHARMACODYNAMICS, AND ANTITUMOR ACTIVITY OF E-602, A BI-SIALIDASE FUSION PROTEIN, IN ADVANCED CANCER (GLIMMER-01)

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Background E-602 is a novel, first-in-class fusion protein of engineered human sialidases, neuraminidase (Neu2), and the human IgG1 Fc region. The sialidase moieties of E-602 cleave terminal sialic acid residues from sialoglycans on diverse immune cell subsets and tumor cells. Sialoglycans are immunosuppressive in cancer, associated with poorer outcomes across numerous tumor indications, and have emerged as a critical glyco-immune checkpoint. In preclinical studies, sialidase-mediated cleavage of terminal sialic acids improves antitumor immunity by restoring the immune function of exhausted-like T cells and enhancing dendritic cell priming and naive T cell activation.1 In multiple syngeneic mouse tumor models, sialidase treatment has demonstrated antitumor activity as monotherapy1 and additive antitumor activity when combined with anti-programmed death-1 (PD-1)/programmed death-ligand 1 (PD-L1) blockade. E-602 has a wide safety margin, is not an immune agonist and does not stimulate cytokine activation in an in vitro PBMC cytokine release assay.1,2 In humans, E-602, via desialylation of tumor cells and immune cells, is expected to have antitumor activity either as monotherapy or in combination with an anti-PD-1 agent.

Methods A Phase 1/2, first-in-human, open label, dose escalation and expansion study of E-602 administered as monotherapy and in combination with an anti-PD-1 agent is ongoing to evaluate the safety, pharmacokinetics, pharmacodynamics, and antitumor activity in participants with advanced cancers. Phase 1 of the study consists of 4 planned dose escalation cohorts of E-602 monotherapy and 2 planned dose escalation cohorts of E-602 in combination with an anti-PD-1 agent. Phase 1 is treating eligible participants with advanced melanoma, ovarian, non-small cell lung, colorectal, pancreatic, breast, gastric/esophageal junction, head and neck, or urothelial cancers. Utilizing a modified 3+3 study design in Phase 1, the safety of the dose regimens is under evaluation to identify the maximum tolerated dose and/or recommended Phase 2 dose. Additional participants (backfill) may be enrolled in the Phase 1 cohorts to obtain additional safety, pharmacokinetic or pharmacodynamic data. Phase 2 will include up to 3 disease indications, evaluating E-602 as monotherapy and/or in combination with an anti-PD-1 agent utilizing a Simon’s minimax 2-stage design. Pre and on-treatment biopsies to further explore the pharmacodynamic effects of E-602 are required for the Phase 1 backfill and Phase 2 participants.

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Trial Registration The study is registered on clinicaltrials.gov as NCT05259696.

REFERENCES

Ethics Approval The study is approved by the Advarra institutional Ethics Board, approval number Pro00058627 and participants gave informed consent before taking part.