PEGASUS GI, A PLATFORM STUDY OF SAR444245 (THOR-707, A PEGYLATED RECOMBINANT NON-ALPHA IL2) WITH ANTI-CANCER AGENTS OF PARTICIPANTS WITH ADVANCED AND METASTATIC GASTROINTESTINAL CANCER

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Background SAR444245 (THOR-707) is a recombinant human IL-2 molecule that includes a PEG moiety irreversibly bound to a novel amino acid via click chemistry to block the alpha-binding domain while retaining near-native affinity for the beta/gamma subunits. In animal models, SAR444245 showed anti-tumor benefits, but with no severe side effects, both as single agent and when combined with anti-PD1 comparing with historical data from aldesleukin. Preclinical study demonstrated SAR444245 enhances ADCC function of cetuximab. The HAMMER trial, which is the FIH study, shows preliminary encouraging clinical results: initial efficacy and safety profile with SAR444245 monotherapy and in combination with pembrolizumab or with cetuximab support a non-alpha preferential activity, validating preclinical models. The Pegasus GI Ph 2 study will evaluate the clinical benefit of SAR444245 in combination with pembrolizumab or cetuximab for the treatment of participants with advanced or metastatic gastrointestinal cancer [esophageal squamous cell carcinoma (ESCC), gastric cancer (GC) or gastro-esophageal junction adenocarcinoma (GEJ), Hepatocellular carcinoma (HCC) or colorectal cancer (CRC)]

Methods Pegasus GI will enroll approximately 280 patients in 7 separate cohorts concurrently (4 cohorts) or sequentially (3 cohorts). In cohort A, 2–3 line (L) ESCC participants who have progressed after checkpoint inhibitor (CPI)-based therapy will receive SAR444245 + pembrolizumab. In cohorts B1, B2 & B3 participants with GC and GEJ cancers will receive SAR444245 + pembrolizumab. Cohort B1 & B2 will enroll 1–3L CPI-naïve patients. Cohort B3 will enroll 2–4L patients post CPI-based therapy). In cohort C, 2–3L HCC participants who have progressed after CPI-based therapy will receive SAR444245 + pembrolizumab. In cohorts D1 and D2, 3–6L CRC participants will receive SAR444245 + pembrolizumab (any RAS) or SAR444245 + cetuximab (RAS-wild type) SAR444245 is administered IV at a dose of 24 ug/kg Q3W until disease progression or completion of 35 cycles. Pembrolizumab is administered as per label, Q3W for up to 35 cycles. Cetuximab is administered per label, QW until PD. The study primary objective is to determine the antitumor activity of SAR444245 in combination with other anticancer therapies. Secondary objectives are to assess safety profile, other indicators of antitumor activity, the pharmacokinetic profile and immunogenicity of SAR444245. The study will be conducted in the US, France, Germany, Spain, Italy, Belgium, Netherlands, Poland, Russia, South Korea and China

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Ethics Approval All applicable ECs are obtained

Consent All participant consents are obtained

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