551 PEGASUS SKIN, A STUDY OF SAR444245 (THOR-707, A PEGYLATED RECOMBINANT NON-ALPHA IL2) WITH CEMIPLIMAB FOR THE TREATMENT OF PARTICIPANTS WITH ADVANCED UNRESECTABLE OR METASTATIC SKIN CANCERS

[1]PARK John, [2]Adyb Baakili*, [2]Brigitte Demers, [3]Rao Saleem, [2]Alice Gosselin, [3]Giovanni Abbadessa, [4]Paolo A Ascierto. [1]*Macquarie University, Macquarie, Australia*; [2]*Sanofi-Aventis, Vitry-sur-Seine, France*; [3]*Sanofi, Cambridge, MA, USA*; [4]*Instituto Nazioanel Tumori IRCCS, Naples, Italy*

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. 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 supporting non-alpha preferential activity, validating preclinical models. The Pegasus Skin Phase 1/2 study will evaluate the clinical benefit of SAR444245 in combination with cemiplimab (anti-PD1) for the treatment of participants with cutaneous squamous cell carcinoma (CSCC) or melanoma

Methods Pegasus Skin (NCT04913220) will enroll approximately 80 participants in 2 separate cohorts. In cohort A, participants with a locally advanced, unresectable or metastatic melanoma will receive SAR444245 + cemiplimab as first line (1L) therapy. In cohort B, participants with locally advanced or metastatic CSCC who have not received moe than 2 prior lines of systemic therapy and are not candidates for curative surgery or radiation will receive SAR444245 + cemiplimab. The study will start with a dose escalation to determine the recommended phase 2 dose (RP2D) of SAR444245 when combined with cemiplimab. The starting dose will be 16 µg/kg Q3W (DL1) with a possibility to de-escalate to 8 µg/kg Q3W (DL -1) or escalate to 24 µg/kg Q3W (DL2) based on the occurrence of DLT and overall assessment of safety. Participants enrolled in the Dose Escalation and treated at the RP2D selected for Dose Expansion will be included in the total number of participants for efficacy and safety evaluation. Participants will receive study treatment until disease progression, unacceptable toxicity, or completion of 35 cycles. Cemiplimab will be administered 350 mg per label, Q3W

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Trial Registration NCT04913220

Ethics Approval All applicable ECs are obtained

Consent All participant consents are obtained

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