### BACKGROUNDS

Tumor necrosis factor receptor-2 (TNFR2) drives immune escape and tumor proliferation, and is highly expressed on tumor cells, immunosuppressive cells in the tumor microenvironment, including regulatory T cells (Tregs) and myeloid-derived suppressor cells (MDSCs). SIM1811-03 is a humanized IgG1 monoclonal antibody that targets TNFR2, which demonstrated antitumor activity in preclinical models as single agent. SIM1811-03 is being evaluated in the First-in-Human study in patients with advanced solid tumors and cutaneous T-cell lymphomas (CTCL) here we report the data based on Chinese population.

### METHODS

The study enrolled participants with advanced solid tumors who were not eligible for standard of care treatment. Participants received one dose of SIM1811-03 in cycle 0 and subsequently once every 2 weeks (Q2W) in dose from 0.5mg/kg to 25mg/kg. Based on emerging data, every 3 weeks(Q3W) schedule in 40mg/kg was tested for single agent. The primary objectives were to determine the maximum tolerated dose (MTD) or recommended dose (RD) in the dose escalation part for expansion and to evaluate preliminary anti-tumor activity using either RECIST v1.1 for solid tumors or the global response score for CTCL (Olsen 2011) in expansion part. The secondary objectives were to assess safety and tolerability and to characterize pharmacokinetics (PK) and pharmacodynamics (PD) profiles of SIM1811-03.

### RESULTS

As of April 18, 2023, 22 patients in dose escalation part received SIM1811-03 monotherapy at doses of 0.5 mg/kg (n=3), 1.5 mg/kg (n=4), 5 mg/kg (n=4), 15 mg/kg (n=4), 25 mg/kg (n=4) Q2W and 40 mg/kg Q3W (n=3). Median age was 51 years (range: 30-68) (Table 1). No dose-limiting toxicity (DLT) was observed and the MTD was not reached. Majority of adverse events were Grade 1 or 2. There were two subjects with Grade 3/4 treatment-related adverse event (TRAE). Two patients experienced treatment-related serious adverse event (SAE), one had peripheral edema and the other platelet count increase (Table 2, Table 3).

#### Pharmacokinetics

**After SIM1811-03 infusion:**
- All doses from 0.5 to 15 mg/kg, the drug concentrations decreased rapidly and the PK profile showed a target-mediated drug disposition (TMDD) property (Figure 2);
- At doses >15 mg/kg, the drug exposure were dose-proportional (Figure 2);
- The terminal elimination half-life was approximately 12 days at doses higher than 15 mg/kg.
- A slight accumulation of SIM1811-03 exposure (1.28 to 2.14 folds) was observed on Cycle 3.

- Figure 2. Mean ± SD Serum Pharmacokinetics Profiles (semi-log scale) after Single and Multiple Doses of SIM1811-03 Infusion.
- Figure 3. TNFR2 Receptor Occupancy in CD14+ and CD16+ Cells of Peripheral Blood after SIM1811-03 Infusion.
- Figure 4. sTNFR2 Release in Plasma after SIM1811-03 Infusion.

### CONCLUSIONS

SIM1811-03 was well tolerated without and DLT reported in participants with advanced solid tumors across all dose levels explored and the MTD was not reached. The preliminary PK and PD results supported 40mg/kg every 3-week to be selected as the recommended dose for expansion and for combinations with PDL1-1 inhibitors. Clinical trial information: NCT05781386.