Background Expression of LAG-3, an inhibitory immunoreceptor, has been linked to reduced T-cell proliferation and cytokine production. LAG525 is a humanized IgG4 anti-LAG-3 antibody which inhibits LAG-3 binding to MHC class II. Spartalizumab is a humanized IgG4 anti-PD-1 mAb which inhibits PD-1 binding with its ligands PD-L1 and PD-L2. Preclinical data have shown promising antitumor activity when blocking LAG-3 and PD-1.

Methods The Phase II part of the first-in-human study (NCT02460224) explored LAG525 + spartalizumab in patients with advanced/metastatic non-small cell lung cancer (NSCLC), cutaneous and non-cutaneous melanoma, renal cell carcinoma (RCC), mesothelioma, or triple-negative breast cancer (TNBC). The dose/schedule of LAG525 and spartalizumab was 400 mg IV Q3W and 300 mg IV Q3W, respectively. Half of patients naïve to anti-PD-1/PD-L1 received LAG525 at 600 mg IV Q4W and spartalizumab at 400 mg IV Q4W. The primary endpoint was overall response rate (ORR) using RECIST v1.1.

Conclusions NIZ985 is safe and tolerable at both TIW and QW dosing ± spartalizumab. It displays approximately dose-proportional, time-dependent PK, and a biomarker and lymphocyte response profile consistent with target engagement. Limited antitumor activity was reported during dose escalation; however, preliminary responses in both IO-experienced and IO-naïve patients were seen in combination with spartalizumab that warrant further investigation.

Ethics Approval The study was approved by an independent ethics committee and/or institutional review board at each participating site.