Background ATOR-1015 is a human CTLA-4 x OX40 bispecific antibody developed as a first in class tumor-localizing CTLA-4 antibody for improved efficacy and reduced toxicity.

Methods The study (NCT03782467) is a first-in-human dose escalation study followed by an expansion part. In the dose escalation patients with refractory solid malignancies are enrolled and the expansion part will enroll patients with cutaneous or mucosal malignant melanoma. Patients receive ATOR-1015 intravenously Q2W as a single agent until confirmed progressive disease, unacceptable toxicity or withdrawal of consent. Intra-patient dose escalation is allowed. The primary objective is to assess the safety and tolerability of ATOR-1015. Secondary objectives include pharmacokinetics, immunogenicity, pharmacodynamics, and clinical efficacy as assessed by iRECIST. Pharmacodynamic analyses include serum cytokines, immunophenotyping of peripheral blood mononuclear cells. Tumor biopsies before and after ATOR-1015 will be analyzed.

Results As of June 26, 2020, 23 patients have been exposed to ATOR-1015. The median age of the patients is 54 years (range 40–72). Patients have received a median of 5 prior lines of therapy (range 1–16). Most common cancer type is colorectal cancer. Dose levels from 0.043 mg to 600 mg have been evaluated and declared safe. Dose escalation is ongoing, and currently two patients have been enrolled at 750 mg dose level. The median time on study was 8.4 weeks (range 0.1–34.3). Five patients are on study and 18 patients have discontinued. Reasons for discontinuation included clinical deterioration (n=10), disease progression (n=5), death due to disease progression (n=2), and investigator’s decision (n=1). Twelve of the 23 patients experienced a drug-related adverse event (AE). Two patients experienced a grade 3 drug-related AE, for all other patients AEs were grade 1 or 2. Infusion-related reactions (IRR) were reported in nine patients. Predominant symptoms of the IRR were chills, rash and pain. Potentially immune-related AEs grade 1 were reported in three patients: one patient had rash, one vitiligo, and one exanthema and eczema. No dose-limiting toxicities have occurred. Best response is stable disease. Pharmacokinetic data show dose proportional kinetics up to 600 mg. Preliminary biomarker analysis shows pharmacodynamic activity of ATOR-1015.

Conclusions ATOR-1015 has been safe and well-tolerated up to 600 mg. Currently 750 mg is under evaluation. Best response is stable disease. Following the dose escalation phase, an expansion cohort for patients with advanced malignant melanoma will be initiated.

Ethics Approval The study is approved by the Ethic Boards in Sweden and Denmark.