Background ATRC-101 is an engineered, fully human, monoclonal antibody identified via the Atreca discovery platform that targets a novel tumor-specific ribonucleoprotein complex. Methods ATRC-101-A01 is a Phase 1b dose escalation and expansion trial of ATRC-101 administered to participants with select solid tumors as monotherapy every 3 (Q3W-Mono) or 2 (Q2W-Mono) weeks and in combination with pembrolizumab (Q3W-Pembro). Participants in Q3W-Pembro must have had suboptimal response to prior/ongoing anti-PD-1/PD-L1 and deemed to potentially benefit from addition of ATRC-101. Objectives include safety (primary), pharmacokinetics, immunogenicity, recommended dose for expansion, and antitumor activity (RECIST v1.1). Biomarker analyses include immunohistochemical staining for target expression and CD8+ T cell infiltration in baseline and on-treatment tumor biopsies. For participants described herein, target expression was analyzed retrospectively.

Results As of data cut-off (February 15, 2022), 50 heavily pretreated participants (median prior lines of therapy 5, range 1–11) received ≥1 dose of ATRC-101 (Q3W-Mono, n=37; Q2W-Mono, n=9; Q3W-Pembro, n=4). ATRC-101 was administered at 0.3 mg/kg (n=3), 1 mg/kg (n=6), 3 mg/kg (n=12), 10 mg/kg (n=13), and 30 mg/kg (n=16). Tumor types included colorectal (n=24), breast (n=8), ovarian (n=7), non-small cell lung (NSCLC, n=5), melanoma (n=3), head and neck squamous cell (n=2), and urothelial (n=1).

Dose escalation has been completed for Q3W-Mono and is ongoing for other cohorts. To date, no dose-limiting toxicities have been reported and no maximum tolerated dose identified. The dose for ongoing cohorts is 30 mg/kg.

Treatment-emergent adverse events (TEAEs) are summarized in Table 1. None resulted in treatment discontinuation or dose reduction. Grade ≥3 TEAEs occurred in 13 (26%) participants. Grade ≥3 TEAEs considered by investigators as related to ATRC-101 occurred in 3 (6%) participants (tumor pain, headache, small intestinal obstruction).

There was one partial response (NSCLC in Q3W-Mono (30 mg/kg) and one complete response (melanoma) in Q3W-Pembro (10 mg/kg). The latter participant had previously progressed during treatment with nivolumab. An additional 5 participants experienced stable disease (SD) as best response, with reductions in target lesions. Target expression, as detected retrospectively by immunohistochemical analysis of screening tumor biopsies, was associated with achievement of SD or better and with reduction in the sum of diameters of target lesions.

Conclusions ATRC-101, without and with pembrolizumab, has been well tolerated and has demonstrated anti-tumor activity among target expressers. Enrollment in specific expansion cohorts now requires pretreatment tumor biopsies demonstrating ATRC-101 target expression (H-score ≥50) by immunohistochemistry. Updated data will be presented at the meeting.

Trial Registration NCT04244552

Ethics Approval This trial was approved by the institutional review board or ethics committee as required for each participating site.