Interim Update of The ATRC-101 Phase 1b Trial in Advanced Solid Tumors

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ATRC-101: Novel Tumor-Specific Engineered Antibody Discovered via Atreca’s Platform

Lung adenocarcinoma patient undergoing treatment with nivolumab (anti-PD-1)

Target appears to be a RNP particle expressed on cancer cells


NSCLC, non-small cell lung cancer; RNP, ribonucleoprotein; PD-1, programmed death 1.

* "Reactive" samples had moderate to high signal overall with ≥ 40% malignant cells positive (N = total samples). Samples were largely from treatment-naïve patients. Percentages based on samples from all subtypes within solid tumor type.
ATRC-101 Activity in EMT6/CT26 Models Driven by Innate and Adaptive Responses

CD, cluster of differentiation; M-MDSC, monocytic myeloid-derived suppressor cells; NK, natural killer; PBS, phosphate buffered saline.


CD, cluster of differentiation; M-MDSC, monocytic myeloid-derived suppressor cells; NK, natural killer; PBS, phosphate buffered saline.
ATRC-101: Proposed Mechanism of Action

Systemically dosed ATRC-101 antibody delivers its tumor antigen to cells of the innate immune system, leading to a remodeling of the tumor microenvironment and an adaptive immune response against tumor.

Chemokines, cytokines, and interferons

Macrophage

Dendritic cell

T cell

Tumor-draining lymph node

ATRC-101

RNP complex

Tumor cell

Innate

Adaptive


RNP, ribonucleoprotein.
## ATRC-101: Phase 1b Trial Design

### OBJECTIVES

- Characterize safety
- Evaluate pharmacokinetics
- Determine RDE
- Measure initial clinical activity
- Analyze target expression
- Determine indication/s for expansion

### ATRC-101 Monotherapy

**Dose Escalation**
- Q3W & Q2W

**Dose Expansion**
- Q3W only

**Target-enriched Expansion**
- Q3W 30 mg/kg

**ATRC-101 Monotherapy**
- Ovarian cancer
- NSCLC
- CRC
- Breast cancer
- Acral melanoma

**Simon 2 stage design:** the null hypothesis of response rate is 5% for efficacy expansion.

### ATRC-101 + Pembrolizumab

**Dose Escalation**
- Q3W

**Target-enriched Expansion**
- Q3W 30 mg/kg

**ATRC-101 + Pembrolizumab**
- NSCLC
- CRC*
- Melanoma
- HCC
- HNSCC
- ESCC
- UC
- TNBC

**Simon 2 stage design:** the null hypothesis of response rate is 8% for efficacy expansion.

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*MSI-H or dMMR.  
CRC, colorectal cancer; dMMR, mismatch repair deficient; ESCC, esophageal squamous cell carcinoma; HCC, hepatocellular carcinoma; HNSCC, head and neck squamous cell carcinoma; MSI-H, microsatellite instability-high; NSCLC, non-small cell lung cancer; PD-1, programmed death-1; PD-L1, programmed death-ligand 1; Q2W, every 2 weeks; Q3W, every 3 weeks; RDE, recommended dose for expansion; TNBC, triple-negative breast cancer; UC, urothelial carcinoma.
# ATRC-101: Baseline Characteristics

*Most Participants Have Received Multiple Prior Lines of Therapy*

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>Overall (N = 71)</th>
<th>Monotherapy Q3W (n = 48)</th>
<th>Monotherapy Q2W (n = 14)</th>
<th>Pembrolizumab Combination (n = 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median years (range)</td>
<td>62 (27–86)</td>
<td>63 (27–79)</td>
<td>53 (42–74)</td>
<td>58 (41–86)</td>
</tr>
<tr>
<td>ECOG PS at baseline, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>24 (34)</td>
<td>18 (38)</td>
<td>4 (29)</td>
<td>2 (22)</td>
</tr>
<tr>
<td>1</td>
<td>47 (66)</td>
<td>30 (63)</td>
<td>10 (71)</td>
<td>7 (78)</td>
</tr>
<tr>
<td>Cancer type, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRC</td>
<td>30 (42)</td>
<td>18 (38)</td>
<td>12 (86)</td>
<td>0</td>
</tr>
<tr>
<td>Ovarian</td>
<td>10 (14)</td>
<td>9 (19)</td>
<td>1 (7)</td>
<td>—</td>
</tr>
<tr>
<td>Breast</td>
<td>9 (13)</td>
<td>9 (19)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Melanoma</td>
<td>8 (11)</td>
<td>6 (13)</td>
<td>0</td>
<td>2 (22)</td>
</tr>
<tr>
<td>NSCLC</td>
<td>7 (10)</td>
<td>6 (13)</td>
<td>0</td>
<td>1 (11)</td>
</tr>
<tr>
<td>HNSCC</td>
<td>3 (4)</td>
<td>—</td>
<td>0</td>
<td>3 (33)</td>
</tr>
<tr>
<td>ESCC</td>
<td>1 (1)</td>
<td>—</td>
<td>—</td>
<td>1 (11)</td>
</tr>
<tr>
<td>HCC</td>
<td>1 (1)</td>
<td>—</td>
<td>—</td>
<td>1 (11)</td>
</tr>
<tr>
<td>Small Bowel*</td>
<td>1 (1)</td>
<td>—</td>
<td>1 (7)</td>
<td>—</td>
</tr>
<tr>
<td>Urothelial</td>
<td>1 (1)</td>
<td>—</td>
<td>—</td>
<td>1 (11)</td>
</tr>
<tr>
<td>Lines of prior cancer medications, median (range)</td>
<td>5 (1–12)</td>
<td>5 (1–12)</td>
<td>6 (1–8)</td>
<td>3 (1–5)</td>
</tr>
<tr>
<td>Prior therapy with checkpoint inhibitor, n (%)</td>
<td>34 (48)</td>
<td>22 (46)</td>
<td>3 (21)</td>
<td>9 (100)</td>
</tr>
</tbody>
</table>

*Protocol deviation.*

CRC, colorectal cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; ESCC, esophageal squamous cell carcinoma; HCC, hepatocellular carcinoma; HNSCC, head and neck squamous cell carcinoma; NSCLC, non-small cell lung cancer; Q2W, every 2 weeks; Q3W, every 3 weeks.

Data Extracted 17-Feb-2023
# ATRC-101: Analysis Sets

## Analysis Sub-sets

<table>
<thead>
<tr>
<th>Analysis Sub-sets</th>
<th>Monotherapy n, (%)</th>
<th>Pembrolizumab Combination n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safety Set (N = 71)</td>
<td>62</td>
<td>9</td>
</tr>
<tr>
<td>Relevant Dose (3-10-30 mg/kg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>H-score result</td>
<td>41 (77)</td>
<td>9 (100)</td>
</tr>
<tr>
<td>RECIST v1.1</td>
<td>49 (92)</td>
<td>7 (78)</td>
</tr>
<tr>
<td>RECIST v1.1 &amp; H-score result</td>
<td>38 (72)</td>
<td>7 (78)</td>
</tr>
<tr>
<td>RECIST v1.1 &amp; target positive</td>
<td>17 (32)</td>
<td>6 (67)</td>
</tr>
<tr>
<td>Best Overall Response &amp; H-score result</td>
<td>41 (77)</td>
<td>8 (89)</td>
</tr>
<tr>
<td>Best Overall Response &amp; target positive</td>
<td>17 (32)</td>
<td>7 (78)</td>
</tr>
</tbody>
</table>

*Defined as the number of participants who have received at least one dose of ATRC-101.
†Defined as successful determination of H-score in a pre-treatment biopsy within the 3-10-30 mg/kg set.
‡Defined as ≥ 1 post-baseline tumor assessment within the 3-10-30 mg/kg set.
§Defined as evaluable for a RECIST v1.1 or clinical response assessment within the 3-10-30 mg/kg set.
ǁDefined as target positive screening H-Score ≥ 50 and target negative H-Score < 50 within the 3-10-30 mg/kg set.

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**Enrolled and dosed**

N = 71

**Relevant Dose (3-10-30 mg/kg) set**

n = 62

**H-score result set**

n = 50 (81%)

**Best Overall Response**

n = 61 (98%)

**RECIST v1.1 Evaluable patients**

n = 56 (90%)

**Best Overall Response**

+ H-score result

n = 49 (79%)

**RECIST v1.1**

+ H-score result

n = 45 (73%)

**Best Overall Response**

+ target positive set

n = 24 (39%)

**RECIST v1.1**

+ target positive set

n = 23 (37%)

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**RECIST**, Response Evaluation Criteria in Solid Tumors.

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**ATRC**, Analysis Sets

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**Enrolled and dosed**

N = 71

**Relevant Dose (3-10-30 mg/kg) set**

n = 62

**H-score result set**

n = 50 (81%)

**Best Overall Response**

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‡Defined as ≥ 1 post-baseline tumor assessment within the 3-10-30 mg/kg set.
§Defined as evaluable for a RECIST v1.1 or clinical response assessment within the 3-10-30 mg/kg set.
ǁDefined as target positive screening H-Score ≥ 50 and target negative H-Score < 50 within the 3-10-30 mg/kg set.
ATRC-101: Favorable Safety Profile Observed in Phase 1b

Adverse events reported in ≥ 5% of participants in safety set (N = 71)

All AEs Reported

<table>
<thead>
<tr>
<th>AEs – by participant</th>
<th>Treatment Emergent n (%)</th>
<th>Treatment Related n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>67 (94)</td>
<td>35 (49)</td>
</tr>
<tr>
<td>Grade 2</td>
<td>47 (66)</td>
<td>18 (25)</td>
</tr>
<tr>
<td>Grade 3</td>
<td>23 (32)</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Grade 4</td>
<td>4 (6)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Grade 5</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Serious AEs</td>
<td>17 (24)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>AEs Leading to Dose Interruptions</td>
<td>16 (23)</td>
<td>6 (8)</td>
</tr>
<tr>
<td>AEs Leading to Drug Discontinuations</td>
<td>2 (3)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

Treatment-Related AEs causing treatment interruptions (n = 6):
- Infusion-related reaction
- Tachycardia
- Elevated LFT laboratory values
- Nausea
- Small intestinal obstruction
- Fatigue

*Grading by Common Terminology Criteria for AEs, Version 5.0. AE, adverse event; ALK, anaplastic lymphoma kinase; ALT; alanine transaminase; AST; alanine transaminase; LFT, liver function test; NCI, National Cancer Institute.

Data Extracted 17-Feb-2023
ATRC-101: H-Score Cutoff Predicts Probability of Disease Control

H-score ≥ 50 discriminates probability of disease control* (Best overall response and H-score data set)

**Monotherapy (n = 41)**

- Fisher’s Exact: $P = 0.05$
- **H-score < 50**
  - n = 24
  - SD: 25%
- **H-score ≥ 50**
  - n = 17
  - SD: 53%

**Overall (n = 49)**

- Fisher’s Exact: $P = 0.021$
- **H-score < 50**
  - n = 25
  - SD: 24%
- **H-score ≥ 50**
  - n = 24
  - SD: 50%

*ATRC-101 Target Expression at Screening

*Disease control = CR + PR + SD. CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease.

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ATRC-101: Anti-tumor Activity Associated with Target Expression

Change in SOD over time and durability of responses
(RECIST v1.1 and target negative monotherapy set)

Monotherapy (n = 21)

Overall (n = 22)

Q2W, every 2 weeks; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; SOD, sum of diameters of target lesions.

Data Extracted 17-Feb-2023
ATRC-101: Anti-tumor Activity Associated with Target Expression

Change in SOD over time and durability of responses
(RECIST v1.1 and H-score set)

Monotherapy (n = 38)
Overall (n = 45)

*Lymph nodes deemed non-pathologic (<10 mm) and considered a complete response.
Q2W, every 2 weeks; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; SOD, sum of diameters of target lesions.

Data Extracted 17-Feb-2023
ATRC-101: Anti-tumor Activity Observed in Multiple Tumor Types

Change in SOD over time and durability of responses in RECIST v1.1 and target positive set (n = 23)

*Lymph nodes deemed non-pathologic (<10 mm) and considered a complete response.
CRC, colorectal cancer; ESCC, esophageal squamous cell carcinoma; HNSCC, head and neck squamous cell carcinoma; NSCLC, non-small cell lung cancer; Q2W, every 2 weeks; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; SOD, sum of diameters of target lesions.

Data Extracted 17-Feb-2023
A TRC-101: Anti-tumor Activity Observed in Multiple Tumor Types

Change in SOD by H-score, cancer type, and treatment
(RECIST v1.1 and H-score set n=45)

H-score < 50
(n = 22)

H-score ≥ 50
(n = 23)

Participant
Best Change in SOD from Baseline
-80% -60% -40% -20% 0% 20% 40% 60% 80%

*Lymph nodes deemed non-pathologic (<10 mm) and considered a complete response.
CRC, colorectal cancer; ESCC, esophageal squamous cell carcinoma; HNSCC, head and neck squamous cell carcinoma; NSCLC, non-small cell lung cancer; RECIST, Response Evaluation Criteria in Solid Tumors; SOD, sum of diameters of target lesions.

Data Extracted 17-Feb-2023
ATRC-101: Longer PFS Associated with Target Expression

PFS based on H-score in monotherapy subset and overall
(Best overall response and H-score data set)

Monotherapy (n = 41)

H-score < 50 vs H-score ≥ 50
HR: 0.47 95% CI: [0.23, 0.95]
Median PFS for H-score ≥ 50: 72 days
Median PFS for H-score < 50: 39 days
Log rank $P = 0.034$

Overall (n = 49)

H-score < 50 vs H-score ≥ 50
HR: 0.4 95% CI: [0.21, 0.78]
Median PFS for H-score ≥ 50: 100 days
Median PFS for H-score < 50: 39 days
Log rank $P = 0.0058$

CI, confidence interval; HR, hazard ratio; PFS, progression-free survival.
**Conclusions – Key Takeaways**

**ATRC-101**

**Was well tolerated**
- No DLTs up to 30 mg/kg dose level and in combination with pembrolizumab
- No treatment discontinuation due to toxicities

**Demonstrated durable disease control across a range of tumor types in heavily pretreated subjects and many cases, after failure of prior CPI therapy**

**Delivered a progression-free survival advantage for patients whose tumor expressed target**

**ATRC-101 therefore has the potential to**

**Address unmet needs in multiple indications**
- Activity and disease control seen for melanoma, NSCLC, HNSCC, ovarian cancer

**Become a component of multiple treatment regimens**
- Safety profile makes it possible to explore combinations with established regimens
- Data supports continuing to explore combination therapy with CPI

CPI, checkpoint inhibitor; DLT, dose-limiting toxicity; HNSCC, head and neck squamous cell carcinoma; NSCLC, non-small cell lung cancer.