



ATRC-101 Clinical Data Webcast

July 29, 2021

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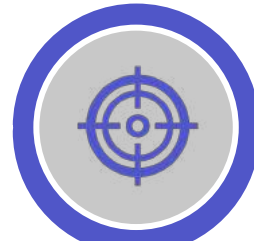
Agenda

- Background: ATRC-101 discovery, preclinical data, and mechanistic insights
- ATRC-101 Phase 1b Clinical Trial
- Summary and Future Development Plans
- Platform Update
- Q&A

Top-line Summary



ATRC-101 was well tolerated by participants



Disease control is associated with target expression



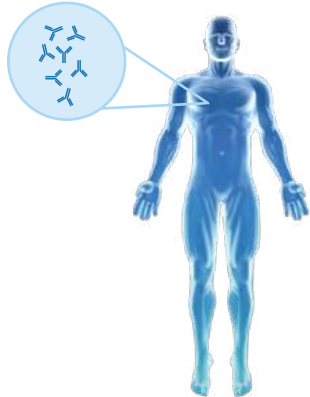
Biomarker data are consistent with the ATRC-101 proposed mechanism of action



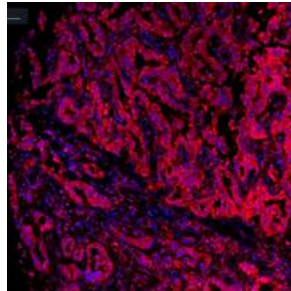
Background on ATRC-101

ATRC-101: A New Way to Target Cancer

Engineered version of a patient antibody discovered via the Atreca platform



Lung adenocarcinoma patient
with active anti-tumor
immune response



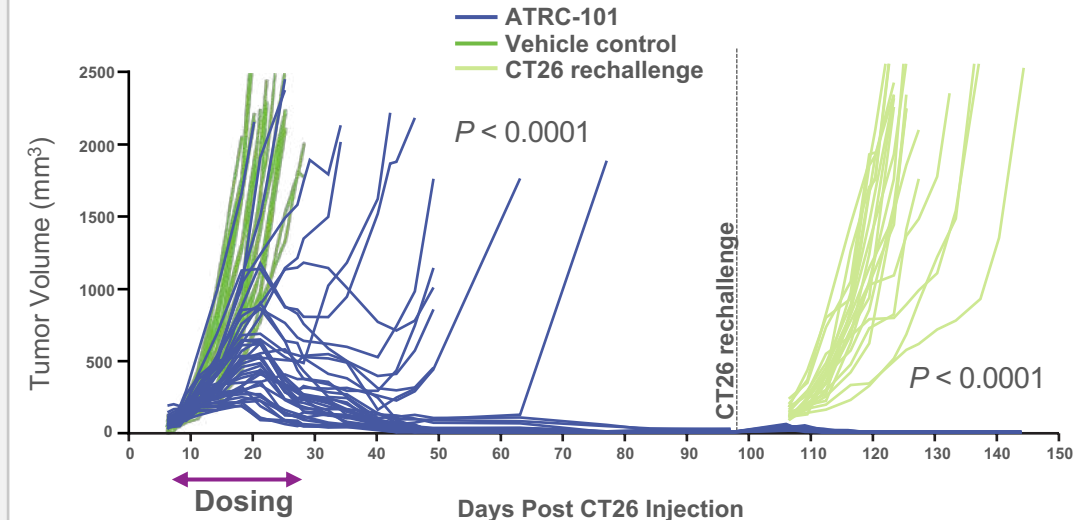
ATRC-101 binds its target in
multiple tumor types from
different patients



ATRC-101 reactivity is tumor-specific across multiple cancer types

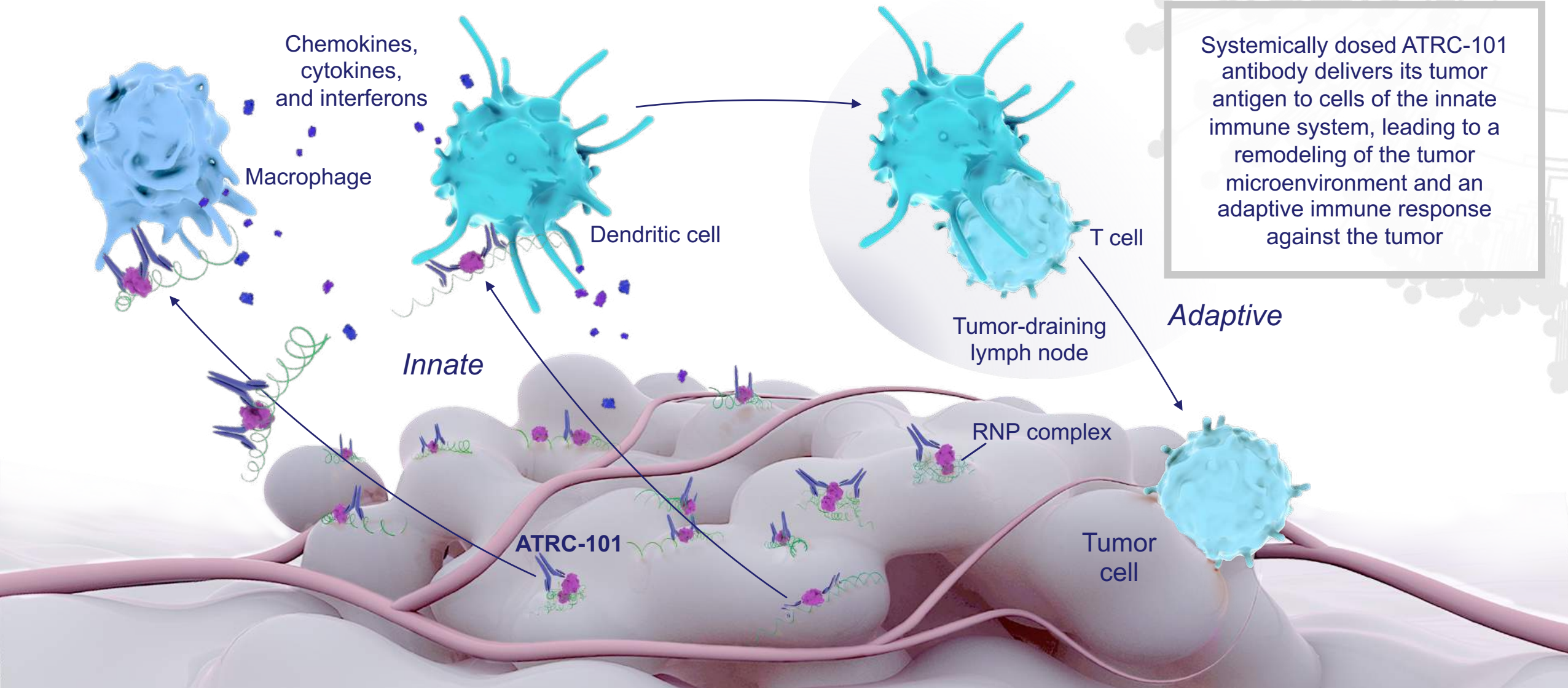
- ATRC-101 reactivity has been seen in ~50% or more of samples from patients with melanoma, NSCLC, and breast, ovarian, and colorectal cancer
- ATRC-101 appears to target a ribonucleoprotein (RNP) complex with over 20 proteins, the most prominent being polyadenylate-binding protein 1 (PABP-1)

ATRC-101 inhibits tumor growth and leads to immune memory in the CT26 syngeneic model



- Large tumors can be eradicated in this model by continued dosing with ATRC-101
- Immune memory prevents re-establishment of tumors after tumor clearance by a second CT26 injection (also observed in the EMT6 model)

Novel ATRC-101 Mechanism of Action: Driver Antigen Engagement





ATRC-101 Phase 1b Clinical Trial

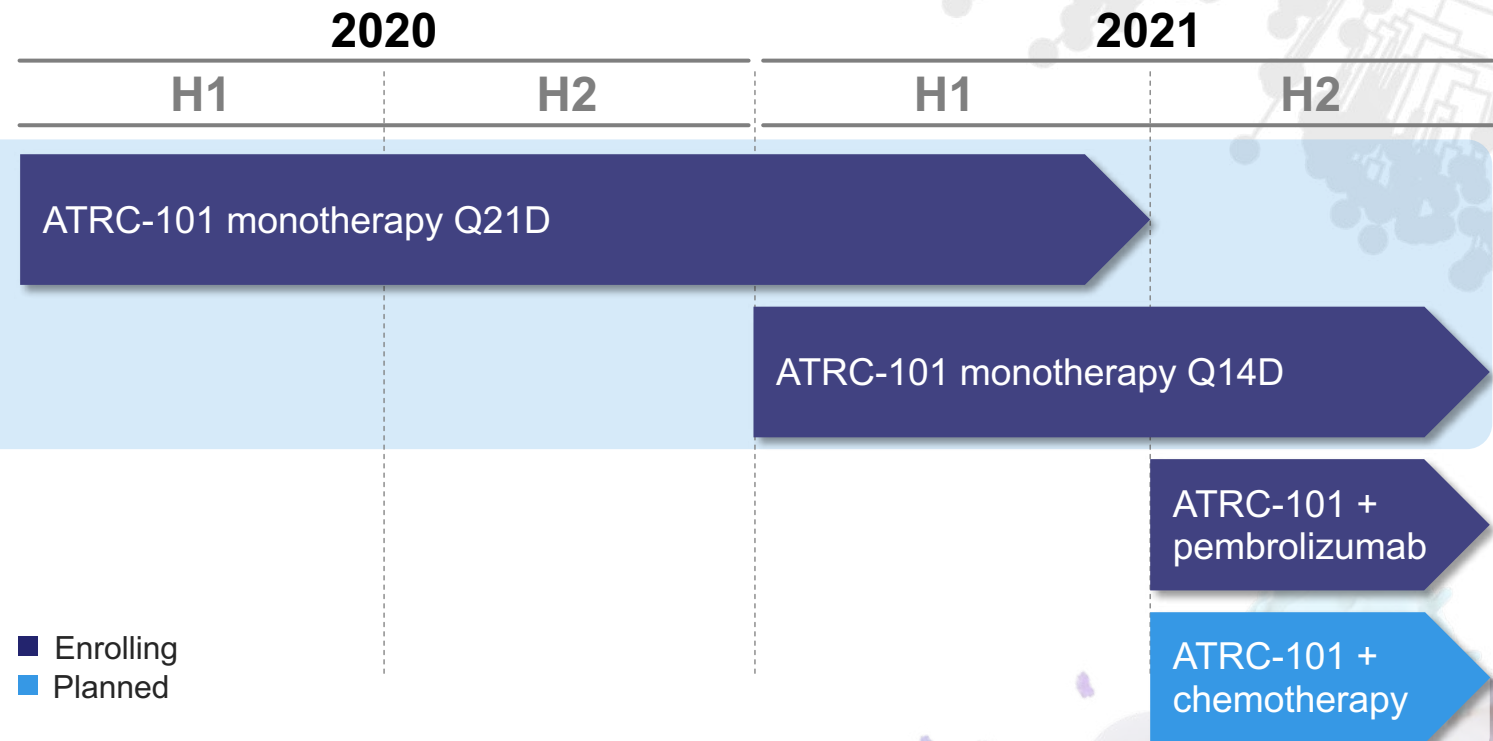
Phase 1b Trial Study Design and Cohort Enrollment Status

OBJECTIVES

- Characterize safety
- Determine MTD or RP2D
- Measure initial clinical activity
- Analyze target expression retrospectively
- Characterize tumor lymphocyte infiltration and other potential biomarkers of activity in tumors, plasma, and PBMCs

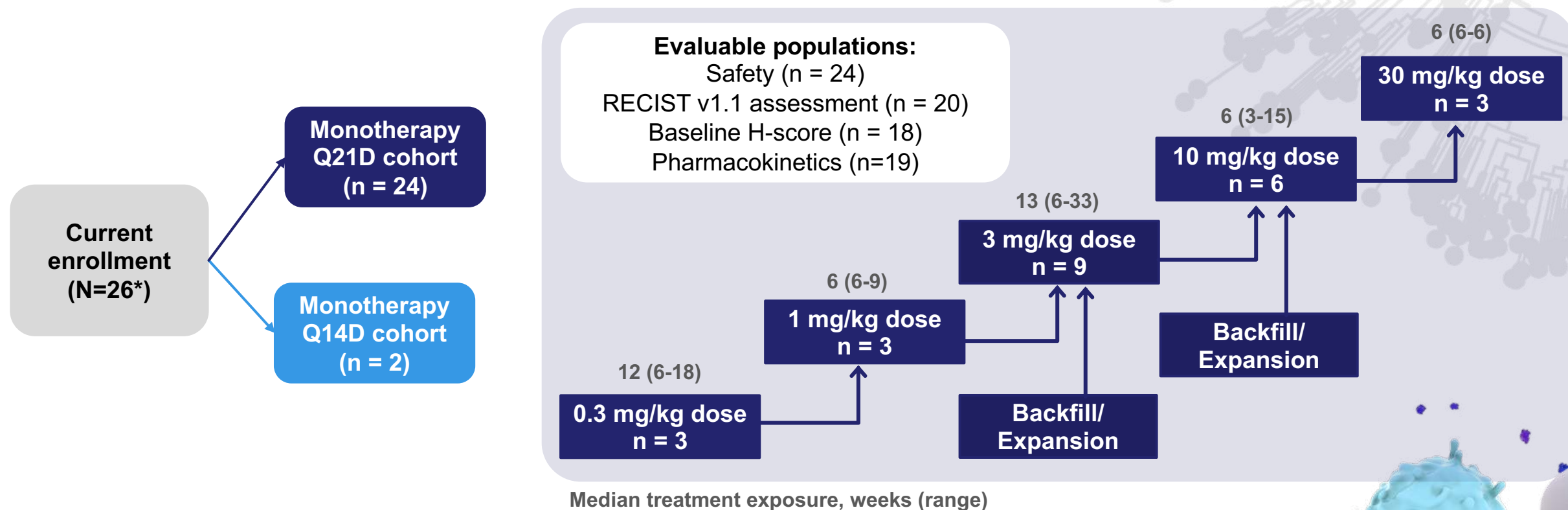
MONOTHERAPY ARM

- Open-label, dose-escalation, adaptive 3+3 design
- IV infusion
- Enrolling participants with advanced solid tumor types that demonstrated >50% reactivity to ATRC-101 in preclinical studies, including:
 - Ovarian cancer
 - NSCLC
 - Colorectal cancer
 - Breast cancer
 - Acral melanoma



IV, intravenous; MTD, maximum tolerated dose; NSCLC, non-small cell lung cancer; PBMC, peripheral blood mononuclear cell; Q14D, every 14 days; Q21D, every 21 days; RP2D, recommended phase 2 dose.

Enrollment, Evaluable Populations, and Treatment Duration as of July 16, 2021, Cutoff



*One more participant in 10 mg/kg Q21D cohort enrolled but not evaluable.
Statistical inferences of the clinical data in this presentation are exploratory in nature.
Q14D, every 14 days; Q21D, every 21 days.

Baseline Characteristics for the Monotherapy Q21D Cohort

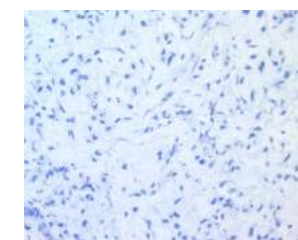
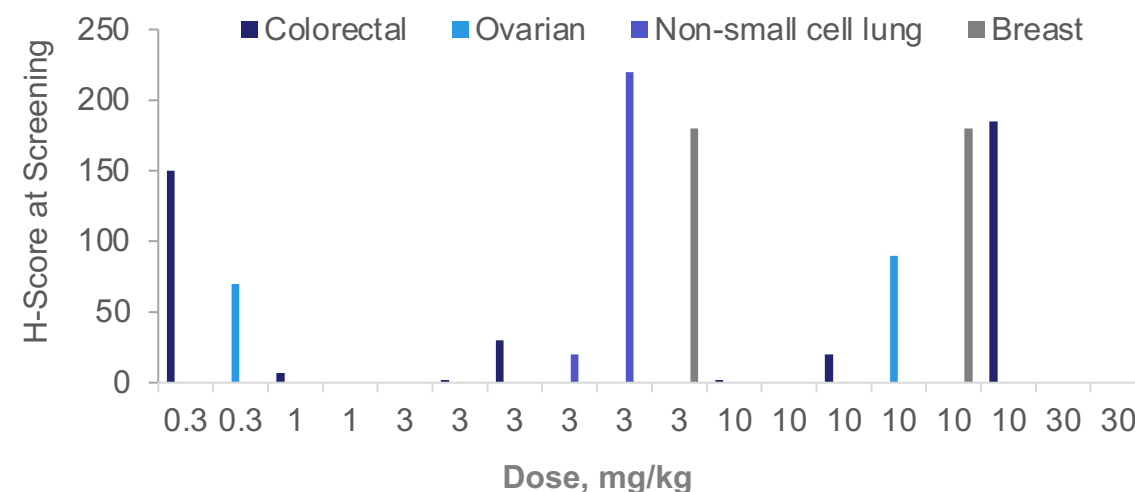
Most Participants Had Received Multiple Prior Lines of Therapy

Baseline characteristics	Overall N = 24
Age, median years (range)	57 (27–75)
Race, n (%)	
White	19 (79.2)
Asian	3 (12.5)
Black or African American	1 (4.2)
Other	1 (4.2)
ECOG PS at baseline, n (%)	
0	6 (25.0)
1	18 (75.0)
Participants with biopsies, n (%)	
Obtained	23 (95.8)
Evaluable	18 (75.0)
Cancer type, n (%)	
Colorectal	13 (54.2)
Ovarian	5 (20.8)
Breast	3 (12.5)
Non-small cell lung	2 (8.3)
Acral melanoma	1 (4.2)
Lines of prior cancer medications, n (%)	
0	1 (4.2)*
1	1 (4.2)
2	2 (8.3)
>2	20 (83.3)
Median (range)	5 (0–11)*
Prior therapy with checkpoint inhibitor, n (%)	12 (50.0)

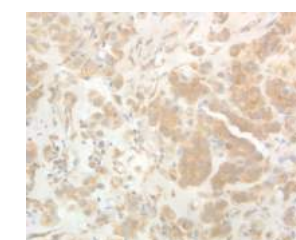
*Value of 0 prior lines corresponds with a missing data point.

Expression of ATRC-101 target was highly variable

ATRC-101 target measured by H-score in evaluable participants (n = 18)



H-score = 0

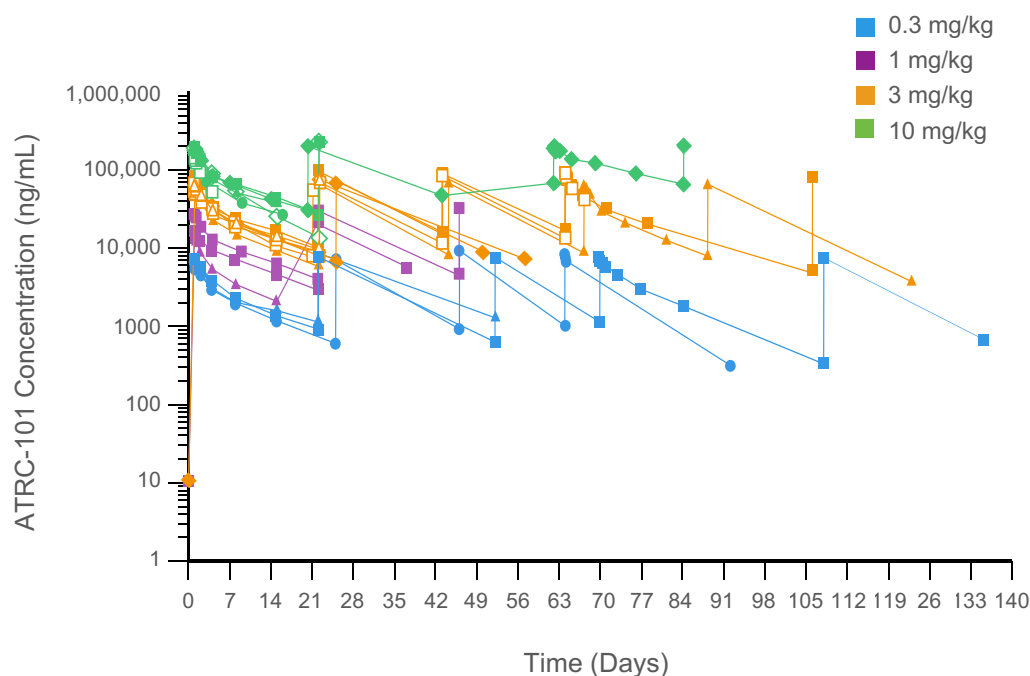


H-score = 180

ATRC-101 Serum Concentrations Appeared to Be Dose Proportional



Average half-life was 10.5 days and was relatively consistent across dose levels



PK assessments	0.3 mg/kg	1 mg/kg	3 mg/kg	10 mg/kg
C_{max} for 1 st dose (ng/mL), mean \pm SD	7030 \pm 418	19,300 \pm 6800	63,800 \pm 10,800	168,000 \pm 22,700
$t_{1/2}$ for 1 st dose (day), mean \pm SD	12.5 \pm 3.78	9.86 \pm 1.49	11.0 \pm 1.21	8.83 \pm 3.61
AUC_{all} (day \cdot ng/mL), mean \pm SD	246,000 \pm 90,500	325,000 \pm 183,000	1,640,000 \pm 1,080,000	1,900,000 \pm 2,580,000
Accumulation ratio*, mean \pm SD	1.15 \pm 0.12	1.33 \pm 0.22	1.17 \pm 0.14	1.22 \pm 0.04

- Maximal concentration and exposure appear to be dose proportional
- Minimal accumulation observed after multiple doses

*Accumulation ratio calculated by dividing C_{max} after last dose by C_{max} after first dose.

AUC_{all} , area under the curve inclusive of all available timepoints; C_{max} , maximum concentration, PK, pharmacokinetics, SD, standard deviation; $t_{1/2}$, half-life.

Adverse Events Summary

No Dose-Limiting Toxicities Observed



Eight participants experienced grade ≥ 3 treatment-emergent adverse events (N = 24)

Treatment-emergent adverse events reported as grade ≥ 3 in ≥ 1 participant, n (%)	Grade 1–2	Grade ≥ 3
Any	22 (91.7)*	8 (33.3)
Sepsis	0	2 (8.3)
Nausea	8 (33.3)	1 (4.2)
Anemia	4 (16.7)	1 (4.2)
Tumor pain	3 (12.5)	1 (4.2)
Blood alkaline phosphatase increased	2 (8.3)	1 (4.2)
Abdominal abscess	0	1 (4.2)
Acute kidney injury	0	1 (4.2)
Acute respiratory failure	0	1 (4.2)
Biliary tract infection	0	1 (4.2)
Hepatic failure	0	1 (4.2)
Hypoxia	0	1 (4.2)
Malignant ascites	0	1 (4.2)
Radiation-associated pain	0	1 (4.2)
Respiratory failure	0	1 (4.2)
Small intestinal obstruction	0	1 (4.2)
Vertebral foraminal stenosis	0	1 (4.2)

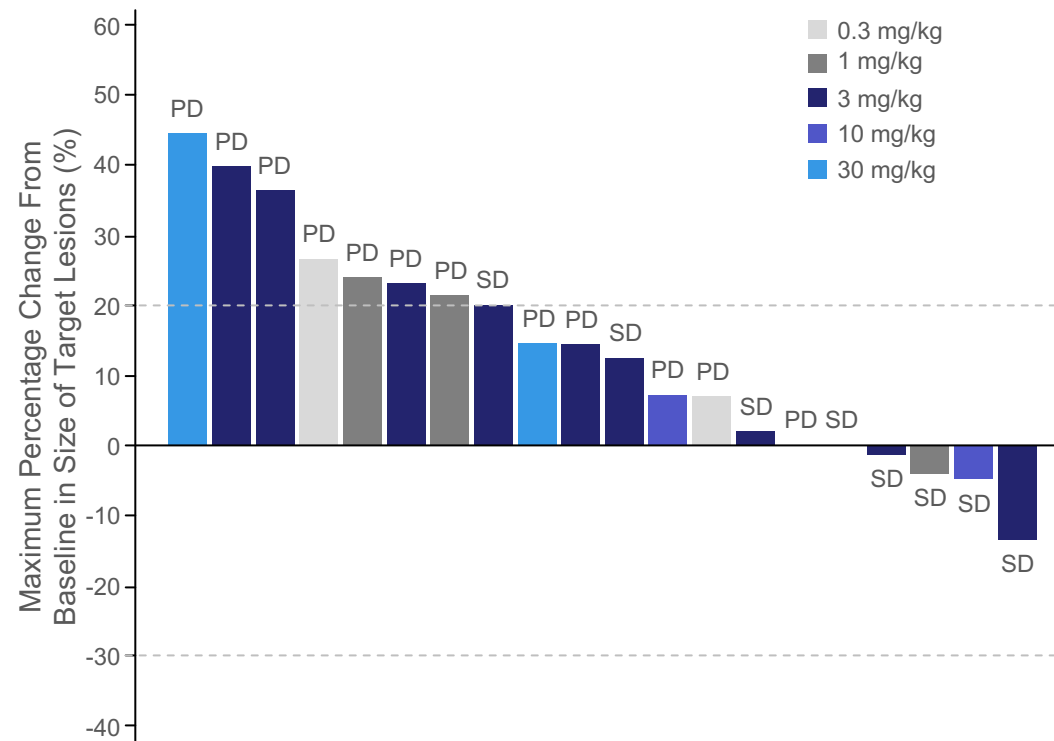
*Includes any participant with an adverse event of any grade.

Treatment-related adverse events reported as grade 1-2 in > 1 participant or grade ≥ 3 in ≥ 1 participant, n (%)	Grade 1–2	Grade ≥ 3
Any	15 (62.5)*	1 (4.2)
Fatigue	5 (20.8)	0
Nausea	4 (16.7)	0
Tumor pain	4 (16.7)	0
Pain	3 (12.5)	0
Blood alkaline phosphatase increased	2 (8.3)	0
Chills	2 (8.3)	0
Decreased appetite	2 (8.3)	0
Dyspnea	2 (8.3)	0
Gastritis	2 (8.3)	0
Pyrexia	2 (8.3)	0
Small intestinal obstruction	0	1 (4.2)

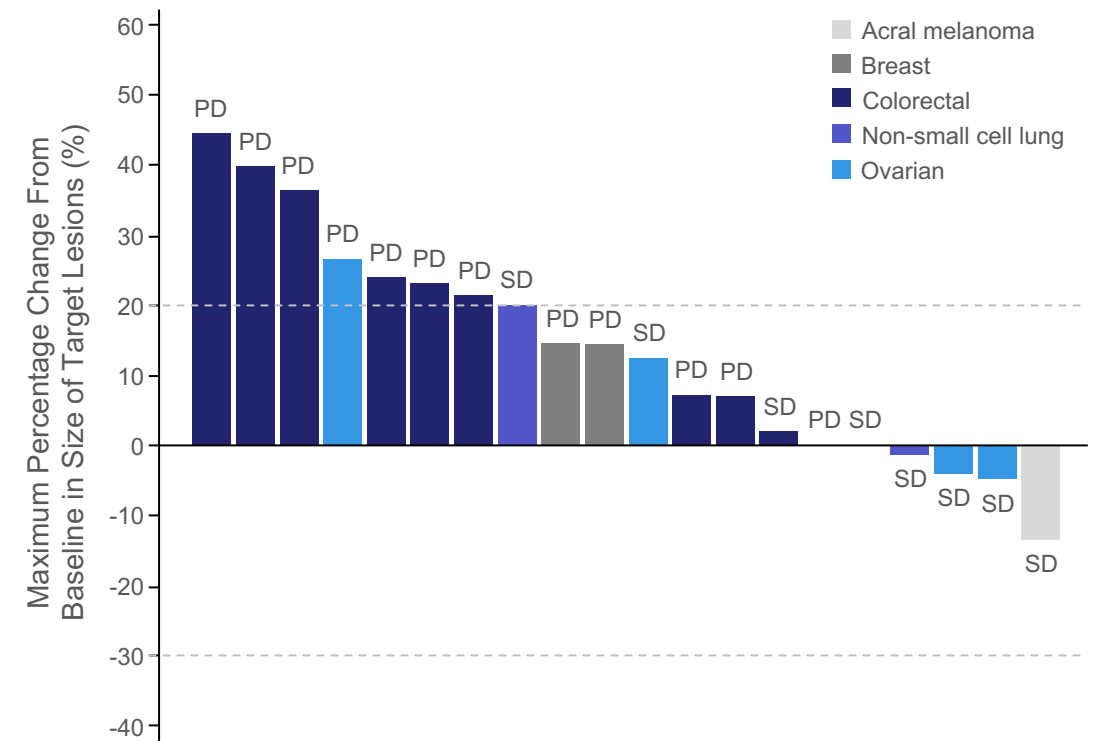
Disease Control and Tumor Reductions

SD Observed in 8 Participants and Tumor Reduction in 4

Tumor reductions and RECIST response by dose



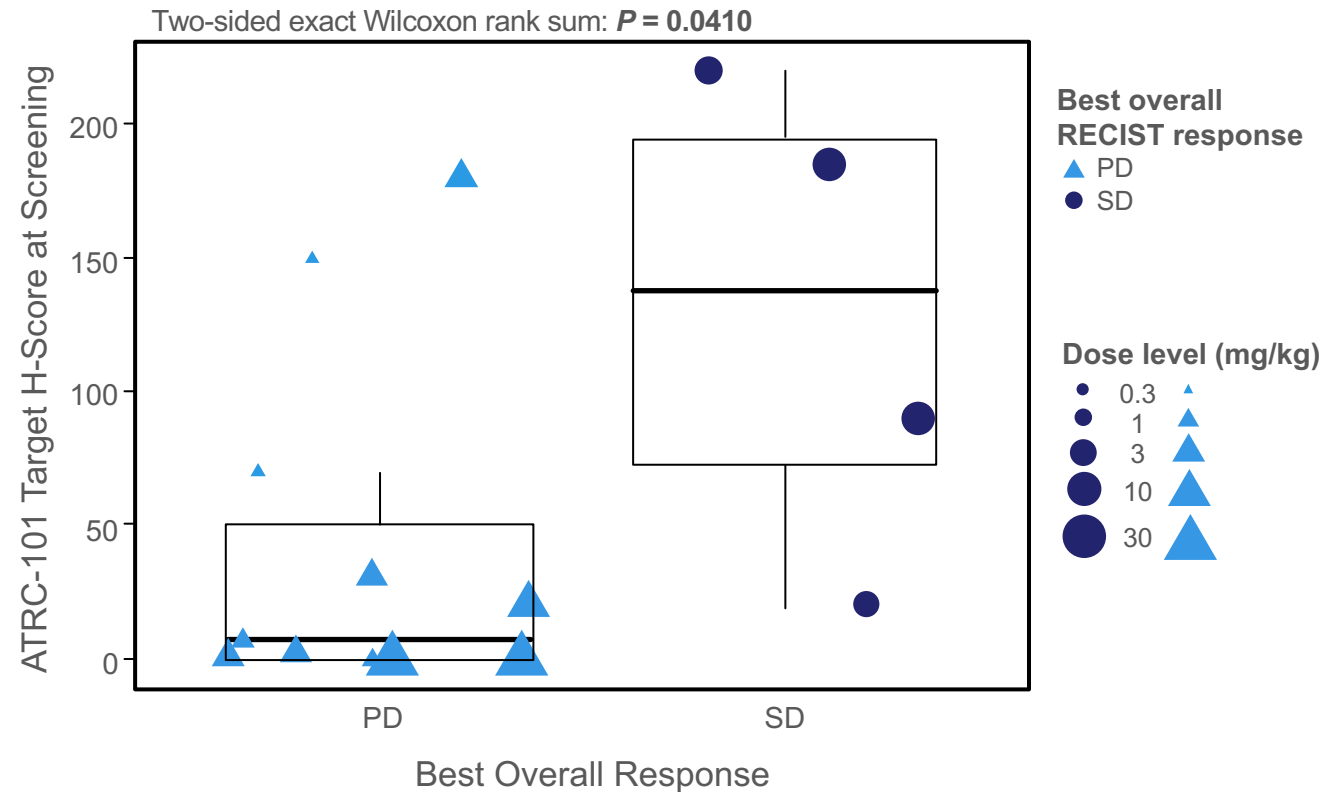
Tumor reductions and RECIST response by tumor type



PD, progressive disease; RECIST, response evaluation criteria in solid tumors; SD, stable disease.

Disease Control Is Associated With Target Expression

Best RECIST response by ATRC-101 target expression

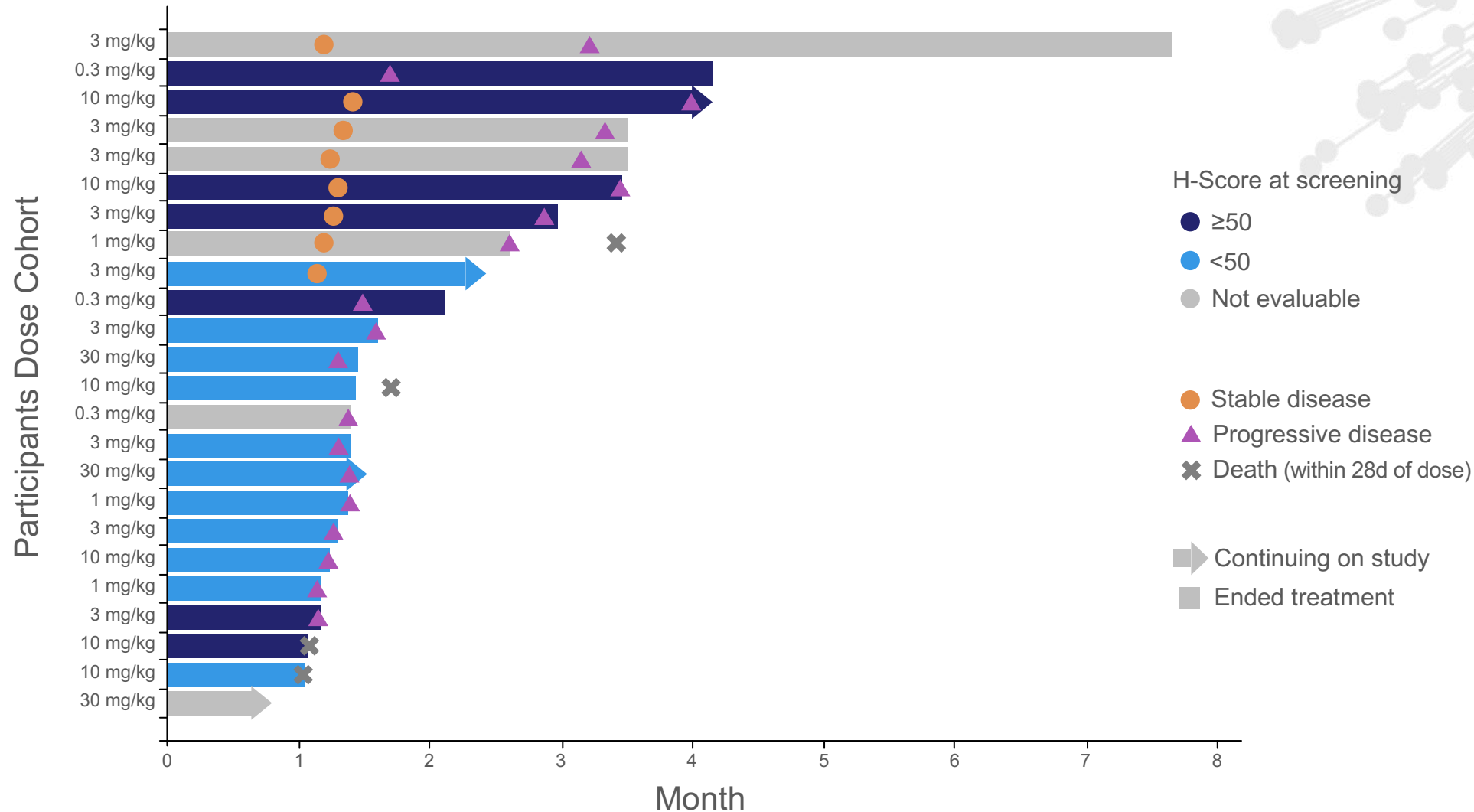


Includes data from 15 RECIST-evaluable participants with H-scores at screening

- **3 of 6 (50%) with H-scores ≥ 50 achieved SD**
- **1 of 9 (11%) with an H-score < 50 achieved SD**
- Statistical significance remains when participants without tumor assessments ($n = 3$) are assumed to have PD

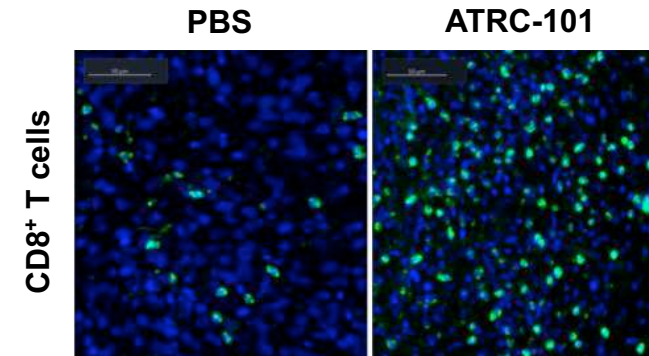
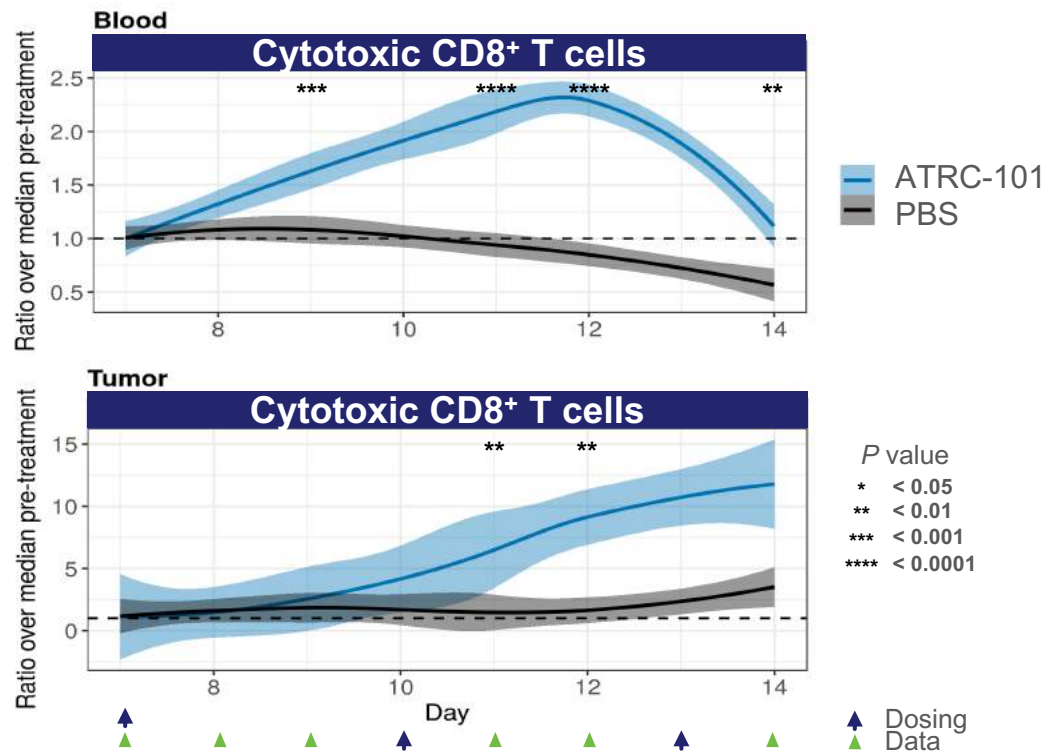
Treatment Duration by Target Expression and Dose

Multiple Participants Treated Beyond Radiographic Progression



ATRC-101 Changes the Immune Cell Profile of the Tumor Microenvironment and Blood in Animal Models

ATRC-101 dosing increases CD8⁺ T cells in EMT6 mouse blood and tumors

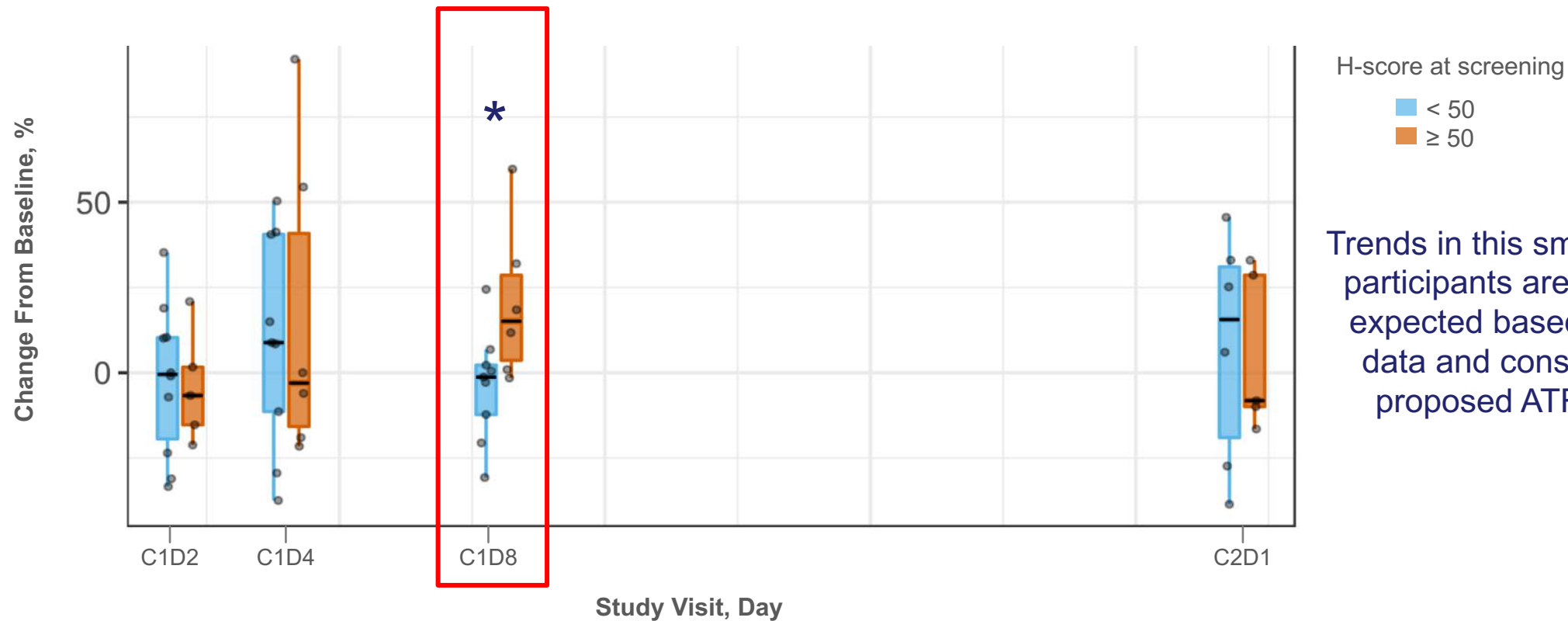


- Cytotoxic CD8⁺ T cells in blood were significantly higher in EMT6 mice treated with ATRC-101 by Day 9
- CD8⁺ T cells appear in the tumor in significant numbers after a brief delay, consistent with their activation in and trafficking from lymph nodes
- Data on other cell types (eg, dendritic cells, NK cells, and macrophages) and cytokines and chemokines were also consistent with the Atreca-hypothesized MOA

CD8⁺ T Cell Expansion in Peripheral Blood After Treatment with ATRC-101 is Associated With Target Expression



Trend toward increased CD8⁺ T cells at treatment day 8



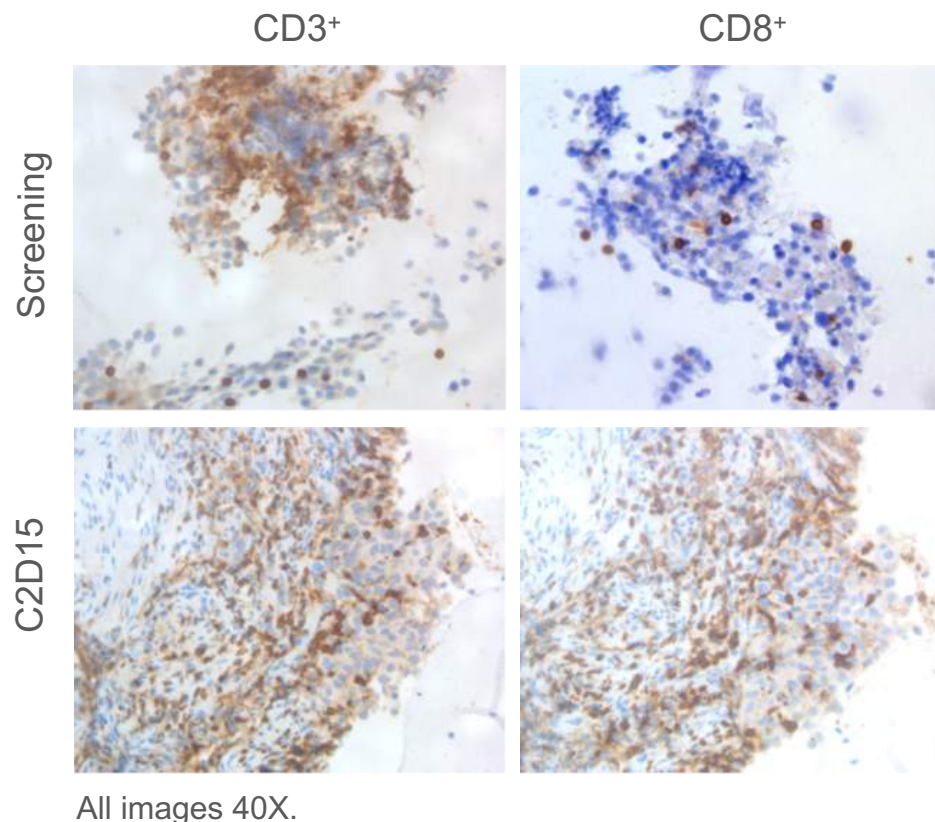
*P < 0.05 by Wilcoxon rank-sum test.
C, cycle; D, day; MOA, mechanism of action.

Influx of Cytotoxic T Cells in a Participant with Ovarian Cancer

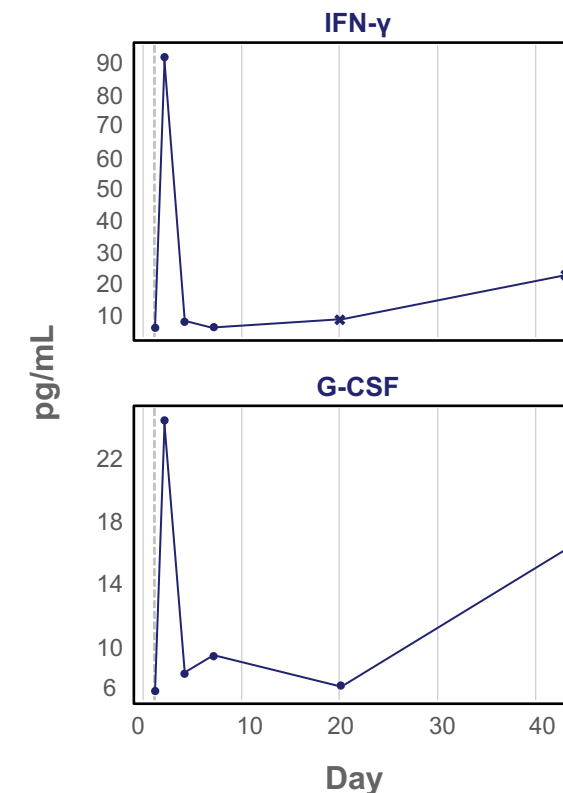
PARTICIPANT INFORMATION

- 69-year-old woman with ovarian cancer
- Lines of prior therapy: 4
- Baseline target H-score: 90
- ATRC-101 exposure: 5 cycles at 10 mg/kg
- Best RECIST response: SD
- Best % tumor reduction: ~4.5%
- Grade 1 and 2 adverse events observed, none \geq Grade 3

Tumor enrichment of CD8⁺ T cells



Dynamics of select cytokines during treatment with ATRC-101

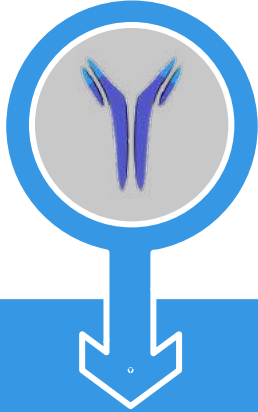


Changes observed with dosing in other cytokines as well



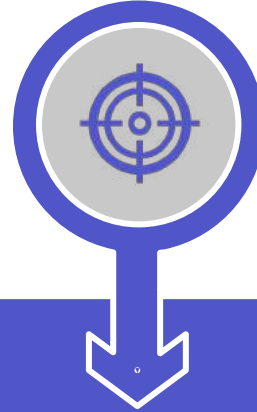
Summary and Future Development Plans

Summary: ATRC-101 exhibits anti-tumor activity consistent with the proposed MOA and was well tolerated at all doses tested



ATRC-101 was well tolerated by participants

- No DLTs observed
- Drug concentration appeared to be dose-proportional



Disease control associated with target expression

- SD in 8 participants and reduction in target-lesion size in 4 of 20 evaluable
- SD in 3 of 6 participants with target expression (screening H-score \geq 50) and response-evaluable tumors



Biomarker data consistent with proposed MOA

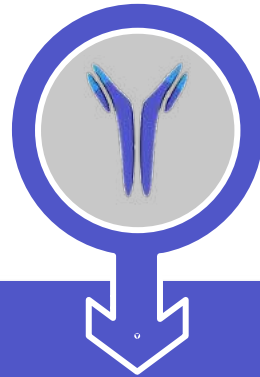
- Expansion of CD8⁺ T cells observed one week after dosing
- CD8⁺ T cell infiltration into tumor observed after dosing

Development Plans and Next Steps



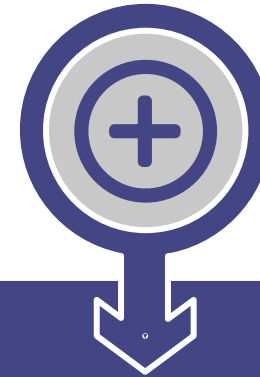
Developing diagnostic to select participants based on target expression

- Expansion of monotherapy cohort will further inform and validate diagnostic



Monotherapy: Treating additional participants at 30 mg/kg

- Continuing to enroll per current protocol
- Expecting to initiate an efficacy cohort (n ≥ 40) at 30 mg/kg
- Anticipating to report additional monotherapy data by mid-2022



Combination with pembrolizumab

- Observed CD8⁺ T cell dynamics further support preclinical rationale
- Enrolling participants with advanced solid tumors, including HNSCC, esophageal SCC, HCC, and urothelial, at a starting dose of 10 mg/kg
- Anticipating to report initial data in mid-2022



Combination with chemotherapy

- Rationale: Increased target expression upon dosing with chemotherapy observed in preclinical models
- Anticipating to report initial data in late-2022



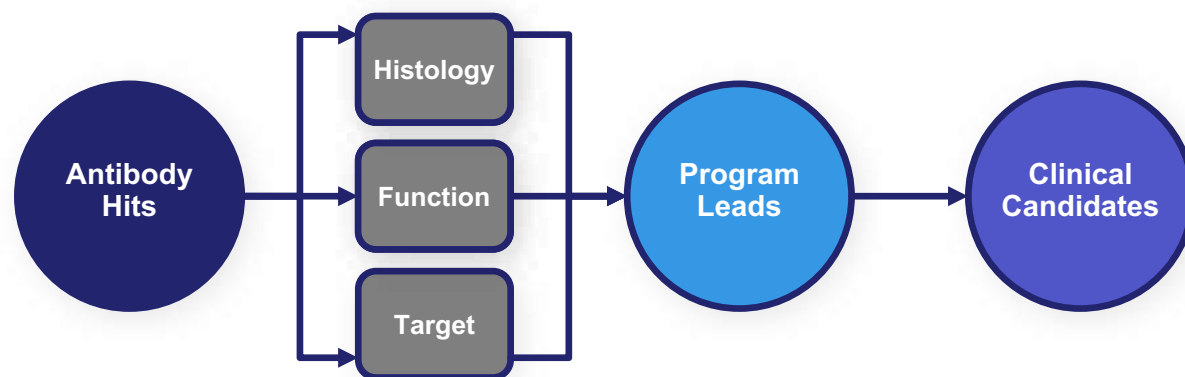
Platform Update

Discovery Platform Continues to Evolve and Deliver

Multiple opportunities for near-term IND candidates with different targets and MOAs



Platform



- Phage display-based Immune Repertoire Capture® (P-IRC™) joins traditional IRC® as a complementary and productive approach to generating “hit” antibodies
- Target identification platform continues to evolve with a greater breadth of approaches in-house, delivering an increasing number of targets (42 confirmed to date)

Pipeline

- EphA2 program continues to progress with Fv optimization delivering improved properties
- Emerging Atreca “ADC Engine” delivering multiple novel antibodies displaying activity *in vivo* in ADC format
- Multiple weaponization formats driving tumor-targeted immune cell activation displaying activity *in vivo* and *in vitro* with Atreca antibodies



Q&A