# AVENTINE-1, a phase 1/2 study of AVZO-1418, an EGFR-HER3 bispecific antibody-drug conjugate (BsADC) for the treatment of patients with locally advanced or metastatic solid tumors - preliminary phase 1 results

Poster #81

FOR ADDITIONAL INFORMATION

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## KEY TAKEAWAYS

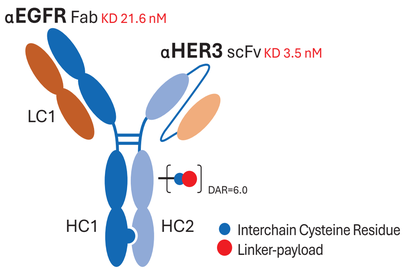
- AVZO-1418 is a potential best-in-class EGFR/HER3 bispecific ADC with pan-tumor potential
- 63% overall response rate in EGFRm NSCLC population; multiple responses ≥24 weeks
  - Majority treated with prior 3rd-generation TKI and platinum-based chemotherapy
- Responses across 6 dose levels and 5 tumor types (EGFRm NSCLC, UC, CRC, SCCHN, NSCLC-WT)
- Doses up to 5.5 mg/kg every 2 weeks (n=48)
  - No DLTs
  - Low incidence of hematologic AEs (Grade 3/4 neutrophil count decreased in 6%)
- Rapid development plan with global expansion to pursue monotherapy and combinations in multiple tumor types is ongoing

## BACKGROUND[1-3]

### Dual Targeting of EGFR/HER3 Is a Promising Therapeutic Strategy

- EGFR and HER3 are commonly co-expressed across solid tumor types, including NSCLC[1]
- EGFR inhibition can increase HER3 expression, suggesting that dual EGFR-HER3 targeting may enhance tumor selectivity and improve therapeutic efficacy[2]
- AVZO-1418 is a novel EGFR/HER3 bispecific ADC designed with higher affinity for HER3 than EGFR to enhance payload delivery to EGFR/HER3-expressing tumors while sparing healthy tissue

### Figure 1. AVZO-1418 EGFR/HER3 Bispecific ADC




The design of AVZO-1418 consists of an asymmetric IgG-like bispecific ADC, featuring a Fab arm targeting EGFR with medium affinity and a scFv arm targeting HER3 with high affinity. The antibody is connected via a KIH Fc domain and conjugated through a tetrapeptide-based cleavable linker with a topoisomerase I inhibitor (P1021) payload at DAR of 6.0.[3]

## STUDY DESIGN[4-5]

N=61 Patients Treated as of 19-October-2026

**POPULATION:**

- Prior lines of chemotherapy ≤3 in escalation
- Prior 3rd-generation TKI therapy required for patients with EGFRm NSCLC
- ECOG 0–1
- Asymptomatic CNS disease allowed

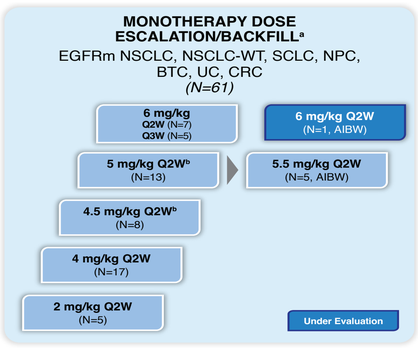
**DESIGN:**

- Bayesian Optimal Interval (BOIN)

**OBJECTIVES:**

- Evaluate safety/tolerability and determine RP2D/MTD

### Figure 2: AVENTINE-1 Phase 1 Study Design




[a]Prior version of protocol allowed for enrollment of SCCHN and TNBC tumor types. [b]Two out of 8 patients at 4.5 mg/kg, 4 out of 13 patients at 5.0 mg/kg Q2W were dosed with AIBW.
Response was assessed by investigator using RECIST v1.1. In addition to cohorts above, Q3W D1D8 dosing schedule and combination therapies will be explored.

## RESULTS

**Data cut-off date of 19-October-2026 is utilized for this presentation with efficacy follow-up through 5-November-2026:**

- Patients with advanced solid tumors treated with AVZO-1418 at 2 mg/kg to 6 mg/kg Q2W and at 6 mg/kg Q3W (N=61)
  - Median follow-up time: 18.0 weeks (min, max: 0.1+, 59.4+)

**Efficacy-evaluable population:**

- Patients with baseline measurable disease treated with AVZO-1418 who had at least 1 evaluable post-baseline scan (N=48), including N=19 with EGFRm NSCLC
  - Study enriched in backfill for EGFRm NSCLC based on early strong signal

N=13 patients not part of efficacy-evaluable population include N=7 ongoing on treatment who have not yet reached post-baseline scan at time of data cut-off date and N=6 patients off treatment prior to an evaluable post-baseline scan (N=1 withdrew consent, N=2 physician decision, N=3 adverse event).

### Table 1. Demographics and Baseline Characteristics

| BASELINE CHARACTERISTIC | | SAFETY POPULATION[a] (N=61) | EFFICACY-EVALUABLE POPULATION[b] | |
|---|---|---|---|---|
| | | | ALL TUMOR TYPES (N=48) | EGFRm NSCLC (N=19) |
| Age (years) | Median (Min, Max) | 65 (27, 77) | 64 (34, 77) | 64 (55, 75) |
| Sex, n (%) | Female | 30 (49) | 22 (46) | 11 (58) |
| Baseline ECOG Score 0 or 1, n (%) | 1 | 49 (80) | 37 (77) | 15 (79) |
| Tumor Type, n (%) | NSCLC-WT | 20 (33) | 14 (29) | 0 |
| | NSCLC-EGFRm | 19 (31) | 19 (40) | 19 (100) |
| | CRC | 6 (10) | 6 (13) | 0 |
| | BTC | 4 (7) | 1 (2) | 0 |
| | SCCHN | 4 (7) | 2 (4) | 0 |
| | UC | 3 (5) | 3 (6) | 0 |
| | Other[c] | 5 (8) | 3 (6) | 0 |
| EGFRm Driver Mutations, n (%) | Exon 19 Deletion | | | 12 (63) |
| | Exon 21 L858R Mutation | | | 6 (32) |
| | Other | | | 1 (5) |
| No. of Prior Lines of Systemic Therapy in Advanced and Metastatic Setting | Median (Min, Max) | 2 (1, 6) | 2 (1, 6) | 2 (1, 4) |
| | 1 | 15 (25) | 13 (27) | 7 (37) |
| | 2 | 25 (41) | 18 (38) | 9 (47) |
| | 3+ | 21 (34) | 17 (35) | 3 (16) |
| Type of Prior Therapy in Advanced and Metastatic Setting, n (%) | Anti PD-(L)1 Immunotherapy | 33 (54) | 21 (44) | 1 (5) |
| | Platinum-Based Chemotherapy | 51 (84) | 39 (81) | 11 (58) |
| | 3rd-gen EGFR TKI | | | 18 (95)[d] |
| | Amivantamab | | | 5 (26) |

- Among EGFRm NSCLC patients (N=19), the median number of prior therapy lines was 2 (range 1-4)
  - All received a 3rd-generation EGFR TKI and 47% received >1 prior TKI

[a]Includes 10 patients treated in China (4 with CRC, 1 with NSCLC-wt, and 5 with EGFRm NSCLC). [b]Patients with baseline measurable disease treated with AVZO-1418 who had ≥1 evaluable post-baseline scan. [c]Other tumor types include TNBC, NPC, OC. [d]One additional patient received 3rd-gen EGFR TKI in adjuvant setting.

### Table 2. Treatment-Emergent Adverse Events

**Generally Well Tolerated With Low Incidence of Hematologic Adverse Events**

| TEAEs OCCURRING IN ≥15% OF PATIENTS BY GRADE | 2 mg/kg - 5.5 mg/kg (N=48) | | TOTAL (N=61) | |
|---|---|---|---|---|
| | GRADE 1-2 N (%) | GRADE 3-4[a] N (%) | GRADE 1-2 N (%) | GRADE 3-4[b] N (%) |
| Nausea | 31 (65) | 0 | 39 (64) | 0 |
| Alopecia | 24 (50) | 0 | 30 (49) | 0 |
| Fatigue | 15 (31) | 3 (6) | 18 (30) | 5 (8) |
| Anemia | 14 (29) | 2 (4) | 18 (30) | 4 (7) |
| Vomiting | 13 (27) | 1 (2) | 19 (31) | 1 (2) |
| Stomatitis | 11 (23) | 2 (4) | 14 (23) | 5 (8) |
| Headache | 13 (27) | 0 | 18 (30) | 0 |
| Diarrhea | 9 (19) | 0 | 15 (25) | 1 (2) |
| Neutrophil count decreased | 6 (13) | 3 (6) | 9 (15) | 7 (11) |
| Constipation | 12 (25) | 0 | 14 (23) | 0 |
| White blood cell count decreased | 6 (13) | 2 (4) | 8 (13) | 6 (10) |
| Decreased appetite | 11 (23) | 0 | 13 (21) | 0 |
| Hypokalemia | 5 (10) | 2 (4) | 8 (13) | 4 (7) |
| Dry eye | 7 (15) | 0 | 11 (18) | 0 |

**Generally well tolerated at doses up to 5.5 mg/kg (N=48)**

- No DLTs
- Three patients (6%) experienced Grade ≥3 events of neutrophil count decreased
- No prophylactic G-CSF required
- Majority of TEAEs/TRAEs did not lead to dose modification

**Treatment-related adverse events, n (%):**

- Grade ≥3: 11 (23%)
- SAEs: 5 (10%)
- Leading to dose reduction: 7 (15%)
- Leading to treatment discontinuation: 1 (2%)
- Grade 2 pneumonitis reported in 1 patient

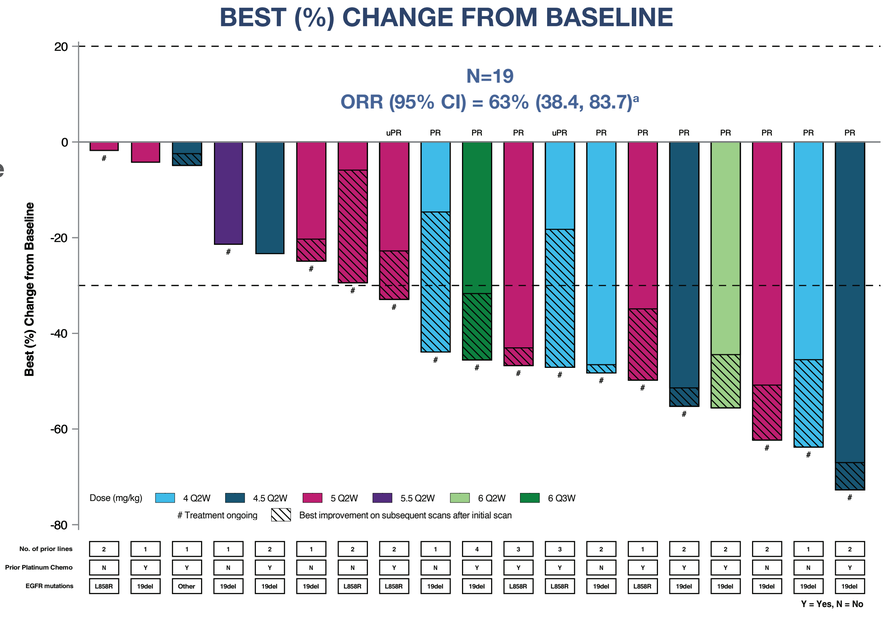
**6 mg/kg actual body weight (N=12) exceeded the MTD[c]**

TEAEs by preferred term and maximum grade. [a]Additional G4+ TEAEs from 2 to 5.5 mg/kg: unrelated: G4 respiratory failure, G5 cardiorespiratory arrest, G4 hypertriglyceridemia, G5 pneumonia; related: G4 platelet count decreased (leading to treatment discontinuation), in 1 patient each. [b]Additional G4+ TEAEs at 6 mg/kg Q2W or Q3W: G4 acute gastroenteritis/pancytopenia (related, leading to treatment discontinuation) and G5 aspiration (unrelated) in same patient, G4 neutrophil count decreased (related, leading to treatment discontinuation). [c]Two DLTs were observed at 6 mg/kg Q2W and Q3W actual body weight dosing cohorts each.

### Figure 3. 63% Response Rate in Pre-Treated EGFRm NSCLC

**Majority Received Prior 3rd-Gen TKI and Platinum-based Chemotherapy**

- Tumor reduction achieved in all 19 patients
- Responses across 5 dose levels




### Table 3. Efficacy Outcomes by RECIST v1.1

| Response | EGFRm NSCLC Patients (N=19) |
|---|---|
| ORR (95% CI) | 63% (38.4, 83.7) |
| cPR, n (%) | 10 (53) |
| uPR[a], n (%) | 2 (11) |
| SD, n (%) | 6 (32) |
| PD, n (%) | 1 (5) |
| DCR (95% CI) | 95% (74.0, 99.9) |

[a]Two patients with uPR on treatment awaiting confirmatory scans

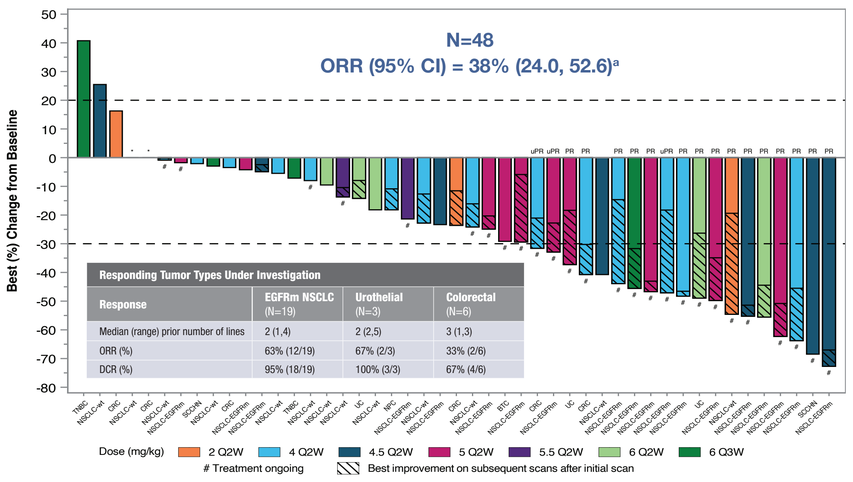
- 15 patients remain on treatment including:
  - 11 responders
  - 4 with tumor reductions (3 with >20% from baseline) awaiting next scans

Efficacy follow-up through 5-November-2026. All patients received 3rd-generation EGFR TKI. [a]10 confirmed PR and 2 unconfirmed PR awaiting confirmatory scans.

### Figure 4. 38% Response Rate Across Multiple Tumor Types

**Responses in 5 tumor types (EGFRm NSCLC, UC, CRC, SCCHN, NSCLC-WT) across 6 dose levels**

- 26 patients remain on treatment including 17 of 18 responders

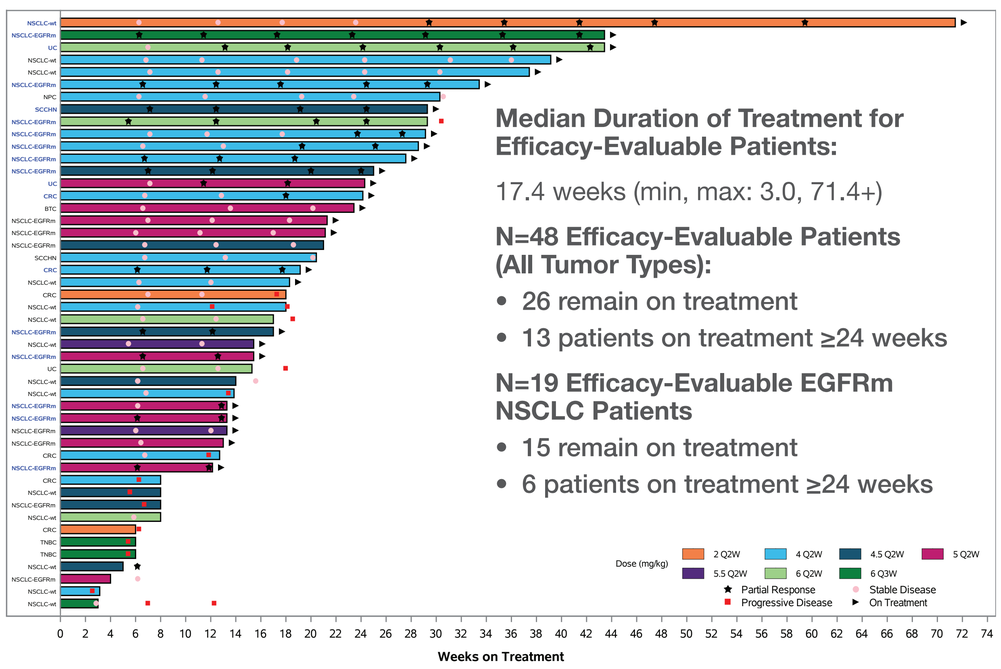



**Responding Tumor Types Under Investigation**

| Response | EGFRm NSCLC (N=19) | Urothelial (N=3) | Colorectal (N=6) |
|---|---|---|---|
| Median (range) prior number of lines | 2 (1,4) | 2 (2,5) | 3 (1,3) |
| ORR (%) | 63% (12/19) | 67% (2/3) | 33% (2/6) |
| DCR (%) | 95% (18/19) | 100% (3/3) | 67% (4/6) |

Efficacy follow-up through 5-November-2026. *Patients with NSCLC-WT and CRC with 0% change from baseline were treated at 4.5 mg/kg and 4 mg/kg Q2W, respectively. [a]15 confirmed PR and 3 unconfirmed PR awaiting confirmatory scans.

### Figure 5: Treatment Exposure: Efficacy-Evaluable Patients N=48




**Median Duration of Treatment for Efficacy-Evaluable Patients:**

17.4 weeks (min, max: 3.0, 71.4+)

**N=48 Efficacy-Evaluable Patients (All Tumor Types):**

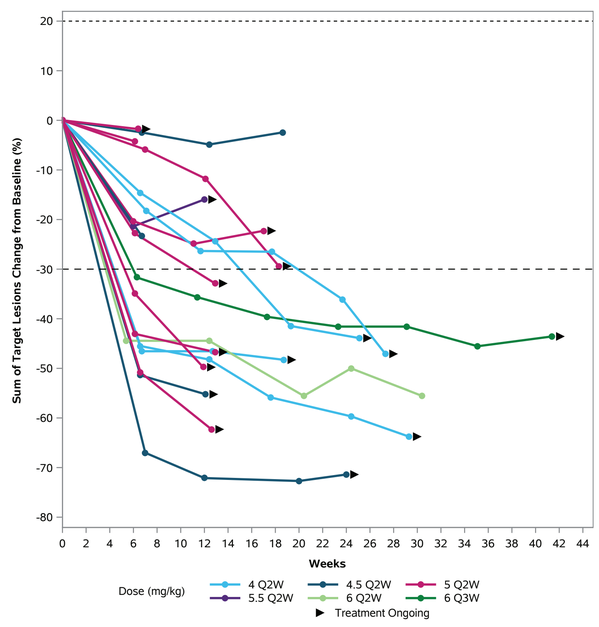
- 26 remain on treatment
- 13 patients on treatment ≥24 weeks

**N=19 Efficacy-Evaluable EGFRm NSCLC Patients**

- 15 remain on treatment
- 6 patients on treatment ≥24 weeks

Efficacy follow-up through 5-November-2026. Tumor type noted in blue text are patients with responses.

### Figure 6. Deepening Tumor Reduction Over Time in EGFRm NSCLC





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## DEFINITIONS

ADC, antibody-drug conjugate; AE, adverse event; AIBW, adjusted ideal body weight; BTC, biliary tract cancer; CI, confidence interval; CNS, central nervous system; cPR, confirmed partial response; CR, complete response; CRC, colorectal cancer; DAR, drug-to-antibody ratio; DCR, disease control rate (CR+PR+uPR+SD); DLT, dose-limiting toxicity; ECOG, Eastern Cooperative Oncology Group; EGFR, epidermal growth factor receptor; Fab, fragment antigen-binding; Fc, fragment crystallizable; G-CSF, granulocyte colony-stimulating factor; HER3, human epidermal growth factor receptor 3; IgG, immunoglobulin G; KIH, knob-into-hole; MTD, maximum tolerated dose; NPC, nasopharyngeal carcinoma; NSCLC, non-small cell lung cancer; OC, ovarian cancer; ORR, objective response rate (CR+PR+uPR); PD, progressive disease; PD-(L)1, programmed cell death (ligand) 1; PR, partial response; Q2W, every 2 weeks; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; RP2D, recommended Phase 2 dose; SAE, serious adverse event; SCCHN, squamous cell carcinoma of the head and neck; scFv, single-chain variable fragment; SCLC, small cell lung cancer; SD, stable disease; TEAE, treatment-emergent adverse event; TKI, tyrosine kinase inhibitor; TNBC, triple-negative breast cancer; TRAE, treatment-related adverse event; UC, urothelial cancer; uPR, unconfirmed partial response; WT, wild type.


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