Phase 1 first-in-human multicenter open-label study of ZW191, a folate receptor α (FRα)–targeting antibody-drug conjugate (ADC), in patients with advanced solid tumors: Part 1 dose-escalation results

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Disclosure information

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Dr. Patricia LoRusso

I have the following relevant financial relationships to disclose:

Participation on a Data Safety Monitoring Board or Advisory Board for AbbVie, Takeda, IQVIA, Glaxo-Smith Kline, Pfizer, QED Therapeutics, AstraZeneca, EMD Serono, Kyowa Kirin Pharmaceutical Development, Kineta, Inc., Zentalis Pharmaceuticals, Molecular Templates, I-Mab, Seagen, Stemline, Compass, Mekanistic, Mersana Therapeutics, Qualigen, NeuroTrials, Actuate Therapeutics, Atreca Development, Cullinan, Amgen, DrenBio, Quanta Therapeutics, Schrödinger, Boehringer Ingelheim, and member of imCORE Alliance-Roche

ZW191 antibody-drug conjugate binds FRα, which is highly expressed in advanced solid tumors

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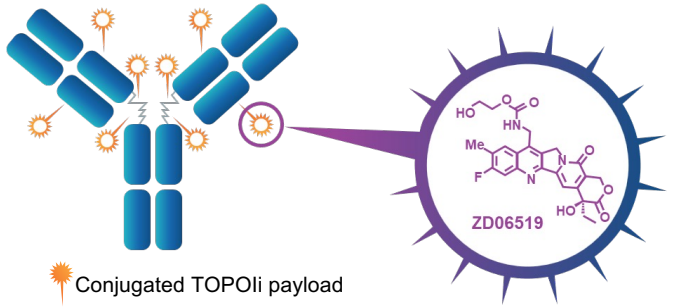
- Folate receptor alpha (FRα) is a clinically validated therapeutic target highly expressed in ovarian cancer (OC), endometrial cancer (EC), and non–small cell lung cancer (NSCLC), with limited expression in normal tissue[1-3]
- ZW191's antibody selectively binds to a distinct epitope of FRα and shows high levels of internalization and tumor penetration in nonclinical models[4]
- ZWI-ZW191-101 (NCT06555744) is an ongoing, phase 1, open-label, 2-part, global study evaluating safety, tolerability, pharmacokinetics, and antitumor activity of ZW191 in participants with advanced solid tumors[5,6]

- FRα-targeting antibody
- Novel TOPOIi payload (ZD06519)
- Protease cleavable linker



ZW191 has a DAR of ~8.[4]

DAR: drug-antibody ratio; EC: endometrial cancer; FRα: folate receptor alpha; NSCLC: non–small cell lung cancer; OC: ovarian cancer; TOPOIi: topoisomerase I inhibitor.

1. Köbel M, et al. *Br J Cancer*. 2014;111(12):2297-2307. **2.** O'Shannessy DJ, et al. *Oncotarget*. 2012;3(4):414-425. **3.** Senol S, et al. *Int J Clin Exp Pathol*. 2015;8(5):5633-5641. **4.** Lawn S, et al. Poster presented at American Association of Cancer Research Annual Meeting; April 5-10, 2024; San Diego, CA. Abstract #1862. **5.** ClinicalTrials.gov. A study of ZW191 in participants with solid tumors. NCT06555744. Updated March 06, 2026. https://clinicaltrials.gov/study/NCT06555744. **6.** LoRusso P, et al. Poster presented at: AACR-NCI-EORTC, 2025; Boston, MA. #LB-A011.

ZWI-ZW191-101 study design

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PART 1 KEY ELIGIBILITY CRITERIA

- ≥18 years old with recurrent:
  - Platinum-resistant OC (epithelial & clear cell)
  - EC (serous or endometrioid)
  - NSCLC (adenocarcinoma)
- Exhausted available treatments
- Retrospective FRα expression
- ECOG PS score of 0 or 1

IN PROGRESS

PART 1: DOSE ESCALATION

OC, EC, and NSCLC

PART 2A: DOSE OPTIMIZATION

OC

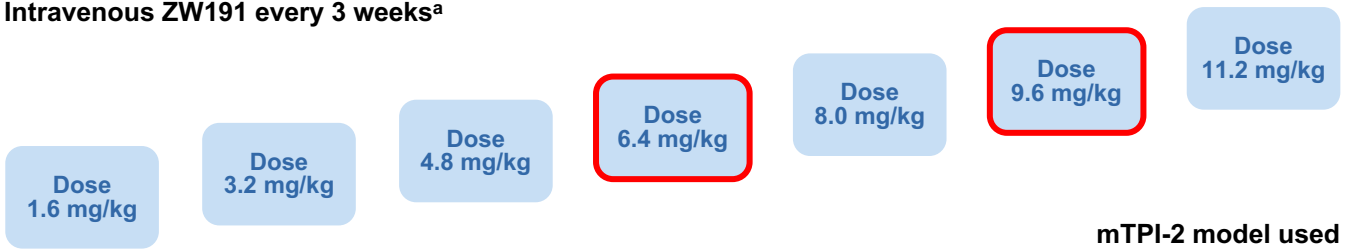
Randomized 1:1:
6.4 mg/kg (n=30)
9.6 mg/kg (n=30)

PART 2B: DOSE EXPANSION

EC n=20

NSCLC n=20

Intravenous ZW191 every 3 weeks[a]



mTPI-2 model used

[a]21-day dose-limiting toxicities evaluation period. CT/MRI testing every 6 weeks (first 4 assessments) or every 9 weeks timed from Cycle 1 Day 1. Safety follow-up was 30 days post–last dose of ZW191; survival follow-up was every 3 months from last dose of ZW191 for up to 2 years.

PRIMARY ENDPOINTS

- ❑ Safety and tolerability
- ❑ MTD
- ❑ RDE

KEY SECONDARY ENDPOINTS

- ❑ Activity
- ❑ PK
- ❑ Immunogenicity

Reported here Part 1 safety and efficacy results (median f/u 7 mo) as of 9 March 2026 data cut

CT: computed tomography; EC: endometrial cancer; ECOG PS: Eastern Cooperative Oncology Group performance status; FRα: folate receptor alpha; f/u: follow-up; mo: months; MRI: magnetic resonance imaging; MTD: maximum tolerated dose; mTPI-2: modified toxicity probability interval version 2 (keyboard design); NSCLC: non–small cell lung cancer; OC: ovarian cancer; PK: pharmacokinetics; RDE: recommended doses for expansion.

ClinicalTrials.gov. A study of ZW191 in participants with solid tumors. NCT06555744. Updated March 06, 2026. https://clinicaltrials.gov/study/NCT06555744.

Demographic and baseline characteristics

Overall population	1.6 mg/kg (n=3)	3.2 mg/kg (n=3)	4.8 mg/kg (n=6)	6.4 mg/kg (n=12)	8.0 mg/kg (n=12)	9.6 mg/kg (n=12)	11.2 mg/kg (n=3)	Total (n=51)
Female, n (%)	3 (100)	3 (100)	6 (100)	11 (92)	11 (92)	12 (100)	3 (100)	**49 (96)**
Median age (range), years	62 (58-68)	64 (59-73)	59 (35-71)	59 (48-79)	59 (52-68)	64 (40-74)	59 (55-65)	**60 (35-79)**
Race, n (%)								
Asian	1 (33)	1 (33)	5 (83)	9 (75)	7 (58)	10 (83)	2 (67)	**35 (69)**
White	2 (67)	1 (33)	1 (17)	3 (25)	4 (33)	1 (8)	1 (33)	**13 (25)**
Black or African American	0	0	0	0	0	1 (8)	0	**1 (2)**
Other/not reported	0	1 (33)	0	0	1 (8)	0	0	**2 (4)**
Baseline ECOG PS, n (%)								
0	1 (33)	1 (33)	3 (50)	6 (50)	5 (42)	8 (67)	1 (33)	**25 (49)**
1	2 (67)	2 (67)	3 (50)	6 (50)	7 (58)	4 (33)	2 (67)	**26 (51)**
Cancer type, n (%)								
Ovarian	2 (67)	2 (67)	5 (83)	5 (42)	8 (67)	10 (83)	3 (100)	**35 (69)**
Endometrial	1 (33)	1 (33)	1 (17)	4 (33)	2 (17)	2 (17)	0	**11 (22)**
Non–small cell lung	0	0	0	3 (25)	2 (17)	0	0	**5 (10)**

ECOG PS: Eastern Cooperative Oncology Group performance status.

Prior systemic treatment

Overall population	1.6 mg/kg (n=3)	3.2 mg/kg (n=3)	4.8 mg/kg (n=6)	6.4 mg/kg (n=12)	8.0 mg/kg (n=12)	9.6 mg/kg (n=12)	11.2 mg/kg (n=3)	Total (n=51)
Median prior lines of therapy (range)	**2 (1-4)**	**3 (2-4)**	**3 (1-7)**	**4 (2-7)**	**3 (2-9)**	**5 (2-6)**	**5 (3-7)**	**3 (1-9)**
PROC	**1.6 mg/kg (n=2)**	**3.2 mg/kg (n=2)**	**4.8 mg/kg (n=5)**	**6.4 mg/kg (n=5)**	**8.0 mg/kg (n=8)**	**9.6 mg/kg (n=10)**	**11.2 mg/kg (n=3)**	**Total (n=35)**
Prior therapy, n (%)								
Platinum	2 (100)	2 (100)	5 (100)	5 (100)	8 (100)	10 (100)	3 (100)	**35 (100)**
Taxane	2 (100)	2 (100)	5 (100)	5 (100)	8 (100)	10 (100)	3 (100)	**35 (100)**
Bevacizumab	2 (100)	2 (100)	3 (60)	4 (80)	8 (100)	7 (70)	3 (100)	**29 (83)**
PARP inhibitor	1 (50)	0	2 (40)	2 (40)	8 (100)	7 (70)	3 (100)	**23 (66)**
Mirvetuximab	0	0	0	0	1 (13)	0	1 (33)	**2 (6)**
EC	**1.6 mg/kg (n=1)**	**3.2 mg/kg (n=1)**	**4.8 mg/kg (n=1)**	**6.4 mg/kg (n=4)**	**8.0 mg/kg (n=2)**	**9.6 mg/kg (n=2)**	**11.2 mg/kg (n=0)**	**Total (n=11)**
Prior therapy, n (%)								
Platinum	1 (100)	1 (100)	1 (100)	4 (100)	2 (100)	2 (100)	0	**11 (100)**
Taxane	1 (100)	1 (100)	1 (100)	4 (100)	2 (100)	2 (100)	0	**11 (100)**
Checkpoint inhibitors	1 (100)	1 (100)	1 (100)	4 (100)	2 (100)	1 (50)	0	**10 (91)**

EC: endometrial cancer; PARP: poly-ADP ribose polymerase; PROC: platinum-resistant ovarian cancer.

Safety and tolerability of ZW191: TEAEs

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ZW191 TEAE, n (%)	1.6 mg/kg (n=3)	3.2 mg/kg (n=3)	4.8 mg/kg (n=6)	6.4 mg/kg (n=12)	8.0 mg/kg (n=12)	9.6 mg/kg (n=12)	11.2 mg/kg (n=3)	Total (n=51)
Any TEAE	2 (67)	3 (100)	6 (100)	12 (100)	12 (100)	12 (100)	3 (100)	**50 (98)**
Grade ≥3 TEAE	2 (67)	2 (67)	4 (67)	4 (33)	6 (50)	8 (67)	2 (67)	**28 (55)**
Serious TEAEs	2 (67)	1 (33)	1 (17)	3 (25)	4 (33)	6 (50)	1 (33)	**18 (35)**
TEAE leading to dose delays	0	1 (33)	2 (33)	6 (50)	2 (17)	7 (58)	2 (67)	**20 (39)**
TEAE leading to dose reduction	0	0	0	2 (17)	4 (33)	3 (25)	0	**9 (18)**
Discontinuations due to TEAEs	0	2 (67)	0	2 (17)	2 (17)	2 (17)	2 (67)	**10 (20)**
Deaths due to TEAEs	0	0	0	0	0	0	1 (33)	**1 (2)[a]**

2 DLTs: 6.4 mg/kg (Gr 3 anemia); 11.2 mg/kg (Gr 3 diarrhea, Gr 4 thrombocytopenia, and Gr 4 sepsis)

[a]Death due to small intestinal perforation (unrelated).

DLT: dose-limiting toxicity; Gr: grade; TEAE: treatment-emergent adverse event.

Safety and tolerability of ZW191: TEAEs

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ZW191 TEAE, n (%)	1.6 mg/kg (n=3)	3.2 mg/kg (n=3)	4.8 mg/kg (n=6)	6.4 mg/kg (n=12)	8.0 mg/kg (n=12)	9.6 mg/kg (n=12)	11.2 mg/kg (n=3)	Total (n=51)
Any TEAE	2 (67)	3 (100)	6 (100)	12 (100)	12 (100)	12 (100)	3 (100)	50 (98)
Grade ≥3 TEAE	2 (67)	2 (67)	4 (67)	4 (33)	6 (50)	8 (67)	2 (67)	28 (55)
Serious TEAEs	2 (67)	1 (33)	1 (17)	3 (25)	4 (33)	6 (50)	1 (33)	18 (35)
TEAE leading to dose delays	0	1 (33)	2 (33)	6 (50)	2 (17)	7 (58)	2 (67)	20 (39)
TEAE leading to dose reduction	0	0	0	2 (17)	4 (33)	3 (25)	0	9 (18)
Discontinuations due to TEAEs	0	2 (67)	0	2 (17)	2 (17)	2 (17)	2 (67)	10 (20)
Deaths due to TEAEs	0	0	0	0	0	0	1 (33)	1 (2)[a]

2 DLTs: 6.4 mg/kg (Gr 3 anemia); 11.2 mg/kg (Gr 3 diarrhea, Gr 4 thrombocytopenia, and Gr 4 sepsis)

[a]Death due to small intestinal perforation (unrelated).

DLT: dose-limiting toxicity; Gr: grade; TEAE: treatment-emergent adverse event.

TEAEs of any grade occurring in ≥20% of participants

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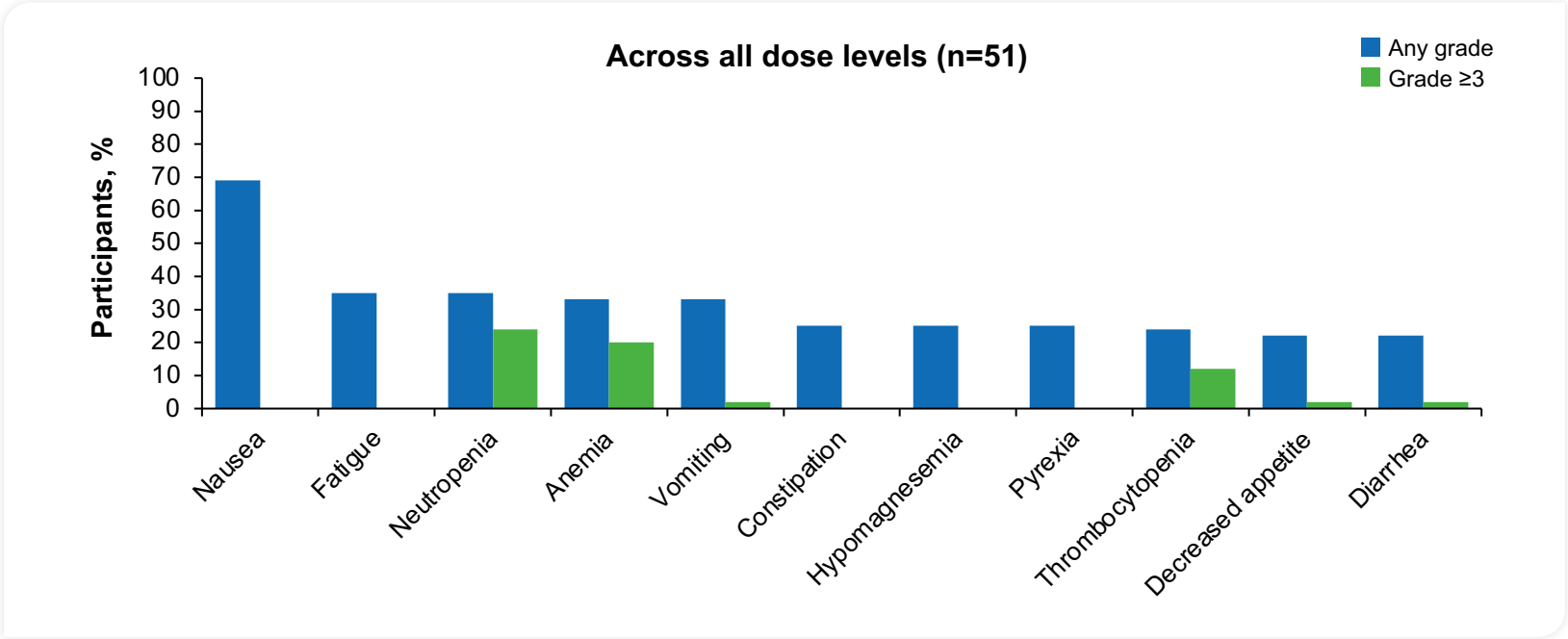
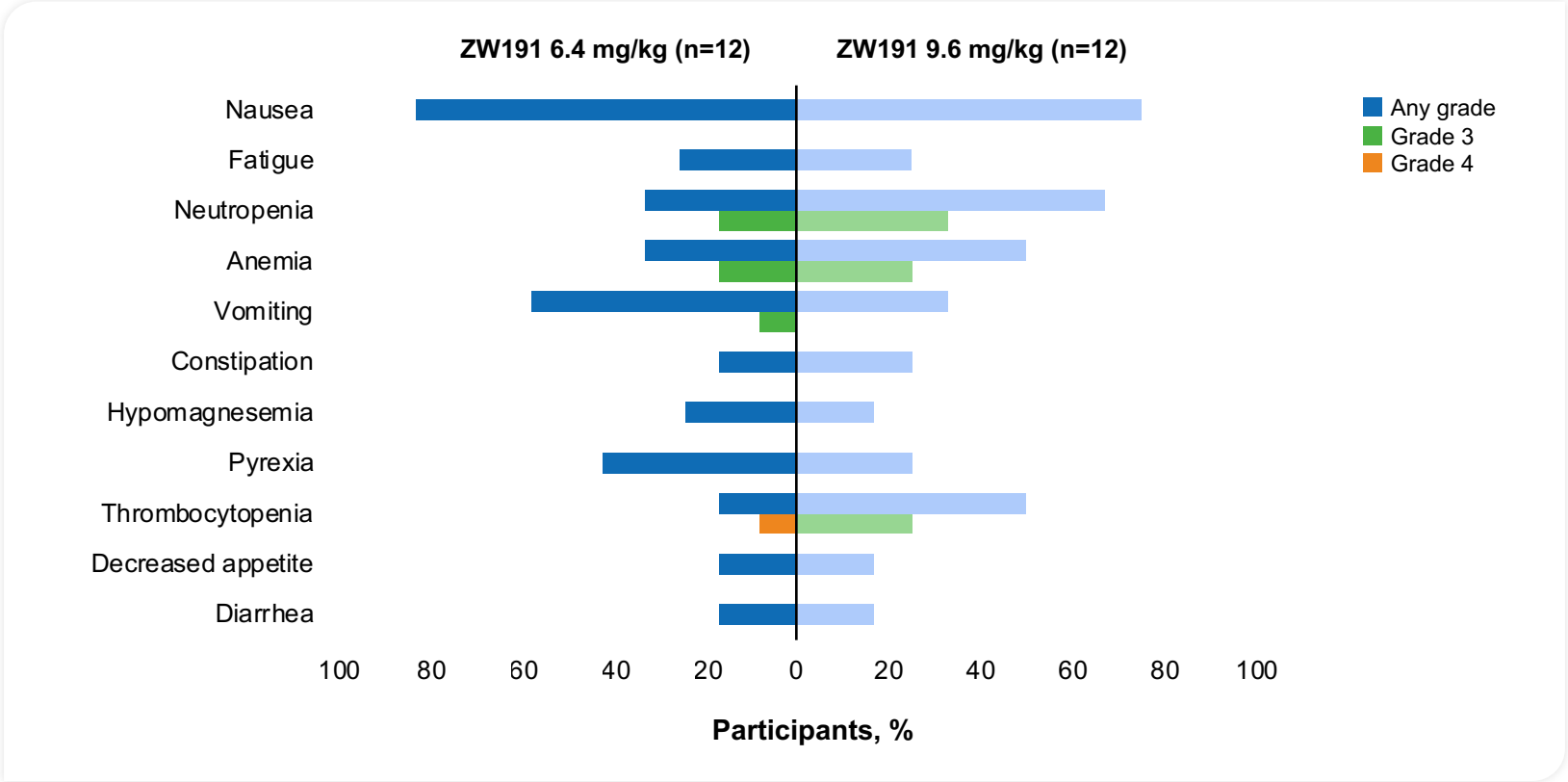


Most common Gr ≥3 TEAEs: neutropenia (n=12), anemia (n=10), and thrombocytopenia (n=6)

Gr: grade; TEAE: treatment-emergent adverse event.

TEAEs of any grade occurring in ≥20% of participants (cont.)



TEAE: treatment-emergent adverse event.

Antitumor activity of ZW191

Ovarian cancer (n=34)

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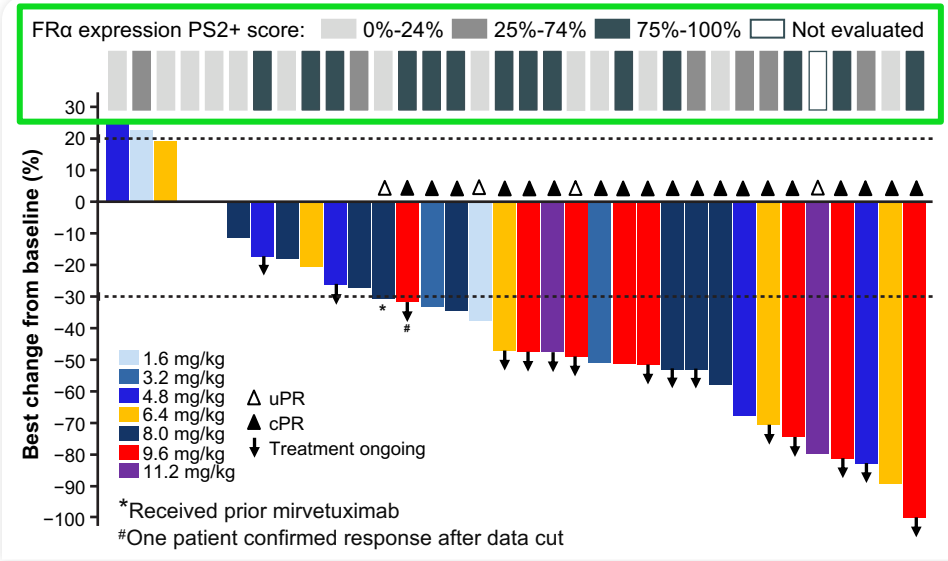

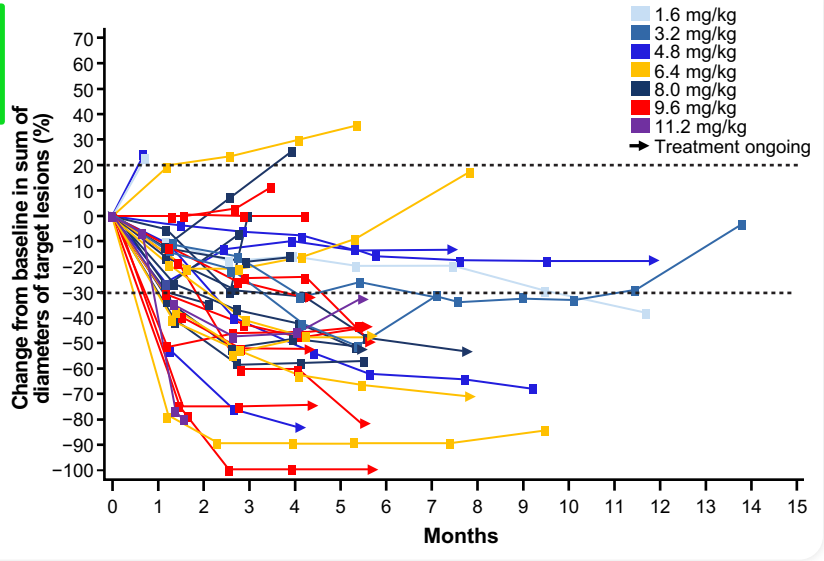

OC	6.4-9.6 mg/kg (n=23)	Total across all dose levels (n=34)
cORR#, % (95% CI)	61% (38.5, 80.3)	56% (37.9, 72.8)
DCR, % (95% CI)	100% (85.2, 100.0)	94% (80.3, 99.3)

As of data cut-off, 34 ovarian cancer participants were response-evaluable by having at least 1 post-baseline scan and were included in the efficacy analysis. Response based on RECIST v1.1 (response and progression defined as –30% and +20% change from baseline, respectively). FRα expression was assessed by immunohistochemistry using archival or newly collected formalin-fixed, paraffin-embedded biopsies with the VENTANA® FOLR1 (FOLR1-2.1) assay. The PS2+ score was defined as the percentage of tumor cells with 2+ and 3+ staining intensity and categorized as low/negative 0%-24%, intermediate 25%-74%, and high 75%-100%. Disease control rate is defined as a best response of complete response, partial response, non-complete response/non-progressive disease, or stable disease per RECIST v1.1. #One patient confirmed response after data cut

CI: confidence interval; cORR: confirmed objective response rate; cPR: confirmed partial response; DCR: disease control response; FRα: folate receptor alpha; OC: ovarian cancer; RECIST v1.1: Response Evaluation Criteria in Solid Tumors, version 1.1; uPR: unconfirmed partial response.

Antitumor activity of ZW191

Endometrial cancer (n=10)

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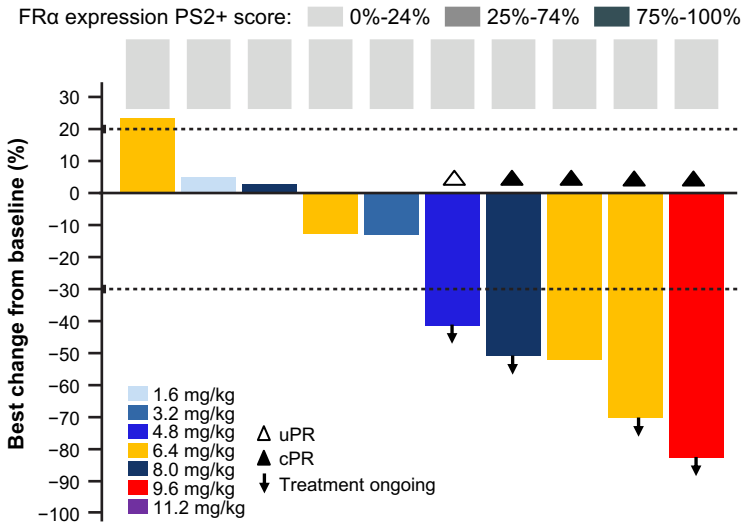

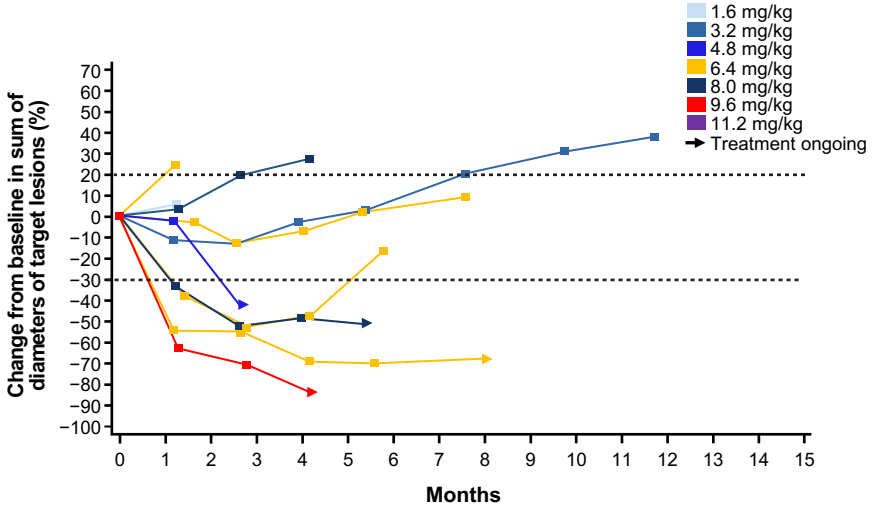

EC	6.4-9.6 mg/kg (n=7)	Total across all dose levels (n=10)
cORR, % (95% CI)	57% (18.4, 90.1)	40% (12.2, 73.8)
DCR, % (95% CI)	86% (42.1, 99.6)	80% (44.4, 97.5)

As of data cut-off, 10 endometrial cancer participants were response-evaluable by having at least 1 post-baseline scan and were included in the efficacy analysis. Response based on RECIST v1.1 (response and progression defined as –30% and +20% change from baseline, respectively). FRα expression was assessed by immunohistochemistry using archival or newly collected formalin-fixed, paraffin-embedded biopsies with the VENTANA® FOLR1 (FOLR1-2.1) assay. The PS2+ score was defined as the percentage of tumor cells with 2+ and 3+ staining intensity and categorized as low/negative 0%-24%, intermediate 25%-74%, and high 75%-100%. Disease control rate is defined as a best response of complete response, partial response, non-complete response/non-progressive disease, or stable disease per RECIST v1.1.

CI: confidence interval; cORR: confirmed objective response rate; cPR: confirmed partial response; DCR: disease control response; EC: endometrial cancer; FRα: folate receptor alpha; RECIST v1.1: Response Evaluation Criteria in Solid Tumors, version 1.1; uPR: unconfirmed partial response.

Duration of treatment and overall response of ZW191

Ovarian and endometrial cancer (n=46)

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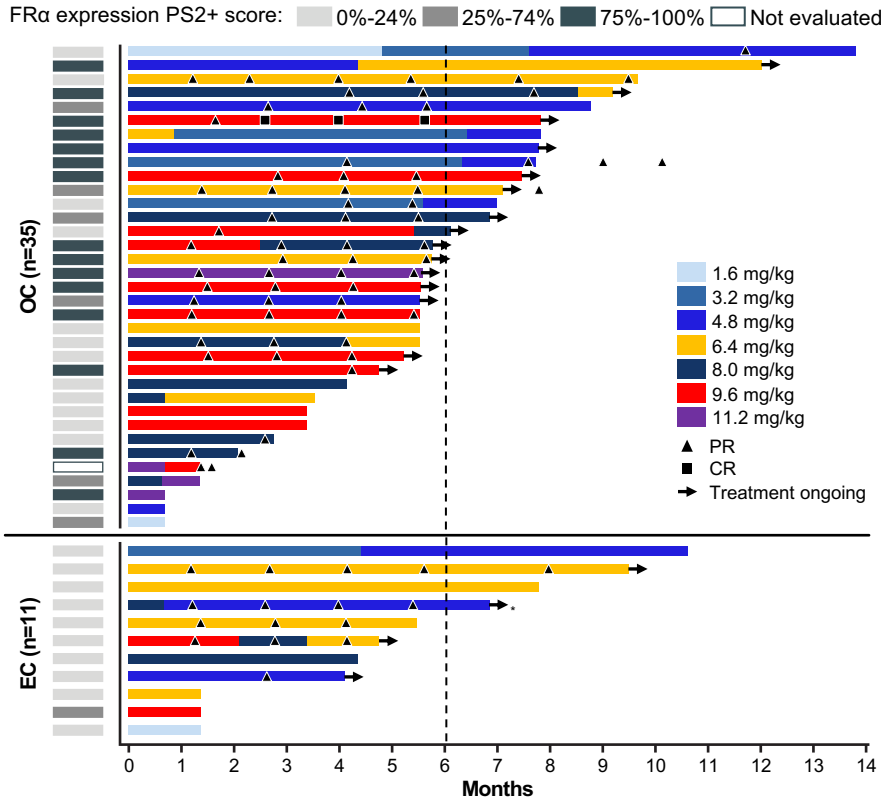

*Dose de-escalation from 8.0 mg/kg to 4.0 mg/kg.

OC and EC	6.4-9.6 mg/kg	Total across dose levels
mTTR, mo (range)	1.4 (1.2-4.2)	1.4 (1.2-4.2)
mDOR, mo (95% CI)	NR (4.2, NR)	NR (4.2, NR)
mPFS, mo (95% CI)	7.6 (4.2, NR)	7.6 (5.5, NR)

FRα expression was assessed by immunohistochemistry using archival or newly collected formalin-fixed, paraffin-embedded biopsies with the VENTANA® FOLR1 (FOLR1-2.1) assay. The PS2+ score was defined as the percentage of tumor cells with 2+ and 3+ staining intensity and categorized as low/negative 0%-24%, intermediate 25%-74%, and high 75%-100%.

CI: confidence interval; CR: complete response; EC: endometrial cancer; FRα: folate receptor alpha; mDOR: median duration of response; mo: months; mPFS: median progression-free survival; mTTR: median time to response; NR: not reached; OC: ovarian cancer; PR: partial response.

Pharmacokinetics of ZW191

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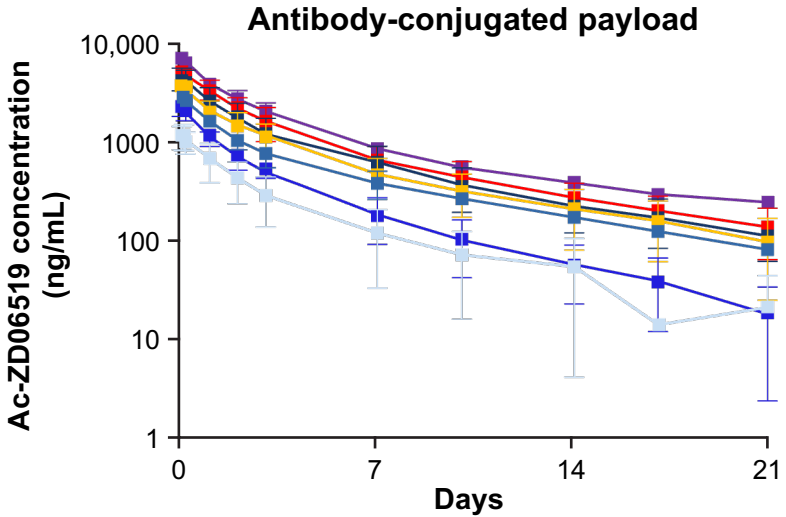

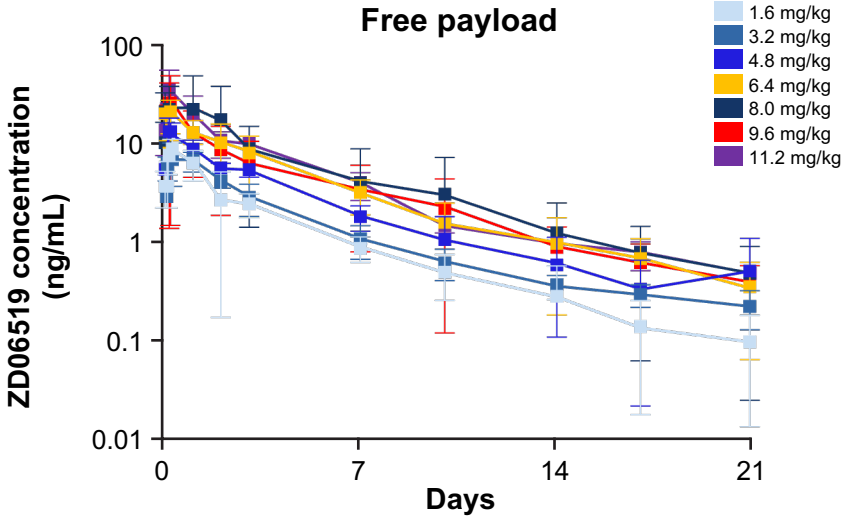

- PK analysis (n=47): exposure generally increased in a dose-proportional manner for all 3 analytes of ZW191; PK exposure at Cycle 4 was slightly higher than at Cycle 1
- Following first IV infusion, concentrations declined with a mean terminal half-life of approximately 6.5 days for TAb and 5.9 days for ac-ZD06519

ac-ZD06519: antibody-conjugated payload; IV: intravenous; PK: pharmacokinetic; TAb: total antibody; ZD06519: free payload.

Conclusions

ZW191 demonstrated a broad therapeutic window and demonstrated competitive efficacy in both high and low FRα-expressing tumors, justifying further investigation, as monotherapy and/or in combination

- ZW191 was well tolerated and safely administered up to 11.2 mg/kg
- 6.4-9.6 mg/kg demonstrated compelling efficacy regardless of FRα expression in heavily pretreated patients
  - cORR in platinum-resistant ovarian cancer: 61%
  - cORR in endometrial cancer: 57%
  - mDOR not reached
  - mPFS (95% CI) in ovarian and endometrial cancer: 7.6 mo (4.2, NR)

Part 2a dose optimization is ongoing at dose levels 6.4 mg/kg and 9.6 mg/kg

CI: confidence interval; cORR: confirmed objective response rate; FRα: folate receptor alpha; mDOR: median duration of response; mo: months; mPFS: median progression-free survival; NR: not reached.

Acknowledgments & Support

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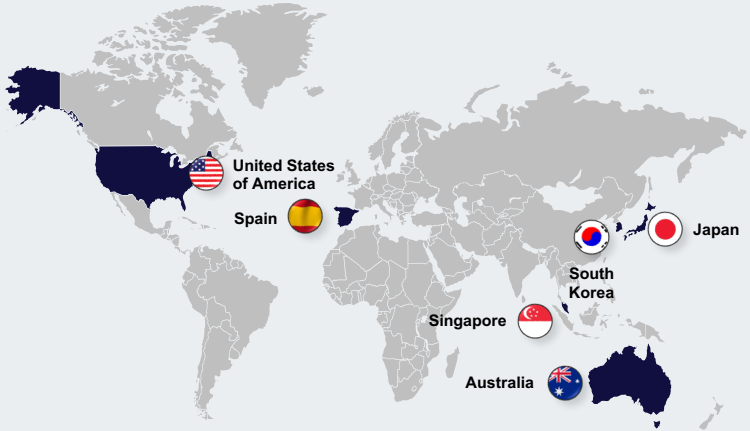
ZWI-ZW191-101 is ongoing at 27 sites across multiple regions, including North America, Europe, and the Asia-Pacific



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