



Initial Results from the Phase 1 Trial of ZW191, an Antibody-Drug Conjugate Targeting Folate Receptor- α

ENA 2025 Highlights

October 23, 2025

Nasdaq: ZYME | zymeworks.com



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The above assumptions, risks and uncertainties are not exhaustive. Forward-looking statements are made as of the date hereof and, except as may be required by law, Zymeworks undertakes no obligation to update, republish, or revise any forward-looking statements to reflect new information, future events or circumstances, or to reflect the occurrences of unanticipated events.

Agenda

1 ZW191: Design Considerations



Stuart Barnscher
Senior Director, ADC Development
Zymeworks

2 ZW191: Highlights from ENA 2025



Dr. Patricia LoRusso DO, PhD (hc)
Professor of Medicine
Yale Cancer Center

3 ZW191: Next Steps



Sabeen Mekan, MD
Senior Vice President, Clinical Development
Zymeworks

4 Q&A

ZW191: Design Considerations



Stuart Barnscher

Senior Director, ADC Development
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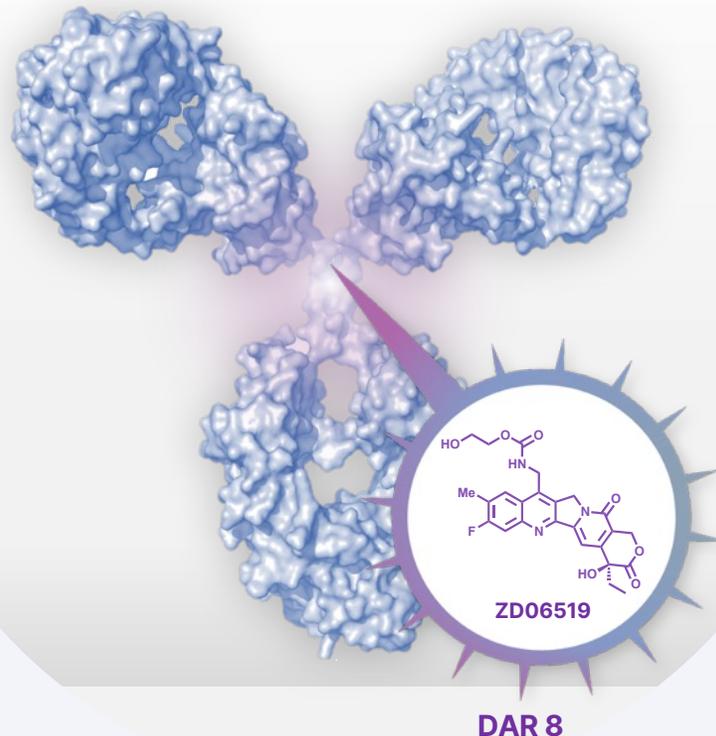
ZW191: an FR α -targeting ADC Differentiated by Design

Antibody Selected for Optimal ADC Properties

- Novel IgG1 antibody¹
- Distinct epitope¹
- High levels of **internalization**²
- Superior **payload delivery**²
- Enhanced **tumor penetration**²

Enables targeting of low FR α tumors with enhanced anti-tumor activity

ZW191



Linker-Payload Selected to Balance Efficacy and Tolerability

- Novel topoisomerase-1 inhibitor³
- Peptide cleavable linker³
- **Moderate potency** (1-10 nM)³
- Strong **bystander activity**^{1,2,3}
- **Validated Ab-linker stability**^{2,4}

Supports tolerability, high protein dosing, and targeting of low/heterogeneous FR α tumors

ZW191: Highlights from ENA 2025



Dr. Patricia LoRusso DO, PhD (hc)

Professor of Medicine
Yale Cancer Center

ZWI-ZW191-101 Study Design

Part 1: Dose Escalation^a

OC, EC, and NSCLC

Part 2a: Dose Optimization^b

OC

Part 2b: Dose Expansion^c

EC and NSCLC

KEY ELIGIBILITY CRITERIA

- Aged ≥18 years with confirmed diagnosis of recurrent cancers:
 - Platinum-resistant OC (epithelial)
 - EC (serous or endometrioid)
 - NSCLC (adenocarcinoma)
- Exhausted available systemic treatment options^b
- FR α expression evaluated retrospectively
- ECOG PS score of 0 or 1



Ongoing Dose Escalation ZW191 IV Q3W

Dose Level 1
1.6 mg/kg
Q3W

Dose Level 2
Dose 3.2
mg/kg
Q3W

Dose Level 3
Dose 4.8
mg/kg
Q3W

Dose Level 4
Dose 6.4
mg/kg
Q3W

Dose Level 5
Dose 8.0
mg/kg
Q3W

Dose Level 6
Dose 9.6
mg/kg
Q3W

Dose Level 7^d
Dose 11.2
mg/kg
Q3W

mTPI-2 model used

^aCT/MRI testing every 6 weeks (first 4 assessments) or every 9 weeks timed from Cycle 1 Day 1 and a 21-day DLT evaluation period. 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. ^bNo limits on the number of prior treatments received. ^cTo be initiated with recommended doses for optimization based on safety monitoring data from Part 1. ^dParticipants at dose level 7 are ongoing and have not completed the DLT window as of 10 September 2025 data cutoff.

CT: computed tomography; DLT: dose-limiting toxicity; EC: endometrial cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; FR α : folate receptor alpha; IV: intravenous; MRI: magnetic resonance imaging; mTPI-2: modified toxicity probability interval version 2 (keyboard design); NSCLC: non-small cell lung cancer; OC: ovarian cancer; Q3W: once every 3 weeks

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Ongoing treatment, n (%)	1 (33)	2 (67)	3 (75)	9 (90)	10 (91)	8 (100)	2 (100)	35 (85)
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Cancer type, n (%)								
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Non-small cell lung cancer	0	0	0	2 (20)	2 (18)	0	0	4 (10)
Median number of prior lines of therapy (range)	2 (1-4)	3 (2-4)	4 (3-7)	4 (2-7)	3 (2-9)	4 (2-6)	7 (7-7)	3 (1-9)
Number of prior lines of therapy, n (%)								
1-2	2 (67)	1 (33)	0	1 (10)	4 (36)	3 (38)	0	11 (27)
3-4	1 (33)	2 (67)	3 (75)	5 (50)	3 (27)	1 (13)	0	15 (37)
≥5	0	0	1 (25)	4 (40)	4 (36)	4 (50)	2 (100)	15 (37)
Prior lines of therapy (ovarian cancer), n (%)								
Platinum	2 (100)	2 (100)	4 (100)	5 (100)	7 (100)	7 (100)	2 (100)	29 (100)
Taxane	2 (100)	2 (100)	4 (100)	5 (100)	7 (100)	7 (100)	2 (100)	29 (100)
Bevacizumab	2 (100)	2 (100)	3 (75)	4 (80)	7 (100)	4 (57)	2 (100)	24 (83)
Mirvetuxumab	0	0	0	0	1 (14)	0	1 (50)	2 (7)
PARP inhibitor	1 (50)	0	2 (50)	2 (40)	7 (100)	6 (86)	2 (100)	20 (69)

ECOG: Eastern Cooperative Oncology Group; PARP: poly-ADP ribose polymerase

All participants (OC, EC, and NSCLC) received platinum and taxane as prior therapy lines; 1 participant with EC (ZW191 8.0 mg/kg) received a PARP inhibitor as a prior therapy line; 3 participants with NSCLC received checkpoint inhibitors as a prior therapy line.

Data cutoff: September 10, 2025

ZWI-ZW191-101 Results: Baseline Characteristics

Parameter	ZW191 1.6 mg/kg (n=3)	ZW191 3.2 mg/kg (n=3)	ZW191 4.8 mg/kg (n=4)	ZW191 6.4 mg/kg (n=10)	ZW191 8.0 mg/kg (n=11)	ZW191 9.6 mg/kg (n=8)	ZW191 11.2 mg/kg (n=2)	Total (n=41)
Median age (range), years	62.0 (58-68)	64.0 (59-73)	59.0 (35-62)	58.5 (48-79)	58.0 (52-68)	62.0 (40-74)	60.0 (55-65)	59.0 (35-79)
Ongoing treatment, n (%)	1 (33)	2 (67)	3 (75)	9 (90)	10 (91)	8 (100)	2 (100)	35 (85)
Race, n (%)								
Asian	1 (33)	1 (33)	4 (100)	8 (80)	7 (64)	8 (100)	1 (50)	30 (73)
White	2 (67)	1 (33)	0	2 (20)	4 (36)	0	1 (50)	10 (24)
Not reported	0	1 (33)	0	0	0	0	0	1 (2)
Baseline ECOG performance status, n (%)								
0	1 (33)	1 (33)	2 (50)	5 (50)	4 (36)	6 (75)	1 (50)	20 (49)
1	2 (67)	2 (67)	2 (50)	5 (50)	7 (64)	2 (25)	1 (50)	21 (51)
Cancer type, n (%)								
Ovarian cancer	2 (67)	2 (67)	4 (100)	5 (50)	7 (64)	7 (88)	2 (100)	29 (71)
Endometrial cancer	1 (33)	1 (33)	0	3 (30)	2 (18)	1 (13)	0	8 (20)
Non-small cell lung cancer	0	0	0	2 (20)	2 (18)	0	0	4 (10)
Median number of prior lines of therapy (range)	2 (1-4)	3 (2-4)	4 (3-7)	4 (2-7)	3 (2-9)	4 (2-6)	7 (7-7)	3 (1-9)
Number of prior lines of therapy, n (%)								
1-2	2 (67)	1 (33)	0	1 (10)	4 (36)	3 (38)	0	11 (27)
3-4	1 (33)	2 (67)	3 (75)	5 (50)	3 (27)	1 (13)	0	15 (37)
≥5	0	0	1 (25)	4 (40)	4 (36)	4 (50)	2 (100)	15 (37)
Prior lines of therapy (ovarian cancer), n (%)								
Platinum	2 (100)	2 (100)	4 (100)	5 (100)	7 (100)	7 (100)	2 (100)	29 (100)
Taxane	2 (100)	2 (100)	4 (100)	5 (100)	7 (100)	7 (100)	2 (100)	29 (100)
Bevacizumab	2 (100)	2 (100)	3 (75)	4 (80)	7 (100)	4 (57)	2 (100)	24 (83)
Mirvetuxumab	0	0	0	0	1 (14)	0	1 (50)	2 (7)
PARP inhibitor	1 (50)	0	2 (50)	2 (40)	7 (100)	6 (86)	2 (100)	20 (69)

ECOG: Eastern Cooperative Oncology Group; PARP: poly-ADP ribose polymerase

All participants (OC, EC, and NSCLC) received platinum and taxane as prior therapy lines; 1 participant with EC (ZW191 8.0 mg/kg) received a PARP inhibitor as a prior therapy line; 3 participants with NSCLC received checkpoint inhibitors as a prior therapy line.

Data cutoff: September 10, 2025

ZWI-ZW191-101 Results: Baseline Characteristics

Parameter	ZW191 1.6 mg/kg (n=3)	ZW191 3.2 mg/kg (n=3)	ZW191 4.8 mg/kg (n=4)	ZW191 6.4 mg/kg (n=10)	ZW191 8.0 mg/kg (n=11)	ZW191 9.6 mg/kg (n=8)	ZW191 11.2 mg/kg (n=2)	Total (n=41)
Median age (range), years	62.0 (58-68)	64.0 (59-73)	59.0 (35-62)	58.5 (48-79)	58.0 (52-68)	62.0 (40-74)	60.0 (55-65)	59.0 (35-79)
Ongoing treatment at data cutoff								35 (85)
Race, n (%)								
Asian								30 (73)
White								10 (24)
Not reported								1 (2)
Baseline ECOG performance								
0								20 (49)
1								21 (51)
Cancer type, n (%)								
Ovarian carcinoma								29 (71)
Endometrial carcinoma								8 (20)
Non-small cell lung carcinoma								4 (10)
Median number of prior lines of therapy								3 (1-9)
Number of prior lines of therapy								
1-2								11 (27)
3-4								15 (37)
≥5								15 (37)
Prior lines of therapy								
Platinum								29 (100)
Taxane	2 (100)	2 (100)	4 (100)	5 (100)	7 (100)	7 (100)	2 (100)	29 (100)
Bevacizumab	2 (100)	2 (100)	3 (75)	4 (80)	7 (100)	4 (57)	2 (100)	24 (83)
Mirvetuxumab	0	0	0	0	1 (14)	0	1 (50)	2 (7)
PARP inhibitor	1 (50)	0	2 (50)	2 (40)	7 (100)	6 (86)	2 (100)	20 (69)

- Enrollment at dose 11.2 mg/kg was ongoing at time of data cutoff
- 6 (15%) participants had discontinued ZW191 treatment due to disease progression
- Of the 41 participants, 35 (85%) were continuing on ZW191 treatment as of data cutoff

ECOG: Eastern Cooperative Oncology Group; PARP: poly-ADP ribose polymerase

All participants (OC, EC, and NSCLC) received platinum and taxane as prior therapy lines; 1 participant with EC (ZW191 8.0 mg/kg) received a PARP inhibitor as a prior therapy line; 3 participants with NSCLC received checkpoint inhibitors as a prior therapy line.

Data cutoff: September 10, 2025

ZWI-ZW191-101 Results: Safety Data Summary

TRAE, n (%)	ZW191 1.6 mg/kg (n=3)	ZW191 3.2 mg/kg (n=3)	ZW191 4.8 mg/kg (n=4)	ZW191 6.4 mg/kg (n=10)	ZW191 8.0 mg/kg (n=11)	ZW191 9.6 mg/kg (n=8)	ZW191 11.2 mg/kg (n=2)	Total (n=41)
Any TRAE	1 (33)	3 (100)	3 (75)	8 (80)	10 (91)	6 (75)	2 (100)	33 (80)
Grade ≥3 TRAE	0	1 (33)	0	1 (10)	4 (36)	1 (13)	0	7 (17)
TRAE leading to dose interruption	0	2 (67)	0	0	1 (9)	0	0	3 (7)
TRAE leading to dose reduction	0	0	0	1 (10)	1 (9)	0	0	2 (5)
DLT event ^a	0	0	0	1 (20)	0	0	0	1 (4)

a. Percentages calculated based on the number of participants in the DLT evaluable set (n=25; n=5 at dose level 6.4 mg/kg). Treatment is ongoing and not all participants have completed the DLT window. DLT: dose-limiting toxicity; TRAE: treatment-related adverse event; AE: adverse event.

Data cutoff: September 10, 2025

No serious TRAEs, discontinuations due to AEs, or deaths

ZWI-ZW191-101 Results: TRAEs of Any Grade Occurring in ≥15% of Participants

ZW191 TRAEs, ^a n (%)	1.6 mg/kg (n=3)		3.2 mg/kg (n=3)		4.8 mg/kg (n=4)		6.4 mg/kg (n=10)		8.0 mg/kg (n=11)		9.6 mg/kg (n=8)		11.2 mg/kg (n=2)		Total (n=41)	
	All grade	Grade ≥3	All grade	Grade ≥3	All grade	Grade ≥3	All grade	Grade ≥3	All grade	Grade ≥3	All grade	Grade ≥3	All grade	Grade ≥3	All grade	Grade ≥3
Any TRAE	1 (33)	0	3 (100)	1 (33)	3 (75)	0	8 (80)	1 (10)	10 (91)	4 (36)	6 (75)	1 (13)	2 (100)	0	33 (80)	7 (17)
Nausea	0	0	2 (67)	0	2 (50)	0	6 (60)	0	7 (64)	0	5 (63)	0	2 (100)	0	24 (59)	0
Fatigue	1 (33)	0	2 (67)	0	1 (25)	0	1 (10)	0	3 (27)	0	1 (13)	0	0	0	9 (22)	0
Anemia	0	0	0	0	0	0	2 (20)	1 (10)	4 (36)	3 (27)	1 (13)	0	0	0	7 (17)	4 (10)
Diarrhea	1 (33)	0	1 (33)	0	0	0	1 (10)	0	4 (36)	0	0	0	0	0	7 (17)	0
Vomiting	0	0	0	0	1 (25)	0	3 (30)	0	1 (9)	0	2 (25)	0	0	0	7 (17)	0
Alopecia	1 (33)	0	0	0	0	0	2 (20)	0	2 (18)	0	1 (13)	0	0	0	6 (15)	0

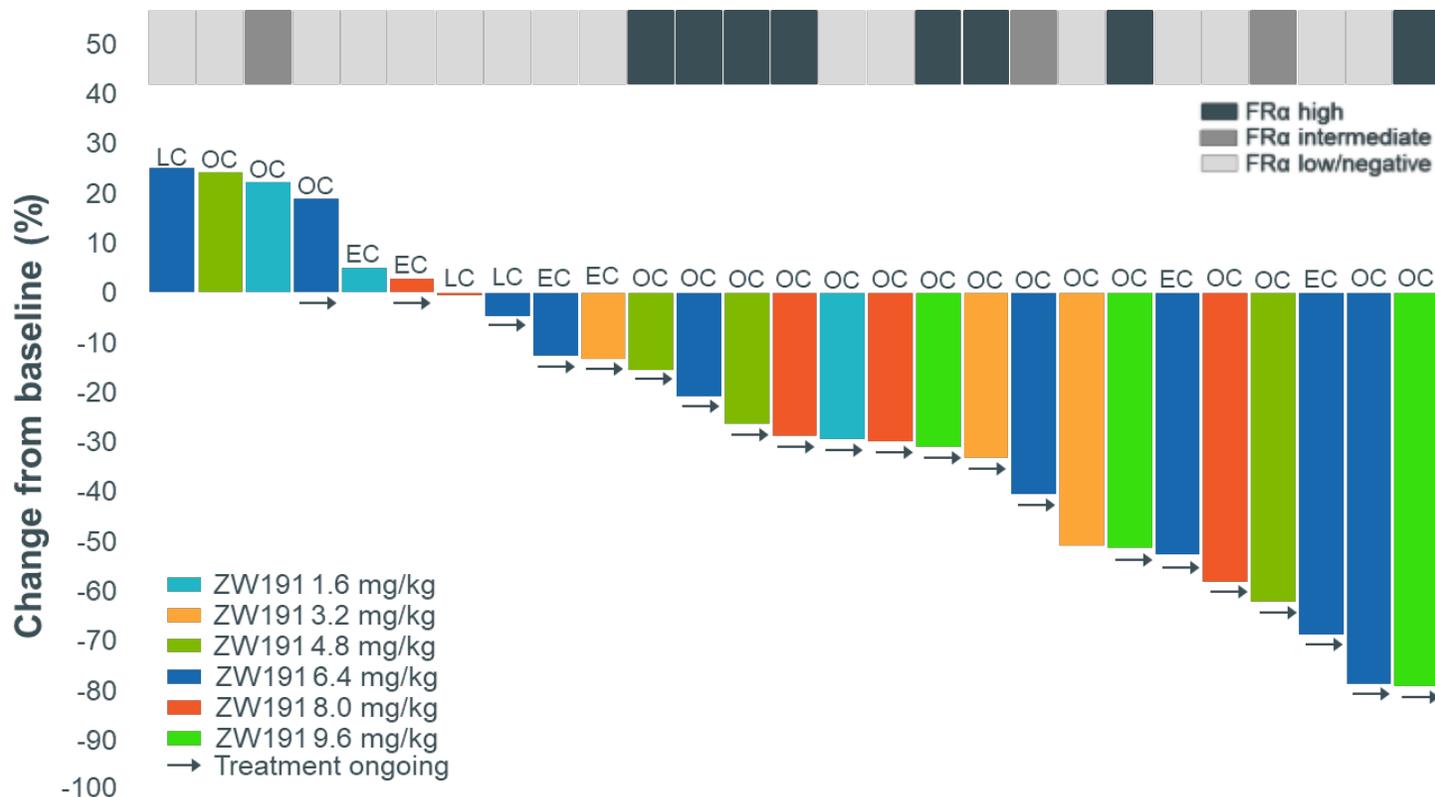
TRAE: treatment-related adverse event

Data cutoff: September 10, 2025

7 participants reported Grade ≥3 TRAEs; the most common were anemia (4), neutropenia (2), and thrombocytopenia (2)

ZWI-ZW191-101 Results: Anti-tumor Activity

Best percent change in target lesion size from baseline (n=27)



27 participants were response-evaluable by having at least 1 post-baseline scan.
 Response based on RECIST v1.1 (response and progression defined as -30% and +20% change from baseline, respectively).
 EC: endometrial cancer; FRA: folate receptor alpha; LC: non-small cell lung cancer; OC: ovarian cancer; RECIST v1.1: Response Evaluation Criteria in Solid Tumors, version 1.1

Data cutoff: September 10, 2025

Preliminary efficacy for response-evaluable participants with gynecological cancer

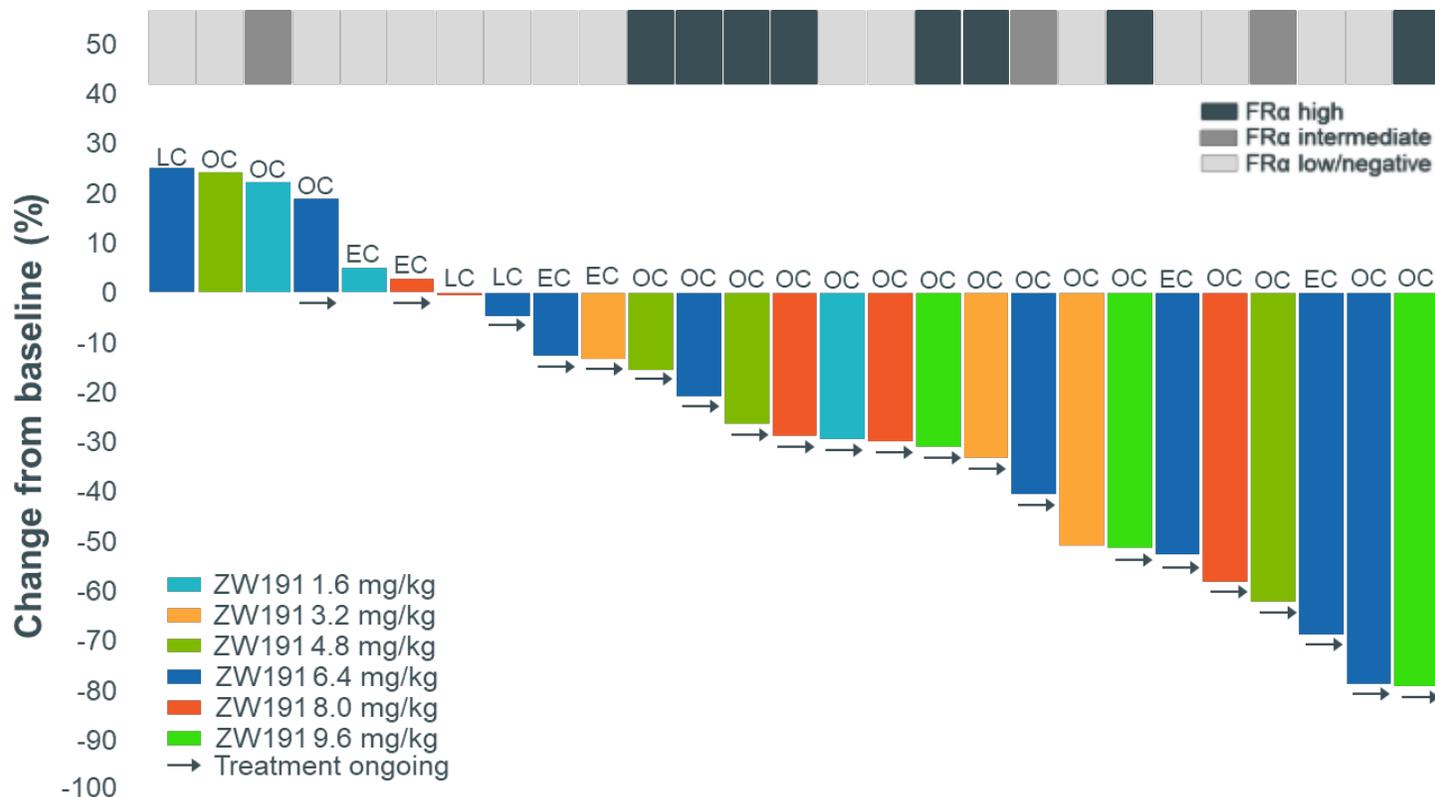
Best response	ZW191 1.6 mg/kg (n=3)	ZW191 3.2 mg/kg (n=3)	ZW191 4.8 mg/kg (n=4)	ZW191 6.4 mg/kg (n=7)	ZW191 8.0 mg/kg (n=4)	ZW191 9.6 mg/kg (n=3)	ZW191 6.4-9.6 mg/kg (n=14)	Total (n=24)
PR, n (%) ^a	0	2 (67)	1 (25)	4 (57)	2 (50)	3 (100)	9 (64)	12 (50)
cPR, n (%)	0	2 (67)	1 (25)	3 (43)	1 (25)	0	4 (29)	7 (29)
SD, n (%)	1 (33)	1 (33)	2 (50)	3 (43)	2 (50)	0	5 (36)	9 (38)
PD, n (%)	2 (67)	0	1 (25)	0	0	0	0	3 (13)

^aPR includes confirmed and unconfirmed. The 5 participants with unconfirmed PR are all awaiting confirmation.
 Note: Percentages are out of gynecological cancer (OC and EC) participants.
 cPR: confirmed partial response; EC, endometrial cancer; OC, ovarian cancer; PD: progressive disease; PR: partial response; RECIST v1.1: Response Evaluation Criteria in Solid Tumors version 1.1; SD: stable disease

Data cutoff: September 10, 2025

ZWI-ZW191-101 Results: Anti-tumor Activity

Best percent change in target lesion size from baseline (n=27)



27 participants were response-evaluable by having at least 1 post-baseline scan.
 Response based on RECIST v1.1 (response and progression defined as -30% and +20% change from baseline, respectively).
 EC: endometrial cancer; FRA: folate receptor alpha; LC: non-small cell lung cancer; OC: ovarian cancer; RECIST v1.1: Response Evaluation Criteria in Solid Tumors, version 1.1

Data cutoff: September 10, 2025

Preliminary efficacy for response-evaluable participants with gynecological cancer

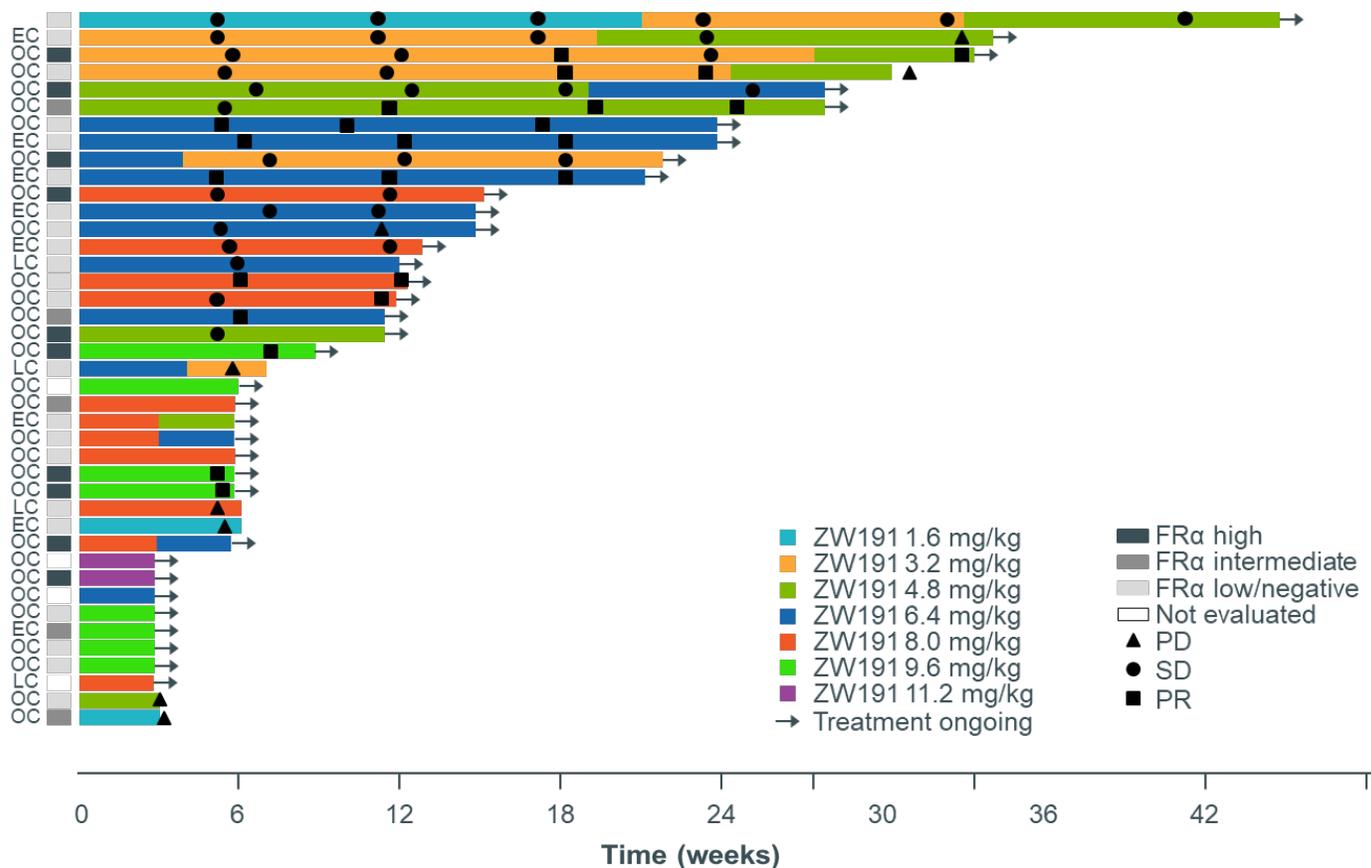
Best response	ZW191 1.6 mg/kg (n=3)	ZW191 3.2 mg/kg (n=3)	ZW191 4.8 mg/kg (n=4)	ZW191 6.4 mg/kg (n=7)	ZW191 8.0 mg/kg (n=4)	ZW191 9.6 mg/kg (n=3)	ZW191 6.4-9.6 mg/kg (n=14)	Total (n=24)
PR, n (%) ^a	0	2 (67)	1 (25)	4 (57)	2 (50)	3 (100)	9 (64)	12 (50)
cPR, n (%)	0	2 (67)	1 (25)	3 (43)	1 (25)	0	4 (29)	7 (29)
SD, n (%)	1 (33)	1 (33)	2 (50)	3 (43)	2 (50)	0	5 (36)	9 (38)
PD, n (%)	2 (67)	0	1 (25)	0	0	0	0	3 (13)

^aPR includes confirmed and unconfirmed. The 5 participants with unconfirmed PR are all awaiting confirmation.
 Note: Percentages are out of gynecological cancer (OC and EC) participants.
 cPR: confirmed partial response; EC, endometrial cancer; OC, ovarian cancer; PD: progressive disease; PR: partial response; RECIST v1.1: Response Evaluation Criteria in Solid Tumors version 1.1; SD: stable disease

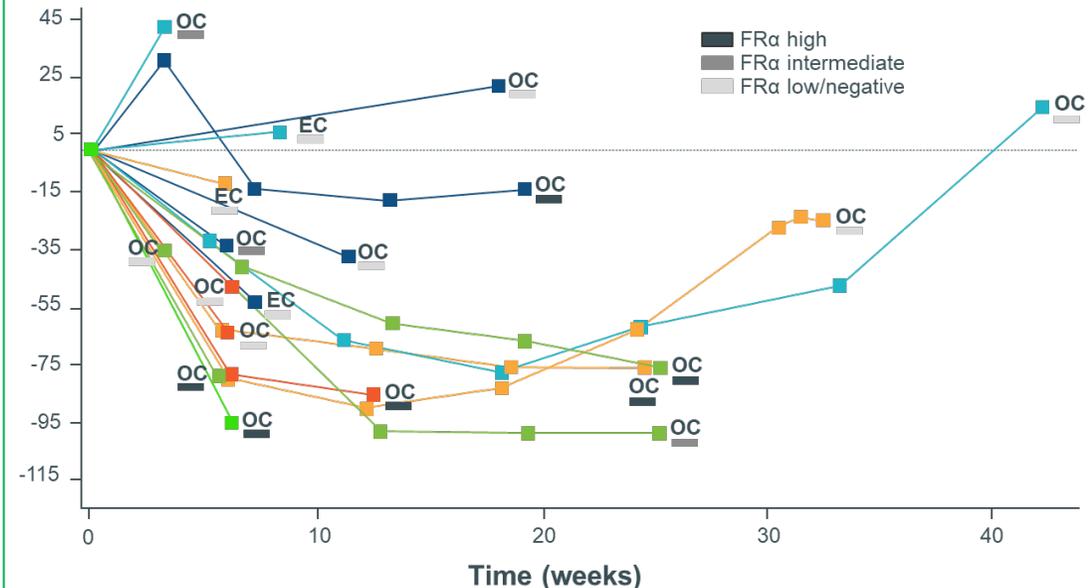
Data cutoff: September 10, 2025

ZWI-ZW191-101 Results: Anti-tumor Activity

Duration of treatment and overall response (n=41)



Percent change from baseline in CA-125 (n=19)



CA-125: cancer antigen 125; EC: endometrial cancer; FRα: folate receptor alpha; LC: non-small cell lung cancer; OC: ovarian cancer; PD, progressive disease; PR, partial response; SD, stable disease

Data cutoff: September 10, 2025

- **ZW191 has been safely administered during dose escalation up to 11.2 mg/kg, with the majority of participants still on treatment**
 - Low rates of dose modifications, dose delays, and Grade ≥ 3 AEs
 - No discontinuations due to AEs
- **Preliminary efficacy is promising, starting at 3.2 mg/kg Q3W**
 - ORRs (uPR + cPR) between 6.4 mg/kg to 9.6 mg/kg were: **53%** (overall) and **64%** (GYN cancers)
 - Anti-tumor activity is observed across all FR α expression levels
- **These data represent a broad therapeutic window for ZW191 and support further investigation in advanced solid tumors**

ZW191: Next Steps



Sabeen Mekan, MD

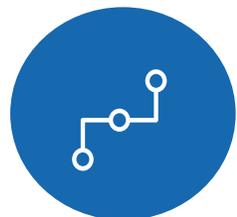
Senior Vice President, Clinical Development
Zymeworks

Advancing ZW191 to Dose Optimization



Data-Driven Development

- Building confidence in our ADC platform through safety, pharmacokinetics, and efficacy with emerging clinical data



Optimization & Differentiation

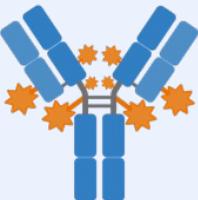
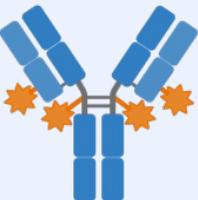
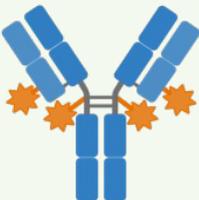
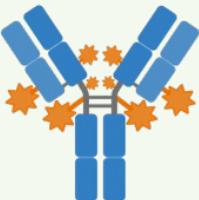
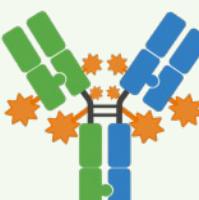
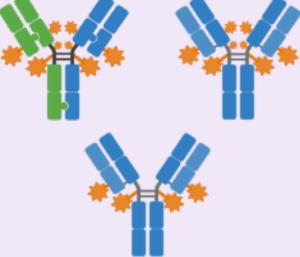
- 11.2 mg/kg dose defined as MTD since this data-cut
- Randomized dose optimization to begin in 4Q-2025 in platinum resistant ovarian cancer at 9.6 and 6.4 mg/kg doses (~30 pts/cohort)
- Early data supports best-in-class potential



Strategic Growth Potential

- Emerging data will inform registration and combination strategies, including earlier-line opportunities
- In parallel, partnership discussions are underway to further refine and accelerate development

ZW191 Phase 1 Data Provides Promising Evidence of Capabilities of ADC Platform and Design Philosophy

	Clinical Assets		Preclinical Assets			Next Gen
						
	ZW191	ZW251	ZW220	ZW327	ZW318	
Target	FR α	GPC3	NaPi2b	Ly6E	PTK7	Various
Payload	ZD06519 (TOPO1i)	ZD06519 (TOPO1i)	ZD06519 (TOPO1i)	ZD06519 (TOPO1i)	ZD06519 (TOPO1i)	Targeted small molecule, Novel cytotoxic, dual payload
Target Indications	OVCA, EC, NSCLC	HCC	OVCA, EC, NSCLC	Pan Tumor	NSCLC, TNBC	Various



zymeworks

Q&A

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