LBA40

MADRID 2026 ESMO congress

Randomized dose optimization of ZW191 in heavily pretreated patients with platinum-resistant ovarian cancer (PROC)

Jung-Yun Lee,[1] David Sommerhalder,[2] Jose Alejandro Pérez-Fidalgo,[3] Daniel S.W. Tan,[4] Kosei Hasegawa,[5] Patricia LoRusso,[6] Kenichi Harano,[7] David M. O'Malley,[8] Sarah E. Church,[9] Lin Lu,[9] Sabeen Mekan,[9] Maggie Weinstein,[9] David Shao Peng Tan[10]

[1] Yonsei Cancer Center and Severance Hospital, Seoul, Republic of South Korea
[2] NEXT Oncology, San Antonio, TX, US
[3] Hospital Clínico de València, INCLIVA, Valencia, Spain
[4] National Cancer Centre, Singapore
[5] Saitama Medical University International Medical Center, Hidaka, Saitama, Japan
[6] Yale New Haven Hospital, New Haven, CT, US
[7] National Cancer Center Hospital East, Kashiwa, Chiba, Japan
[8] The Ohio State University and the James Comprehensive Cancer Center, Columbus, OH, US
[9] Zymeworks BC Inc., Vancouver, BC, Canada
[10] National University Cancer Institute, Singapore, and Yong Loo Lin School of Medicine, National University of Singapore, Singapore



EUROPEAN SOCIETY FOR MEDICAL ONCOLOGY (ESMO) MEETING, MADRID, SPAIN, OCTOBER 23–27, 2026

ESMO

Disclosure information

Jung-Yun Lee, MD, PhD

I have the following relevant financial relationships to disclose:

Personal financial relationships

- Honoraria – Abbvie, AstraZeneca, Daiichi Sankyo, Eisai, GSK, MSD, Roche, Takeda
- Consulting/Advisory/Steering Committee – Abbvie, AstraZeneca, CanariaBio, Corcept, Daiichi Sankyo, Eisai, Genmab, GII, GSK, ImmunoGen, Lilly, Merck, MSD, Pfizer, Regeneron, Seagen, Sutro, TORL-bio

Institutional financial interest

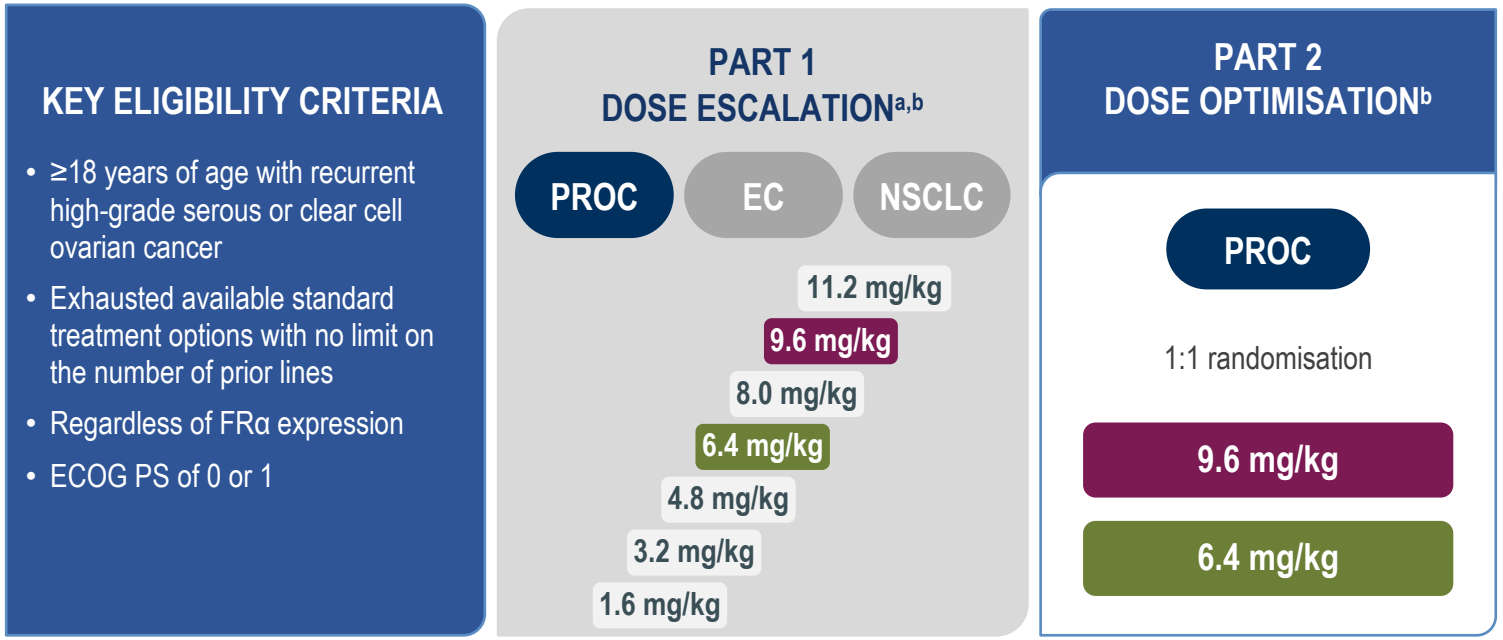
- Abbvie, Advenchen, Ascendis Pharma, Alkermes, AstraZeneca, Beone, BergenBio, BMS, CanariaBio, Corcept, Cellid, CKD, Clovis Oncology, Daiichi Sankyo, Eisai, Genemedicine, Genmab, GII, GSK, ImmunoGen, Janssen, Kelun, Lilly, Merck, Mersana, MSD, Novartis, Onconic Therapeutics, ONO, Pfizer, Regeneron, Roche, Seagen, Sutro, Synthon, Takeda, TORL-bio, Zentalis, Zymeworks

All authors met ICMJE authorship criteria and had full access to relevant data.

Content of this presentation is copyright and responsibility of the author. Permission is required for re-use.

Background and study design

- Treatment options remain limited for heavily pretreated patients with platinum-resistant ovarian cancer (PROC), including those with high-grade serous and clear cell histology[1]
- Folate receptor alpha (FRα) is highly expressed in ovarian cancer and other solid tumours, making it a promising therapeutic target[2]
- ZW191 is an FRα-targeted antibody-drug conjugate comprising a protease-cleavable linker and a novel topoisomerase I inhibitor payload (ZD06519; drug-to-antibody ratio: 8)[3]
- ZWI-ZW191-101 (NCT06555744) is an ongoing, first-in-human, phase 1 global study evaluating the safety, tolerability, and antitumour activity of ZW191 in patients with advanced solid tumours[4]



[a]21-day dose-limiting toxicities evaluation period. [b]ZW191 administered IV every 3 weeks. 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.

We report efficacy and safety results at 6.4 and 9.6 mg/kg in participants with PROC, with a median follow-up of 7 months

Data cutoff 10 September 2026.

CT: computed tomography; EC: endometrial cancer; ECOG PS: Eastern Cooperative Oncology Group performance status; IV: intravenously; MRI: magnetic resonance imaging; NSCLC: non-small cell lung cancer.

1. Richardson DL, et al. *JAMA Oncol*. 2023;9(6):851-859. **2.** Köbel M, et al. *Br J Cancer*. 2014;111(12):2297-2307. **3.** Lawn S, et al. *Clin Cancer Res*. 2026;32(13):2748-2764. **4.** A study of ZW191 in participants with solid tumors. ClinicalTrials.gov. Updated 7 May 2026. Accessed 2 October 2026. https://clinicaltrials.gov/study/NCT06555744.

Content of this presentation is copyright and responsibility of the author. Permission is required for re-use.

Patients were heavily pretreated and had a wide range of FRα expression

Demographics and baseline characteristics	6.4 mg/kg (n=37)	9.6 mg/kg (n=43)	Total (N=80)
Age, years, median (range)	61 (42-78)	61 (40-79)	61 (40-79)
≥65 years, n (%)	15 (41)	20 (47)	35 (44)
Race, n (%)			
Asian	27 (73)	33 (77)	60 (75)
White	9 (24)	9 (21)	18 (23)
Other	1 (3)	1 (2)	2 (2)
Baseline ECOG PS, n (%)			
0	20 (54)	24 (56)	44 (55)
1	17 (46)	19 (44)	36 (45)
Histology, n (%)			
High-grade serous	32 (86)	39 (91)	71 (89)
Clear cell	5 (14)	4 (9)	9 (11)

Prior therapies	6.4 mg/kg (n=37)	9.6 mg/kg (n=43)	Total (N=80)
Prior lines of therapy, median (range)	4 (1-10)	4 (2-9)	4 (1-10)
Prior lines of therapy, n (%)			
1-2	12 (32)	8 (19)	20 (25)
3-4	9 (24)	15 (35)	24 (30)
≥5	16 (43)	20 (47)	36 (45)
Prior systemic therapy, n (%)			
Platinum and taxane	37 (100)	43 (100)	80 (100)
Bevacizumab	32 (86)	35 (81)	67 (84)
PARP inhibitor	18 (49)	27 (63)	45 (56)
Checkpoint inhibitor	7 (19)	10 (23)	17 (21)
Mirvetuximab soravtansine	2 (5)	2 (5)	4 (5)

Median baseline FRα H-score was 145 (range, 0-300) and median PS2+ was 45% (range, 0%-100%)

ECOG PS: Eastern Cooperative Oncology Group performance status; FRα: folate receptor alpha; H: histochemical; PARP: poly adenosine diphosphate–ribose polymerase; PS2+: positive score ≥2+.

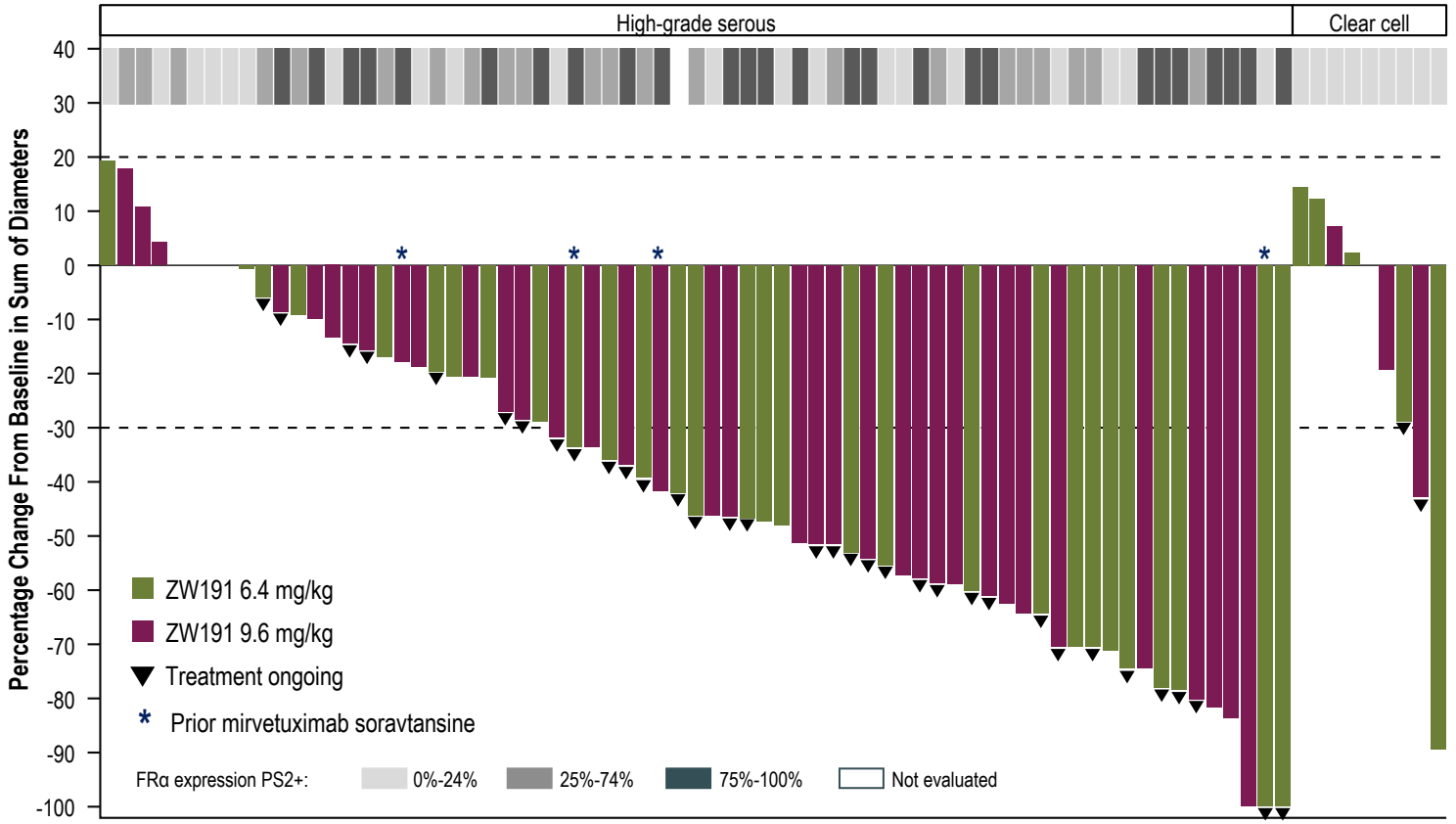
Content of this presentation is copyright and responsibility of the author. Permission is required for re-use.

cORR was 65% at 6.4 mg/kg and 55% at 9.6 mg/kg in high-grade serous PROC

High-grade serous PROC	6.4 mg/kg (n=31)	9.6 mg/kg (n=38)
cORR, % (95% CI)	**64.5** (45.4, 80.8)	**55.3** (38.3, 71.4)
DCR, % (95% CI)	**100** (88.8, 100.0)	**92.1** (78.6, 98.3)
Clear cell PROC	**6.4 mg/kg (n=5)**	**9.6 mg/kg (n=4)**
cORR, % (95% CI)	**20.0** (0.5, 71.6)	**0** (0, 60.2)
DCR, % (95% CI)	**80.0** (28.4, 99.5)	**100** (39.8, 100.0)

Note: Response-evaluable patient data only. All clear cell patients had low/negative FRα level.

- cORR (95% CI) in HGSOC by FRα PS2+ categories
  - High ≥75% (n=26): **69.2%** (48.2%, 85.7%)
  - Intermediate 25%-74% (n=22): **50.0%** (28.2%, 71.8%)
  - Low/negative 0%-24% (n=20): **55.0%** (31.5%, 76.9%)



Analysis populations: All enrolled (N=80); response-evaluable (n=78); FRα-evaluable (n=77). Three patients had confirmed responses after the data cut date. One response-evaluable patient with non-evaluable FRα data was excluded from the FRα subgroup analysis.
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+ was defined as the percentage of tumour cells with 2+ and 3+ staining intensity and categorised as low/negative 0%-24%, intermediate 25%-74%, and high 75%-100%.

cORR: confirmed objective response rate; DCR: disease control rate; FRα: folate receptor alpha; HGSOC: high-grade serous ovarian carcinoma; PROC: platinum-resistant ovarian cancer; PS2+: positive score ≥2+.

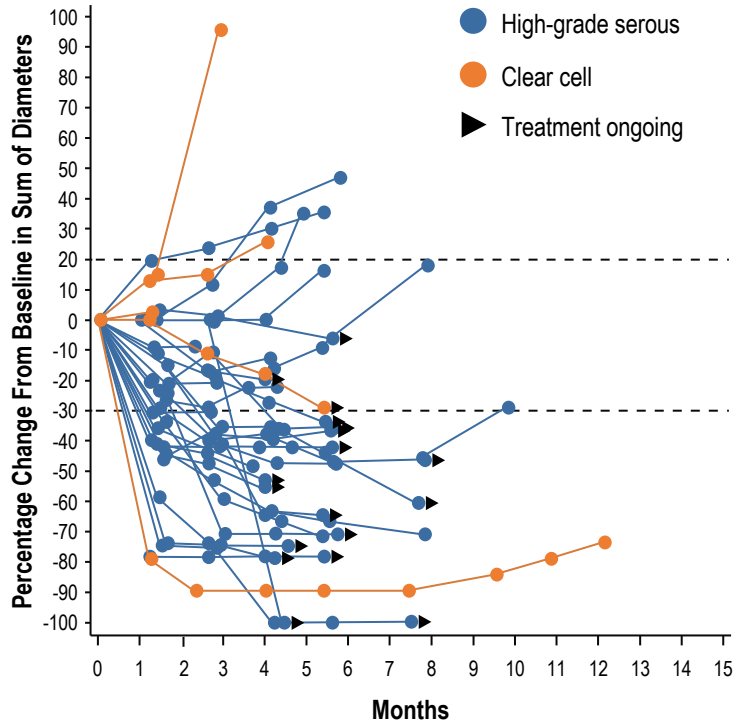
Content of this presentation is copyright and responsibility of the author. Permission is required for re-use.

MADRID 2026 ESMO congress

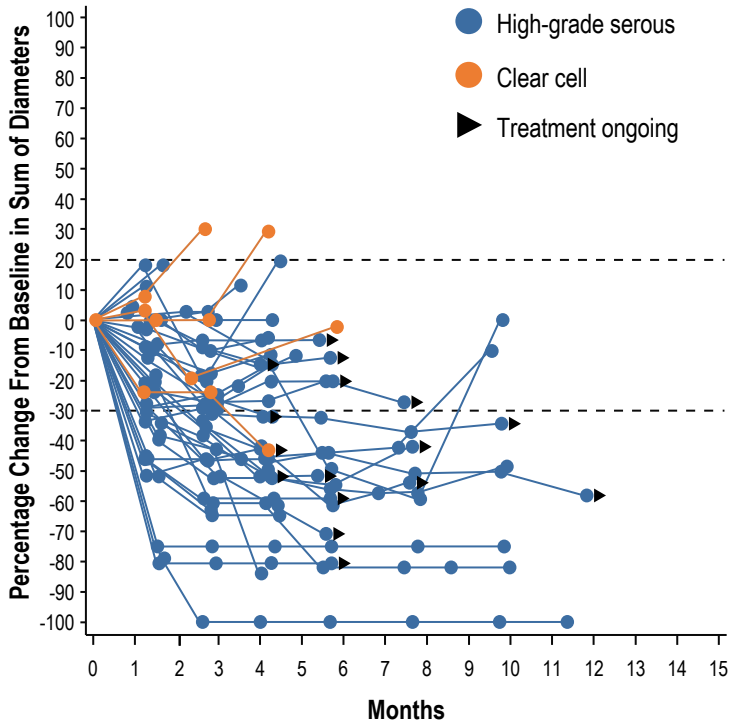
Responses to ZW191 were deep and durable

mDOR was not reached with 45% of participants continuing treatment

ZW191
6.4 mg/kg



ZW191
9.6 mg/kg



	6.4 mg/kg	9.6 mg/kg
HIGH-GRADE SEROUS		
mDOR[a]	NR	NR
mPFS, mo (95% CI)	7.9[b] (4.9, NR)	9.8 (4.4, 9.9)
6-month PFS, % (95% CI)	61.5 (38.4, 78.1)	61.4 (41.6, 76.2)
CLEAR CELL		
mPFS, mo (95% CI)	4.0 (1.2, NR)	5.0 (2.6, NR)

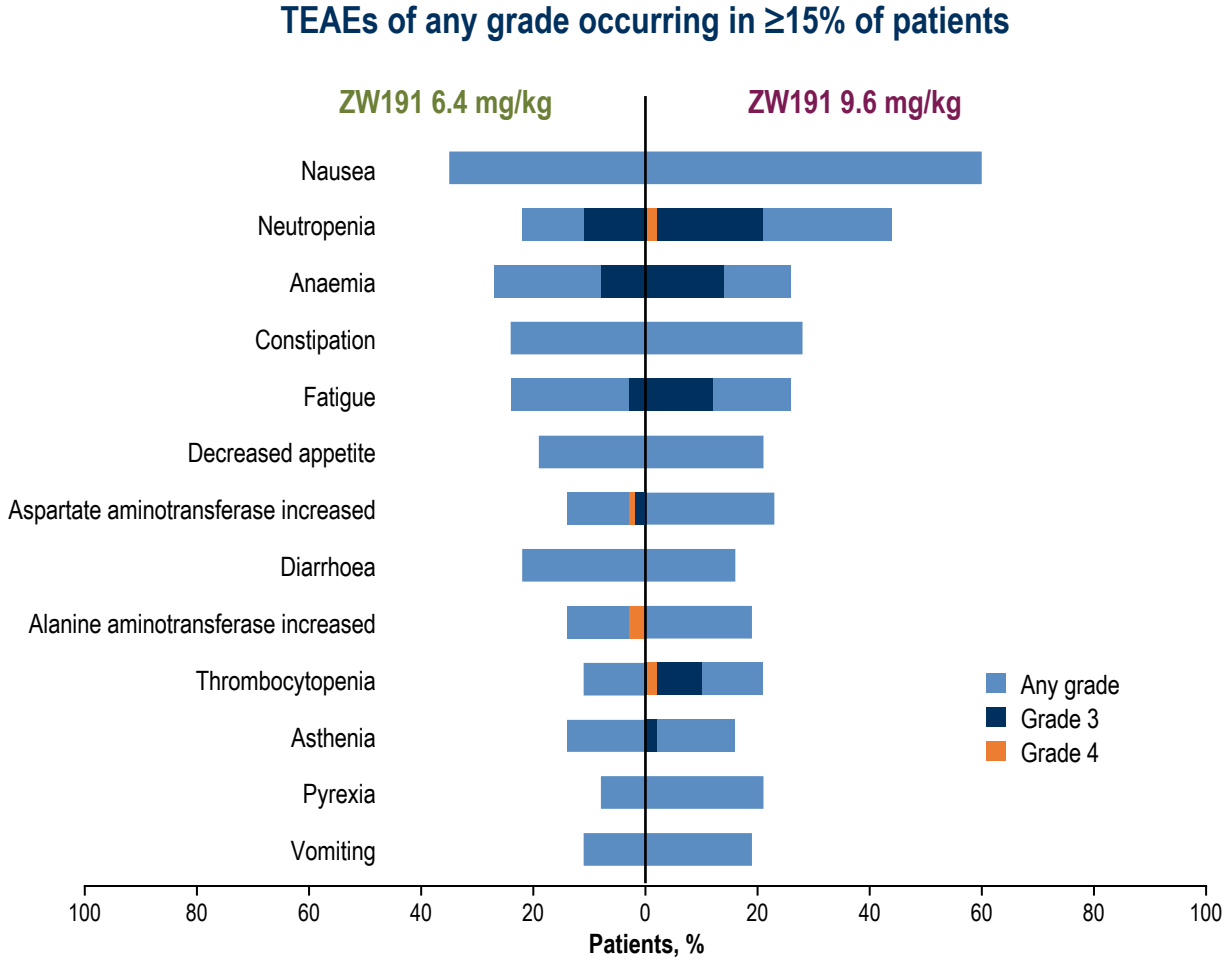
[a]At median 7 months follow-up. [b]Event rate was 44% as of data cut with majority of patients on treatment. mPFS is expected to evolve.

mPFS was evaluated based on all enrolled patients with PROC (N=80).
mDOR: median duration of response; mPFS: median progression-free survival; NR: not reached; PFS: progression-free survival; PROC: platinum-resistant ovarian cancer.

Content of this presentation is copyright and responsibility of the author. Permission is required for re-use.

ZW191 was well tolerated

TEAE, n (%)	6.4 mg/kg (n=37)	9.6 mg/kg (n=43)
Any TEAE	35 (95)	43 (100)
Grade ≥3 TEAE	20 (54)	32 (74)
Grade ≥3 TRAE	8 (22)	19 (44)
Serious TEAEs	16 (43)	23 (53)
Serious Grade ≥3 TEAE	14 (38)	19 (44)
TEAE leading to dose reduction	2 (5)	14 (33)
Discontinuations due to TEAEs	5 (14)	8 (19)
Deaths due to TEAEs	0	0



TEAE: treatment-emergent adverse event; TRAE: treatment-related adverse event.

Content of this presentation is copyright and responsibility of the author. Permission is required for re-use.

Conclusions

ZW191 demonstrated impressive efficacy in heavily pretreated PROC across FRα expression

- Impressive efficacy at doses 6.4 and 9.6 mg/kg across FRα expression in HGSOC
  - cORR was 65% at 6.4 mg/kg and 55% at 9.6 mg/kg
  - Strong activity was observed in high FRα expression with cORR of 69%
  - Promising activity was observed in negative/low and intermediate FRα expression with cORR of 55% and 50%, respectively
  - mDOR has not been reached
  - 6-month PFS was ~61% at both doses with majority of patients remaining on treatment
- Favourable safety profile with low rate of adverse events, including cytopenias, particularly at 6.4 mg/kg

These findings will guide optimal dosing for further clinical development

cORR: confirmed objective response rate; FRα: folate receptor alpha; HGSOC: high-grade serous ovarian carcinoma; mDOR: median duration of response; mPFS: median progression-free survival; PFS: progression-free survival; PROC: platinum-resistant ovarian cancer.

Content of this presentation is copyright and responsibility of the author. Permission is required for re-use.