Zymeworks Portfolio Update

ZW209 Licensing Agreement and New Clinical Data for ZW191

OCTOBER 27, 2026

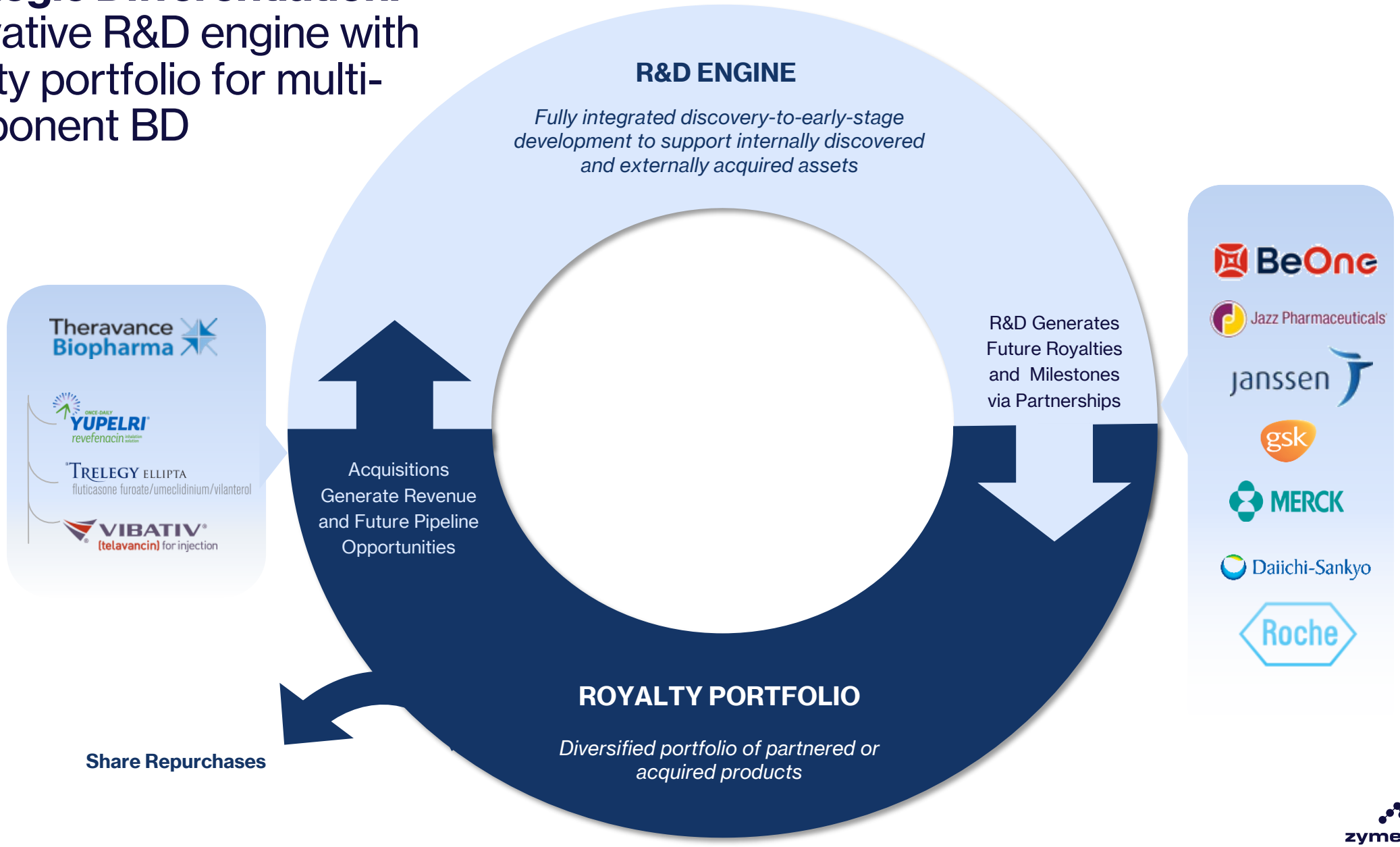
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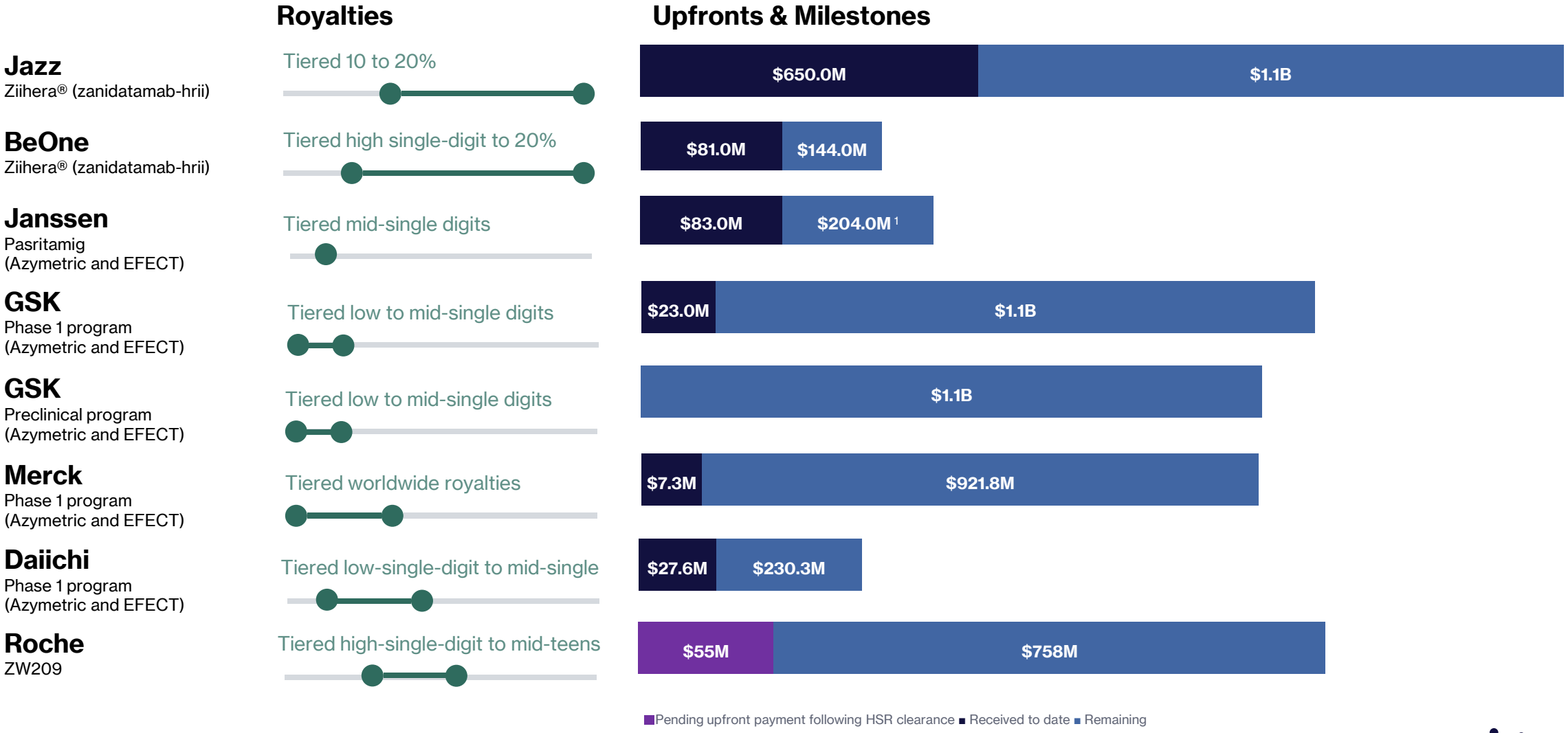
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Strategic Differentiation: innovative R&D engine with royalty portfolio for multi-component BD



Zymeworks partnering model has paid almost $1B



*Bars not to scale. Values rounded to the nearest million

1. 204.0M remaining milestones are related to Pasritamig only, and do not include additional milestones that may be payable in relation to another deprioritized asset.

Differentiated pipeline of multifunctional therapeutics

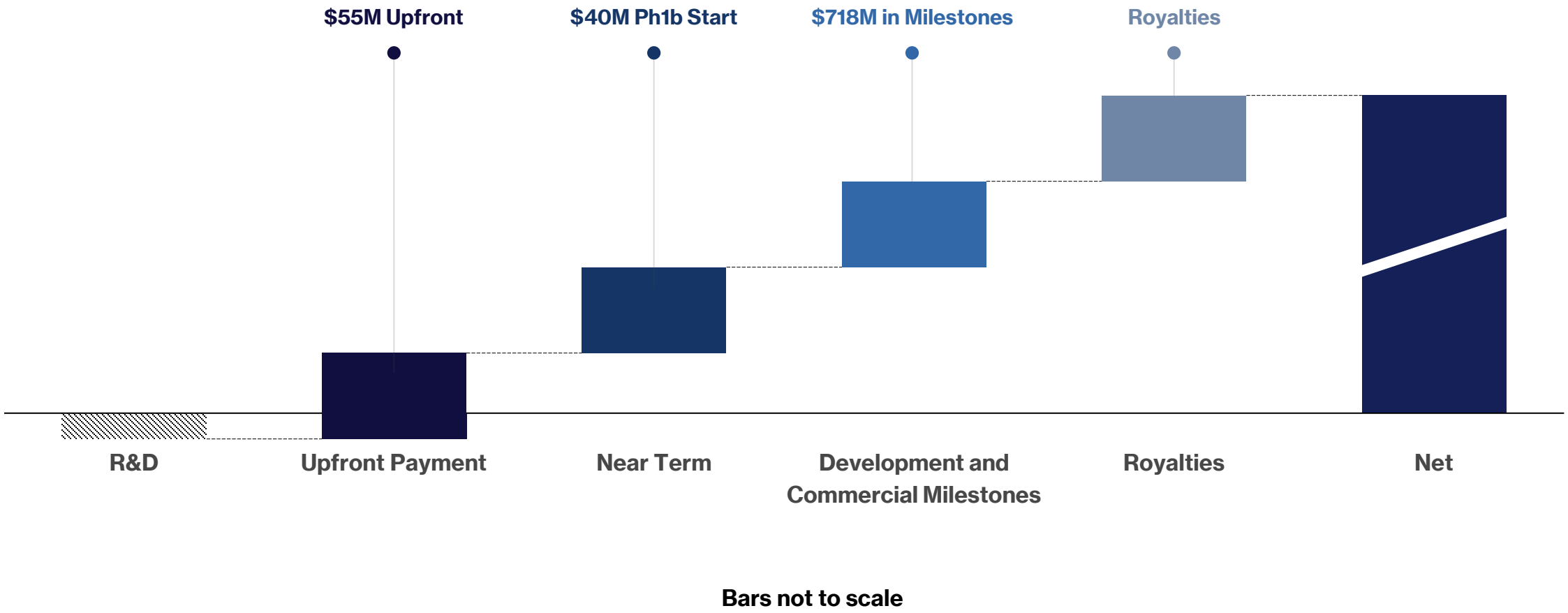
Program	Technology	Target	Indication	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
Solid Tumor Oncology: Antibody-Drug Conjugates (ADC)								
ZW191 Topo1i ADC | DAR 8 | Fc WT	ZD06519 Payload	FRα	Gynecological Thoracic			NCT06555744		
ZW251 Topo1i ADC | DAR 4 | Fc WT	ZD06519 Payload	GPC3	HCC, CGT, sqNSCLC			NCT07164313		
ZW220 Topo1i ADC | DAR 4 | Fc Mut	ZD06519 Payload	NaPi2b	Gynecological Thoracic					
ZW327* Topo1i ADC | DAR 8 | Fc Mut	ZD06519 Payload	Ly6E	Multiple indications					
ZW427* RASi ADC | DAR 8 | Fc Silent	RASi Payload	Ly6E	Lung and GI					
ZW418* RASi ADC | DAR 8 | Biparatopic	RASi Payload	Biparatopic PTK7	Lung					
ZW439* RASi ADC | DAR 8 | Fc Silent	RASi Payload	Claudin18.2	Pancreatic					
Solid Tumor Oncology: Multispecific Antibody Therapeutics (MSAT)								
ZW209 Trispecific TCE | Tri-TCE Costim	Azymetric™, Novel anti-CD3 Conditional CD28	DLL3 x CD3 x CD28	Thoracic			Anticipated IND in 2026		
ZW239 Trispecific TCE | Tri-TCE Costim	Azymetric™, Novel anti-CD3 Conditional CD28	CLDN18.2 x CD3 x CD28	Digestive System					
Autoimmune & Inflammatory Diseases								
ZW1528 Dual Cytokine Blocker	Azymetric™ Hetero-Fab | YTE	IL4Rα x IL-33			Anticipated regulatory submission in 2027			
ZW1572 Dual Cytokine Blocker	Azymetric™ Hetero-Fab | YTE	IL4Rα x IL-31						

ZW209: Roche Licensing Agreement Overview



Adam Schayowitz
Head of R&D

Meaningful return from upfront with substantial potential upside from milestones and royalties



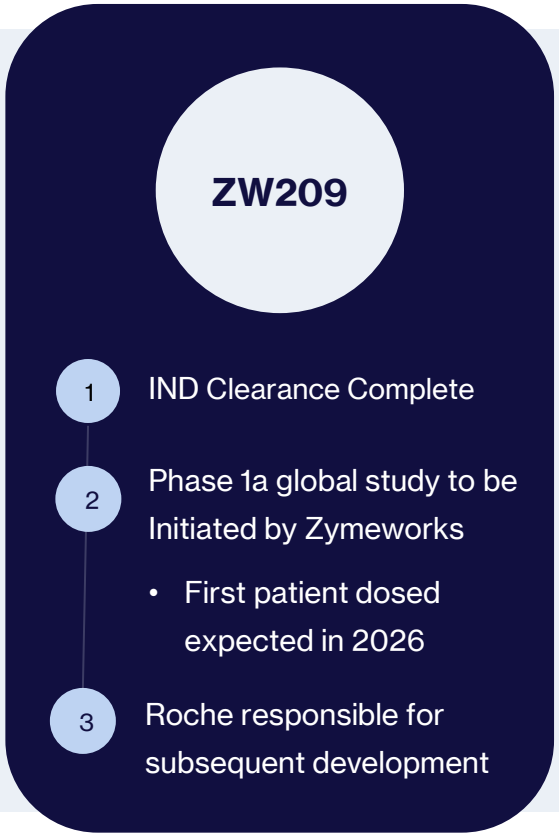
Bars not to scale

Royalties: high-single-digit to mid-teen digits, into the 2040s

Roche to fund all research and development of ZW209, including the Phase 1a trial. Roche will be responsible for subsequent development and commercialization.

Collaboration combines Zymeworks' innovation while leveraging Roche's capabilities to accelerate and expand development

- ZW209 development leverages Zymeworks proprietary, and clinically validated, Azymetric™ platform
- Zymeworks' utilizes decades of extensive paratope and format exploration to enable discovery of optimal TriTCEs
- Zymeworks to run the global Phase 1a study, leveraging proven development capabilities for speed and execution, with no handover required.



- Global capabilities to accelerate and broaden development across multiple lines of therapy
- Roche brings commercial experience in first line ES-SCLC with established prescribers, payer and trial networks.
- Roche's pipeline includes additional programs which may provide combination

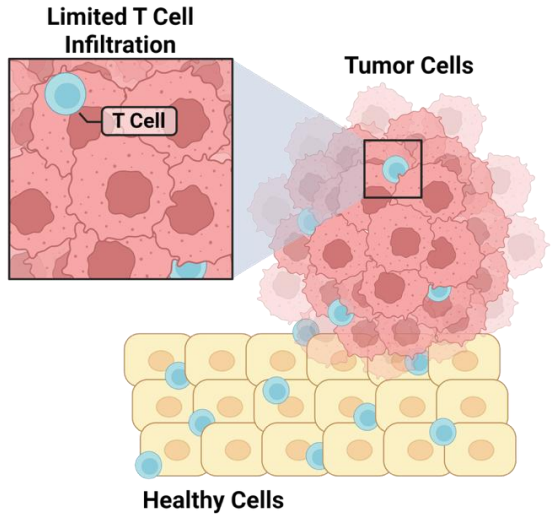
ES-SCLC: Extensive-stage small-cell lung cancer
Agreement remains subject to HSR clearance

ZW209: Preclinical Development

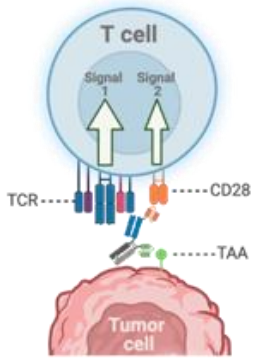


Paul Moore
Chief Scientific Officer

Zymeworks Trispecific Co-Stimulatory TCE: Overcoming Lack of Efficacy and Durability of Responses in Solid Tumors by Incorporating Conditional Costimulation



Low T cell infiltration and T cell anergy remain challenges in the treatment of solid tumors with traditional bispecific T Cell Engagers



Zymeworks' Next Generation Solution:

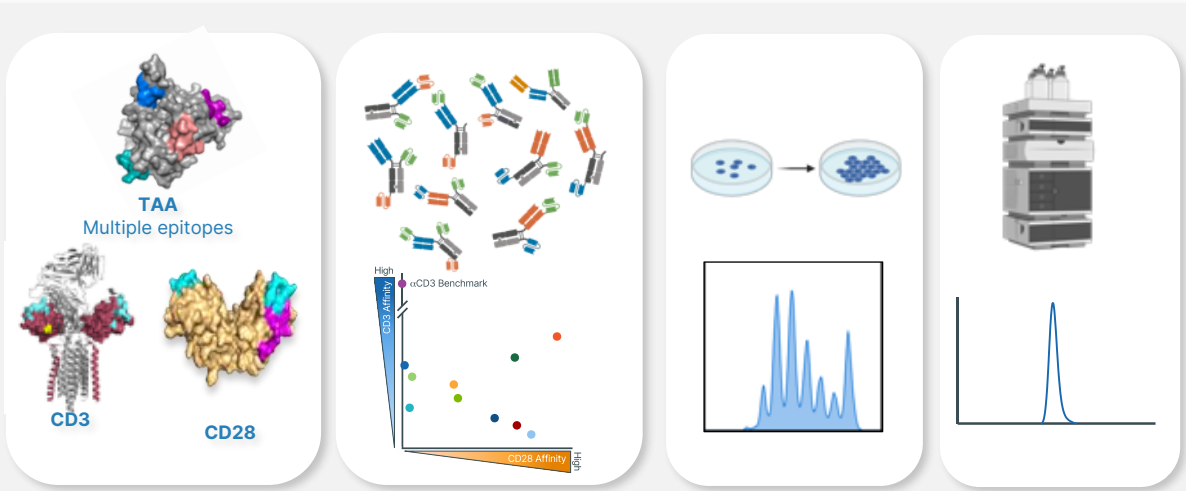
- Balanced CD3 and CD28 affinity engagement
- Conditional CD28 binding that only binds in cis with CD3 engagement
- Strict target-dependent activity and T cell activation
- Identified via Azymetric™ screening of various antibody geometries and CD3 and CD28 paratope affinities

CD28 biology provides ideal costimulatory pathway to integrate with CD3 TCE to enhance and sustain anti-tumor T cell responses

CD3: cluster of differentiation 3 protein complex and T cell co-receptor; TAA: tumor associated antigen; TCE: T cell engager; TCR: T cell receptor; TriTCE Co-Stim: trispecific T cell engager co-stimulatory program.
Arvedson T et al. Ann Rev Cancer Biol 2022.

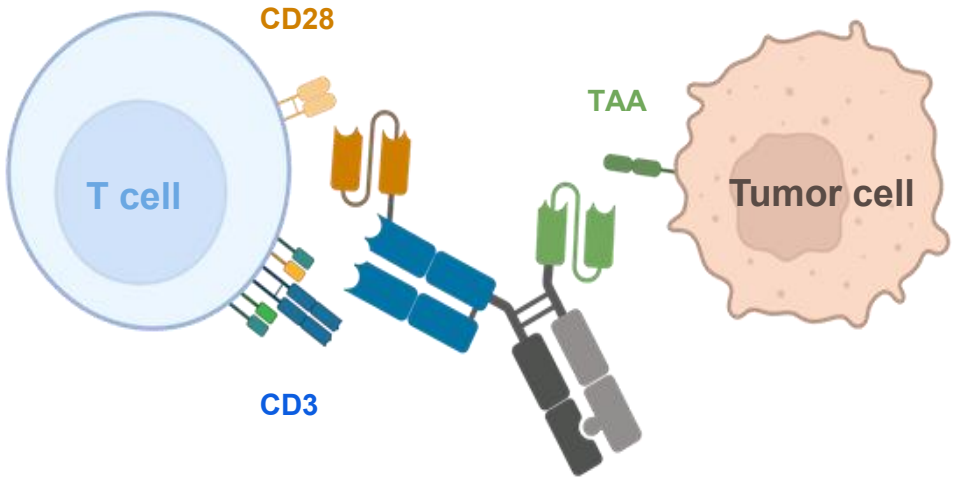
Extensive Paratope And Format Exploration Enables Discovery Of Optimal Costimulatory TCEs

Computational & AI Guided Paratope Engineering | **Azymetric™ Enabled HTP Format Engineering & Production** | ***in vitro* Activity & Differentiation** | **Early Developability Assessment**



Iterative HTP lab-in-loop screening

Locked CD3/CD28 geometry:
optimized for efficient conditional *cis* CD28 co-stimulation and strict TAA dependence

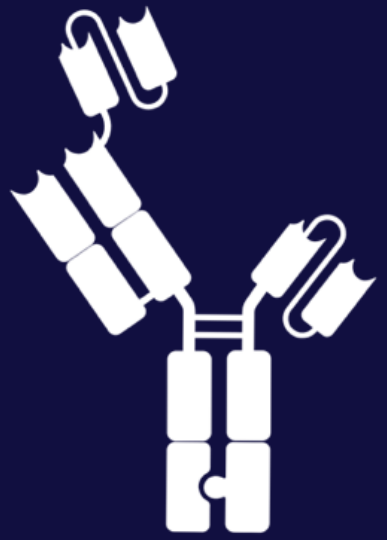


Future TriTCE Co-stim Programs

Program	Technology	Target(s)	Indication	Discovery	Candidate Selection	Preclinical	Phase 1	Phase 2	Phase 3
Oncology									
ZW209 Trispecific TCE | TriTCE Co-Stim	Azymetric™, EFECT™, TriTCE Co-Stim	DLL3	Thoracic						
ZW239 Trispecific TCE | TriTCECo-Stim	Azymetric™, EFECT™, TriTCE Co-Stim	CLDN18.2	Digestive System						
ZW335 Trispecific TCE | TriTCE Co-Stim	Azymetric™, EFECT™, TriTCE Co-Stim	Undisclosed	Colorectal Cancer						
ZW1953 Logic-gated TCE | TriTCE Co-Stim	Azymetric™, EFECT™, TriTCE Co-Stim	Undisclosed	AML						
ZW437 Trispecific TCE | TriTCE Co-Stim	Azymetric™, EFECT™, TriTCE Co-Stim	Undisclosed	Multi-indication solid tumor						
ZW463 Trispecific TCE | TriTCE Co-Stim	Azymetric™, EFECT™, TriTCE Co-Stim	Undisclosed	Prostate Cancer						
Novel Target TriTCE Co-Stim Trispecific TCE | TriTCE Co-Stim	Azymetric™, EFECT™, TriTCE Co-Stim	Undisclosed	Multi-indication solid tumor						

ZW209

Trispecific T cell engager (TriTCE) Designed to Target DLL3-expressing Solid Tumors



Expected Phase 1 Initiation, in collaboration with Roche, in 2026.

Optimized design

- Potential first-in-class TriTCE Co-Stim targeting eradication of DLL3-expressing tumor cells through simultaneous engagement of CD3 and CD28 on T cells
- Optimized DLL3, CD3, CD28 binding affinities and coordinated binding geometry using Azymetric™ and EFECT™ platforms
- Leverages obligate cis-T cell binding and conditional CD28 engagement to prevent unintended T cell activation and T cell fratricide, while enabling tumor-targeted cytotoxicity

Differentiated profile

- Superior in vitro and in vivo pharmacology profile relative to DLL3 x CD3 bispecifics including Tarlatamab
- Integrated co-stimulation increases target-dependent T cell proliferation, survival and anti-tumor activity
- No T cell activation or cytokine activation in absence of DLL3 target cells, no T cell fratricide
- Well tolerated at high dose in nonhuman primates displaying antibody like pharmacokinetics

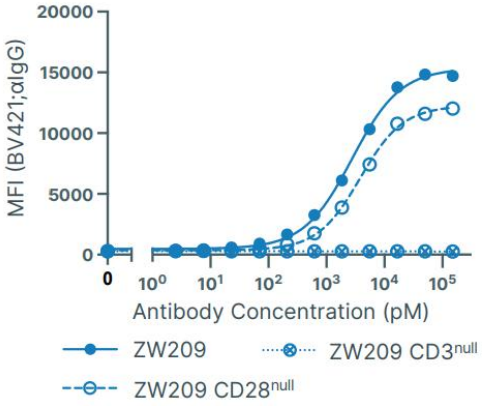
Significant patient need

- DLL3 is expressed on the surface of SCLC and other neuroendocrine tumors but rarely on the surface of normal cells
- SCLC accounts for about 15% of all lung cancer diagnoses in the U.S. each year[1]

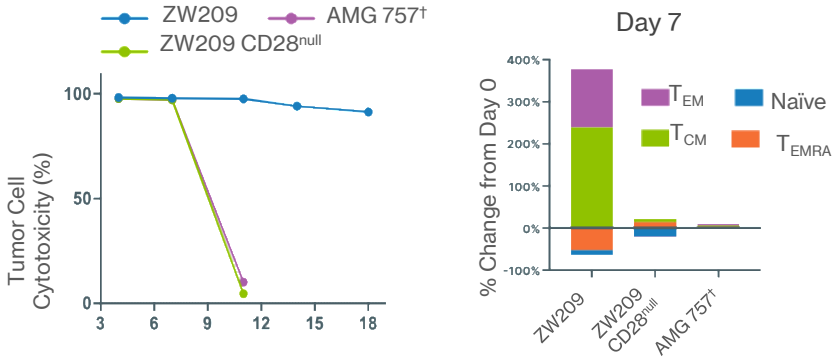
1. https://www.yalemedicine.org/conditions/small-cell-lung-cancer
DLL3: Delta-like ligand 3; SCLC: Small Cell Lung Cancer; TAA: tumor-associated antigen; TriTCE: Tri-specific T Cell Engager.

ZW209: DLL3 TCE designed for optimal T cell activation

Conditional binding of CD28, requiring co-engagement of CD3

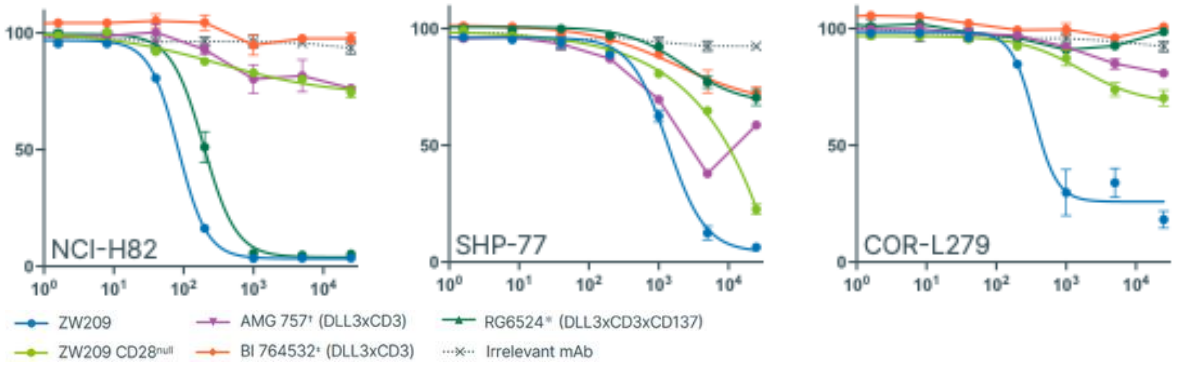


Sustained cytotoxicity relative to bispecific TCEs over repeated stimulations



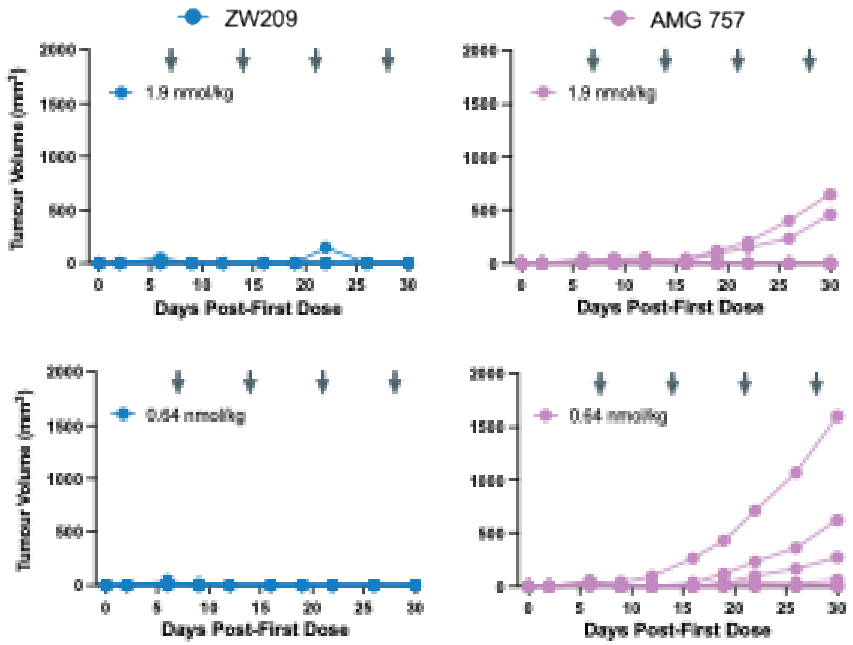
ZW209 supports sustained T cell fitness while expanding memory T cell populations

Improved in vitro potency on DLL3 tumor cells relative to benchmarks



ZW209 displays superior cytotoxicity relative to bispecific and trispecific clinical TCE benchmarks across multiple DLL3-positive SCLC tumor cell lines in assays with low E:T ratio (E:T = 1:4)

Anti-tumor activity in mouse tumor models



ZW209 exhibits in vivo anti-tumor activity in an admixture NCI-H82 xenograft model

- No target-independent cytokine release in PBMC donor-based solid or liquid phase assays
- Well tolerated in human immune engrafted mouse model and NHP with no elevated systemic cytokines. Displays antibody like PK.

Lau D et al., Abstract #7318 presented at AACR 2025; mAb: monoclonal antibody; TCEs: T Cell Engagers. AMG 757/tarlatamab

ZW191: New Clinical Data

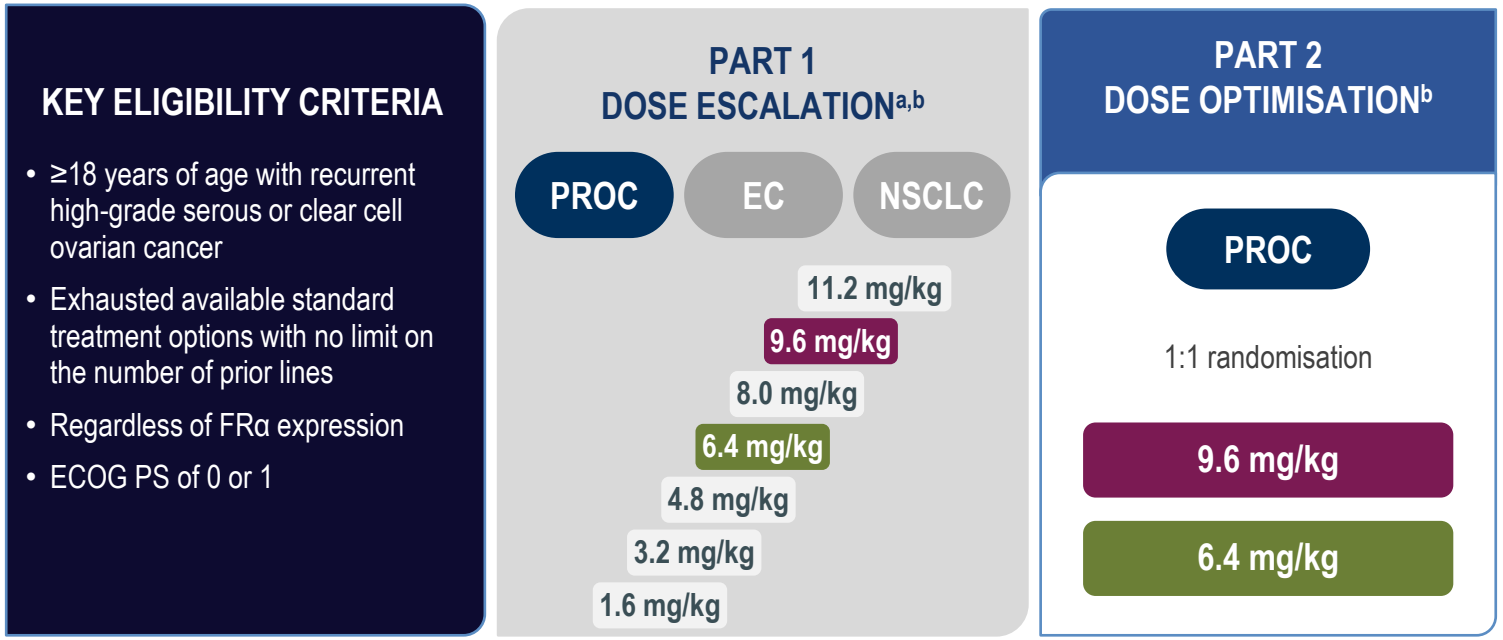


Sabeen Mekan

Chief Medical Officer

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.

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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+.

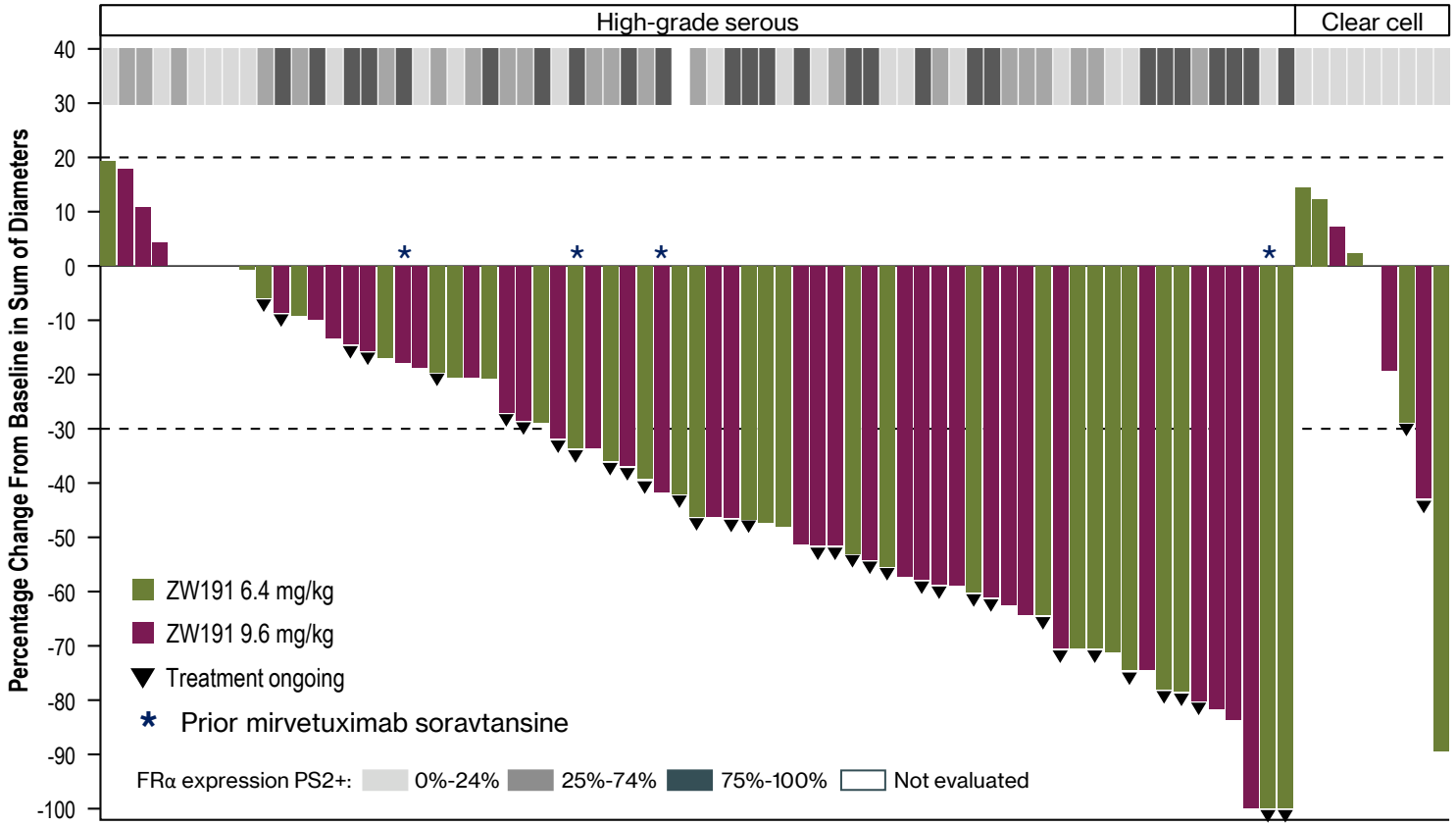
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cORR was 65% at 6.4 mg/kg and 55% at 9.6 mg/kg in high-grade serous PROC

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%.

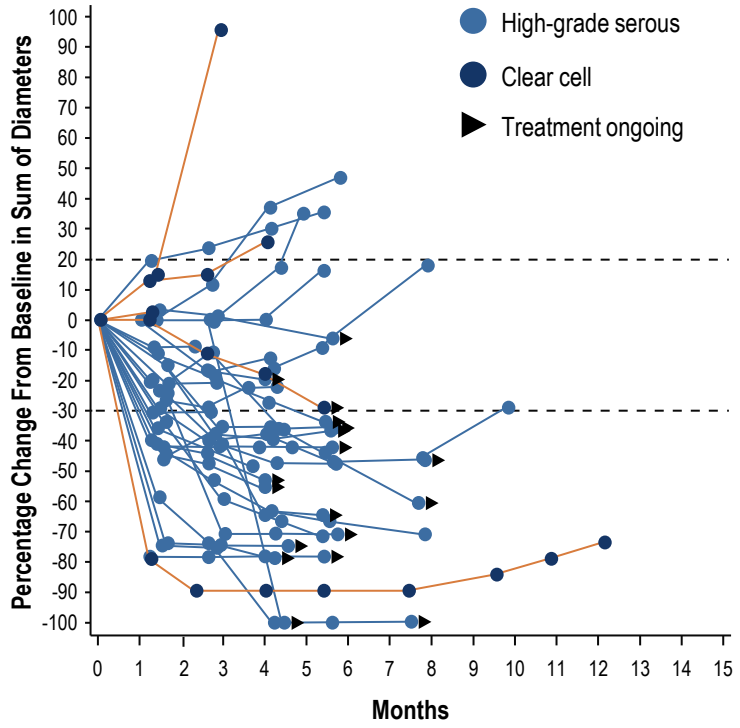
cORR: confirmed objective response rate; DCR: disease control rate; FRα: folate receptor alpha; HGSOC: high-grade serous ovarian carcinoma; PROC: platinum-resistant ovarian cancer; PS2+: positive score ≥2+.

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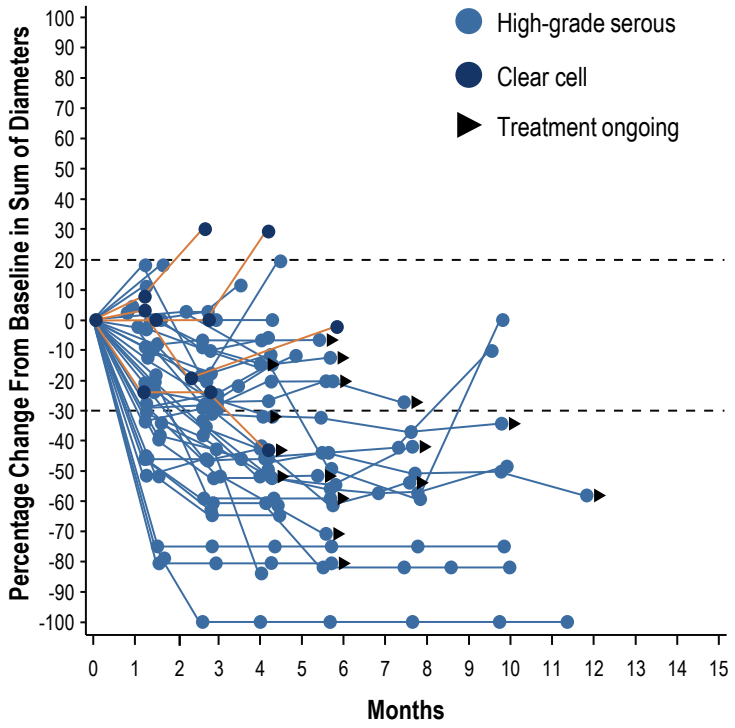
Responses to ZW191 were deep and durable

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).

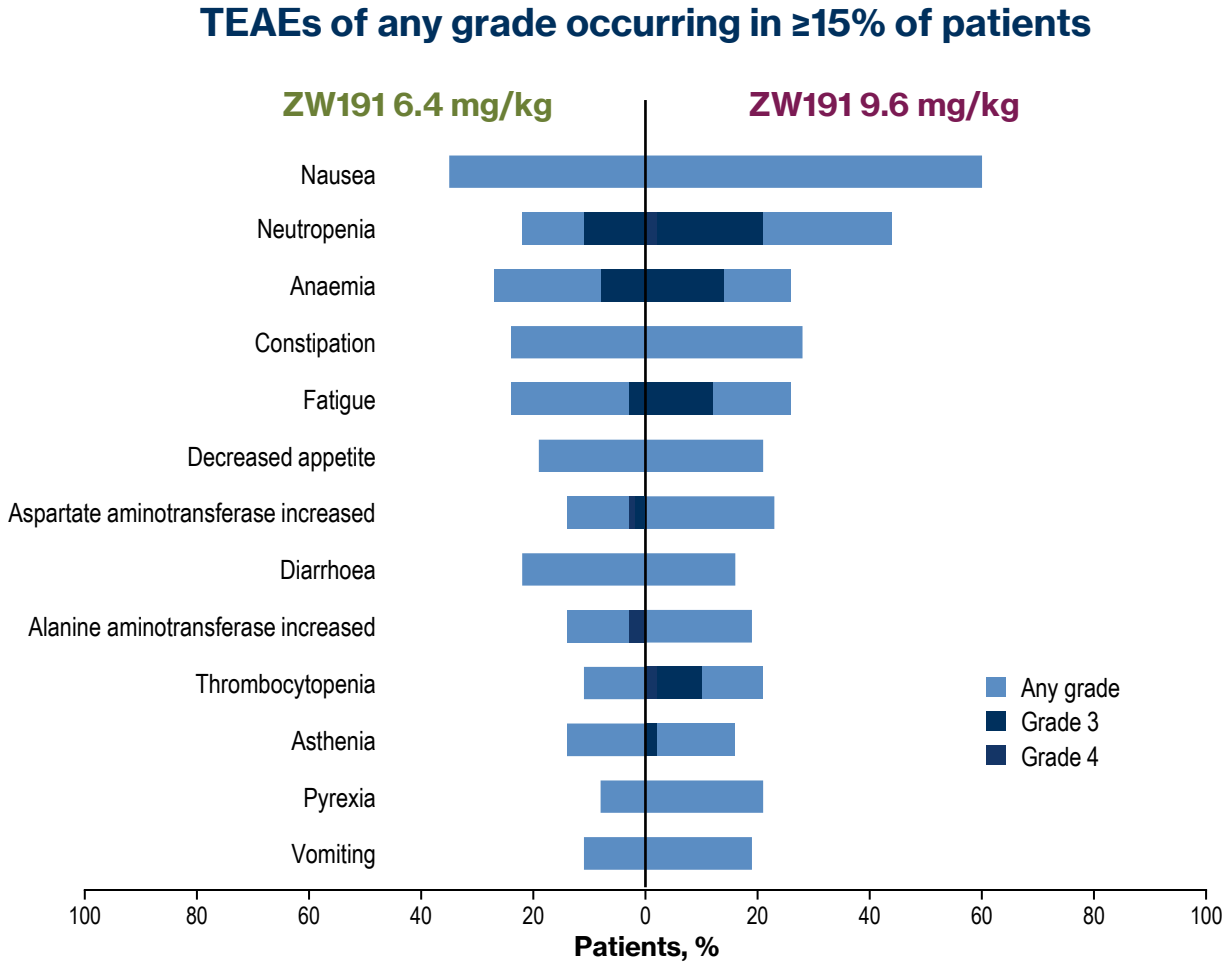
mDOR: median duration of response; mPFS: median progression-free survival; NR: not reached; PFS: progression-free survival; PROC: platinum-resistant ovarian cancer.

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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.

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Zymeworks originated programs highlighted at ESMO

Abstract	Title	Key Highlights
LBA40	Randomized dose optimization of ZW191 in heavily pretreated patients with platinum-resistant ovarian cancer (ZYME)	• cORR of 64.5% at the 6.4 mg/kg dose in patients with high-grade serous PROC • mDOR not yet reached at either dose level at median 7 months follow-up, with six-month PFS rate of 61% in both groups • Favorable tolerability profile, particularly at 6.4 mg/kg, supports continued clinical development in partnership or through a strategic collaboration
LBA79	Zanidatamab (zani) + chemotherapy (CT) ± tislelizumab (TIS) for first-line (1L) HER2-positive (HER2+) advanced/metastatic gastroesophageal adenocarcinoma (mGEA): Second interim analysis (IA) from HERIZON-GEA-01 (JAZZ)	• Nearly 40% of patients alive at three years with Ziihera plus tislelizumab and chemotherapy, irrespective of PD-L1 status, achieving a median OS of 27 months • Mature HERIZON-GEA-01 results show Ziihera plus chemotherapy delivered statistically significant and clinically meaningful OS benefit, reducing the rate of death by 24% versus trastuzumab plus chemotherapy • Median OS reached 27.0 months (95% confidence interval [CI]: 23.7–32.2), the longest reported in a Phase 3 trial in this setting. The Ziihera plus tislelizumab and chemotherapy regimen reduced the risk of death by 35% (hazard ratio [HR] 0.65; 95% CI: 0.52–0.80), improving from an HR of 0.72 at the first interim analysis.
2946P	Exposure-Adjusted Analyses of Safety Patterns in HERIZON-GEA-01: Zanidatamab With and Without Tislelizumab and Chemotherapy in 1L HER2-Positive Metastatic Gastroesophageal Adenocarcinoma	• In the exposure-adjusted event rate analysis, after accounting for differences in treatment exposure, all grade and grade ≥3 diarrhea TEAE rates were generally comparable between the zanidatamab + tislelizumab + Chemotherapy and zanidatamab + CT arms • In the per-cycle analysis, diarrhea TEAE incidence generally decreased over successive treatment cycles, during which CT could be reduced or discontinued per protocol or standard of care –TEAEs leading to zanidatamab or trastuzumab discontinuation also generally decreased over successive cycles in each treatment arm

Closing



Adam Schayowitz

Head of R&D

Executing on a model that combines R&D and acquisitions to compound value for shareholders

Early-stage partnering provides funding for future R&D and shared risk profile

1

Immediate revenue

Upfronts and development milestones

2

Strategic validation

Early-stage partnering and shared risk

3

Compounding platform

Commercial milestones and future royalties

R&D provides upside optionality

1

Ongoing pipeline development

- ZW191 & ZW251 Phase 1 trials

2

Partnerships & Spinouts

Evaluating opportunities both within wholly owned pipeline and acquired assets from Theravance Biopharma

3

Continued innovation in R&D

Pan-RAS ADC platform unveiled with three new candidates

Q&A



Adam Schayowitz
EVP & Head of R&D



Paul Moore
Chief Scientific Officer



Sabeen Mekan
Chief Medical Officer



Ken Galbraith
Chair & Chief Executive Officer