Design of ZW191: preclinical insights and clinical potential

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World ADC London
February 25, 2026

Zymeworks is a global clinical stage biotechnology company

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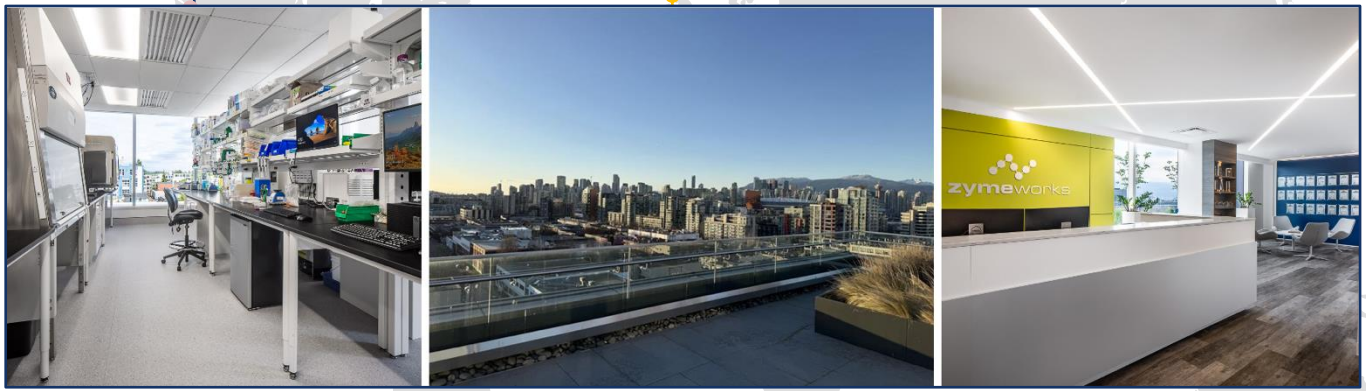
Vancouver, BC

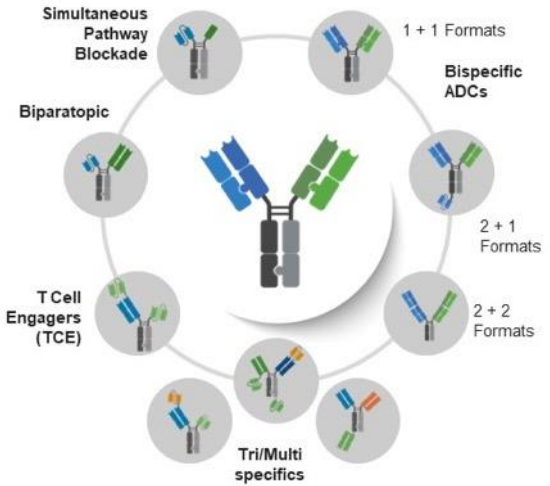
R&D labs for ADCs & MSATs



Zymeworks R&D: pushing the boundaries of antibody-based therapeutics through multispecifics and antibody drug conjugates

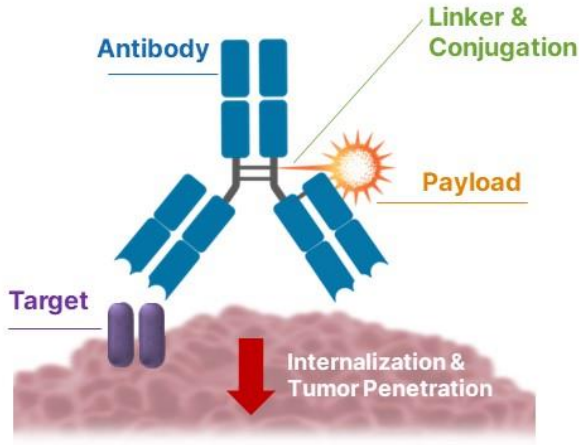
MULTISPECIFIC ANTIBODIES

Unlocking new biology and therapeutic possibilities through optimal design and format



ANTIBODY-DRUG CONJUGATES

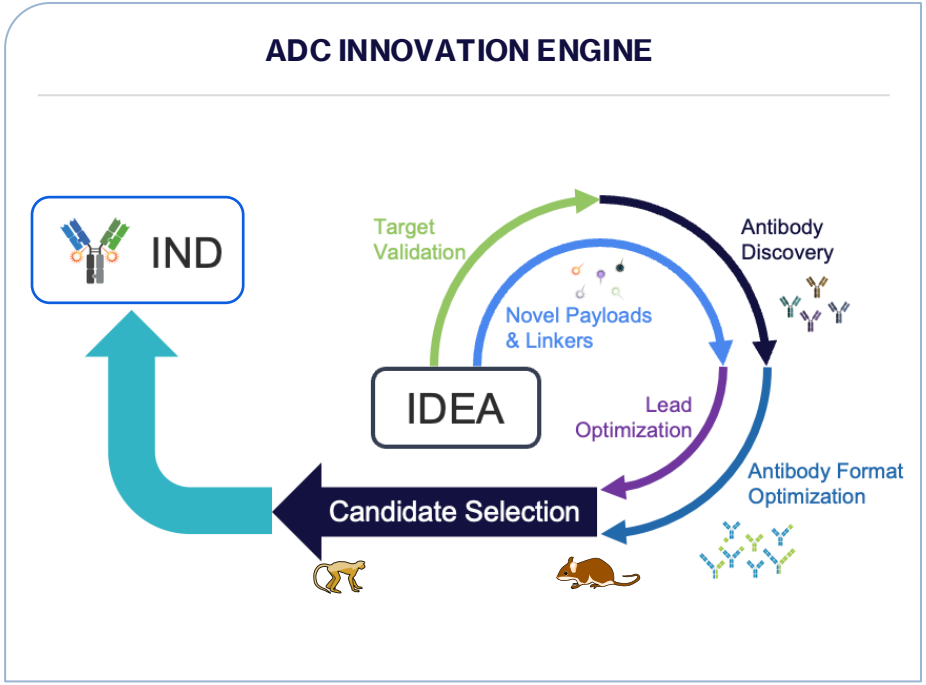
Utilizing antibodies to more effectively deliver small molecules through optimal linker-payload design and antibody format



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	Digestive System (HCC)			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					
Solid Tumor Oncology: Multispecific Antibody Therapeutics (MSAT)								
Zanidatamab Bispecific	Azymetric™	HER2	Multiple indications			Development partners: Jazz Pharmaceuticals and BeOne		
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 2026			
ZW1572 Dual Cytokine Blocker	Azymetric™ Hetero-Fab | YTE	IL4Rα x IL-31						

Integrated innovation engine to generate fit-for-purpose ADCs



Target Validation	• **Unbiased fit-for-purpose** target identification workflow • Pursuit of **novel targets** for broad therapeutic application
Antibody Discovery	• Multiple species & immunization strategies • Antibodies selected for **optimal ADC properties**
Novel Payload Development	• Payload mechanisms **tailored to priority indications** • Emphasis on **drug-like properties** of payloads
Format Optimization	• Innovating across **multiple antibody formats** • Tuning valency, format, and paratope to optimize engagement

Integrated ADC team with expertise across all facets of ADC design

Stuart Barnscher
Senior Director,
Preclinical Programs
ADC Therapeutic
Development

Jamie Rich, PhD
Senior Director,
Technology
ADC Therapeutic
Development

Raffaele Colombo, PhD
Director Medicinal Chemistry

Dunja Urosev, PhD
Associate Director Antibody
Discovery & Engineering

Sam Lawn, PhD
Principal Scientist & Group Lead
In Vivo Biology & PK

Laurence Madera, PhD
Principal Scientist & Group Lead
Target Validation

Luying Yang, PhD
Sr. Scientist & Group Lead
Analytics

Andrea Hernandez, BSc
Sr. Scientist & Group Lead
In Vitro Biology

Vincent Fung, BSc
Scientist & Group Lead
Bioconjugation

Select Publications

"Design and evaluation of ZD06519, a novel camptothecin payload for antibody drug conjugates"; M.E. Petersen et al, *Mol. Cancer Ther.*, 2024, 23:606-618.

"The Journey of Antibody Drug Conjugates: Lessons Learned from 40 Years of Development"; R. Colombo et al, *Cancer Discov.*, 2024, 14(11): 2089-2108.

"The Therapeutic Window of Antibody Drug Conjugates: A Dogma in Need of Revision"; R. Colombo and J.R. Rich, *Cancer Cell*, 2022, 40(11):1255-1263.

"ZW191, a FRα-targeted topoisomerase 1 inhibitor ADC with a differentiated antitumor efficacy and tolerability profile"; S. Lawn et al, *Clin. Cancer Res.*, 2026, in press.

"ZW327, A Topoisomerase-1 Inhibitor ADC Designed to Target Ly6E-Expressing Tumors"; S.D. Barnscher, 16th World ADC San Diego, November 5, 2025.

Extensive portfolio of ADC assets

6+ ADC programs at various stages of development

- **ZW191:** Ph1 development
- **ZW251:** Ph1 development
- **ZW220:** IND submission-ready
- **ZW327:** PCD-ready
- **ZW318:** PCD-ready
- **ZW418:** pre-candidate nomination
- **Multiple early & late discovery programs**

7+ ADC platform technologies

- TOPO1i drug-linker technology
- RASi drug-linker technology
- PreCysion site specific conjugation
- Biparatopic ADCs
- Bispecific ADCs
- TLR7 agonist drug-linker technology
- Auristatin & Hemiasterlin drug-linker technology

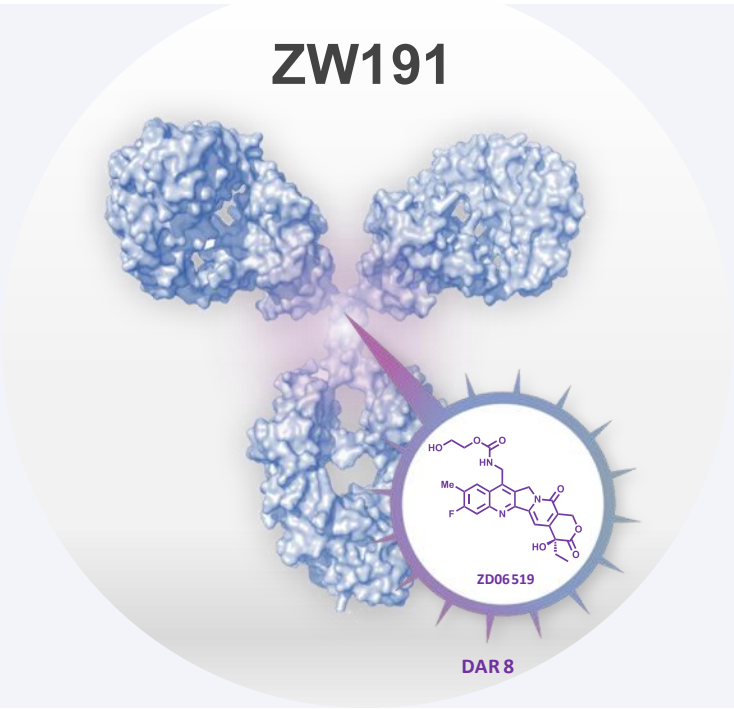
20+ ADC patent families

- **Antibodies and ADCs: 13**
- **Linkers & payloads: 6**
- **Site specific conjugation: 1**

ZW191: A FRα-targeting Topoisomerase-1 Inhibitor ADC

Optimized design

- Novel topoisomerase-1 inhibitor[1]
- **Moderate potency** (1-10 nM)[1]
- Peptide **cleavable linker**[1]
- **Validated Ab-linker stability**[3,4]
- Strong **bystander activity**[1,2,3]
- **High drug-to-antibody ratio** of 8[2]
- IgG1 selected for **strong internalization**[2,3]



Differentiated profile

- Phase 1 trial preliminary efficacy data, shows 64% overall response rate in gynecological cancers at doses ≥6.4mg/kg[5]
- Manageable safety profile, with low rates of dose modifications, dose delays, and Grade ≥3 TRAE[5]
- Opportunity to treat broader range of FRα-expressing cancers

1 M.E. Petersen, M.G. Brant et al, Mol Cancer Ther 2024; 23(5):606-618.
2 Lawn S et al. Abstract # 2641 presented at American Association for Cancer Research annual meeting 2023.
3 Lawn S. et al. Abstract # 1862 presented at American Association for Cancer Research annual meeting 2024
4 Colombo R. Mol Cancer Ther (2023) 22 (12_Supplement): IA003.
5 LoRusso P. et al. Abstract # LB-A011 Presented at AACR-NCI-EORTC 2025;

ZW191: A FRα-targeting Topoisomerase-1 Inhibitor ADC

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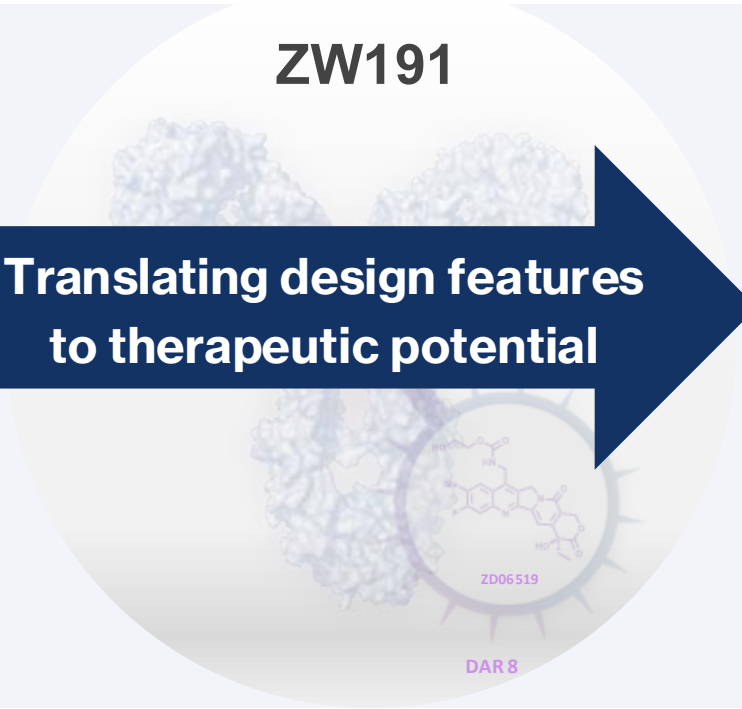
ZW191



Translating design features to therapeutic potential

Differentiated profile

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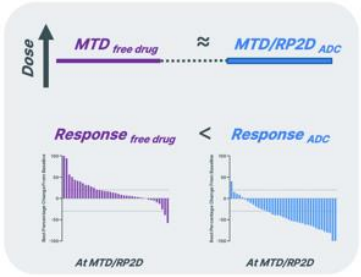
ZW191's TOPO1i payload was selected for moderate potency and bystander activity

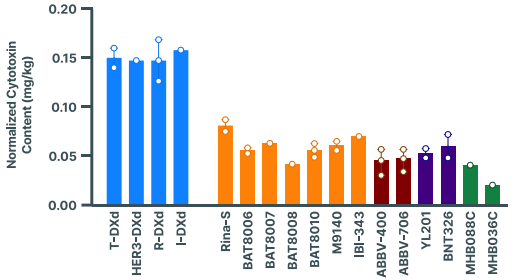
Hypotheses:

- ADC dose and toxicity profile is governed *primarily* by payload MoA and potency ∴ moderate payload potency can drive higher ADC doses to saturate target and efficiently penetrate solid tumors
- Bystander activity may be critical to treat low and heterogenous antigen-expressing tumors

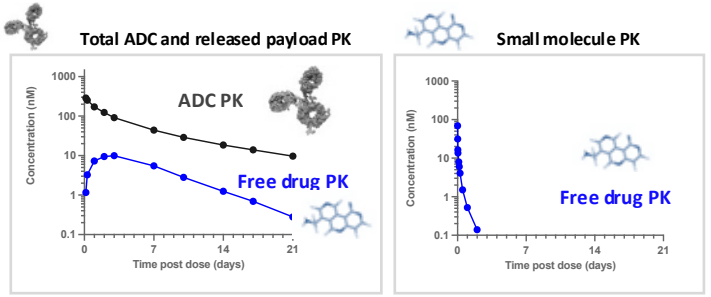
1 Conjugation does not improve payload MTD[1]



2 More potent payloads limit protein dose[2]

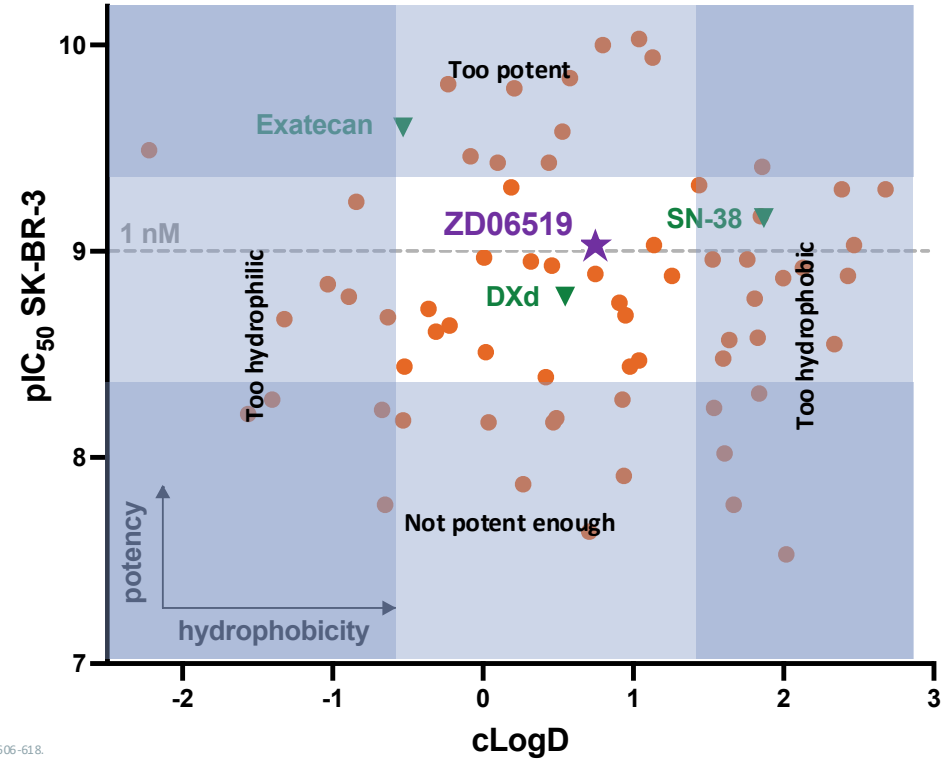


3 Bystander activity is a key payload feature[2]



1. R. Colombo and J.R. Rich, Cancer Cell 2022, 40(11):1255-1263; 2. R. Colombo et al, Cancer Discov 2024, 14(11):2089–2108

The ZW191 payload, ZD06519, was selected from >100 possible candidates with a range of potency and polarity



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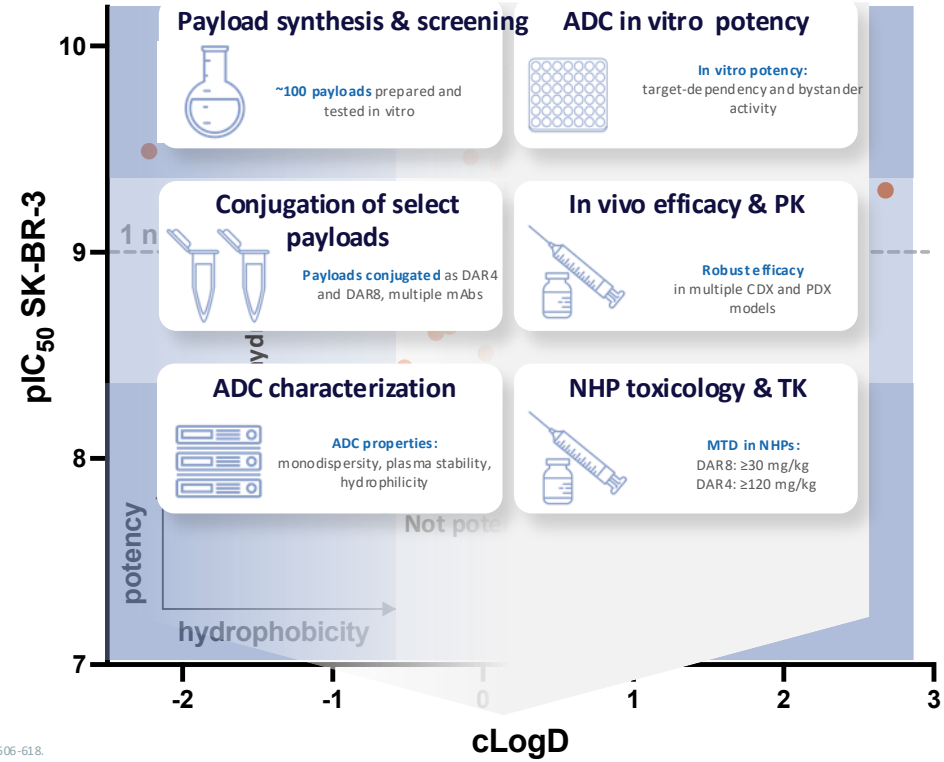
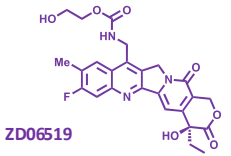
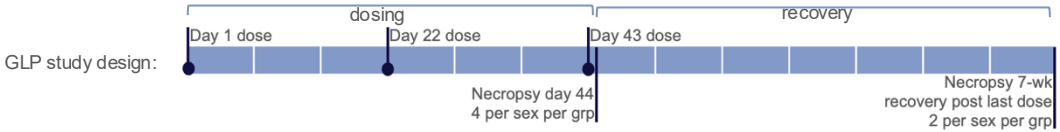


Lead selection and application



M.E. Petersen, M.G. Brant et al, Mol Cancer Ther 2024, 23(5):606-618.

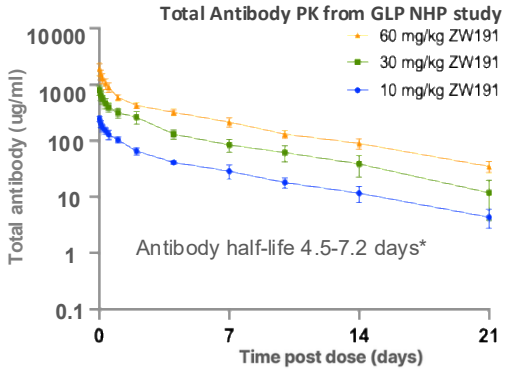
ZW191 is well tolerated in non-human primates



Dose mg/kg (Q3W x3)	n	Clinical observations	Histopathology	Clinical Chemistry	Hematology & coagulation	Adverse effects	HNSTD
10	4F, 4M	None	None	↑ AST, ALT (n=1)	No effects	None	60 mg/kg
30	6F, 6M	Emesis/vomitus	↓ Thymic lymphocytes; ↓ PACS (n=2)	↑ AST, ALT			
60	6F, 6M	Liquid/discolored feces; Emesis/vomitus; ↓ activity level (n=1)	↓ Thymic lymphocytes; ↓ PACS (n=1)	↑ AST, ALT ↑ CK			

- No mortality or body weight effects
- No ophthalmic effects
- All effects were non-adverse and reversible
- **HNSTD in NHP of 60 mg/kg**

ZW191 has a favorable pharmacokinetic (PK) profile



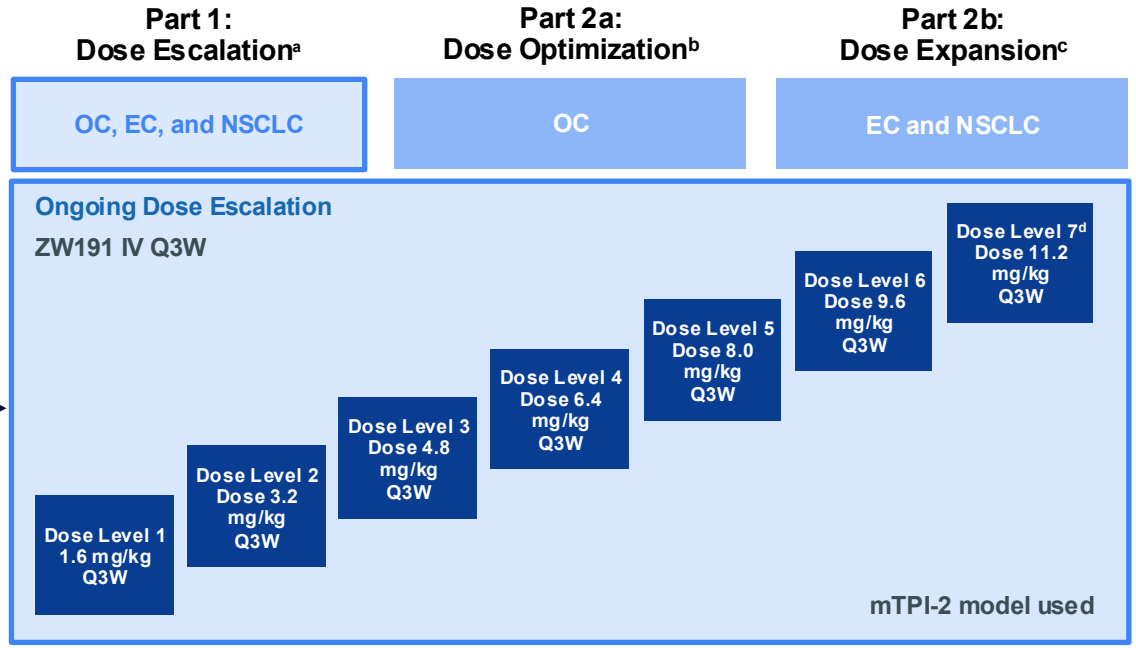
- **ZW191 displays favorable PK** and is **well tolerated in NHP at exposure levels** above those projected to be efficacious
- A **best-in-class HNSTD** provides flexibility to **explore a wider dose range in the first-in-human Phase 1 trial**

ALT: alanine aminotransferase; AST: aspartate aminotransferase; CK: creatine kinase; GMP: good manufacturing practices; HNSTD: highest non-severely toxic dose; MTD: maximum tolerated dose; NHP: non-human primates; PACS: pancreatic acinar cell secretion.
* across dose levels and dose cycles

ZWI-ZW191-101 Study Design

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]
- FRα expression evaluated retrospectively
- ECOG PS score of 0 or 1



High doses of ZW191 were achievable as predicted from selection of moderate payload potency and high HNSTD from GLP NHP study

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; FRα: 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

ZW191 demonstrates a favorable clinical safety profile
Contribution of moderate payload potency

TRAE, n (%) Data cutoff: September 10, 2025	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)**

No serious TRAEs, discontinuations due to AEs, or deaths reported

Presented at 2025 AACR-NCI-EORTC Conference on Molecular Targets and Cancer Therapeutics

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.
LoRusso P. et al. Abstract # LB-A011 Presented at AACR-NCI-EORTC 2025.
DLT: dose-limiting toxicity; TRAE: treatment-related adverse event; AE: adverse event.

ZW191 Demonstrated a Favorable Clinical Safety Profile

Contribution of moderate payload potency

TRAEs of any Grade/Grade ≥3 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

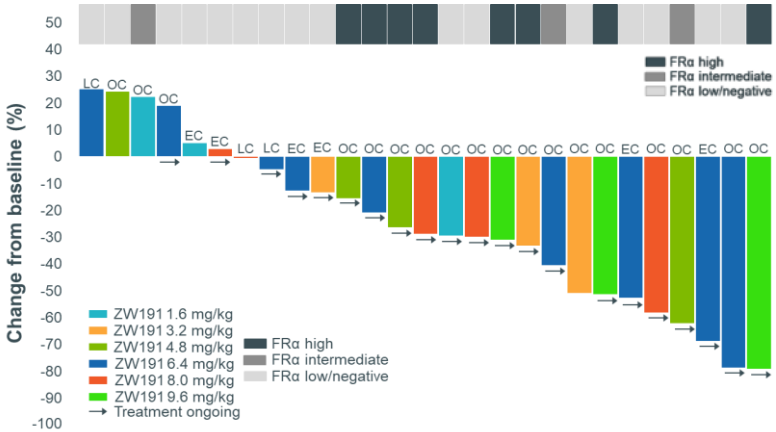
Data cutoff: September 10, 2025

7 participants reported Grade ≥3 TRAEs; the most common were anemia (10%), neutropenia (5%), and thrombocytopenia (5%)

ZWI-ZW191-101 | preliminary clinical results
Contribution of moderate payload potency

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

Data cutoff: September 10, 2025



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).

Preliminary efficacy for response-evaluable participants with gynecological cancer

Data cutoff: September 10, 2025

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)

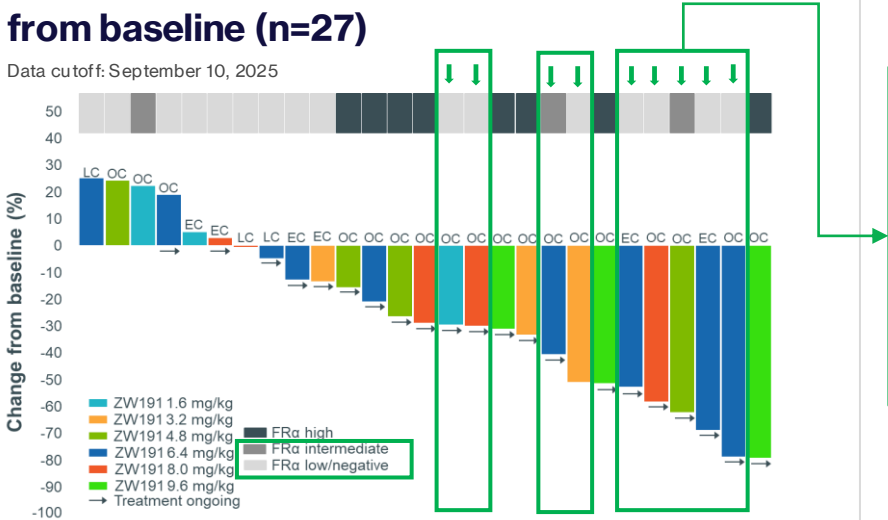
a. PR includes confirmed and unconfirmed. The 5 participants with unconfirmed PR are all awaiting confirmation.
Note: Percentages are out of gynecological cancer (OC and EC) participants.

Higher doses, through selection of moderate payload potency, may be driving better responses
64% ORR at doses of 6.4 – 9.6 mg/kg

LoRusso P. et al. Abstract # LB-A011 Presented at AACR-NCI-EORTC 2025.
EC: endometrial cancer; FRα: folate receptor alpha; LC: non-small cell lung cancer; OC: ovarian cancer; RECIST v1.1: Response Evaluation Criteria in Solid Tumors, version 1.1; cPR: confirmed partial response; EC, endometrial cancer; OC, ovarian cancer; PD: progressive disease; PR: partial response; SD: stable disease

ZWI-ZW191-101 | preliminary clinical results
Contribution of bystander active payload

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



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Response based on RECIST v1.1 (response and progression defined as -30% and +20% change from baseline, respectively).

Preliminary efficacy for response-evaluable participants with gynecological cancer

- Anti-tumor activity is observed across all FRα expression levels
  - Activity observed in intermediate FRα expressing tumors (H-score: 75-199)
  - Activity observed in low/negative FRα expressing tumors (H-score: 0-74)
- Opportunity to treat broader range of FRα-expressing cancers

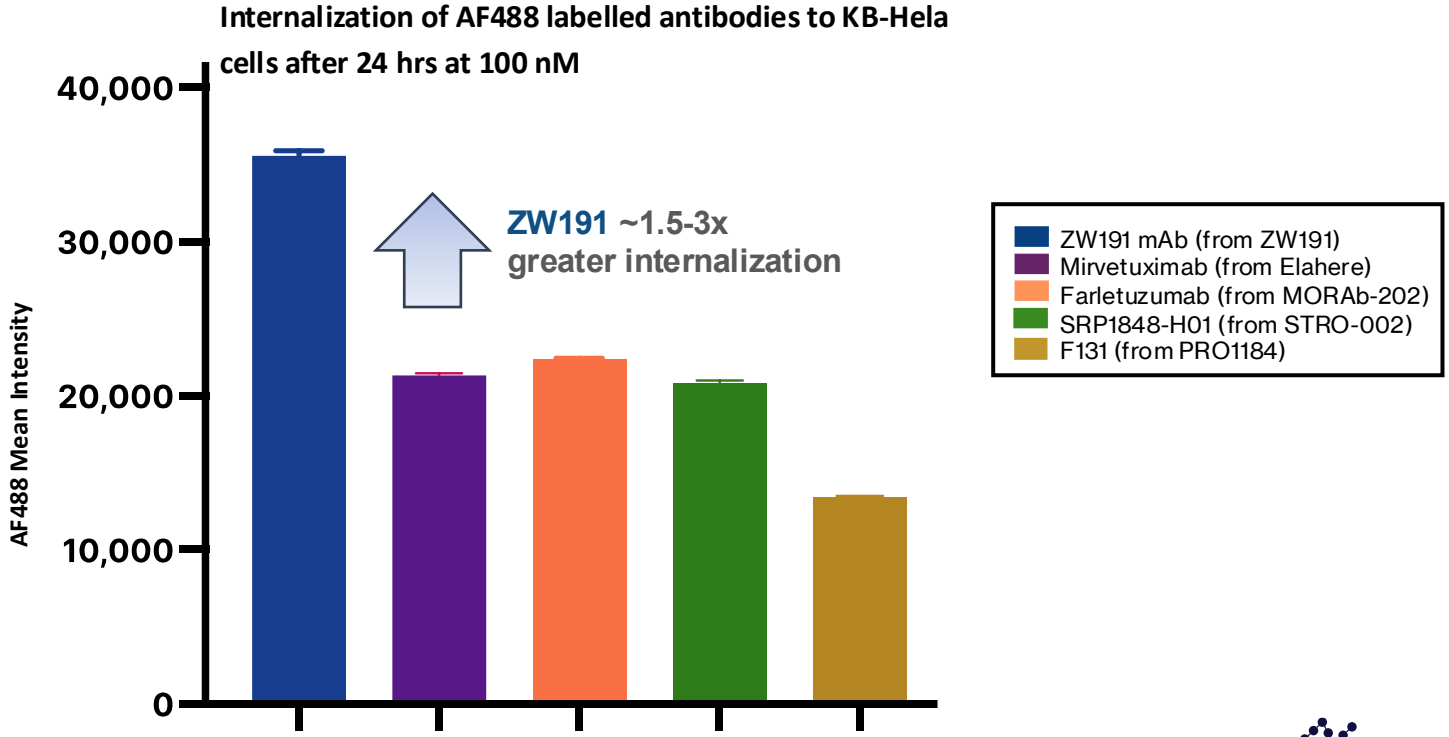
FRα expression was measured by immunohistochemistry on archival or newly collected formalin-fixed, paraffin-embedded biopsies with the VENTANA® FOLR1 (FOLR1-2.1) assay

Payload bystander activity may contribute to the activity observed in FRα intermediate and FRα low/negative tumors

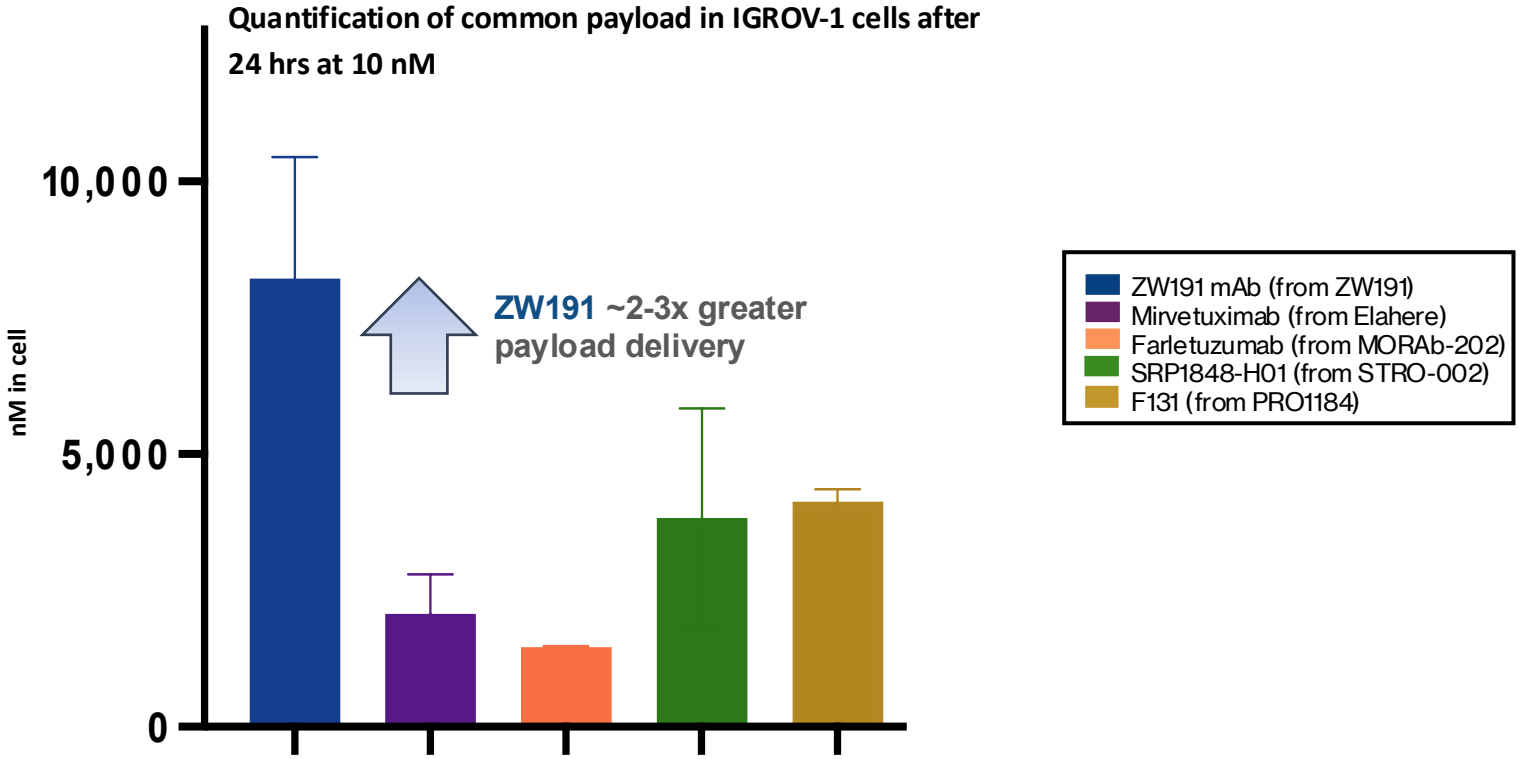
LoRusso P. et al. Abstract # LB-A011 Presented at AACR-NCI-EORTC 2025.
EC: endometrial cancer; FRα: folate receptor alpha; LC: non-small cell lung cancer; OC: ovarian cancer; RECIST v1.1: Response Evaluation Criteria in Solid Tumors, version 1.1; cPR: confirmed partial response; EC, endometrial cancer; OC, ovarian cancer; PD: progressive disease; PR: partial response; SD: stable disease

ZW191's antibody was selected for strong internalization

Hypothesis: greater levels of internalization may lead to activity in low expressing antigen settings and activity may be observed at doses below MTD

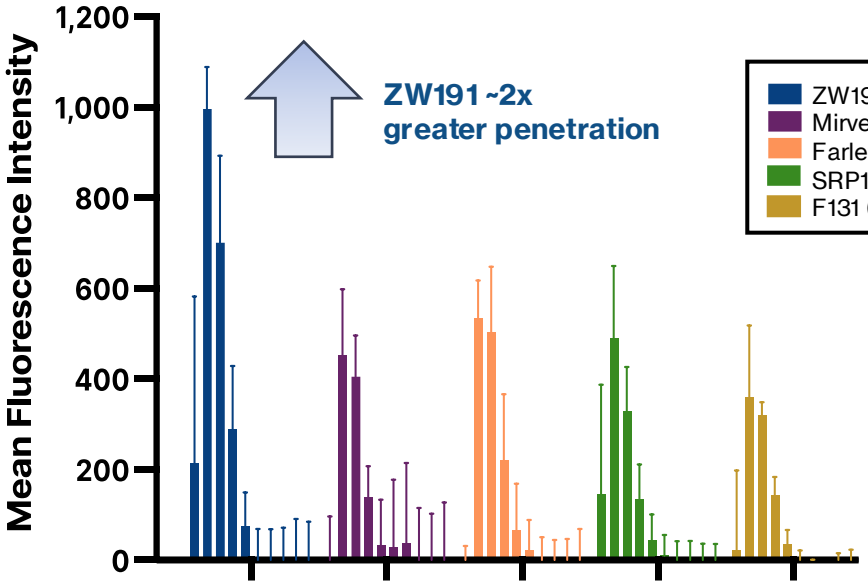


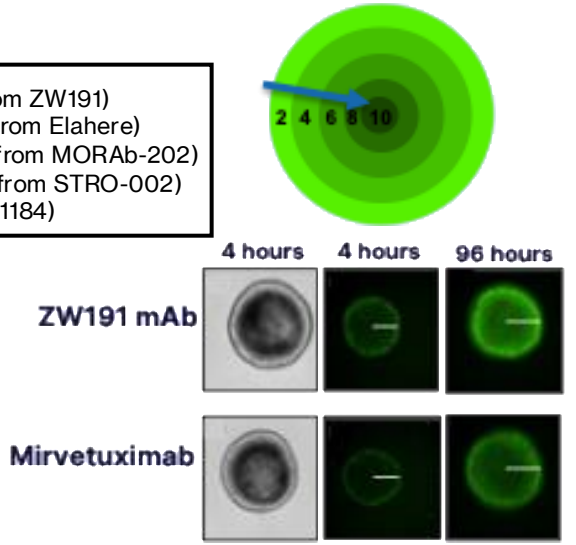
ZW191 internalization leads to payload delivery



ZW191's mAb demonstrates highly effective penetration to 3D tumor cell spheroids

Fluorescence AUC: **2300** 1100 1300 1100 900

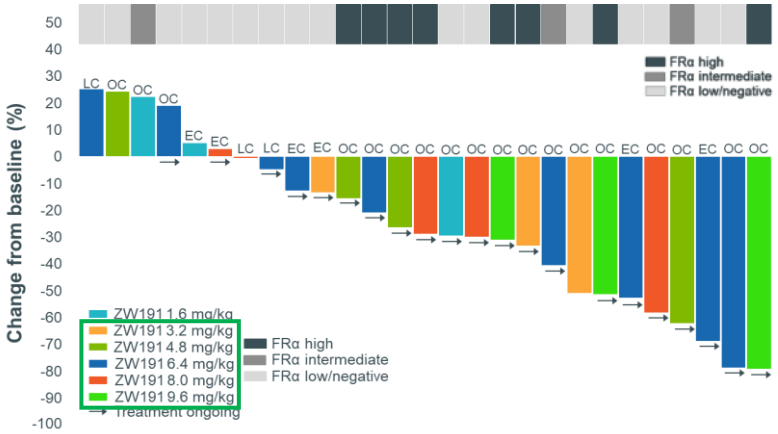




ZWI-ZW191-101 | preliminary clinical results
Contribution of strong internalizing antibody

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

Data cutoff: September 10, 2025



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).

Preliminary efficacy for response-evaluable participants with gynecological cancer

Data cutoff: September 10, 2025

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)

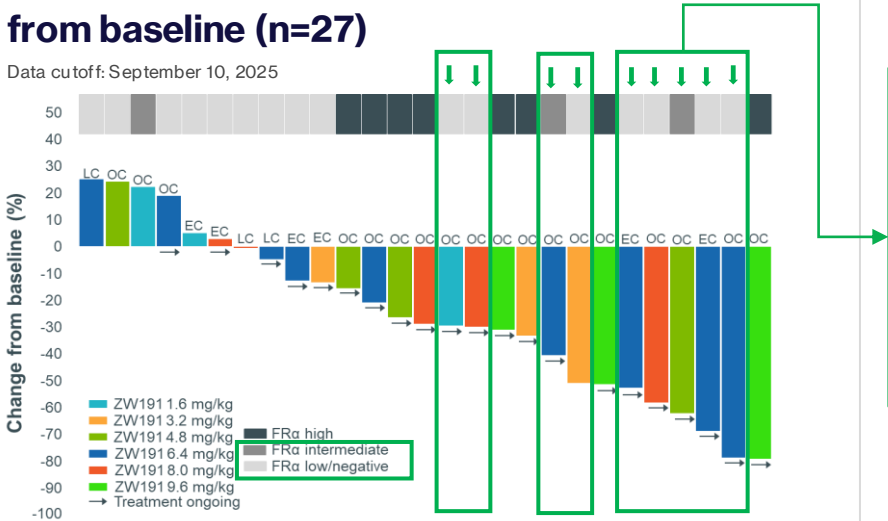
a. PR includes confirmed and unconfirmed. The 5 participants with unconfirmed PR are all awaiting confirmation.
Note: Percentages are out of gynecological cancer (OC and EC) participants.

Activity observed below 11.2 mg/kg MTD
Broad therapeutic window from 3.2mg/kg to 9.6 mg/kg

LoRusso P. et al. Abstract # LB-A011 Presented at AACR-NCI-EORTC 2025.
EC: endometrial cancer; FRα: folate receptor alpha; LC: non-small cell lung cancer; OC: ovarian cancer; RECIST v1.1: Response Evaluation Criteria in Solid Tumors, version 1.1; cPR: confirmed partial response; EC, endometrial cancer; OC, ovarian cancer; PD: progressive disease; PR: partial response; SD: stable disease

ZWI-ZW191-101 | preliminary clinical results
Contribution of strong internalizing antibody

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).

Preliminary efficacy for response-evaluable participants with gynecological cancer

- Anti-tumor activity is observed across all FRα expression levels
  - Activity observed in intermediate FRα expressing tumors (H-score: 75-199)
  - Activity observed in low/negative FRα expressing tumors (H-score: 0-74)
- Opportunity to treat broader range of FRα-expressing cancers

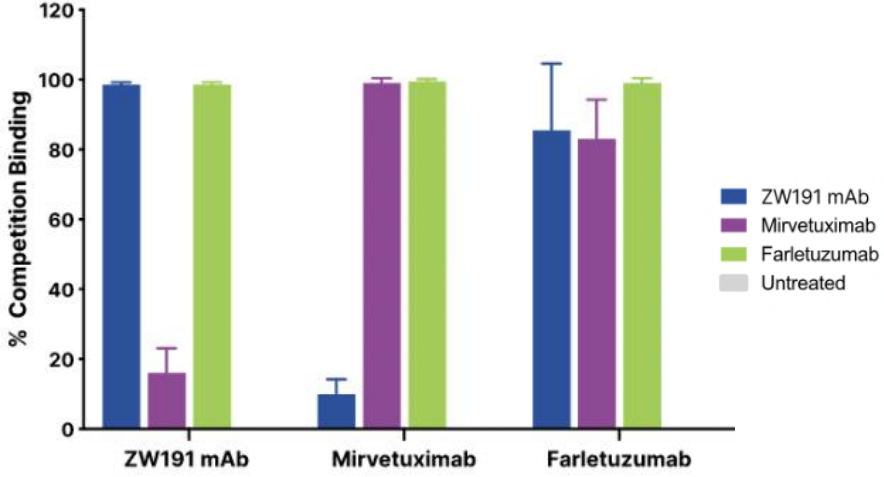
FRα expression was measured by immunohistochemistry on archival or newly collected formalin-fixed, paraffin-embedded biopsies with the VENTANA® FOLR1 (FOLR1-2.1) assay

Strong antibody internalization may contribute to the activity observed in FRα intermediate and FRα low/negative tumors

LoRusso P. et al. Abstract # LB-A011 Presented at AACR-NCI-EORTC 2025.
EC: endometrial cancer; FRα: folate receptor alpha; LC: non-small cell lung cancer; OC: ovarian cancer; RECIST v1.1: Response Evaluation Criteria in Solid Tumors, version 1.1; cPR: confirmed partial response; EC, endometrial cancer; OC, ovarian cancer; PD: progressive disease; PR: partial response; SD: stable disease

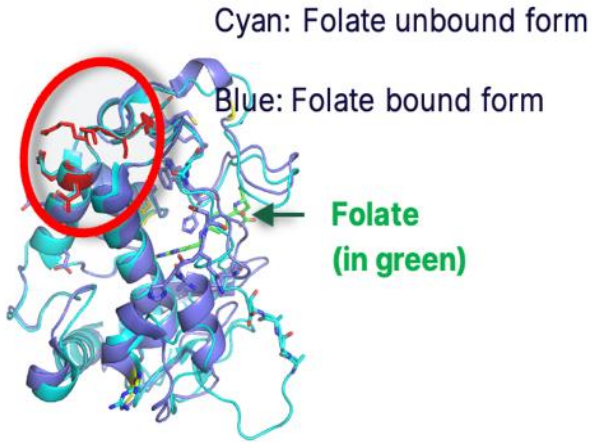
The ZW191 mAb binds to a unique epitope of FRα

ZW191 binds a distinct FRα epitope space



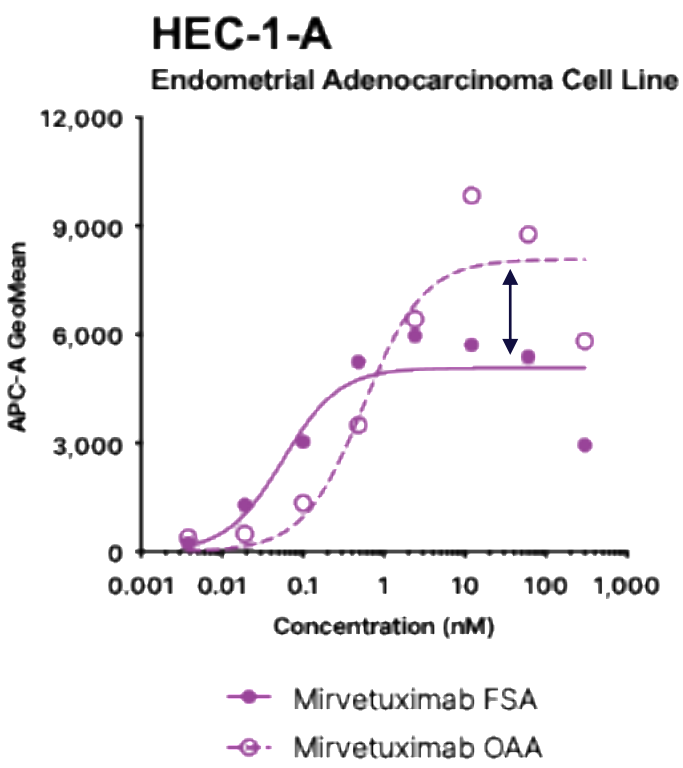
- ZW191 does not compete with MIRV
- ZW191 competes with farletuzumab but shows different competition with mirvetuximab

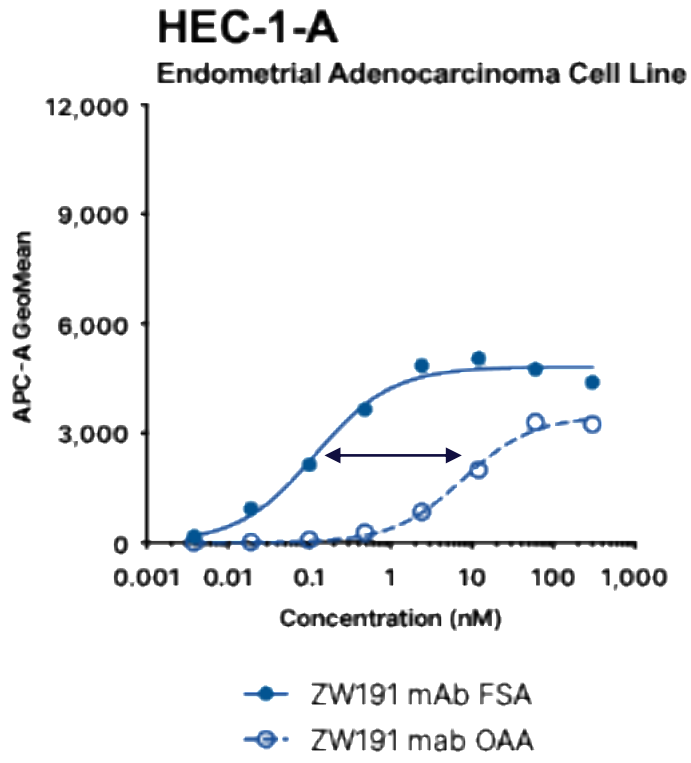
ZW191's FRα epitope at a molecular resolution



Determined by HDX, the ZW191 mAb targets an epitope of FRα that is unaffected by folate binding

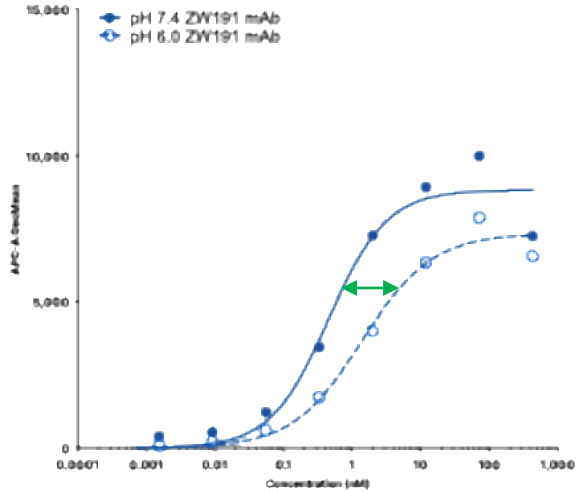
ZW191's mAb demonstrates a distinctive avidity driven binding profile to FRα



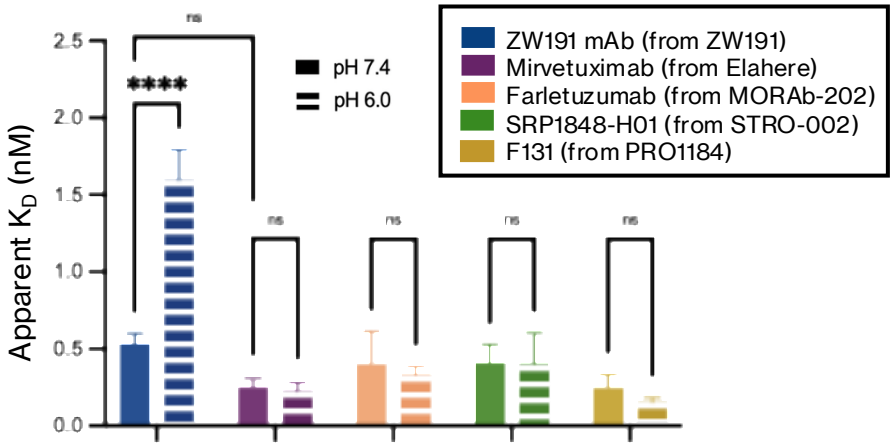


ZW191's mAb demonstrates a distinctive pH sensitive binding profile to FRα

Equilibrium binding profile of ZW191 at pH 7.4 and pH 6.0



Apparent K_D of ZW191 and competitor FRα binding mAbs at pH 7.4 and pH 6.0



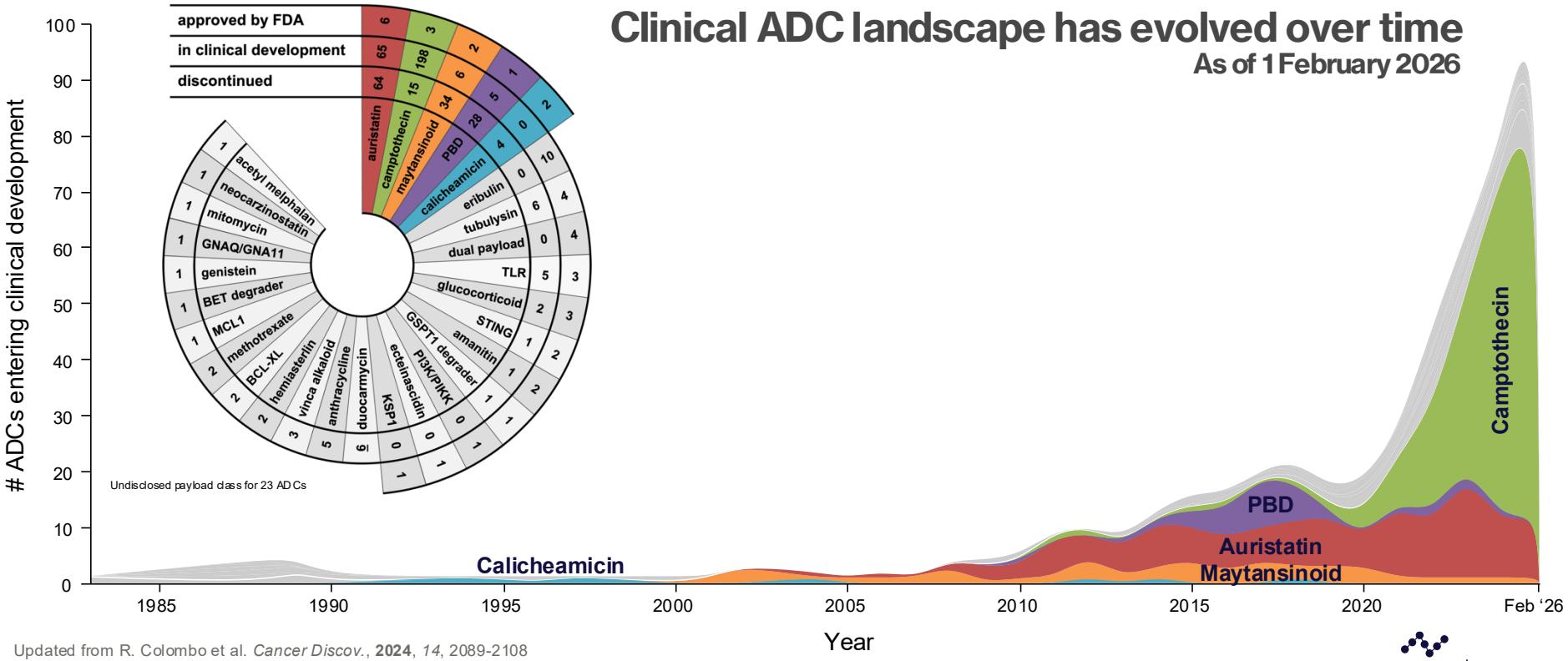
Target/antibody dissociation at lower pH may result in greater intracellular antibody accumulation, possibly due to altered antibody and target recycling following internalization[1]

1 Gera *et al*., Mol Cancer Ther (2024) 23 (9): 1282–1293.

ZW191: from design to clinical potential

- **Moderate payload potency selected for ZW191 contributes to the high MTD of 11.2 mg/kg and favorable safety profile**
  - Low rates of dose modifications, dose delays, and Grade ≥3 AEs
  - No discontinuations due to AEs
  - ORRs (uPR + cPR) between 6.4 mg/kg to 9.6 mg/kg were: **53%** (overall) and **64%** (GYN cancers)
  - Dose expansion at 6.4 mg/kg and 9.6 mg/kg
- **ZW191's strong internalizing antibody paired with a bystander active payload contribute to activity at doses below the MTD and activity in tumors with low/negative and intermediate FRα expression**
  - Preliminary efficacy is promising, starting at 3.2 mg/kg Q3W
  - Anti-tumor activity is observed across all FRα expression levels
  - Opportunity to treat broader range of FRα-expressing cancers

Novel payload development is a priority

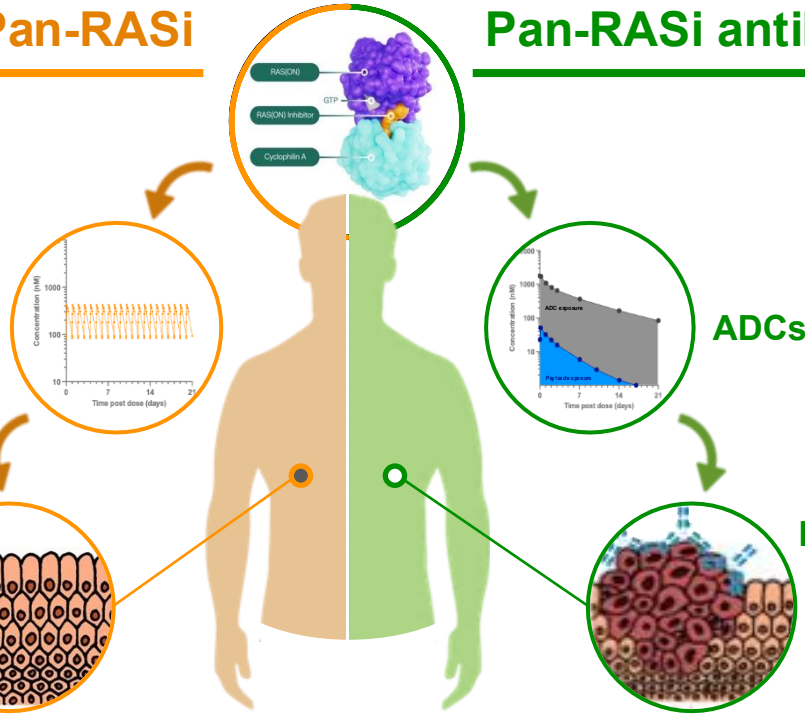


Updated from R. Colombo et al. *Cancer Discov.*, **2024**, *14*, 2089-2108

ADCs May Present an Improved Approach to Treatment of RAS-Driven Cancers

Small molecule Pan-RASi

Pan-RASi antibody conjugate



High daily oral dose

Side effects
(skin, stomatitis, GI tox)

ADCs: Improved tumor exposure

Rasi ADCs opportunities:

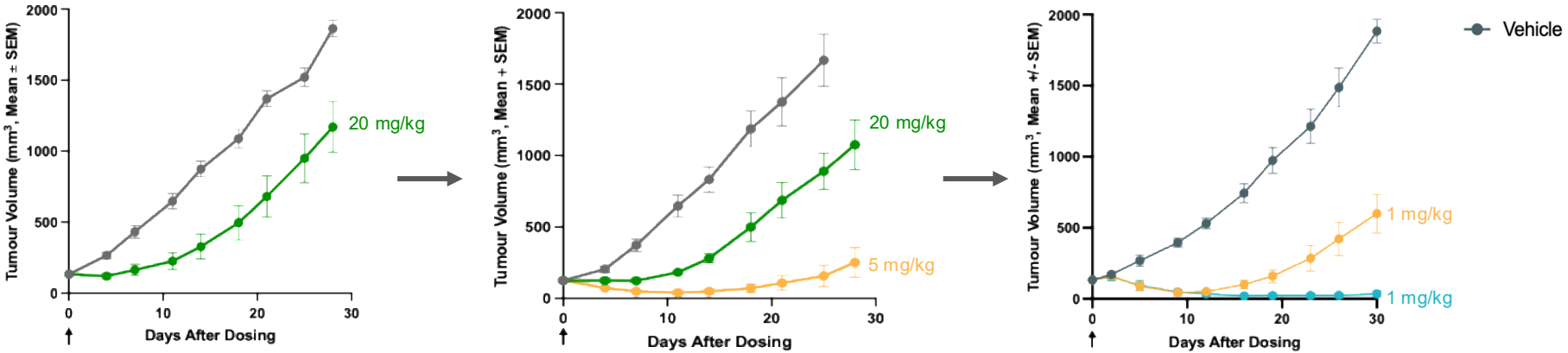
↑ Improved efficacy
↓ Reduced side effects
↑ Improved combination

Optimized RAS Inhibitor ADCs are Highly Active in RAS^{MUT} Xenograft Models

Pan-RASi ADCs:

- Potential application in NSCLC, PDAC, and CRC
- Optimal overlap between TAA expression and RAS-driven tumors

Lung Adenocarcinoma Model (KRAS G12C)



Proof of concept for Pan-RAS inhibitor ADC with clinically validated Pan-RASi

Iterative optimization yields Prototype ADC

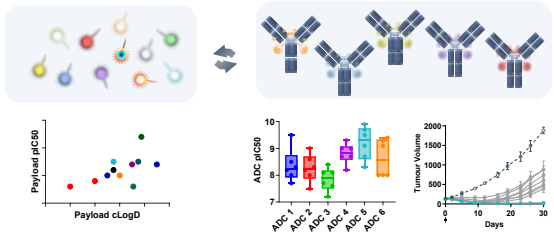
Lead drug linker selected

Platform Development → Three Pipeline Programs

Proof of concept for RASi ADC

Incorporates clinically validated Pan-RASi

Platform development



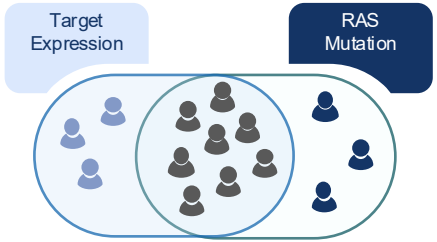
RASi ADC Features

- Novel, potent, bystander-capable pan-RASi
- Novel linkers optimized for favorable PK
- Anti-tumor activity in >20 CDX models
- Decreased RAS suppression in normal tissue
- Murine MTD >200 mg/kg, NHP proof of concept

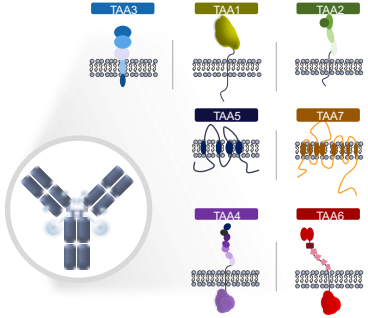
Platform Development

Program Development

Target expression and RAS mutational status



Target-mechanism compatibility



Final candidate selection

ZW418 PTK7 RASi ADC | DAR 8 | Biparatopic	RAS^{MUT} NSCLC
Program #2 TAA RASi ADC	RAS^{MUT} NSCLC, CRC, PDAC
Program #3 TAA RASi ADC	RAS^{MUT} PDAC

Acknowledgements

ADC Therapeutic Development
Zymeworks

Zymeworks Clinical team
- Clinical research
- Clinical operations

Zymeworks Translational team
- Clinical pharmacology
- Biomarkers

Q&A

Stuart Barnscher
Senior Director, ADC Therapeutic Development
Zymeworks