Making a Meaningful Difference

Accelerating the next generation of therapeutics to improve the standard of care for the most challenging diseases in cancer, autoimmune and inflammatory disease

May 2025

Nasdaq: ZYME | zymeworks.com

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Zymeworks: Global Biotech Focused on Targeted Therapies

Starting with Patients

- Focusing on **challenging, multi-factorial diseases with significant unmet medical needs**, including aggressive cancers with historically low survival rates and complex autoimmune and inflammatory disorders that remain difficult to treat
- Focused on **developing best-in-class multifunctional therapeutics** that hold the potential to optimize patient outcomes

Driven by Science & Technology

- Suite of **ADC technologies** combines the **precision of antibodies with the power of potent proprietary payloads** for targeted delivery to cells
- **Clinically validated proprietary MSAT technology, Azymetric™** and suite of MSAT technologies **enhance therapy precision, efficacy, and adaptability**, targeting complex disease mechanisms

Empowered by People

- **Robust leadership team** with decades of experience in drug discovery, development, and commercialization
- **Renowned scientists** and researchers in protein engineering, MSATs, and ADC technologies
- **Global scope**, operating across North America, Europe, and Asia
- **Productive and efficient organization** focused on transformative drug discovery with cash resources of approx. $321.6M[1]

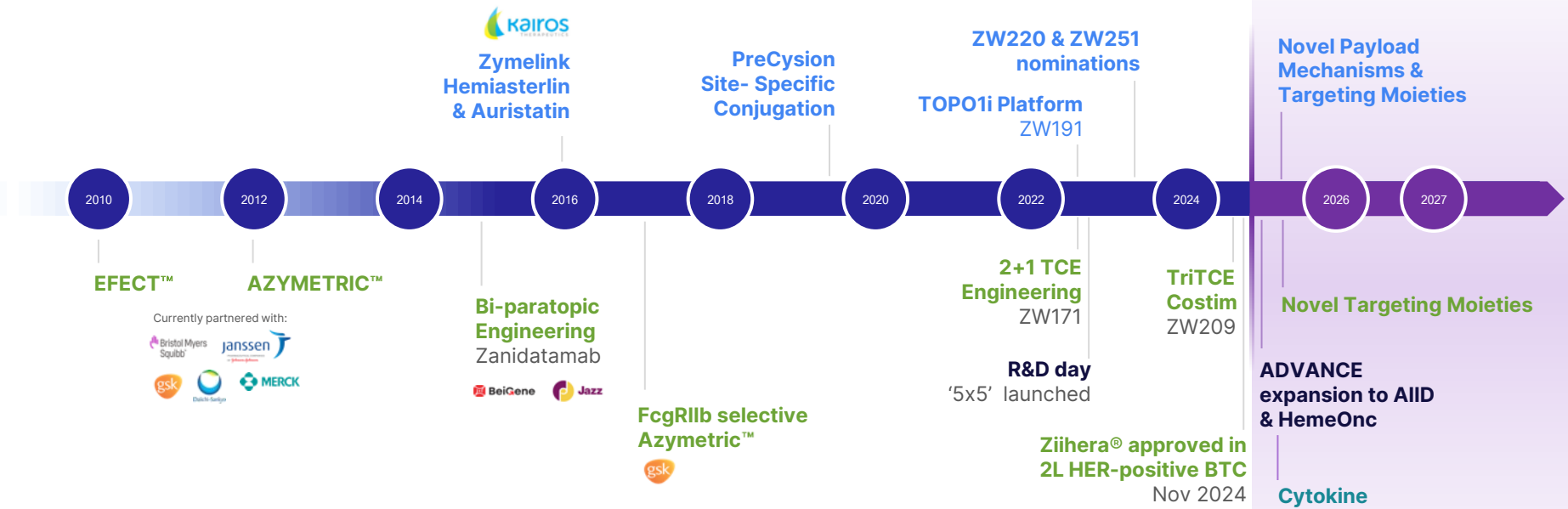
ADC: antibody-drug conjugate; MSAT: multispecific antibody therapeutic
1. Cash, cash equivalents, and marketable securities as of March 31, 2025

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		
ZW220 Topo1i ADC |DAR 4 | Fc Mut	ZD06519 Payload	NaPi2b	Gynecological Thoracic					
ZW251 Topo1i ADC | DAR 4 | Fc WT	ZD06519 Payload	GPC3	Digestive System (HCC)				Anticipated IND mid 2025	
Solid Tumor Oncology: Multispecific Antibody Therapeutics (MSAT)								
Zanidatamab Bispecific	Azymetric™	HER2	Multiple indications					Development partners: Jazz Pharmaceuticals and BeiGene
ZW171 Trivalent TCE | 2+1 Format	Azymetric™ Novel anti-CD3	MSLN x CD3	Gynecological Thoracic			NCT06523803		
ZW209 Trispecific TCE | Tri-TCE Costim	Azymetric™ Novel anti-CD3 Conditional CD28	DLL3 x CD3 x CD28	Thoracic				Anticipated IND 1H 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 IND 2H 2026		
ZW1572 Dual Cytokine Blocker	Azymetric™ Hetero-Fab | YTE	IL4Rα x IL-31						

10+ Years of Pioneering Multifunctional Antibody Development

Leading the development of next generation antibody-drug conjugates



Clinically validated technology drives development of novel multispecific therapeutics

BTC: biliary tract cancer; TCE: t cell engager; TOPO1i: topoisomerase 1 inhibitor; 2L: second-line.

Recent Accomplishments and Near-Term, Upcoming Milestones

5+ **Strategic Partnerships**

Collaborating with industry leaders to accelerate impact

Extended the reach of therapeutic candidates, while **validating our innovative approach** through strategic partnerships with companies including Jazz, BeiGene, GSK, and others.

1 **Internally Developed FDA Approved Drug**

Ziihera® (zanidatamab-hrii)
(HER2 bispecific antibody)

Licensed to Jazz and BeiGene

2L BTC (IHC3+) U.S. FDA Approval

Phase 3 1L BTC confirmatory trial ongoing

Phase 3 1L GEA top-line PFS readout expected 2H25

6 **Nominated Wholly-Owned Candidates**

Multiple Modalities and Therapeutic Areas

2 Clinical Stage Assets in Phase 1 Trials: ZW171 & ZW191

1 IND Planned in 2025:
ZW251

2 INDs Planned in 2026:
ZW209 & ZW1528

zymeworks

2L: second-line; BTC: biliary tract cancer; 1L: first-line; GEA: gastroesophageal adenocarcinoma; IND: investigational new drug application

Strategic Priorities for 2025 and 2026

Build a diverse and differentiated pipeline

Expand solid tumor portfolio with an emphasis on digestive system cancers

Expand R&D portfolio into hematology oncology and AIID

Maintain balanced R&D investment across wholly-owned clinical candidates and preclinical research

Become a leading, global biotech focused on targeted therapies

Enable preclinical, clinical, and TMO groups to manage portfolio of candidates across expanded focus areas

Maintain and potentially expand R&D portfolio through strategic partnering efforts

Continue to build pipeline of new product candidates with validated, strong target profiles

Invest in our people, culture & society

Harness global presence rooted in R&D to foster continued innovation in our patient communities

Maintain an efficient, financially/socially responsible, and productive organization

Enhanced optionality for partnerships and collaborations to share capital and development risk

Use strength of balance sheet to grow and broaden wholly-owned pipeline and next-generation technologies

Focused Therapeutic Areas Provide Diversity to R&D Portfolio and Enhanced Optionality for Partnering and Retained Product Rights

Solid Tumors

- Gynecological cancers
- Thoracic cancers
- Digestive system cancers

Hematological Cancers

- AML
- Multiple myeloma
- Lymphoma

Autoimmune & Inflammatory Disease

- Respiratory diseases
- Rheumatoid arthritis
- Inflammatory bowel diseases

AML: Acute myeloid leukemia

Zanidatamab: $2B+ Peak Sales Potential*

The approval of Ziihera® is the result of over a decade of groundbreaking research and development at Zymeworks

01 Entering market first in BTC with U.S. FDA Approval

- Ziihera® now approved in the U.S. for the treatment of adults with previously treated, unresectable or metastatic HER2+ (IHC3+) 2L BTC. Jazz Pharmaceuticals initiated U.S. launch activities.
- EMA validated MAA; potential approval as early as 2Q 2025
- The CDE NMPA in China has accepted the BLA for zanidatamab for 2L BTC
- Confirmatory Phase 3 trial initiated in 1L BTC

02 Path to approval in 1L GEA with sBLA with top-line results estimated 2H 2025

- HER2+/PD-L1 negative: opportunity to address unmet need and replace trastuzumab[1]
- HER2+/PD-L1 positive: opportunity to replace trastuzumab as HER2-targeted therapy of choice[1]
- Opportunity to explore potential in neoadjuvant populations[1]

03 Expanded opportunity across lines of Breast Cancer (BC)[1]

Expanded opportunity across lines of therapy[1]
- Post T-DXd (Ph3 EmpowHER trial)
- Early lines of therapy (neoadjuvant)
- Novel combinations[1]

Ongoing trials in early breast cancer:
- I-SPY2 Trial (NCT01042379)
- MD Anderson collaboration

04 Broad potential beyond BTC, GEA, and mBC in multiple HER2-expressing indications[2]

- Colorectal
- NSCLC
- Ovarian
- Endometrial
- Pancreatic
- Bladder
- Salivary Gland
- Ampullary
- And other HER2-expressing solid tumors

Strong Track Record of Meaningful Commercial Partnerships

- Licensing agreement with **Jazz Pharmaceuticals** to commercialize Ziihera in U.S., EU, Japan, India, and all other non-APAC territories

  Eligible for up to $500M in regulatory milestones and $862.5M in commercial milestones

- Licensing agreement with **BeiGene** to commercialize Ziihera in APAC (except Japan and India)

  Eligible for up to $164M in development and commercial milestones

- Tiered royalties between 10-20% from Jazz and from the high single digits to 19.5% from BeiGene sales (up to 20% when royalty reduction of 0.5% reaches cap in the low double-digit millions of dollars)

*Adapted from Jazz Pharmaceuticals' Guidance
sBLA: supplemental biologics license application; CDE: Center for Drug Evaluation; NMPA: National Medical Products Administration.
1. Pending regulatory approvals, 2. Funda Meric-Bernstam et al, Zanidatamab, a novel bispecific antibody, for the treatment of locally advanced or metastatic HER2-expressing or HER2-amplified cancers: a phase 1, dose-escalation and expansion study, The Lancet Oncology, Volume 23, Issue 12, 2022, Pages 1558-1570, ISSN 1470-2045, https://doi.org/10.1016/S1470-2045(22)00621-0.

Azymetric™: Adaptable to Different Formats and Applications

Engineering

Set of transferable mutations supporting pure and stable Fc heterodimer formation with exclusive chain pairing during co-expression

Libraries of constant domain Fab mutations available for kappa/kappa, kappa/lamda and lambda/lambda bispecific LC combinations

Flexibility

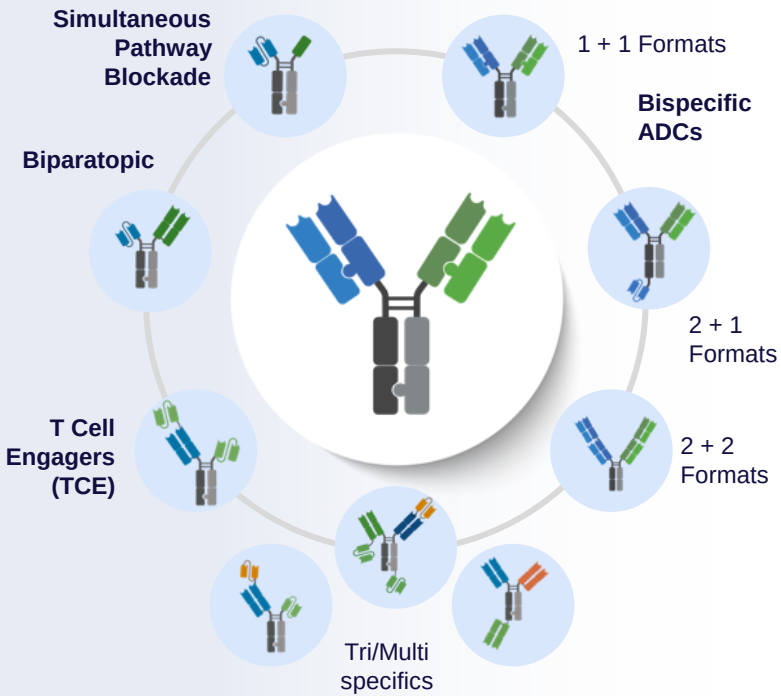
Can employ novel or existing antibody paratopes; human (IgG1, IgG2A, IgG4) and mouse frameworks; other CH2 and glyco-engineering approaches. Compatible with linker/payload conjugation

High-throughput Screening

Best-in-class activity requires screening of alternative targets, epitopes, sequences, target engagement geometries, and mechanisms of action (blocking, lytic, ADC)

Highly Manufacturable

Antibody like yields/stability; leveraged by multiple pharma/biotech with various clinical stage programs in development



Advancing Our Next-Generation Technology in Challenging Diseases

Antibody-Drug Conjugates

Novel Payload Discovery
- Our hypothesis on ADC mechanism guides our approach to novel payload discovery
- Four novel payload mechanisms in discovery to help innovation beyond TOPO1i and auristatin platforms

Optimal Antibody Formats
- Multi-pronged strategy to discover antibodies with enhanced ADC properties
- Antibody format (monospecific, biparatopic, or bispecific) dictated by target characteristics

Therapeutic Application
- Target, payload mechanism, and antibody format selected for enhanced activity in disease indication

Multispecific Antibody Therapeutics

Advanced Protein Engineering Solutions
- FDA approved, clinically validated, and novel engineering solutions enable plug and play building blocks to address complex biological challenges
- Flexibility of Azymetric™ facilitates high throughput multiparameter antibody screening to identify molecules with the desired biology

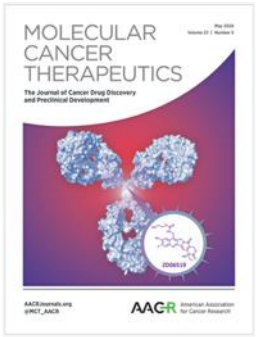
Addressing Biological Challenges in Indications with High Unmet Need
- Designing next generation T cell engagers to overcome biological challenges not addressed with traditional bispecific T cell engagers

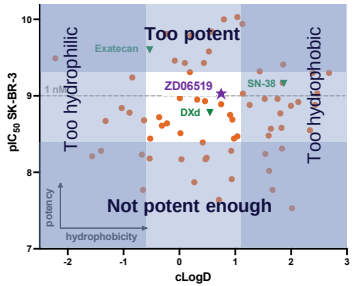
Driving the Forefront of Next Generation T cell Engagers
- Enhancing functionality and specificity to drive deep and durable responses in difficult to treat tumors
- Plug and play platforms enable fast development to rapidly address patient need

Continued execution against 2027+ IND application strategy

Zymeworks Topoisomerase ADC Platform Exemplifies Our Philosophy and Enables Our Pipeline

Antibody-Drug Conjugates





Payload synthesis & screening

~100 payloads prepared and tested in vitro

ADC in vitro potency

In vitro potency: target-dependency and bystander activity

Conjugation of select payloads

Payloads conjugated as DAR4 and DAR8, multiple mAbs

In vivo efficacy & PK

Robust efficacy in multiple CDX and PDX models

ADC characterization

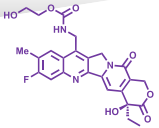
ADC properties: monodispersity, plasma stability, hydrophilicity

NHP toxicology & TK

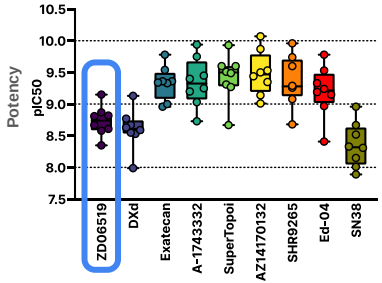
MTD in NHPs:
DAR8: ≥30 mg/kg
DAR4: ≥120 mg/kg

Lead selection and application

ZD06519



- Moderate potency to enable higher ADC dose
- Bystander active
- **ZW191** first in human trial (NCT0655574)
- **ZW251** expected to enter clinic in 2025



M.E. Petersen, M.G. Brant et al, Mol Cancer Ther 2024, 23(5):606-618.
CDX: cell line-derived xenograft, MTD: maximum tolerated dose, NHP: non-human primates, PDX: Patient-derived xenograft, TK: Toxicokinetic

Zymeworks' Engineering Approach: Key Expertise in Format and Geometry Screening to Identify Differentiated Activity

Multispecific Antibody Therapeutics

Potential best-in-class activity requires screening of epitopes, affinities and target engagement geometries

Unique flexibility of Azymetric™ enables format and affinity optimization for potential best-in-class attributes

Discovery of unique biology and differentiation to combination approaches

Biparatopic

Zanidatamab

Optimization of affinity and format for highest biparatopic activity

Unique biparatopic MOA

Superior activity to combination

Multi-Cytokine Blocker

ZW1528 (IL4Rα x IL33)

IgG-like format, manufacturability and PK

IL4Ra and IL33 blockade equivalent to bivalent benchmarks

Unique bispecific activity, potentially superior to combination

2+1 TCE

ZW171 (2+1 MSLN TCE)

Avidity optimization to prevent normal tissues tox

Avidity and format optimization to not bind shed MSLN

Synapse optimization for high activity with minimal cytokine release

Trispecific T Cell Engager

ZW209 (CD28 TriTCE)

Discovery of novel format to prevent non-specific T cell activation

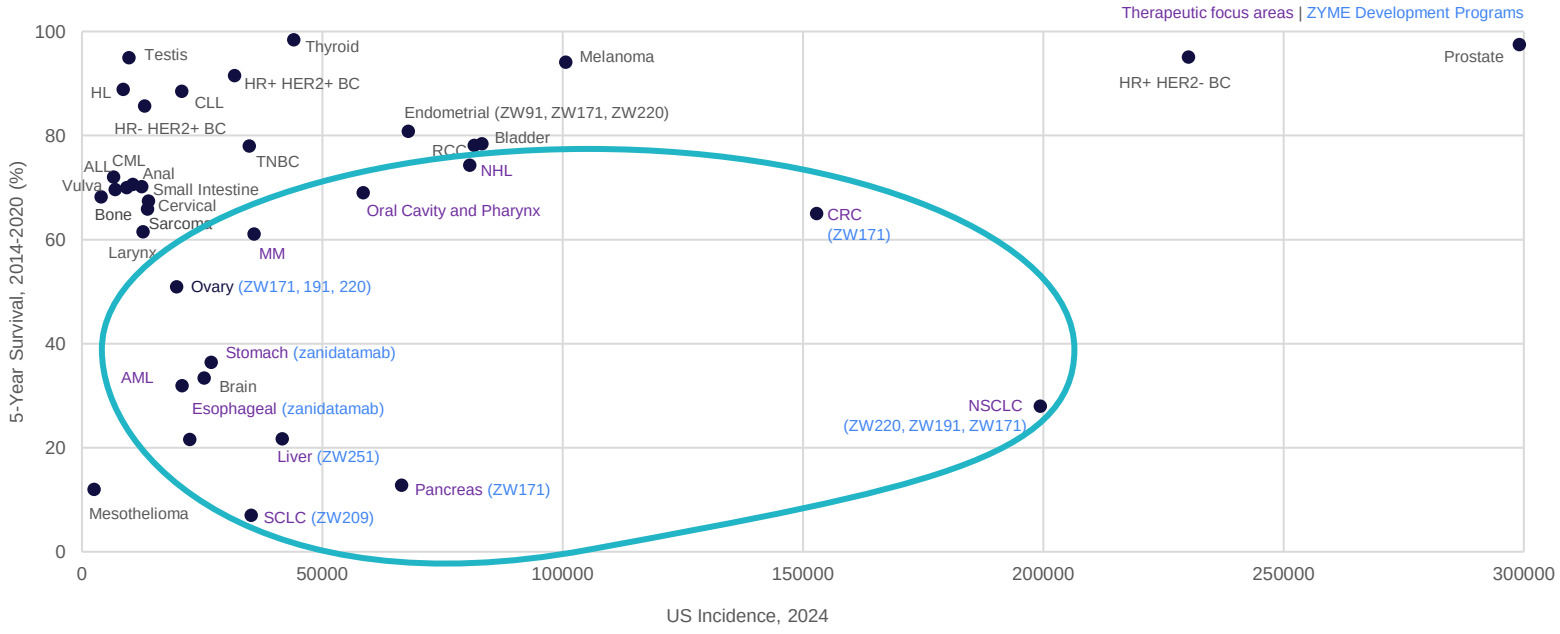
Conditional CD28 activation

Synapse optimization for balanced Signal 1 plus Signal 2

Increased Complexity

Mod: Mechanism of Action: MSLN: Mesothelin, PK: Pharmacokinetic, TCE: T Cell Engager, TriTCE: Trispecific T Cell Engager,

Maintain Focus on Cancers with Highest Unmet Medical Need: Increase GI Tract and Thoracic Cancer Coverage and Expand to Heme-Onc Cancers

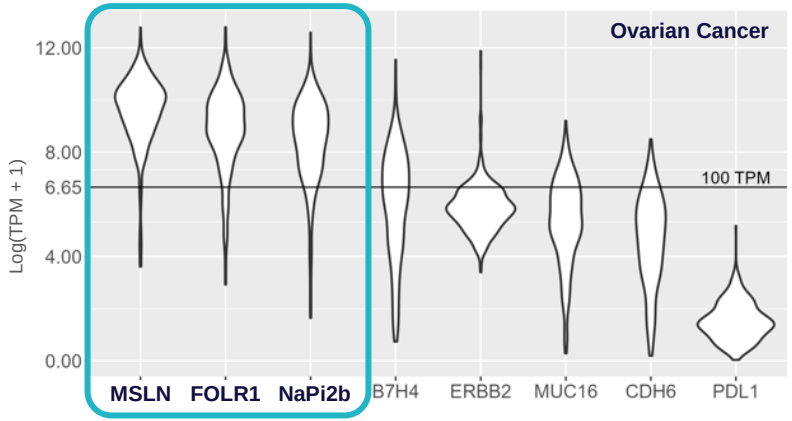


SEER*Explorer, accessed 10 Oct 2022.
AML: AML: Acute myeloid leukemia, CRC: colorectal cancer; MM: Multiple myeloma, NSCLC: Non-small cell lung cancer, SCLC: Small cell lung cancer, NHL: non-Hodgkin lymphoma

Target Selection Driven by Expression Profile, Biology and Clinical Precedence

Selection of an ADC or TCE strategy is driven by target expression, biology including internalization rate, clinical precedence and differentiation to prior therapeutic programs

mRNA Expression Profile of Select Cancer Target in Ovarian Cancer (N=421)



A balanced portfolio of ADCs targeting clinically validated FRα and NaPi2b, along with a T cell engager targeting MSLN, ensures comprehensive coverage and risk mitigation for ovarian cancer and NSCLC, **providing a diversified therapeutic focus on ovarian and lung cancers**.

MSLN, FOLR1 and NaPi2b are each expressed at higher level than other targets pursued in ovarian cancer or NSCLC

TCGA bulk RNA-sequencing data were obtained from TCGA-OV, workflow STAR – Counts from https://portal.gdc.cancer.gov/ repository. The median TPM (Transcript per Million) for each gene in each patient was plotted on a violin plot using ggplot21. This dataset contains 421 samples (patients) from Ovarian Serous Cystadenocarinoma (OV) and 521 sample from lung adenocarcinoma. The width of the shape/violins indicates the density of samples
TPM: transcripts per million 1. Wickham H (2016). ggplot2: Elegant Graphics for Data Analysis. Springer-Verlag New York. ISBN 978-3-319-24277-4, https://ggplot2.tidyverse.org.
ADC: antibody-drug conjugate; TCE: t cell engager; NSCLC: non-small cell lung cancer

ZW171

Bispecific Antibody Designed to Target Gynecological, Thoracic, and Digestive System Cancers

Initiated Phase 1 clinical trial in 2H 2024 (NCT06523803)

Optimized Design[1]

- T cell-engaging bispecific antibody for the treatment of MSLN-expressing solid tumors, built with Azymetric™.
- Unique geometry: Two single-chain fragment variable arms targeting MSLN; one Fab arm targeting the CD3 component of the T cell receptor, redirecting the body's immune system to fight cancer cells.

Differentiated Profile[1]

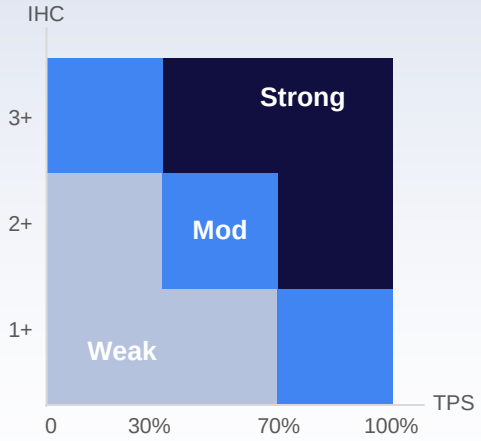
- Enhanced anti-tumor activity and safety profile in preclinical models supports opportunity to overcome clinical limitations of prior MSLN-directed therapies.

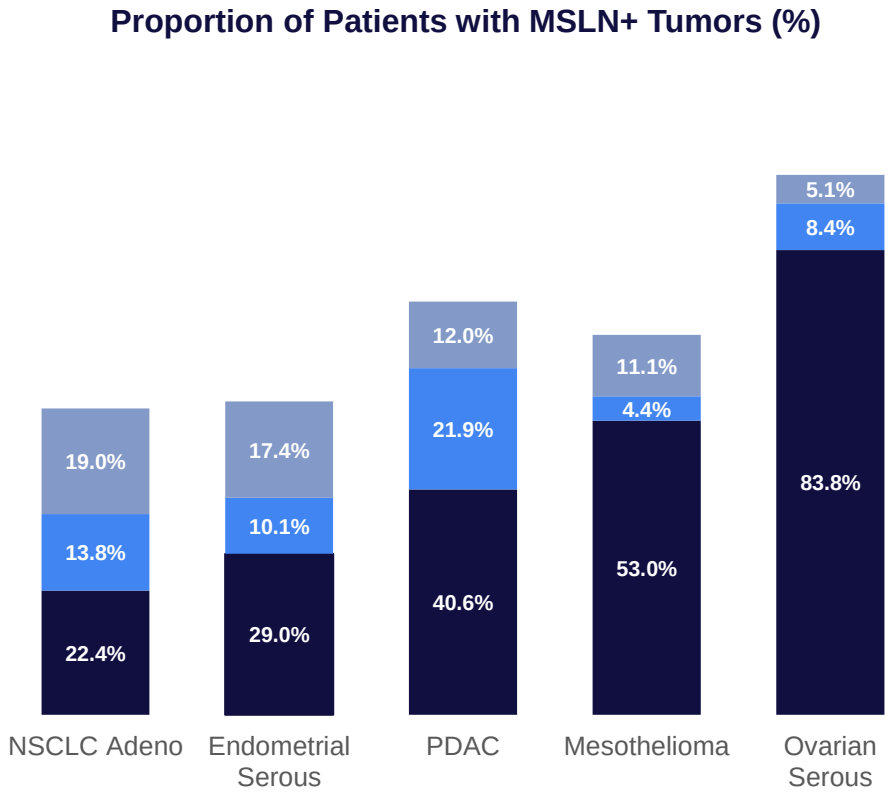
Significant Patient Need

- Strong expression of MSLN in ovarian cancer (~84%) and moderate to strong expression in NSCLC (~36%).[2]
- In the U.S. in 2024[3]:
  - 19K+ new cases of ovarian cancer
  - 234K+ new cases of lung cancer
  - 353K+ new cases of digestive system cancers

MSLN: mesothelin; NSCLC: non-small cell lung cancer; scFV: single-chain variable fragment.
1. Afacan N et al., Abstract #2942 presented at AACR 2023.
2. Weidemann, S. et al. Biomedicines 2021, Apr 7;9(4):397.
3. https://acsjournals.onlinelibrary.wiley.com/doi/10.3322/caac.21820

ZW171: Mesothelin Expression Is Frequent in Ovarian Cancer, Endometrial Cancer, NSCLC, PDAC, and Other Malignancies

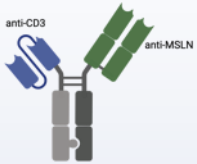
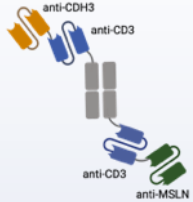




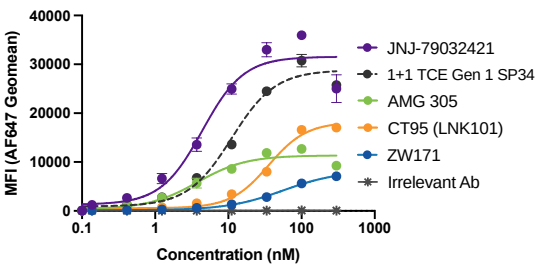
Adapted from Weidemann S, et al Biomedicines. 2021;9(4):397.
IHC: immunohistochemistry; Mod: moderate; MSLN: mesothelin; NSCLC: non-small cell lung cancer; PDAC: pancreatic ductal adenocarcinoma; TPS: Tumor Proportion Score.

ZW171 Exhibits a Wider Therapeutic Window Compared to Next Gen MSLN TCEs

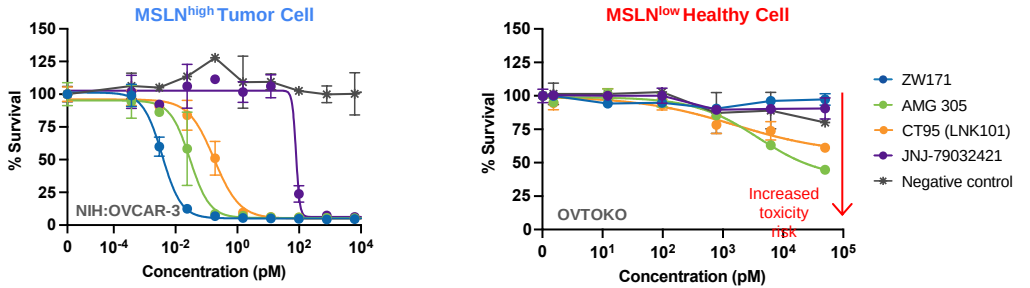
- Enhanced tumor selective cytotoxicity
- No targeting of normal tissues
- Low affinity CD3 binding to mitigate peripheral T cell binding and cytokine release
- Maintains potency in the presence of soluble MSLN

ZW171	CT95[1] (LNK101)	JNJ-79032421[2]	AMG 305[3]
			
2 +1	2 + 2	1 + 1	1 + 1 + 2

Low Binding to T cells



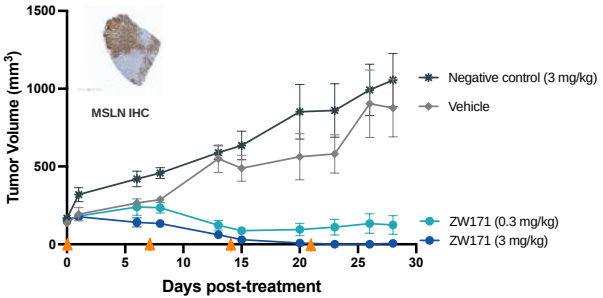
Potent Cytotoxicity in MSLN+ Tumor Cells but not Normal Cells



Afacan N, et al. Presented at: AACR. 2025 (Abstract 3503). Tumor cell lines were cocultured with human PBMCs at an E:T ratio of 5:1. Test articles were titrated and added to wells in duplicate. After 72hr, tumor cell survival was assessed by high-content imaging. Negative control= HAxCD3; 1. CT95: Context Therapeutics Corporate Presentation Dec 2024; 2. JNJ-79032421: https://clinicaltrials.gov/study/NCT06255665?term=JNJ-79032421&rank=1; 3. AMG 305: Pham L et al AACR 2023; https://clinicaltrials.gov/study/NCT05800964.

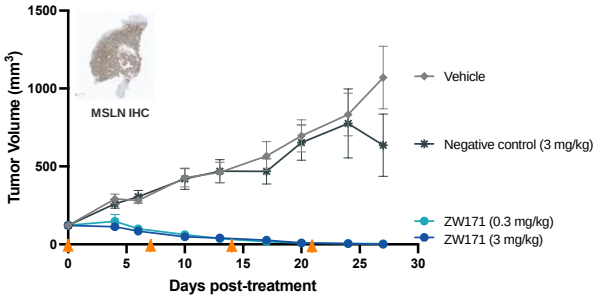
ZW171: Mediates Strong Anti-Tumor Activity in Patient-derived Models

Patient-derived NSCLC Humanized Mouse Model



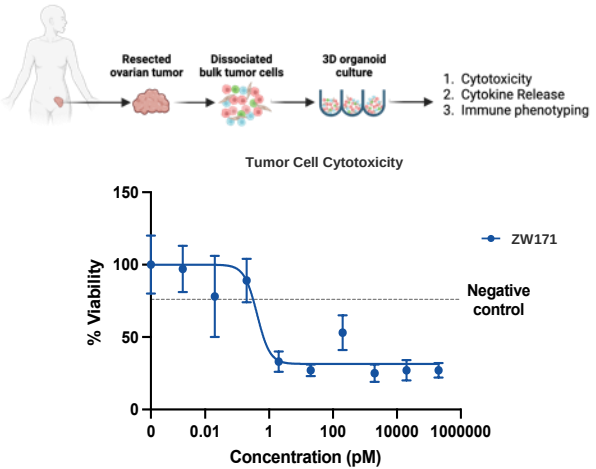
CD34 engrafted mice were engrafted with CTG-2579. When tumors reached 100-200 mm^3, mice were dosed i.v. QW x4 with ZW171 at 3 or 0.3 mg/kg, the neg control (HAxCD3) at 3 mg/kg, or vehicle (H6Su).

Patient-derived Pancreatic Cancer Humanized Mouse Model



CD34 engrafted mice were engrafted with CTG-1375. When tumors reached 100-200 mm^3, mice were dosed i.v. QW x4 with ZW171 at 3 or 0.3 mg/kg, the neg control (HAxCD3) at 3 mg/kg, or vehicle (H6Su).

Ovarian Cancer Model Leveraging Endogenous Tumor T cells



3D patient-derived ovarian carcinoma organoids were generated, and ZW171 activity assessed using KIYATEC proprietary technologies (Lassahn, 2023). Following incubation of organoids with ZW171 for 72hr, tumor cell viability was assessed using a CellTiter-Glo 3D (Promega) assay.

Afacan N, et al. Presented at: AACR. 2025 (Abstract 3503). Lassahn et al., Abstract 2275: Preclinical testing of therapeutic biologics using patient-derived 3D spheroids. Cancer Res 1 April 2023; 83 (7_Supplement): 2275
IHC: immunohistochemistry; IV: intravenous; MSLN: mesothelin; NSCLC: non-small cell lung cancer; QW: every week.

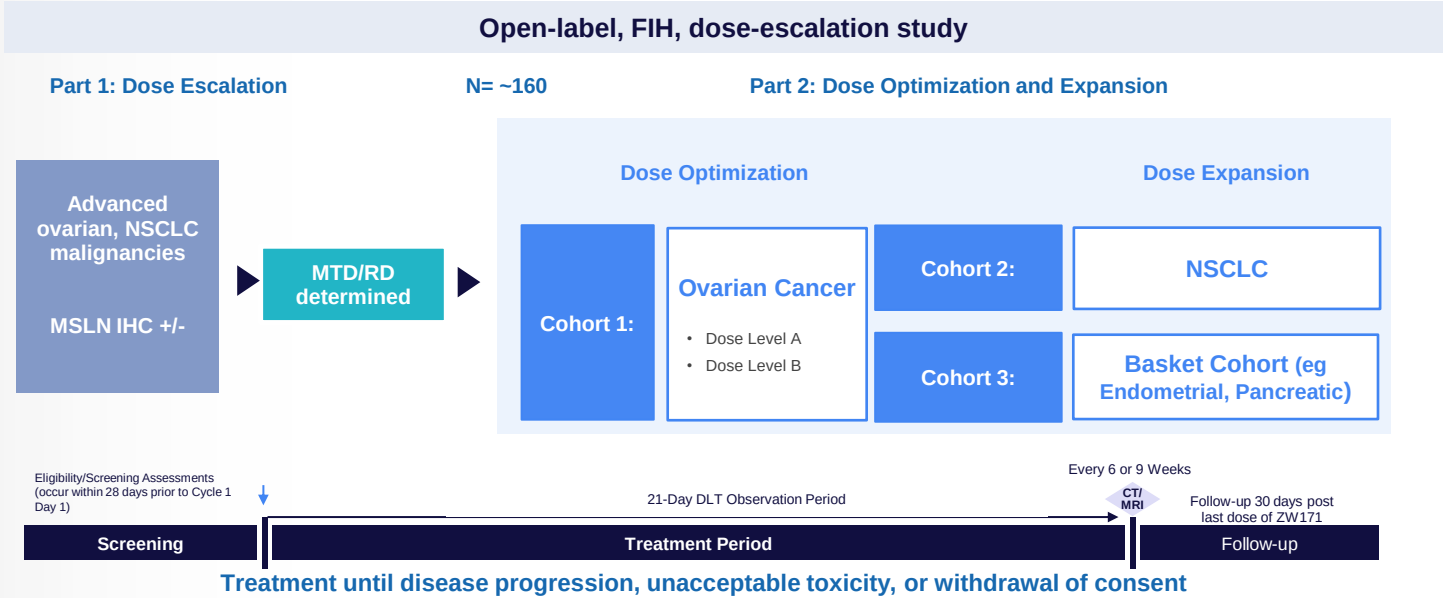
ZW171 Global Phase 1 Study in MSLN-Expressing Solid Tumors (NCT06523803)

USA
FDA IND Approval
Sites Activated

United Kingdom
MHRA CTA Approval
Sites Activated

Germany
EU CTA Approval
Sites Activated

South Korea
MFDS CTA Approval
Site Activated



CT: Computed Tomography; DLT: Dose Limiting Toxicity; FIH: first in human; IHC: immunohistochemistry; MRI: Magnetic Resonance Imaging; MTD: maximum tolerated dose; MSLN: mesothelin; NSCLC: non-small cell lung cancer; RD: recommended dose.

ZW191

ADC Designed to Target FRα-Expressing Tumors

Initiated Phase 1 clinical trial in 2H 2024 (NCT06555744)

Optimized Design[1]

- ADC targeting FRα -expressing tumors including ovarian cancer, other gynecological cancers, and NSCLC.
- Comprised of a humanized IgG1 antibody conjugated to a novel camptothecin-based topoisomerase 1 inhibitor payload technology, ZD06519.
- Drug-to-antibody ratio ~8.
- Validated peptide cleavable linker sequence.

Differentiated Profile

- Differentiated anti-tumor activity in preclinical tumor models with a breadth of FRα expression.[1]
- Favorable safety profile in nonhuman primate (NHP) toxicology studies.[1]
- Favorable PK and is well-tolerated in NHP at exposure levels above those projected to be efficacious.
- Opportunity to treat broader range of FRα-expressing cancers.

Significant Patient Need

- FRα is found in ~75% of high-grade serous ovarian carcinomas[2] and ~70% of lung adenocarcinomas.[3]

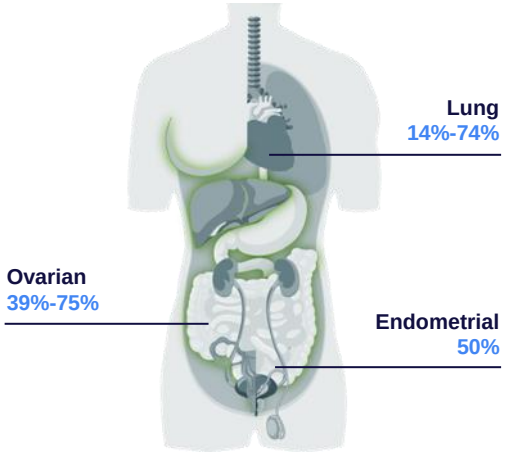
1. Lawn S et al. Abstract # 2641 Presented at AACR 2023.
2. Köbel, M., Madore, J., Ramus, S. et al. Br J Cancer 111, 2297–2307 (2014).
3. O'Shannessy DJ, et al., Oncotarget. 2012 Apr; 3(4):414-25.

FRα-expressing Cancers Represent a Significant Commercial Opportunity[1-7]

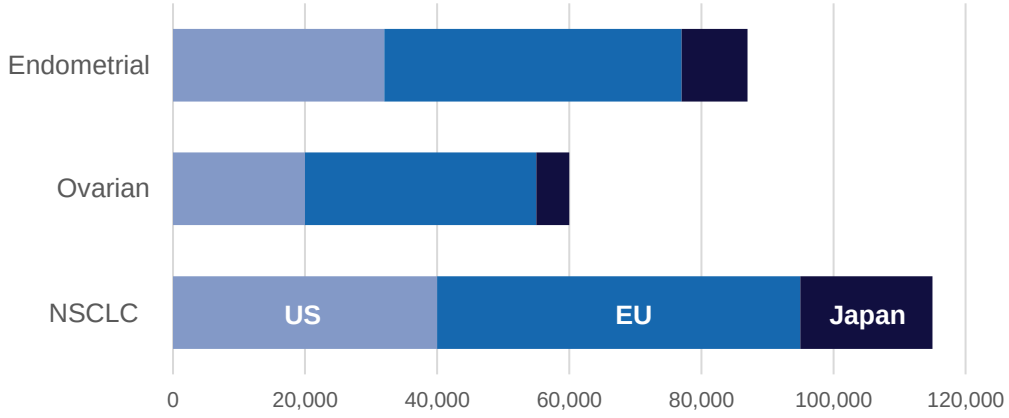
Potential first and best-in-class in
FRα-high endometrial, NSCLC, TNBC, and FRα-mid/low solid tumors

Potential best-in-class opportunity in
FRα-high ovarian cancer

FRα-Expressing Cancers



Estimate of Newly Diagnosed FRα+ Patients In Key Indications



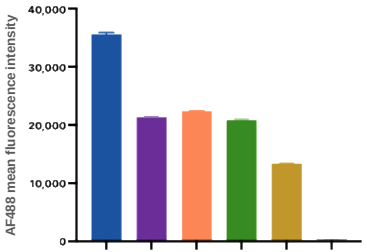
FRα: folate receptor alpha; NSCLC: non-small cell lung cancer; TNBC: triple negative breast cancer

1. Senol S, et al. Int J Clin Exp Pathol. 2015;8(5):5633-5641; 2. Omote S, et al. Med Mol Morphol. 2018;51(4):237-243; 3. Oza AM. SGO. 2021; 4. O'Shannessy DJ, et al. Oncotarget. 2012;3(4):414-425; 5. Nunez MI, et al. J Thorac Oncol. 2012;7(5):833-840; 6. D'Angelica M, et al. Mod Pathol. 2011;24(9):1221-1228; 7. Scaranti M, et al. Nat Rev Clin Oncol. 2020;17(6):349-359.

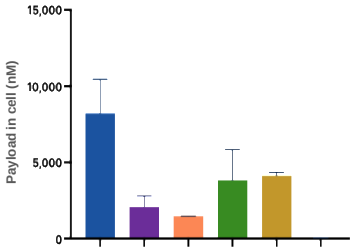
ZW191: Key Design Considerations

ZW191's Novel mAb Drives Superior Internalization, Payload Delivery, and Tissue Penetration

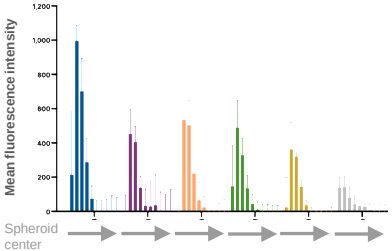
Internalization



Payload Delivery



Tumor Spheroid Penetration

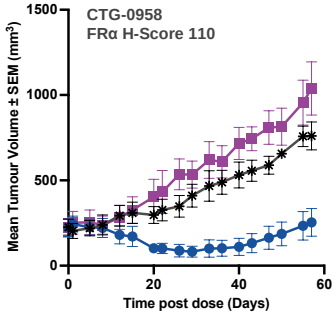


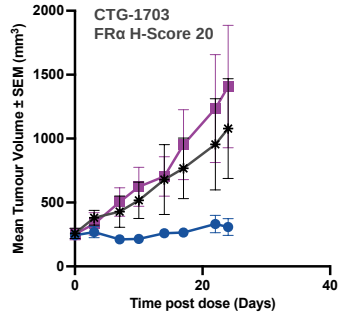
- ZW191 mAb (from ZW191)
- Mirvetuximab (from Elahere™)
- Farletuzumab (from MORAb-202)
- SRP1848-H01 (from STRO-002)
- F131 (from PRO1184)
- Non-targeted control mAb

Internalization of AF488 labelled antibodies to KB-Hela cells after 24 hrs at 100 nM; Mass-spec. quantification of internalized payload following 24-hour treatment of IGROV-1 cells with 10 nM of ADCs comprising ZW191 mAb or other FRα-targeted mAbs conjugated to n auristatin payload; Tumor spheroid penetration of AF488 labelled antibodies as quantified by high content imaging of spheroid layers at 24 hours post-treatment at 50 nM.

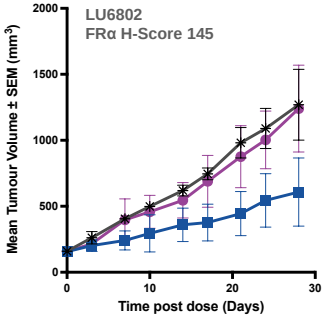
Anti-tumor Activity Across Multiple Tumor Types And Range of FRα Expression (PDX models)

Ovarian Cancer

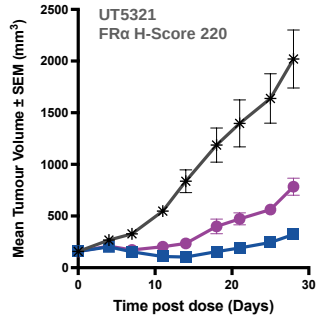




NSCLC



Endometrial



ZW191, 6 mg/kg mirvetuximab soravtansine, 6 mg/kg

Wong J et al., Abstract #3127 presented at American Association for Cancer Research annual meeting 2024
Lawn S. et al. Abstract # 1862 presented at American Association for Cancer Research annual meeting 2024

Differentiation is Critical for ZW191 in the Competitive FRα ADC Space for TOPO1i

A novel design to target FRα

1. **Potential best-in-class antibody**
   The ZW191 antibody was selected for enhanced internalization, payload delivery, and tumor penetration.[1]

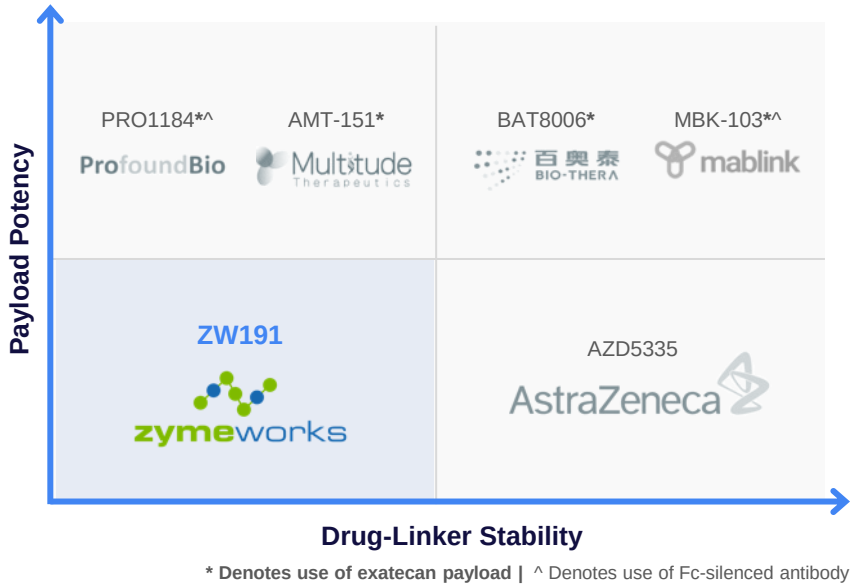
2. **Topoisomerase I inhibitor (TOPO1i) payload mechanism**
   TOPO1i containing ADCs have proven to be an effective mechanism to treat ovarian cancers.[2,3]

3. **Moderate payload potency**
   A moderate potency TOPO1i payload (ZD06519) was selected for ZW191 to enable a higher protein dose, which may be advantageous for target engagement, tumor penetration, and drug exposure.[5] Exatecan is 3-10X more potent than the ZW191 payload.

4. **Moderate antibody-linker stability**
   A 'designed instability' approach was taken with ZW191; all approved ADCs feature an element of linker instability.[4]

5. **Strong bystander activity**
   Strong bystander activity is beneficial when treating tumors with low and heterogenous expression of FRα.[1]

The balance between **drug-linker stability** and **payload potency** differentiates ZW191 from other FRα-TOPO1i ADCs



*** Denotes use of exatecan payload |** ^ Denotes use of Fc-silenced antibody

[1] Lawn S et al. Abstract # 2641 Presented at AACR 2023; [2] Meric-Bernstam F, et al., Journal of Clinical Oncology 2023 41:17; [3] Moore K, et al., j.annonc.2023.09.1924; [4] Colombo R, Barnscher SD, Rich JR. Cancer Res 2023, 83 (7). Abstract #1538 presented at AACR 2023 [5] Lawn S. ZW191: A Potential Best-in-Class TOPO1i ADC for Treatment of FRα-Expressing Solid Tumors, Presented at World ADC London 2023.

ZW191: Global Phase 1 Study in FRα-Expressing Solid Tumors (NCT06555744)

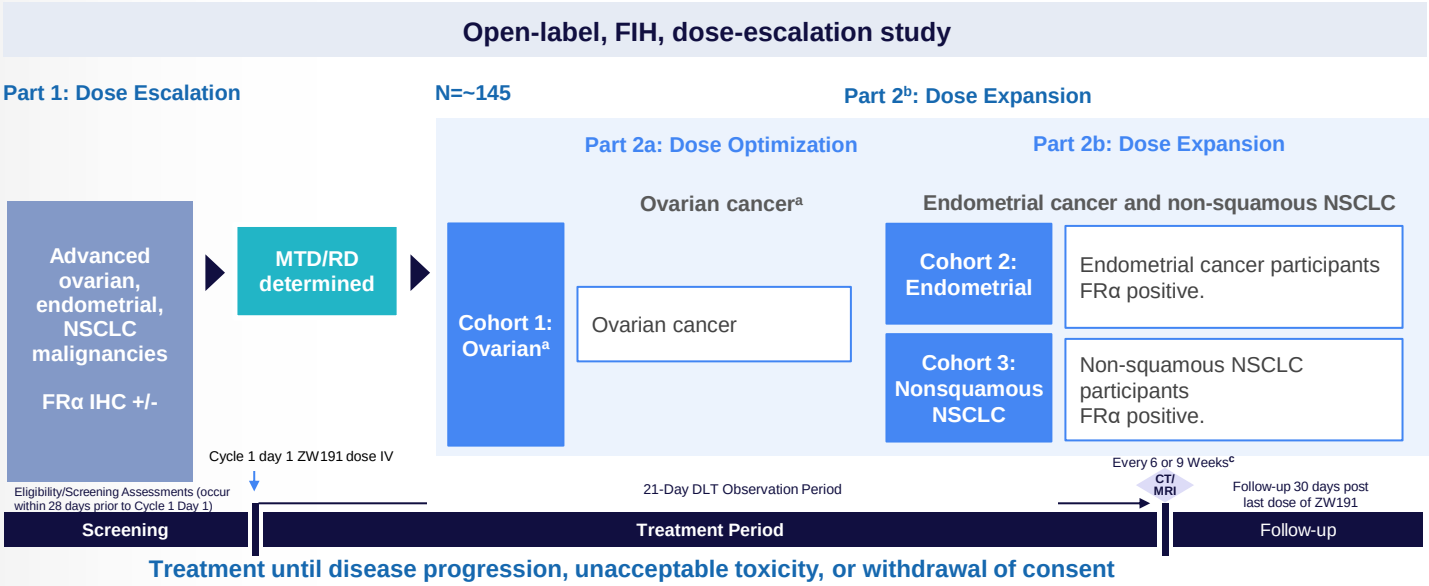
USA
FDA IND Approval
Sites Activated

Japan
PMDA CTN Approval
Sites Activated

Australia
TGA CTA Approval
Sites Activated

South Korea
MFDS CTA Approval
Sites Activated

Singapore
HSA CTA Approval
Sites Activated



[a]Ovarian cancer includes primary peritoneal and fallopian tube cancers. [b]Part 2 will be initiated at dose levels (RDEs) based on the SMC's comprehensive analysis of safety, tolerability, clinical PK, PD, and preliminary antitumor activity data from Part 1. The Part 2 selected doses will be decided at SMC meetings and could be the MTD or RDEs based on comprehensive analysis of safety, tolerability, clinical PK, PD, and antitumor activity data from Part 1. The RDE dose levels may vary across the tumor types in Cohorts 1, 2, and 3. [c]Timed from cycle 1 day 1. Q6W (every 6 weeks) for the first 4 assessments and then Q9W (every 9 weeks) thereafter. ClinicalTrials.gov ID: NCT06555744.
CT/MRI: computed tomography/magnetic resonance imaging; DLT: Dose Limiting Toxicity; FIH: First-in-human; FRα: folate receptor alpha; IHC: immunohistochemistry; IV: intravenous; MTD: maximum tolerated dose; NSCLC: non-small cell lung cancer; RD: Recommended Dose..

ZW251

ADC Designed to Target Glypican 3-Expressing Hepatocellular Carcinoma (HCC)

Expected IND filing by mid-2025

Optimized Design

- Potential first-in-class ADC designed to treat GPC3-expressing HCC with a new MOA
- Composed of a humanized IgG1 antibody conjugated to a novel camptothecin-based topoisomerase 1 inhibitor, ZD06519
- Intermediate drug-to-antibody ratio ~4
- Validated peptide cleavable linker sequence

Differentiated Profile

- Strong preclinical activity in models with a breadth of GPC3 expression[1]
- Exhibited comparable PK to a clinical-stage antibody comparator; PK unaffected by conjugation
- Noteworthy tolerability and no mortality observed in a repeat dose NHP toxicology study up to 60 mg/kg (DAR 8) or 120 mg/kg (DAR 4)

Significant Patient Need

- GPC3 is expressed in 76% of HCC, with high expression observed in ~55% of HCC[2]
- HCC is the most common type of primary liver cancer and the third leading cause of cancer deaths globally[1]

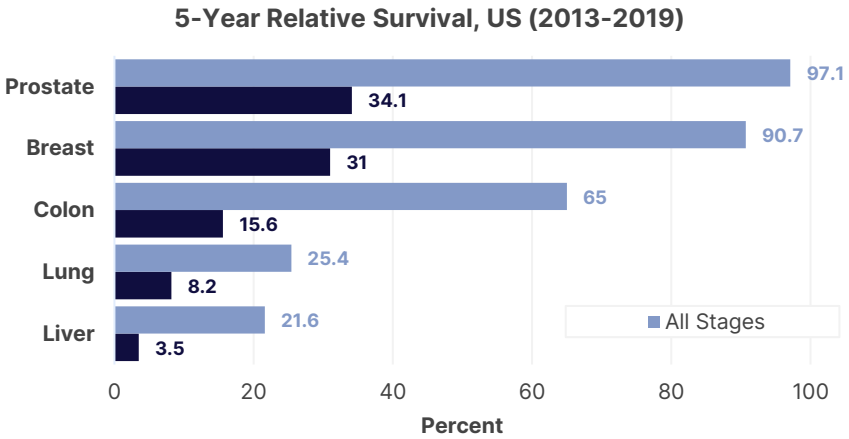
1. https://www.cancer.gov/types/liver/what-is-liver-cancer/causes-riskfactors#:~:text=Worldwide%2C%20liver%20cancer%20is%20the,the%20incidence%20of%20HBV%20infection
2. Wang HL et al., Arch Pathol Lab Med 2008; 2.Madera L et al., Abstract #2658 presented at AACR 2023.

ADC: Antibody Drug Conjugate; DAR: Drug to antibody ratio; GPC3: Glypican-3; HCC: Hepatocellular Carcinoma; NHP: Non-human Primates; PK: Pharmacokinetics.

HCC Epidemiology and Current Treatment

HCC Burden

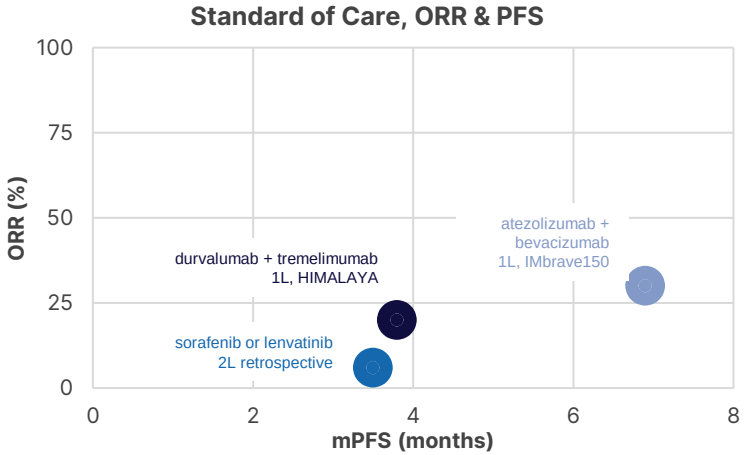
- Globally 6th most common cancer and third most common cause of death from cancer



WHO. International Agency of Cancer Research. Cancer Today. 2020. Available at: https://gco.iarc.fr/today/home. Accessed October 2023 SEER. Cancer Stat Facts. National Cancer Institute. Available at https://seer.cancer.gov/statfacts/

Standard of Care for Systemic HCC

- In the US, most patients receive IO-VEGF or IO-IO combinations in 1L; multi-targeted TKIs are a 2L option



Finn RS et al NEJM 2020; Abou-Alfa GK et al NEJM Evid 2022; Yoo C et al Liver Cancer 2021

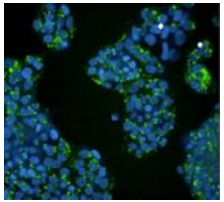
As a first-in-class TOPO1-based ADC for HCC, ZW251 offers the potential of a **new MOA** for patients, and an **opportunity to improve upon the current standard of care**

ZW251: Potential Utility in Hepatocellular Carcinoma

On track for clinical studies in mid-2025

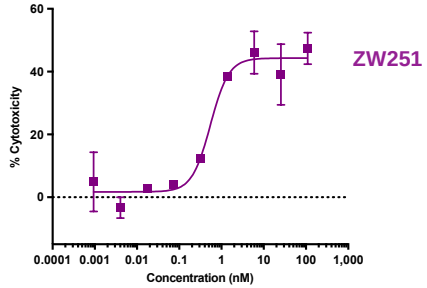
Robust ADC Internalization and Cytotoxicity

ZW251 internalized in HCC cell line



Internalization visualized after 24-hour treatment

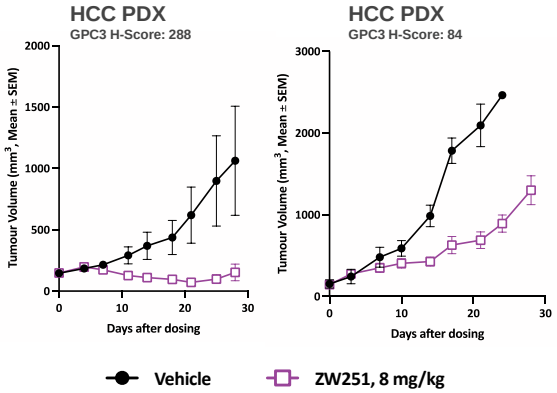
Tumor spheroid cytotoxicity in HCC cell line



Cytotoxicity assessed by cell line spheroids (treatment over 4 days)

Differentiated Modality Demonstrates Anti-tumor Activity

Anti-tumor activity of ZW251 against hepatocellular carcinoma patient derived xenografts expressing high and low GPC3

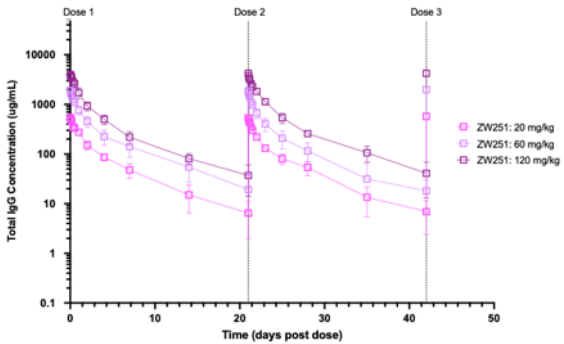


Impressive Tolerability and Dose-proportional PK in NHP

Non-GLP toxicology study in non-human primates dosed 3 times every 3 weeks

Dose	MTD	$T_{1/2}$ (day)
20 mg/kg	≥ 120 mg/kg	4.6
60 mg/kg		4.8
120 mg/kg		5.4

Total IgG in NHP serum



HCC: Hepatocellular carcinoma; PDX: patient derived xenograft; MTD: maximum tolerated dose; T1/2: half-life; GLP: good laboratory practice

Madera L et al., Abstract #2658 presented at AACR 2023; Madera L et al, presentation at World ADC 2023; Madera L et al., Abstract #177 presented at EORTC-NCI-AACR 2024.

ADC: Antibody Drug Conjugate; GPC3: Glypican-3; HCC: Hepatocellular Carcinoma; MTD: Maximum Tolerated Dose; NHP: Non-human Primates; PDx: Patient-derived xenograph; PK: Pharmacokinetics.

ZW220

ADC Designed to Target NaPi2b-Expressing Ovarian Cancer and NSCLC

Optimized Design[1]

- ADC targeting NaPi2b-expressing solid tumors
- Comprised of a humanized IgG1 antibody conjugated to a moderate potency topoisomerase I inhibitor payload technology with bystander activity, ZD06519
- Intermediate drug-to-antibody ratio ~4
- Validated peptide cleavable linker sequence
- FcγR silenced to potentially minimize toxicities driven by cellular uptake via FcγR

Differentiated Profile

- Strong preclinical activity in models with a breadth of NaPi2b expression[2]
- Encouraging tolerability in repeat dose NHP toxicology studies[1]
- Desirable PK and is well tolerated at high doses
- First-in-class ADC potential for NaPi2b-expressing solid tumors

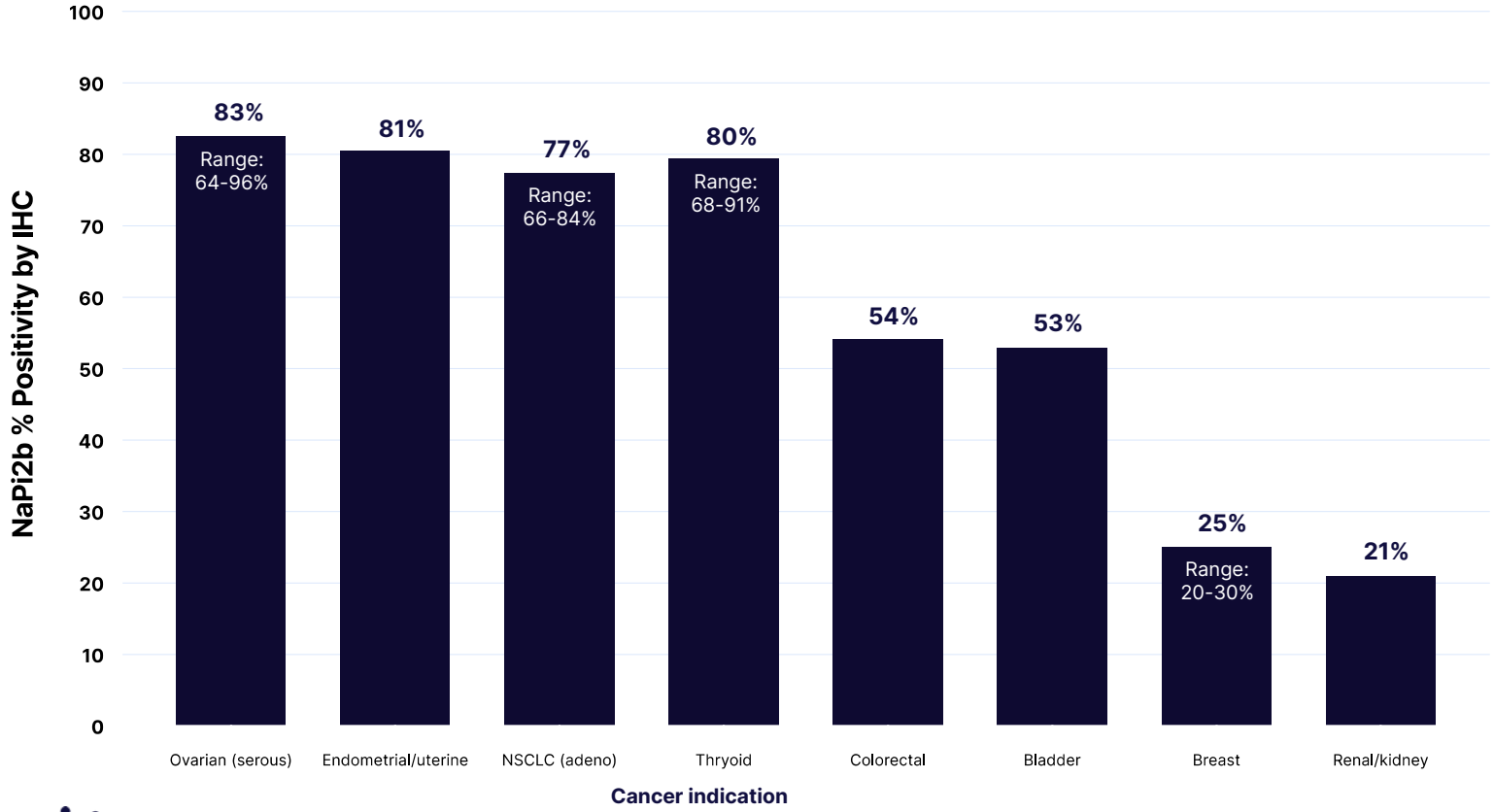
Significant Patient Need

- NaPi2b is found in ~83% of ovarian serous adenocarcinomas[2] and ~77% of NSCLC adenocarcinomas[2]

1. Hernandez Rojas A et al., Abstract #1533 presented at AACR 2023.
2. Lin K, et al. Clin Cancer Res. 2015;21(22):5139–5150 (prevalence % based on 26 cases of ovarian serous adenocarcinomas and 31 cases of non-small cell lung adenocarcinomas).

ADC: Antibody Drug Conjugate; NaPi2b: Sodium-dependent phosphate transporter 2b; NHP: Non-human Primates; NSCLC: non-small cell lung cancer; PK: Pharmacokinetics

NaPi2b is Overexpressed in Multiple Cancers with High Unmet Medical Need

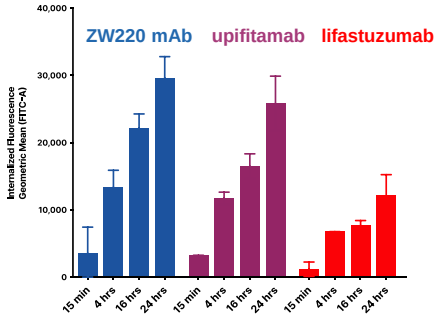


Ovarian
1) Banerjee et al. 2023. ESMO #145
2) Richardson et al. 2022. SGO #76
3) Levan et al. 2017. BMC Cancer
4) Lin et al. 2015. Clin Cancer Res
5) Lopes dos Santos et al. 2013. PLoS One
Endometrial/uterine
1) Horsley et al. 2024. Cancer Res #5085
NSCLC (adeno)
1) Horsley et al. 2024. Cancer Res #5085
2) Heynemann et al. 2022. Clin Lung Cancer
3) Yu et al. 2018. IASLC #12636
4) Zhang et al. 2017. Tumor Biology
5) Lin et al. 2015. Clin Cancer Res
Thyroid
1) Hakim et al. 2021. Anal Cell Pathol
2) Lin et al. 2015. Clin Cancer Res
Colorectal
1) Liu et al. 2018. Biomed Pharmacother
Bladder
1) Ye et al. 2017. Cell Death Dis
Breast
1) Lopes dos Santos et al. 2013. PLoS One
2) Kiyamova et al. 2011. Exp Oncol
Renal/kidney
1) Lopes dos Santos et al. 2013. PLoS One

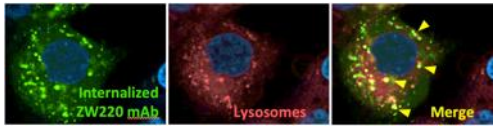
ZW220: Potential Utility in Multiple Cancers

ZW220 Efficiently Internalizes and Co-localizes with Lysosomes

ZW220 (mAb) internalization in Ovarian Cancer cell line

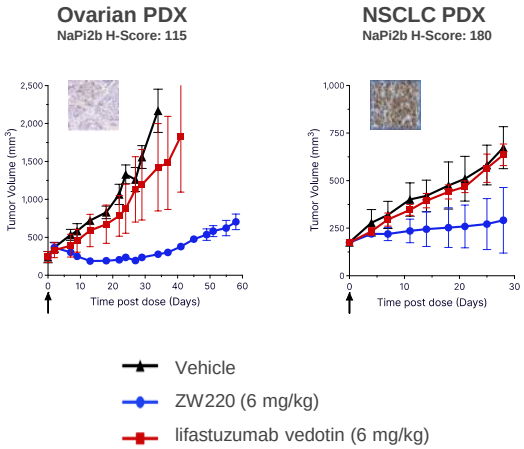


Lysosomal trafficking of ZW220 mAb



Anti-tumor Activity in Ovarian and Lung Cancer Models

Anti-tumor activity of ZW220 and lifastuzumab vedotin against ovarian and lung patient derived xenografts (PDXs) expressing NaPi2b

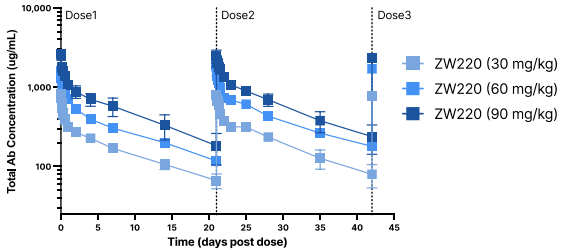


Impressive Tolerability and Dose-proportional PK in NHP

Non-GLP toxicology study in non-human primates dosed 3 times every 3 weeks

Dose	MTD	$T_{1/2}$ (day)
30 mg/kg	≥ 90 mg/kg	10.3
60 mg/kg		9.8
90 mg/kg		8.0

Total IgG in NHP serum



*ZW220 Fc wt surrogate used in non-GLP NHP study

mAb: monoclonal antibody; PDX: patient derived xenograft; MTD: maximum tolerated dose; T1/2: half-life; GLP: good laboratory practice

Hernandez Rojas A et al., Abstract #1533 presented at AACR 2023; Hernandez Rojas A et al. Presentation at World ADC 2023; Hernandez Rojas A et al. *Eur. J. Cancer* (2024), 211, 114535.

zymeworks

ZW209

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

On track for IND submission 1H 2026

Optimized Design

- Potential first-in-class TriTCE that targets DLL3-expressing tumor cells, and CD3 and CD28 on T cells.
- TriTCE with potentially optimized TAA, CD3, CD28 binding affinity and geometry using Azymetric™ and EFECT™ platforms.
- Leverages obligate cis-T cell binding and conditional CD28 engagement to prevent unintended T cell activation, while enabling tumor-targeted cytotoxicity.

Differentiated Profile

- Clean expression profile and absence of on-target, off-tumor side effects observed for DLL3 x CD3 bispecifics provides ideal TriTCE Co-stim target profile.
- Long term cytotoxicity at low effector to T cell ratios, increased T cell proliferation, survival, and anti-tumor activity with reduced cytokine release.
- Validated responsiveness of DLL3-expressing tumors to TCE modality.

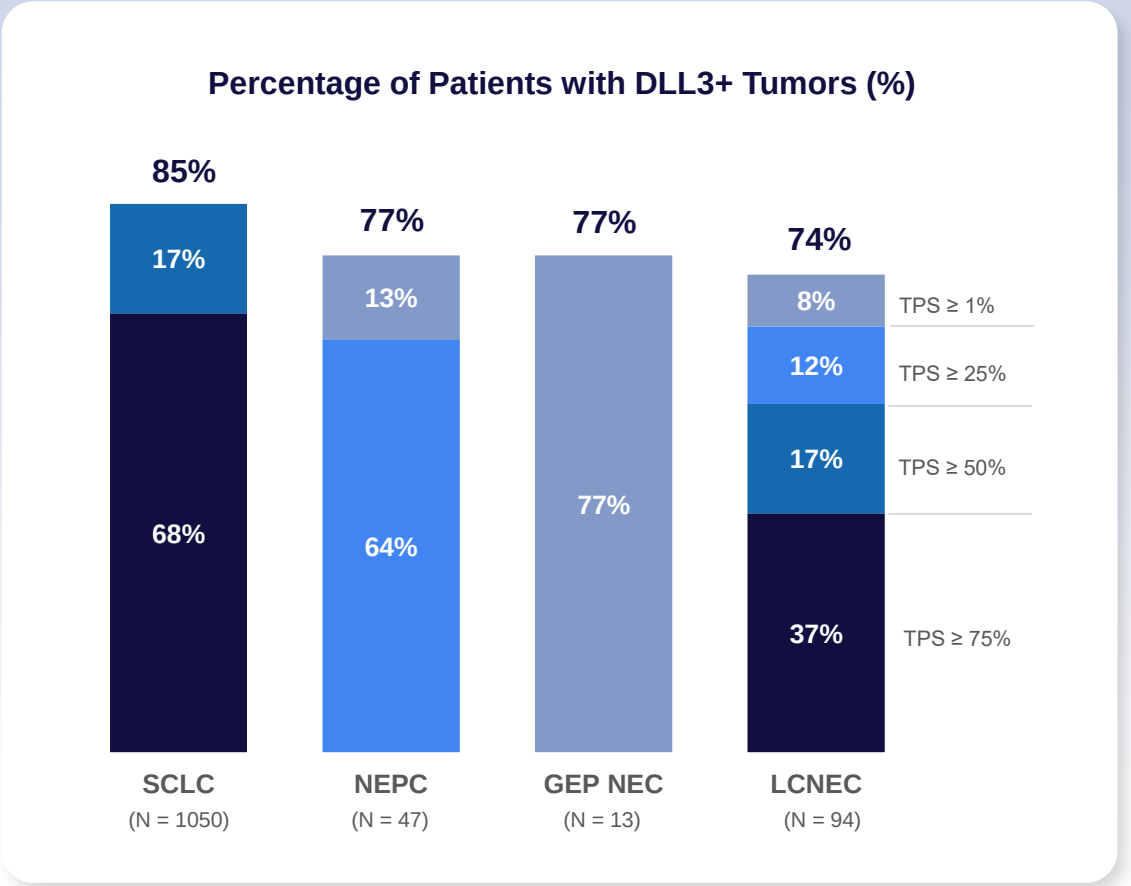
Significant Patient Need

- 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#:~:text=There%20are%20two%20primary%20forms,and%20improving%20quality%20of%20life.
DLL3: Delta-like ligand 3; SCLC: Small Cell Lung Cancer; TAA: tumor-associated antigen; TriTCE: Tri-specific T Cell Engager.

DLL3 is an Ideal Target to Evaluate TriTCE Co-stim Platform, with Opportunities in Multiple Cancers

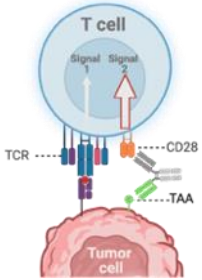
- Responsiveness of DLL3-expressing tumors to TCE modality validated with Imdelltra™ and other DLL3 bispecific TCEs; however, opportunity for improved responses remains
- DLL3 is expressed on the surface of SCLC and other neuroendocrine tumors but rarely on the surface of normal cells
- Clean expression profile and absence of on-target, off-tumor side effects observed for DLL3 x CD3 bispecifics provides ideal TriTCE Co-Stim target profile



Adapted from: Rojo F et al Lung Cancer 2020. International real-world study of DLL3 expression in patients with small cell lung cancer. Puca L et al. Delta-like protein 3 expression and therapeutic targeting in neuroendocrine prostate cancer. Sci Transl Med. 2019. 11: eaav0891. Liverani C et al Endocrine Pathol 2021. Diagnostic and Predictive Role of DLL3 Expression in Gastroenteropancreatic Neuroendocrine Neoplasms. 32:309-27. Hermans BCM et al. DLL3 expression in large cell neuroendocrine carcinoma (LCNEC) and association with molecular subtypes and neuroendocrine profile. Lung Cancer 2019. 138:102-8. DLL3: Delta-like Ligand 3; GEP NEC: Gastroenteropancreatic Neuroendocrine Cancer; LCNEC: Large Cell Neuroendocrine Cancer; NEPC: Neuroendocrine Prostate Cancer; SCLC: Small Cell Lung Cancer TCE, T cell engager; TPS: Tumor Proportion Score.

CD28 Co-stimulatory T Cell Engager Approaches

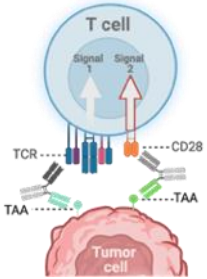
Bispecific CD28 T cell Engagers



CD28 x TAA +/- PD1

Limitations:

Initial clinical activity for CD28-TAA +PD1, but potential toxicity due to autoreactive T cells[1]

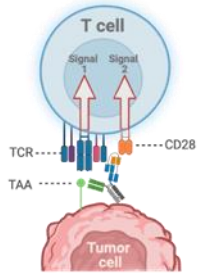


CD28 x TAA + CD3 x TAA

Limitations:

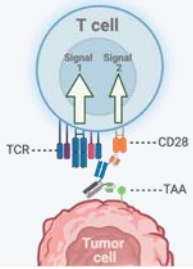
- Optimized for single agent activity and strong CD28 agonism, potential for similar toxicity to CD28-TAA and difficult to optimize by dose adjustment
- Exposure of two molecules at required dose levels potentially suboptimal

Trispecific CD28 T cell Engagers



First Generation:

- High affinity CD3 and CD28 superagonist paratopes[2,3]
- T cell binding, activation and TMDD observed in periphery[2,3]
- Target-independent activity and T cell activation



Zymeworks' Next Generation Solution:

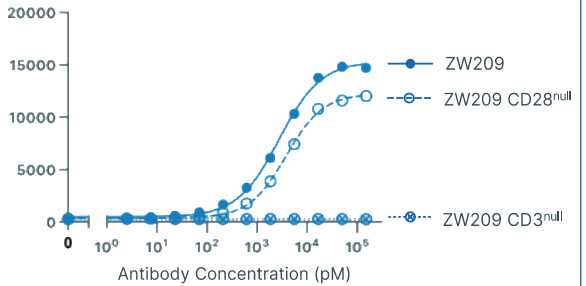
- Balanced low affinity CD3 and CD28 engagement
- Conditional CD28 binding that only binds in cis with CD3 engagement
- Strict target-dependent activity and T cell activation
- Identified via Azymetric™ screening of various antibody geometries and CD3 and CD28 paratope affinities

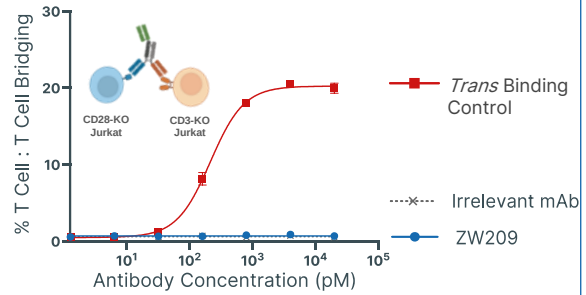
[1]Stein et al., Journal Clinical Oncology (2023); [2]Seung et al., Nature (2022); [3] Promsote et al., Nature Communications (2023)
TAA: tumor-associated antigens, TMDD: Target-mediated drug disposition

ZW209: Mediates Enhanced and Sustained Cytotoxicity

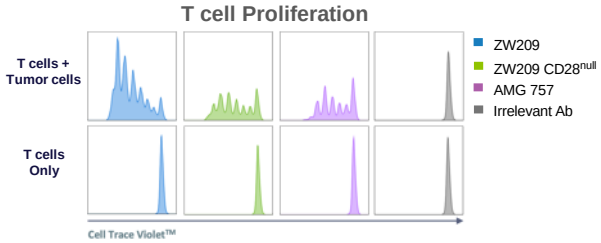
ZW209 demonstrates conditional CD28 binding and target-dependent anti-tumor activity

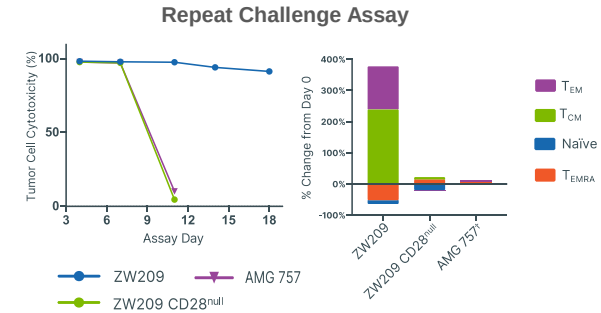
Conditional Binding of CD28, Requiring Co-engagement of CD3; Obligate Cis Binding



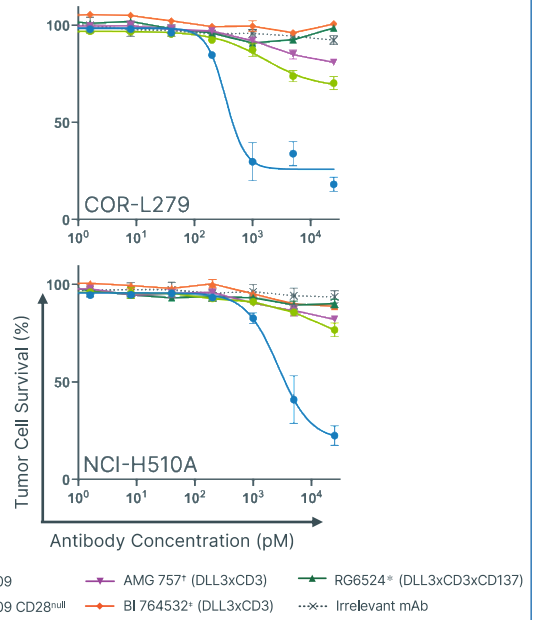


Improved T Cell Proliferation, Memory T Cell Expansion and Sustained Cytotoxicity





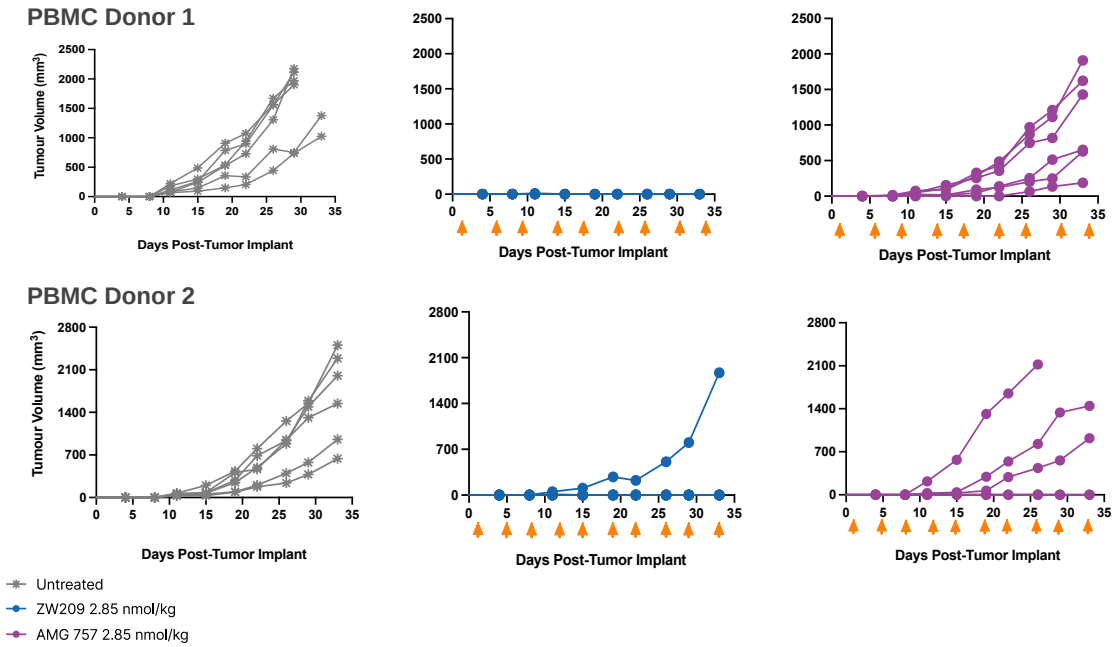
Improved Cytotoxicity Over Bispecifics in Low E:T Conditions



Lau D, et al. Presented at: AACR. 2025 (Abstract 7318). † AMG 757 (DLL3/CD3 BiTE) produced in-house, ‡ BI 764532 (DLL3/CD3 bispecific TCE) produced in-house, * RG6524 (DLL3/CD3/CD137 trispecific TCE), § CD3xCD28xTAA CODV Analog is a CD3xCD28xMSLN trispecific with the same format as the Sanofi Trispecific containing a CD3xCD28 CODV-Fab; produced in-house. ⁋ TGN1412 (hIgG4; biosimilar produced in-house)

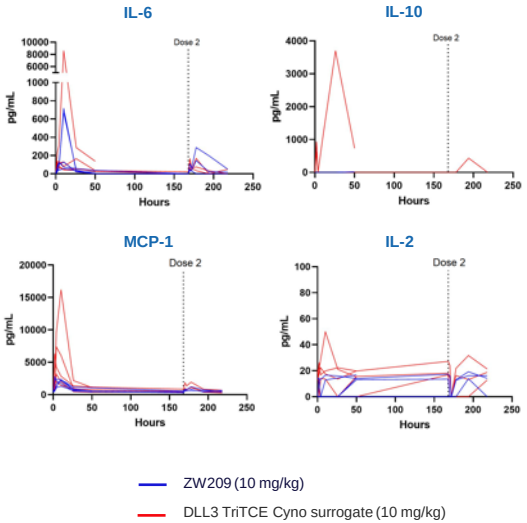
ZW209: Mediates Enhanced Anti-Tumor Activity and Favorable Safety Profile in *In Vitro* and Animal Studies

ZW209 Mediates Enhanced Anti-Tumor Activity *In Vivo* Compared to Benchmark Bispecific TCE in Humanized SCLC Models



Well Tolerated in Non-Human Primates

Transient, Minor Increases in Serum Cytokine Post-Dosing



Note: Peak 10 mg/kg surrogate values are male with ↑ CRP

Lau D, et al. Presented at: AACR. 2025 (Abstract 7318). † AMG 757 (DLL3/CD3 BiTE) produced in-house

AD-VAN-CE Portfolio: Progressing “First In Class” Therapeutics

1. **Focus on novel “first in class” multi-functional therapeutics:** novelty of modality, mechanism of action (MoA), and/or targeting strategy. Disruptive therapeutics with high potential benefit to patients.
2. **Build on competitive edge in ADCs and protein engineering:** cross complementary MoA and pathway axes across Zyme portfolio.
3. **Continue to focus on select therapeutic opportunities in solid tumors:** expand portfolio coverage with GI tract and thoracic cancers.
4. **Expand technology application to Heme-Onc, Autoimmune and Inflammatory Disease:** targeted areas conducive to multi-functional therapeutic intervention; overlap with company expertise.

Antibody-Drug Conjugates

- Novel Payload(s) – beyond TOPO1i
- Bispecific/Biparatopic(s)
- Novel Targets and Target Pairs
- Payload modalities beyond cytotoxics

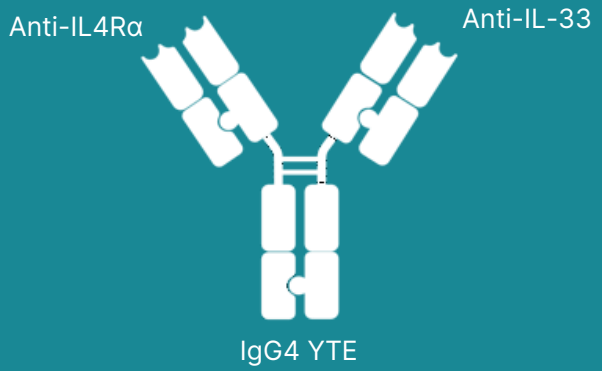
Cell Engagers

- Multispecific T Cell Engagers
- Multi-antigen targeting
- Conditional activation
- Novel targets (e.g. proteomics)
- Intracellular antigens

Cytokine Engineering

- Tumor specific cytokine activation
- Combination Checkpoint Inhibition/cytokine activation
- Chemokine incorporation
- Multi-cytokine blockade (Autoimmune)

ADCs: Antibody Drug Conjugates; GI: Gastrointestinal; MoA: mechanism of action.



ZW1528

Bispecific Designed to Address Respiratory Inflammation

On track for IND submission 2H 2026

Optimized Design

- IL-4Rα x IL-33 bispecific molecule that inhibits multiple pathways within complex pathophysiology of inflammation in diseases such as mixed-type COPD
- In-house antibody discovery of novel anti-IL4Rα and IL-33 paratopes
- Native IgG-like geometry

Differentiated Profile

- Potently blocks two complementary pathways of respiratory inflammation: IL-4Rα and IL-33
- Targets three cytokines in a single biologic
- Offers a unique approach that leverages clinically validated targets
- Demonstrates high manufacturability and incorporates half-life extending Fc modifications
- Aligns with requirements for successful AIID therapeutics

Significant Patient Need

- Mixed-type COPD patients are hospitalized 2-3.6 times more often than those with other COPD phenotypes[1]

1. https://pubmed.ncbi.nlm.nih.gov/25844673/#:~:text=Measurements%20and%20main%20results:%20Of,%3C%200.05%20for%20all%20comparisons).
AIID: Autoimmune and inflammatory disease, COPD: Chronic obstructive pulmonary disease

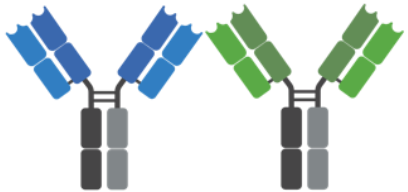
Bispecific Antibody Therapeutics as the Potential Answer to Complex Biology of AIID and Hematology Oncology

Patients

- Serious, difficult-to-treat diseases (e.g., ALL, cHL, MM, COPD, and NHL)
- Contribution of multiple (targetable) pathways
- Large patient population
- Restricted access to advanced therapeutics
- Urgent need for treatments in refractory or multidrug-resistant cases
- Poor outcomes

Clinical Science

+ Clinically validated targets
+ Benefits of combination



– Inconvenience and cost of clinical implementation

Technology

+ Clinically validated platform
+ Compatibility with Fc modifications (HLE)

+ High efficacy, convenient, cost-effective solution

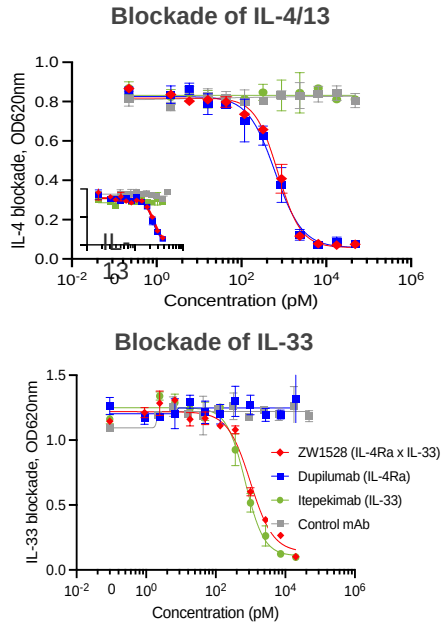
Zymeworks' differentiated multifunctional therapeutics provide opportunity to improve upon existing treatment approaches and current standard of care in areas of high unmet need

ALL:Acute lymphocytic leukemia , cHL: Classical Hodgkin Lymphoma, MM: Multiple myeloma, COPD: Chronic obstructive pulmonary disease, NHL: non-Hodgkin lymphoma, HLE: Half-life extension.

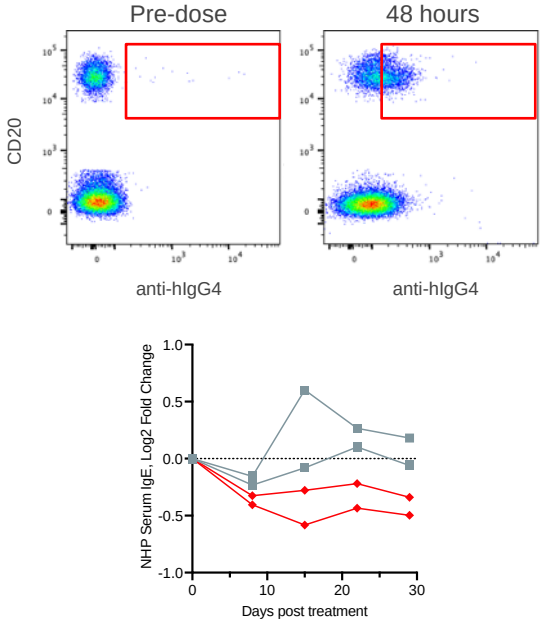
ZW1528: A Potential New Treatment Option in COPD

Potently blocks two complementary pathways of respiratory inflammation, while aligning with requirements for successful AIID therapeutics

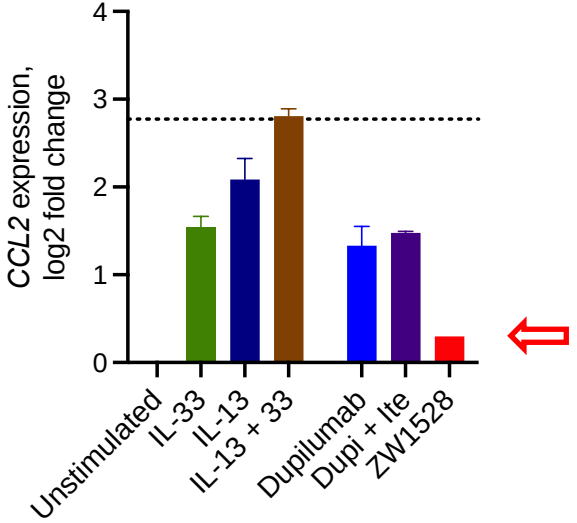
Effectively Blocks of IL-4/13 and IL-33 Signaling



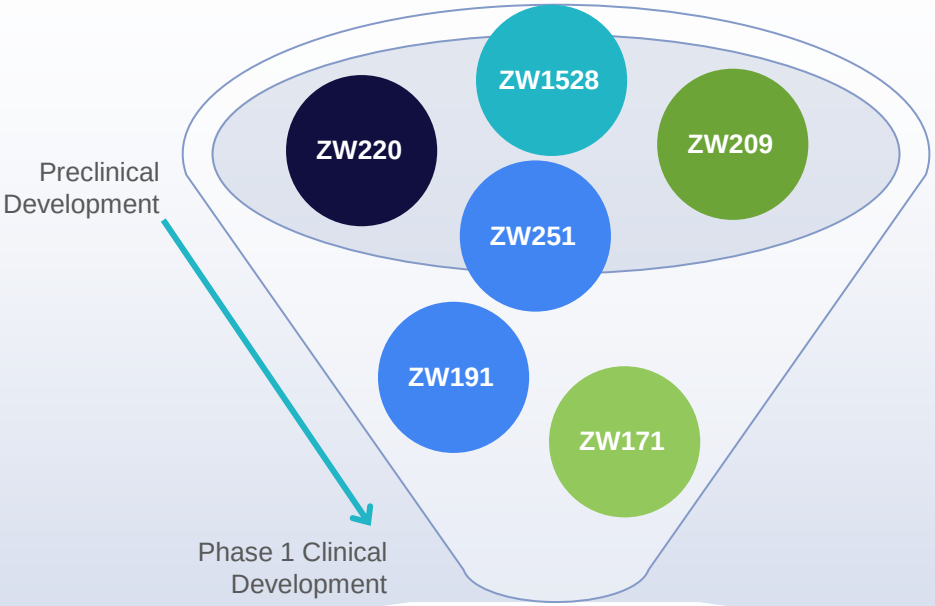
Demonstrates Biomarkers of IL-4Rα/IL-33 Blockade in NHP Up to 6 Weeks After Single Administration



Effectively Blocks Complementary Pathways of Immune Activation



Multiple Candidates in Development Offer Strategic Pivot Points



Decision Pathway Factors

- Optimal dose
- Tolerability and safety
- Early signs of anti-tumor activity
- Proof of targeted therapy: strong relationship between expression levels and anti-tumor activity
- Competitive landscape

Pipeline Resource Allocation

Partnership Optionality

Combination Approaches

Accelerated Development into Phase 2/3

Executive Summary

With nomination of ZW209, 5x5 solid tumor portfolio construction is 18 months ahead of schedule

Recent approval of zanidatamab demonstrates our experience and abilities to develop unique and differentiated therapeutics with clinically meaningful benefits for patients

ADVANCE portfolio broadly diversified into hematological cancers and AIID in addition to solid tumors with initial IND planned for 2H-2026 for ZW1528

Clear decision-making processes to advance or cease development activities on product candidates based on clinical data generated

Enhanced optionality for partnerships and collaborations to share capital and development risk

Strong financial position to provide opportunity for retaining certain product rights

R&D organizational structure in place to drive continued progress in both ‘5x5’ and ADVANCE portfolios

Additional solid tumor research focused on digestive system cancers, including CRC and PDAC

Meaningful Catalyst Events Anticipated Throughout 2025 & 2026

2025

- **Potential regulatory decisions in EU and China expected for zanidatamab** in 2L BTC
- **Initial royalty revenue for Ziihera®** from Jazz collected
- **Expected IND submission for ZW251** (GPC3) by mid-2025
- **Pivotal Phase 3 top-line PFS data readout in 1L GEA for zanidatamab** targeted by our partner Jazz in 2H 2025
- **Potential initial royalty revenue for Ziihera®** from BeiGene

2026

- **Expected IND submission for ZW209** (DLL3) in 1H 2026
- **Expected regulatory submission for ZW1528** (IL4R x IL-33) in 2H 2026
- **Jazz to potentially launch zanidatamab for 1L GEA** in 2026

CASH[1] RUNWAY FORECAST INTO 2H 2027 WHEN COMBINED WITH RECEIPT OF CERTAIN ANTICIPATED REGULATORY MILESTONE PAYMENTS

[1] Cash, cash equivalents, and marketable securities.
Illustrative. Key news flow only.
BTC: Biliary Tract Cancer; GEA: Gastroesophageal adenocarcinoma; GPC3: Glypican-3; sBLA: supplemental biologics license application; PFS: Progression-Free Survival

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