zymeworks

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

January 2025

Nasdaq: ZYME | zymeworks.com

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Furthermore, we are in the process of finalizing our financial results for the fourth quarter and fiscal year 2024, and therefore our finalized and audited results and final analysis of those results are not yet available. The preliminary expectations regarding year-end cash, cash equivalents, and marketable securities are the responsibility of management, are subject to management’s review, and the actual results could differ from management’s expectations. The actual results are also subject to audit by our independent registered public accounting firm and no assurance is given by our independent registered public accounting firm on such preliminary expectations. You should not draw any conclusions as to any other financial results as of and for the year ended December 31, 2024, based on the foregoing estimates. Although Zymeworks believes that such forward-looking statements are reasonable, there can be no assurance they will prove to be correct. 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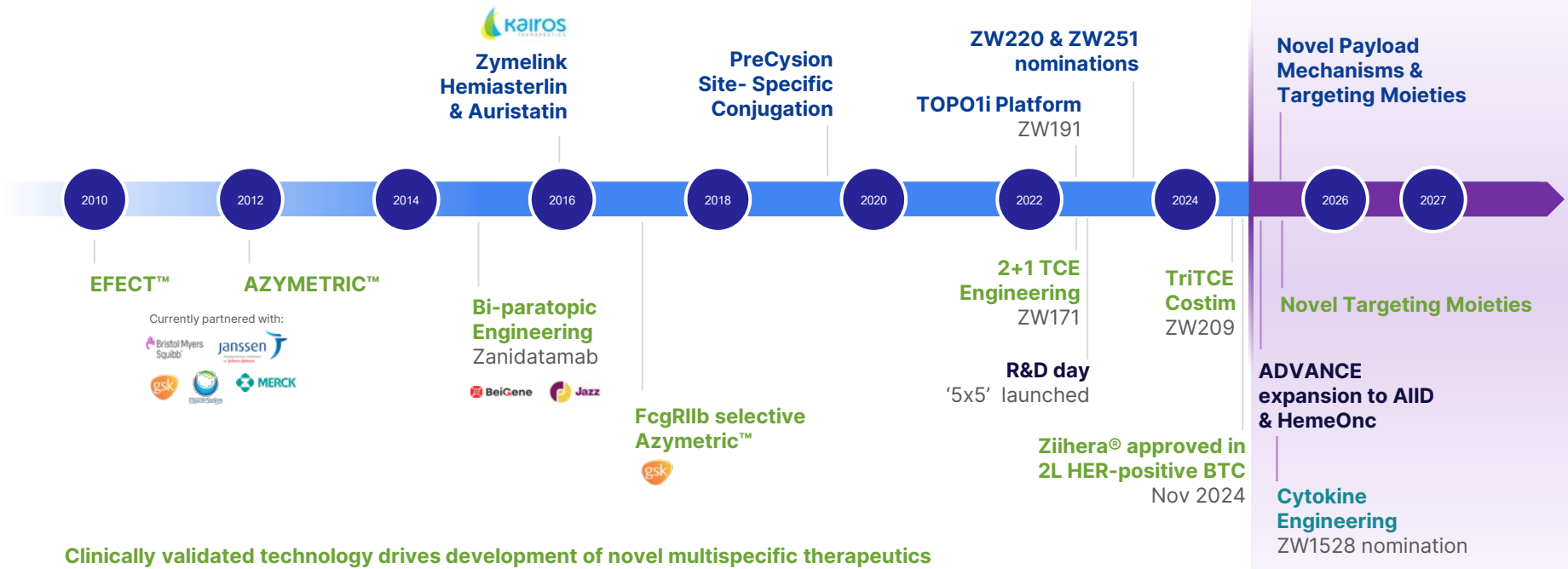
10+ Years of Pioneering Multifunctional Antibody Development

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 2Q25

6 Wholly-Owned Candidates

Multiple Modalities and Therapeutic Areas

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

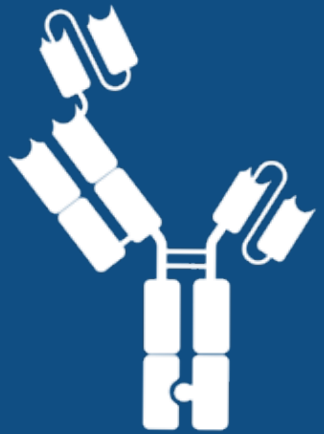
2 INDs Planned in 2025: ZW220 & ZW251

2 INDs Planned in 2026: ZW209 & ZW1528

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

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			IND 1H 2025		
ZW251 Topo1i ADC | DAR 4 | Fc WT	ZD06519 Payload	GPC3	Digestive System (HCC, PDAC)			IND 2H 2025		
Solid Tumor Oncology: Multipecifics 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			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™ Het-Fab | YTE	IL4Rα x IL-33				IND 2H 2026		
ZW1572 Dual Cytokine Blocker	Azymetric™ Het-Fab | YTE	IL4Rα x IL-31						



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

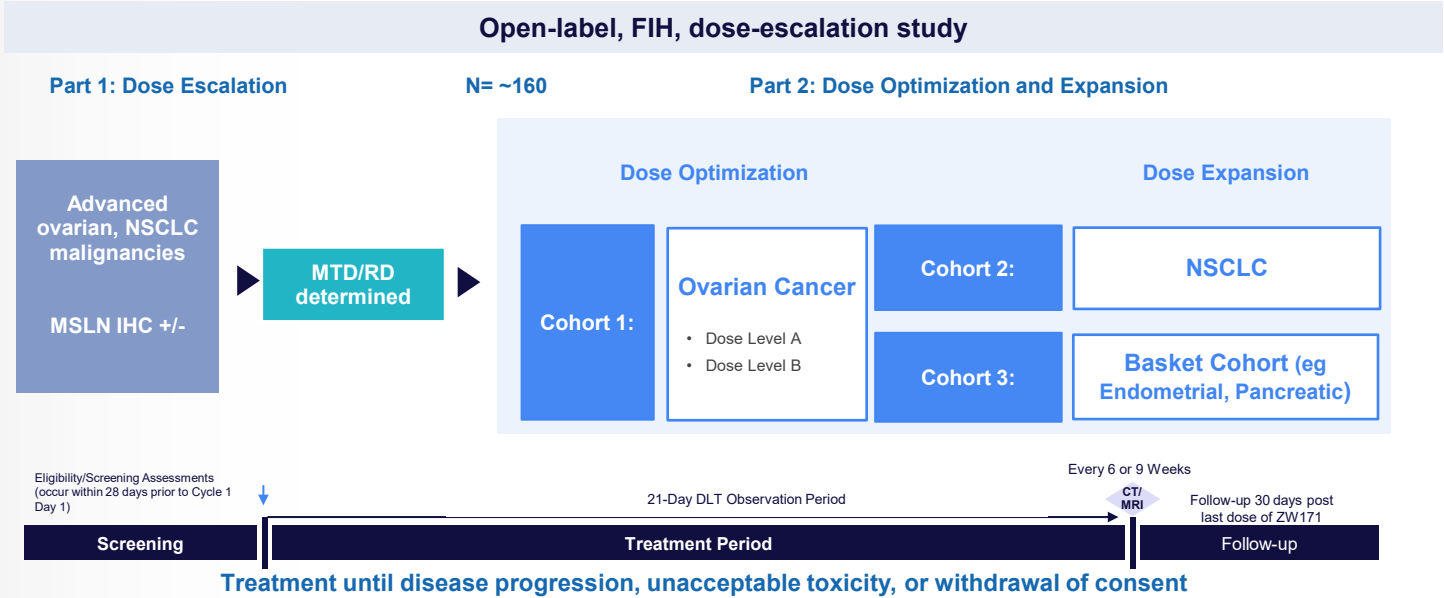
ZW171 Global Phase 1 Study in MSLN-Expressing Solid Tumors (NCT06523803)

USA
US FDA Approval
Sites Activated

United Kingdom
UK MHRA Approval
Sites Activated

Germany
Pending Approval

South Korea
MFDS Approval
Sites 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.

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

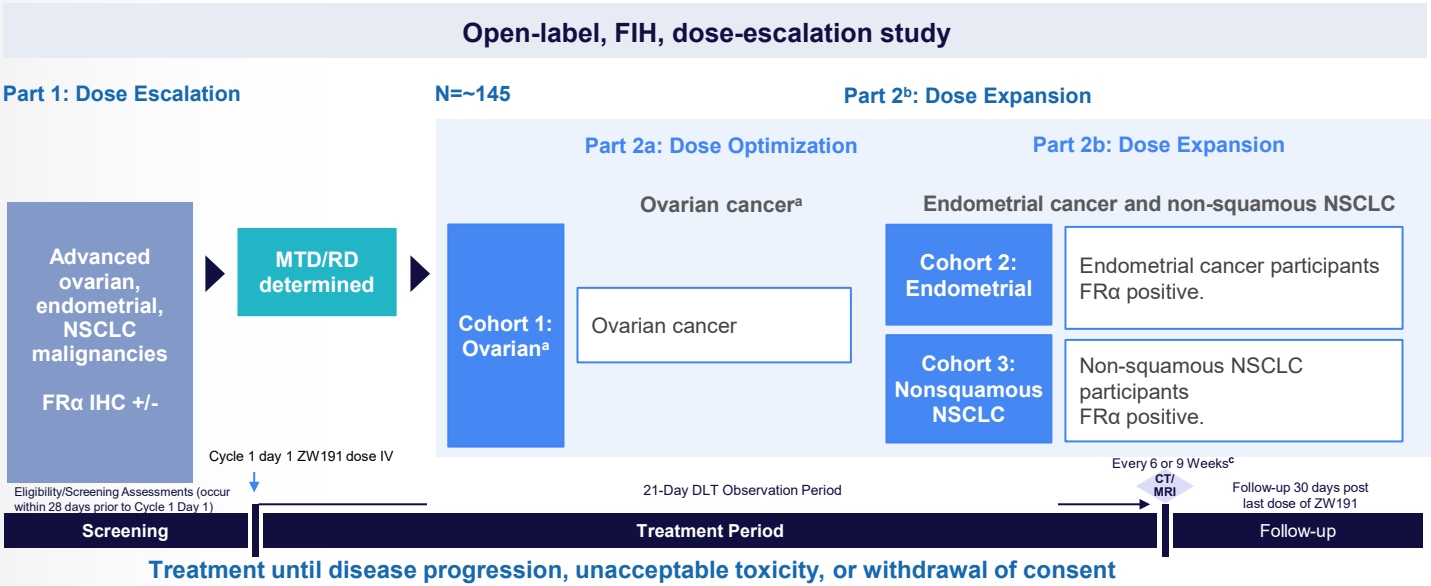
USA
US FDA Approval
Sites Activated

Japan
PMDA Approval
Sites Activated

Australia
TGA Approval
First Site Activated

South Korea
MFDS Approval
Sites Activated

Singapore
HSA Approval
First Site 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..

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

- Muti-specific 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.

Meaningful Catalysts Expected Throughout 2025 & 2026

Pipeline Events

1H 2025

- Expected IND submission for ZW220 (NaPi2b) in 1H 2025
- Pivotal Phase 3 top-line PFS data readout in 1L GEA for zanidatamab targeted by our partner Jazz in 2Q 2025
- Potential regulatory decisions in EU and China expected for zanidatamab in 2L BTC with potential approval as early as 2Q 2025
- Initial royalty revenue for Ziihera® from Jazz

2H 2025

- Expected IND submission for ZW251 (GPC3) in 2H 2025
- Jazz may file a sBLA for zanidatamab in 1L GEA
- Potential Initial royalty revenue for Ziihera® from BeiGene

2026

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

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

[1] cash, cash equivalents, and marketable securities

Illustrative. Key news flow only.

BTC: Biliary Tract Cancer; Gastroesophageal adenocarcinoma; GPC3: Glypican-3; NaPi2b: Sodium Dependent Phosphate transport Protein 2b; sBLA: supplemental biologics license application..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