zymeworks

Making a meaningful difference

A royalty-driven organization differentiated by in-house R&D capabilities developing novel medicines for patients with difficult-to-treat diseases

MAY 2026

Nasdaq: ZYME | zymeworks.com

Legal disclaimer

This presentation and any accompanying oral commentary include “forward-looking statements” or information within the meaning of the applicable securities legislation, including Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements in this presentation and the accompanying oral commentary include, but are not limited to, statements that relate to Zymeworks’ expectations regarding implementation of its strategic priorities and the anticipated benefits thereof, including shareholder returns and the anticipated manner of such returns; anticipated capital allocation strategy; the anticipated benefits of its collaboration agreements, including Zymeworks’ ability to receive any future milestone payments and royalties thereunder; statements relating to potential milestone payments upon regulatory approvals of Ziihera in GEA; industry opportunities for acquisition of new revenue streams or collaborations; statements that relate to Zymeworks’ ability to execute the share repurchase plan, in whole or in part; expected timing and amount of repurchases; Zymeworks’ ability to pursue its business objectives following repurchases under the share repurchase plan; expectations regarding future regulatory filings and approvals and the timing thereof; the timing of and results of interactions with regulators; the timing and status of ongoing and future studies and the related data; clinical development of product candidates and enrollment in clinical trials; anticipated preclinical and clinical data presentations; the potential addressable market of zanidatamab and other product candidates; expectations regarding peak sales; potential safety profile and therapeutic effects of zanidatamab and other product candidates; the commercial potential of technology platforms and zanidatamab and other product candidates; extrapolations or comparisons of results derived from independent studies instead of head-to-head studies are subject to misinterpretation, assumptions or caveats of each study, and may be different from head-to-head comparisons; Zymeworks’ early-stage pipeline; evolution of Zymeworks’ business strategy related to anticipated and potential future royalty streams and existing and potential new partnerships; potential strategic initiatives; Zymeworks’ ability to execute new collaborations and partnerships; the anticipated benefits of its collaboration agreements with Jazz, BeOne and other partners; Zymeworks’ ability to receive any future milestone payments and royalties thereunder; anticipated sufficiency of existing cash resources, when assuming full execution of the share repurchase plan and combined with the assumed receipt of certain anticipated regulatory milestones, to fund Zymeworks’ planned operations beyond 2028; Zymeworks’ ability to satisfy potential regulatory and commercial milestones with existing and future partners; the timing and status of ongoing and future studies and the release of data; anticipated continued receipt of revenue from existing and future partners; Zymeworks’ early stage pipeline; Zymeworks’ strategic priorities; preclinical development progress and expectations for future investigational new drug and foreign equivalent application submissions; and other information that is not historical information. When used herein, words such as “plan”, “believe”, “expect”, “may”, “continue”, “anticipate”, “potential”, “will”, “progress”, “on track”, and similar expressions, or any discussion of strategy, are intended to identify forward-looking statements. In addition, any statements or information that refer to expectations, beliefs, plans, projections, objectives, performance or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking. All forward-looking statements are based upon Zymeworks’ current expectations and various assumptions, including, without limitation, Zymeworks’ examination of historical operating trends. Zymeworks believes there is a reasonable basis for its expectations and beliefs, but they are inherently uncertain. Zymeworks may not realize its expectations, and its beliefs may not prove correct. Actual results could differ materially from those described or implied by such forward-looking statements as a result of various factors, including, without limitation: Zymeworks’ assumptions and estimates regarding its financial condition, future financial performance and estimated cash runway may be incorrect; any of Zymeworks’ or its partners’ product candidates may fail in development, may not receive required regulatory approvals, or may be delayed to a point where they are not commercially viable; Zymeworks may not be able to execute the share repurchase plan, in whole or in part; the anticipated benefits of the share repurchase plan may not be realized; Zymeworks may not achieve milestones or receive additional payments under its collaborations; regulatory agencies may impose additional requirements or delay the initiation of clinical trials; the impact of new or changing laws and regulations; market conditions, including the impact of tariffs; potential negative impacts of FDA regulatory delays and uncertainty around recent policy developments, changes in the leadership of federal agencies such as the FDA, staff layoffs, budget cuts to agency programs and research, and changes in drug pricing controls; the impact of pandemics and other health crises on Zymeworks’ business, research and clinical development plans and timelines and results of operations, including impact on its clinical trial sites, collaborators, and contractors who act for or on Zymeworks’ behalf; zanidatamab may not be successfully commercialized; Zymeworks’ evolution of its business strategy related to anticipated and potential future milestones and royalty streams and existing and potential new partnerships may not be successfully implemented; ongoing and any future clinical trials clinical trials may not demonstrate safety and efficacy of any of Zymeworks’ or its collaborators’ product candidates; Zymeworks’ evolution of its business strategy may not deliver meaningful shareholder returns; Zymeworks may be unsuccessful in actively managing and/or aggregating revenue-generating assets alongside its active R&D operations; Zymeworks may be unable to maintain or enter into new partnerships or strategic collaborations; and the factors described under “Risk Factors” in Zymeworks’ quarterly and annual reports filed with the Securities and Exchange Commission (copies of which may be obtained at www.sec.gov and www.sedarplus.ca). Although Zymeworks believes that such forward-looking statements are reasonable, there can be no assurance they will prove to be correct. Investors should not place undue reliance on forward-looking statements.

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Executing on an established model, positioned for scalable growth

✓ Shareholder returns
⚙ Operational progress

PARTNERSHIP PROGRESS

2H 2024

Recognized revenue of **$2.5M** research **milestone payment from GSK**

FDA approves Ziihera® for the treatment of HER2+ (IHC 3+) BTC resulting in **$25.0M regulatory milestone payment from Jazz**

✓ Completion of **initial $30.0M of share repurchase** program

1H 2025

Recognized revenue of $25.2M in partnership milestone payments*

NMPA conditional approval of Ziihera® for BTC resulting **in $20.0M milestone payment from BeOne**

2H 2025

✓ Completion of **$95.8M of share repurchase** program

✓ **Announced $125.0M share repurchase** program

Recognized revenue of **$25.0M** development **milestone payment from J&J**

HERIZON-GEA-01 Topline Data Readout

1H 2026

Jazz and BeOne completed sBLA for zanidatamab for the treatment of HER2+ GEA

PIPELINE PROGRESS

1H 2025

First patient dosed in the Phase 1 trials of ZW191 and ZW171

2H 2025

Decision to **discontinue development of ZW171**

⚙ **Expansion of Board and management team** focused on strategic BD

1H 2026

Initial clinical data from the Phase 1 trial of ZW191 showcasing best-in-class potential

First patient dosed in the Phase 1 trial of ZW251

*Inclusive of $7.5M payment from BMS, $3.1M clinical milestone payment from Daiichi Sankyo, $14.0M clinical milestone payment from GSK.

Evolving our value proposition

We are transforming from a traditional biotech to a **revenue-generating** organization **differentiated by in-house R&D capabilities**

We are pivoting to this novel strategy to:

Return and compound existing valuable royalty streams in a tax-efficient manner

Enable **internal R&D to focus on its strengths** – delivering highly innovative medicines with early proof of differentiation – while **avoiding costly and binary late-stage development**

Deploy capital with a **focus on best possible risk-adjusted return** to shareholders

Pathways to return and compound value for shareholders

CASH FLOW FROM PARTNERS

BeOne
Johnson&Johnson Innovative Medicine
GSK
Daiichi-Sankyo
MERCK
Jazz Pharmaceuticals

COMPOUND VALUE ALTERNATIVES

- Internal Programs
- Acquired Programs
- Acquired Royalties

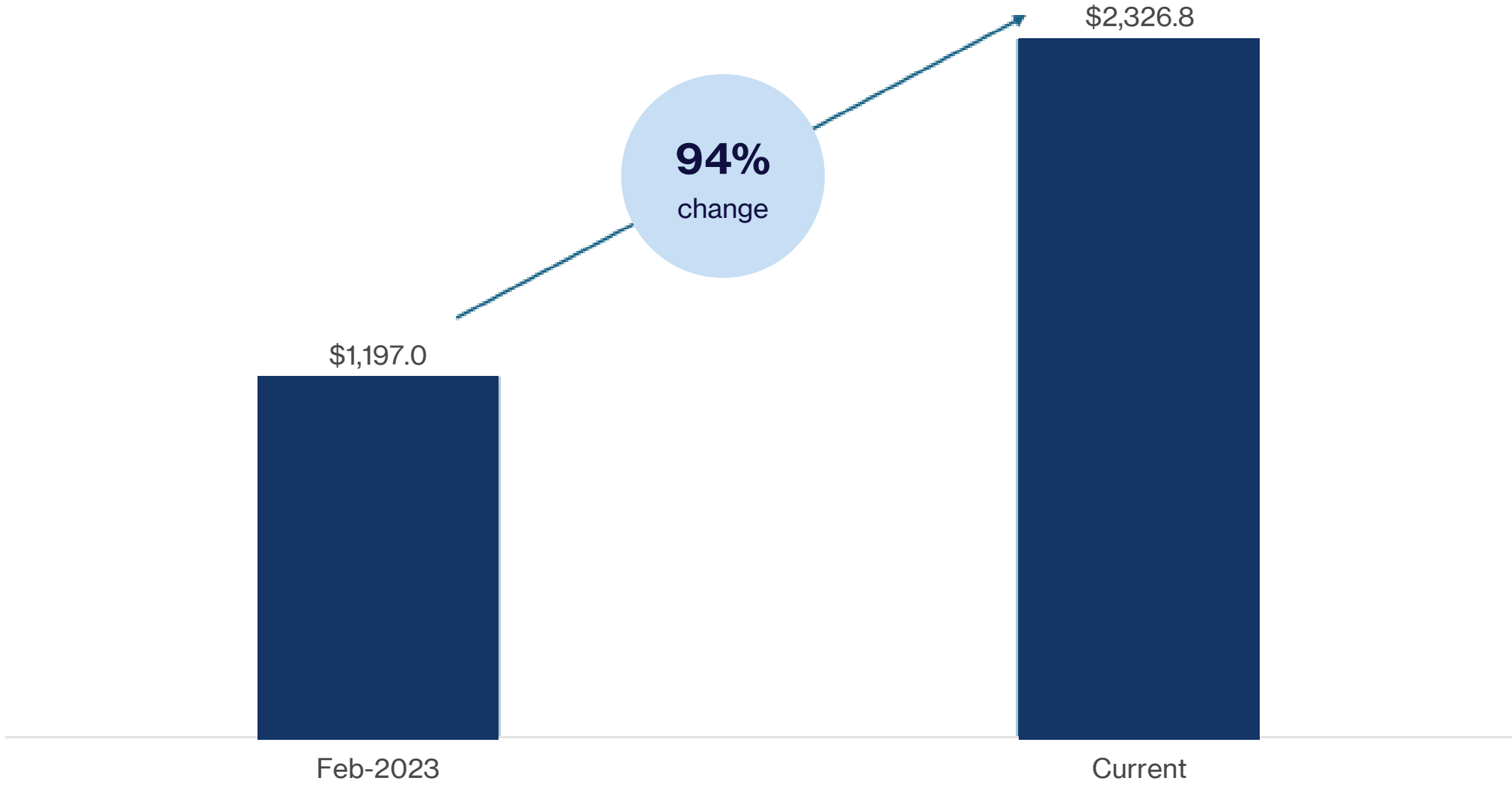
RETURN VALUE ALTERNATIVES

- Share Repurchases
- Special Dividends

We seek to allocate capital based on which path we believe will provide the highest return for shareholders

Ziihera Peak Sales Estimate Over Time

Evolution of Wall Street Consensus | 2023 vs. Now | ($ Millions)



Differentiation of partner focused R&D

Partner driven clinical development

R&D operations self-funded through partnerships and milestones, without dependency on royalty cash flow

Preclinical and early clinical stage development focus

Minimize costly, lengthy, binary late-stage development programs

Ability to leverage internal discovery and external BD

Enables diverse scientific platforms and multiple areas of expertise

Success metrics: partnerships, royalty and milestone generation

Well-positioned with R&D and asset aggregation synergies

	zymeworks	TRADITIONAL ROYALTY BUYERS	TRADITIONAL BIOTECH
Acquire existing royalties	✓	✓	✗
Create synthetic royalties	✓	✓	✗
Unlock trapped royalties	✓	✗	✗
Establish platform collaborations	✓	✗	✓
Partner internal programs	✓	✗	✓
Partner acquired programs	✓	✗	✓

Differentiated pipeline of multifunctional therapeutics

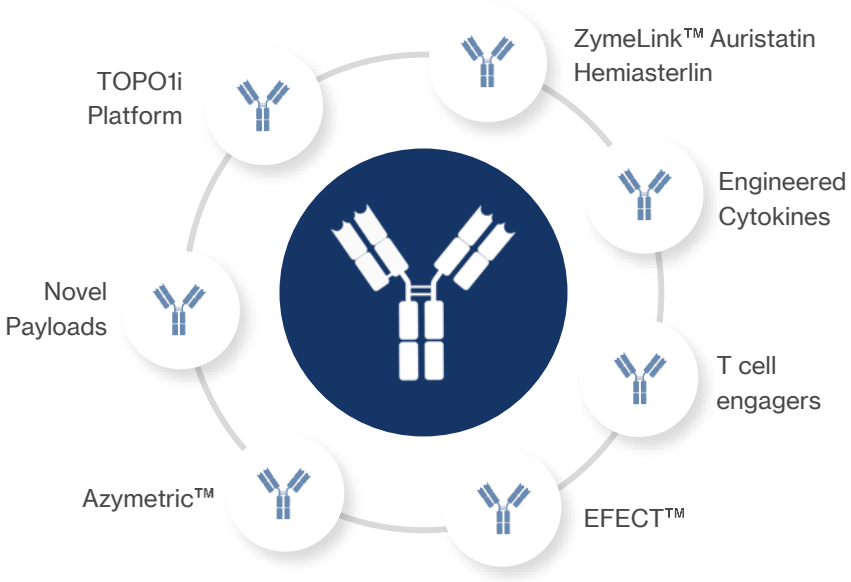
Program	Technology	Target	Indication	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
Solid Tumor Oncology: Antibody-Drug Conjugates (ADC)								
ZW191 Topo1i ADC | DAR 8 | Fc WT	ZD06519 Payload	FRα	Gynecological Thoracic			NCT06555744		
ZW251 Topo1i ADC | DAR 4 | Fc WT	ZD06519 Payload	GPC3	Digestive System (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					
ZW427* RASi ADC | DAR 8 | Fc Silent	RASi Payload	Ly6E	Lung and GI					
ZW418* RASi ADC | DAR 8 | Biparatopic	RASi Payload	Biparatopic PTK7	Lung					
ZW439* RASi ADC | DAR 8 | Fc Silent	RASi Payload	Claudin18.2	Pancreatic					
Solid Tumor Oncology: Multispecific Antibody Therapeutics (MSAT)								
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						

*We intend to advance our future ADC research efforts into clinical studies only with partnerships and collaborations and/or external funding becoming available.

Partnering is central to Zymeworks' history and future

PLATFORM AND DISCOVERY PARTNERSHIPS

Leverage partnerships to extend the reach of Zymeworks' best-in-class platforms and capabilities



MERCK · Daiichi-Sankyo · Johnson&Johnson · GSK

ASSET-BASED / PIPELINE PARTNERSHIPS

Commercial Partners

Jazz Pharmaceuticals

BeOne

zanidatamab

FUTURE PARTNERSHIP OPTIONALITY FOR OUR WHOLLY-OWNED PIPELINE

Oncology programs

Antibody-Drug Conjugates

ZW191
ZW327

ZW251
ZW220

T-cell Engagers

ZW209
ZW239

AIID programs

Bispecifics

ZW1528
ZW1572

Proven execution and financial foundation with Ziihera®

Jazz Pharmaceuticals

UP TO

$440M

Anticipated near-term milestones for global GEA approvals[1]

$400M

Upfront and milestone payments received to date*

$1.3B

Future potential regulatory and commercial milestones***

$2.0B+

Peak sales potential provided by jazz[2]
10-20% tiered royalties

BeOne

$81M

Upfront and milestone payments received to date

$144M

Future potential regulatory and commercial milestones

19.5%

High single-digit royalties from BeOne sales[1]

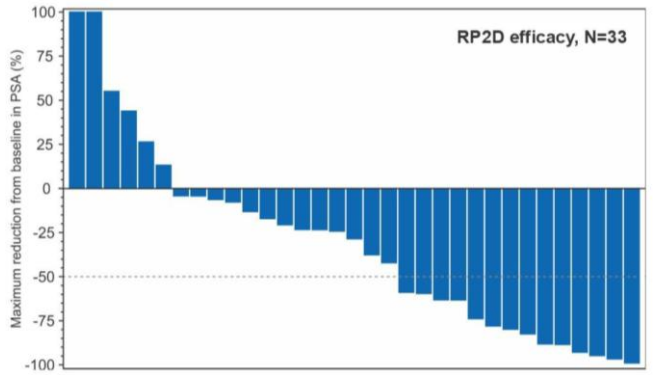
1. Regulatory Approval in GEA anticipated to be received: USA FDA - $250M, European Commission - $100M, PMDA (Japan) - $75M, NMPA (China) - $15M; 2. Referenced in Jazz Pharmaceuticals Corporate Presentation September 4, 2025 *Upfront and milestone payments received through 9/30/2025; **up to 20% when royalty reduction of 0.5% reaches cap in the low double-digit millions of dollars; ***$1.3B inclusive of the $425M of regulatory millstones associated with positive approvals in GEA from Jazz.
GEA: Gastric and esophageal adenocarcinoma

Diverse potential revenue streams from existing platform partnerships

Partner & Phase	Potential Future Milestone Payments	Royalty Rate
Johnson&Johnson Innovative Medicine *Phase 3*	Up to **$434m**	**Tiered worldwide royalties in the mid-single digit percentages**
GSK *Phase 1*	Up to $1.1B	Tiered worldwide royalties in the low to mid-single digit percentages
Daiichi-Sankyo *Preclinical*	Up to $230M	Tiered worldwide royalties from low single digit percentages up to 10%
GSK *Preclinical*	Up to $1.1B	Tiered worldwide royalties in the low single digit percentages
MERCK *Preclinical*	Up to $921.8M	Tiered worldwide royalties on sales

PROMISING UPDATES FROM PASRITAMIG

- **First Phase 3 initiated in September 2025 (NCT07164443):** pasritamig vs placebo in castration-resistant prostate cancer
- **Phase 3 scheduled for 2026 (NCT07225946):** pasritamig with docetaxel vs docetaxel for metastatic castration-resistant prostate cancer
- **J&J guidance of $1-5B in sales[1]**



Encouraging Phase 1 clinical data presented at ASCO 2025*

Except as otherwise indicated, the information is provided as at December 31, 2025. The information included in the table above presents a summary of key aspects of our collaboration and licensing agreements. Figures reflect all potential future milestone payments under the applicable agreement, including, but not limited to, the lead asset. Current stage and therapeutic indication reflects the current preclinical, clinical or commercial stage of development for the most advanced program under the partnership, as applicable. For additional information regarding the terms and conditions of our collaboration and licensing agreements, please refer to "Item 1. Business – Strategic Partnerships and Collaborations" of our Annual Report on Form 10-K for the year ended December 31, 2025 filed with the SEC on March 2, 2026.

1. $1-$5B peak sales opportunity referenced by J&J: https://www.investor.jnj.com/pipeline/novel-therapies/default.aspx

*Data cut-off March 7, 2025. PSA50, >50% decrease from baseline in PSA RP2D, recommended phase 2 dose.

Partnerships that benefit both Zymeworks and our partners

	PEOPLE	PLATFORM	PARTNER
Partner Benefits	**Access** to proven team with deep scientific and engineering expertise	**Unique** combination of biology and engineering enables development of complex therapeutics	**Flexible** model enables partners to tailor collaborations to their strategic priorities
Zymeworks Benefits	**Builds** reputation as partner of choice and knowledge leader across modalities	**Extends** the reach of Zymeworks' novel and differentiated technologies	**Non-dilutive** capital to enable further scientific innovation and builds royalty pipeline

Operating from a strong financial position

+$403M
Cash resources[1] provides a runway beyond 2028[2]

UP TO
$440M
From potential cumulative global GEA approvals

$125M
Share repurchase plan announced in November 2025

$106M
Revenues reported for 2025[3]

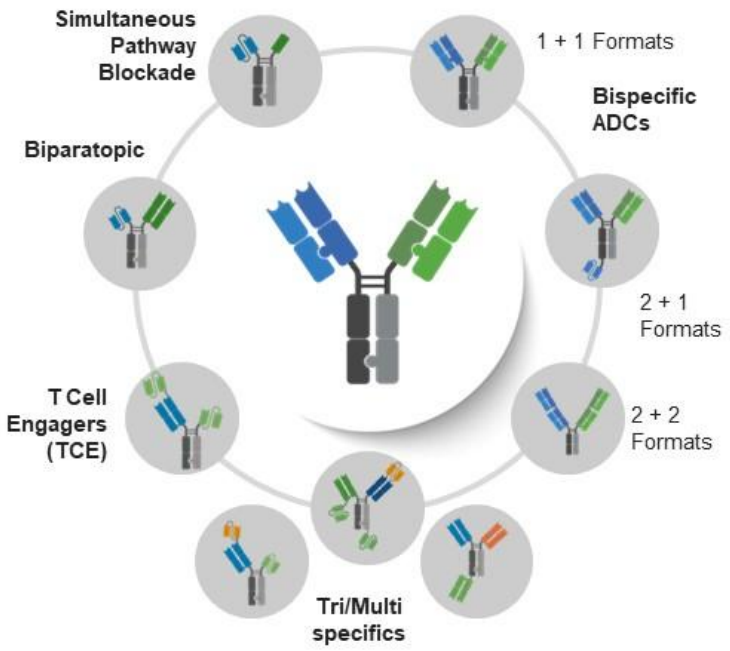
Cash runway expected to fund operations beyond 2028[2], and potential to access additional non-dilutive potentially lower cost of capital financing

1. As of March 31, 2026, the Company had cash resources of approximately $403.8 million, consisting of cash, cash equivalents, and marketable securities.; 2. Assuming the full execution of the $125.0M share repurchase plan, we currently expect our existing cash resources, when combined with anticipated regulatory milestone payments of $440.0 million related to the potential approvals of Ziihera in GEA in the United States, Europe, Japan, and China, as well as the net proceeds from our non-recourse royalty-backed note, to fund our planned operations beyond 2028; 3. Revenues for 2025, reported as of December 31, 2025.

Pushing the boundaries of antibody-based therapeutics through multispecifics and optimized drug conjugates

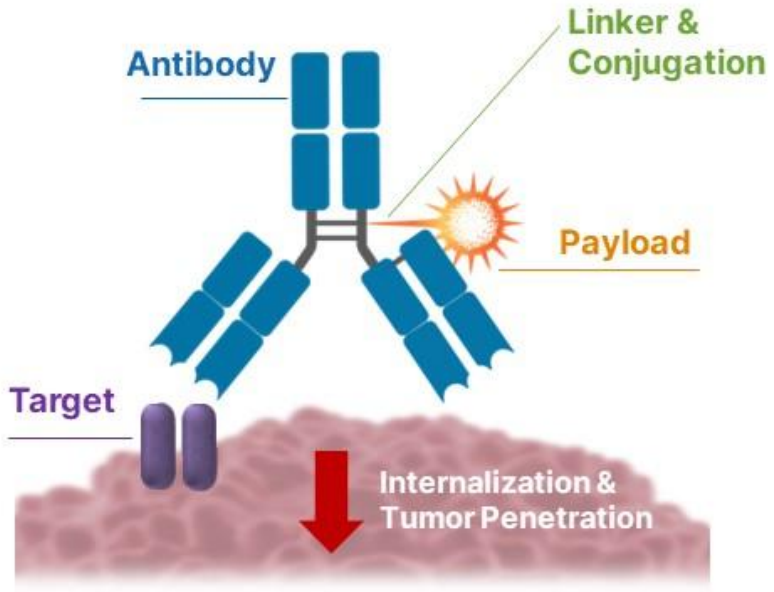
MULTISPECIFIC ANTIBODIES

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



ZW191

ADC Designed to Target FRα-Expressing Tumors

Phase 1 trial ongoing (NCT06555744)

Optimized design[1]

- ADC targeting FRα -expressing tumors including ovarian cancer, other gynecological cancers, and non-small cell lung cancer
- 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]
- Phase 1 trial efficacy data shows confirmed objective response rate (cORR) of 61% at doses 6.4-9.6 mg/kg and 56% cORR across all dose levels in platinum resistant ovarian cancer (PROC)
- Opportunity to treat broader range of FRα-expressing cancers

Significant patient need

- FRα is found in ~75% of high-grade serous ovarian carcinomas[3] and ~70% of lung adenocarcinomas[4]
- The U.S. Food and Drug Administration granted Fast Track designation to ZW191 for the treatment of patients with advanced or metastatic PROC

1. Lawn S et al. Abstract # 2641 Presented at AACR 2023;
2. LoRusso P. et al. Abstract # CT306 Presented at AACR Annual Meeting 2026;
3.Köbel, M., Madore, J., Ramus, S. et al. Br J Cancer 111, 2297–2307 (2014);
4. O'Shannessy DJ, et al., Oncotarget. 2012 Apr; 3(4):414-25.
FRα: Folate receptor alpha;; ADC: Antibody-drug conjugate.

ZW191 demonstrates a favorable clinical safety profile

TRAE, n (%) Data cutoff: March 9, 2026	ZW191 1.6 mg/kg (n=3)	ZW191 3.2 mg/kg (n=3)	ZW191 4.8 mg/kg (n=6)	ZW191 6.4 mg/kg (n=12)	ZW191 8.0 mg/kg (n=12)	ZW191 9.6 mg/kg (n=12)	ZW191 11.2 mg/kg (n=3)	Total (n=51)
Any TRAE	2 (67)	3 (100)	6 (100)	12 (100)	12 (100)	12 (100)	3 (100)	50 (98)
Grade ≥3 TRAE	2 (67)	2 (67)	4 (67)	4 (33)	6 (50)	8 (67)	2 (67)	28 (55)
Serious TRAE	2 (67)	1 (33)	1 (17)	3 (25)	4 (33)	6 (50)	1 (33)	18 (35)
TRAE leading to dose delays	0	1 (33)	2 (33)	6 (50)	2 (17)	7 (58)	2 (67)	20 (39)
TRAE leading to dose reduction	0	0	0	2 (17)	4 (33)	3 (25)	0	9 (18)
Discontinuations due to TEAEs	0	2 (67)	0	2 (17)	2 (17)	2 (17)	2 (67)	10 (20)
Deaths due to TEAEs	0	0	0	0	0	0	1 (33)	1 (2)[a]

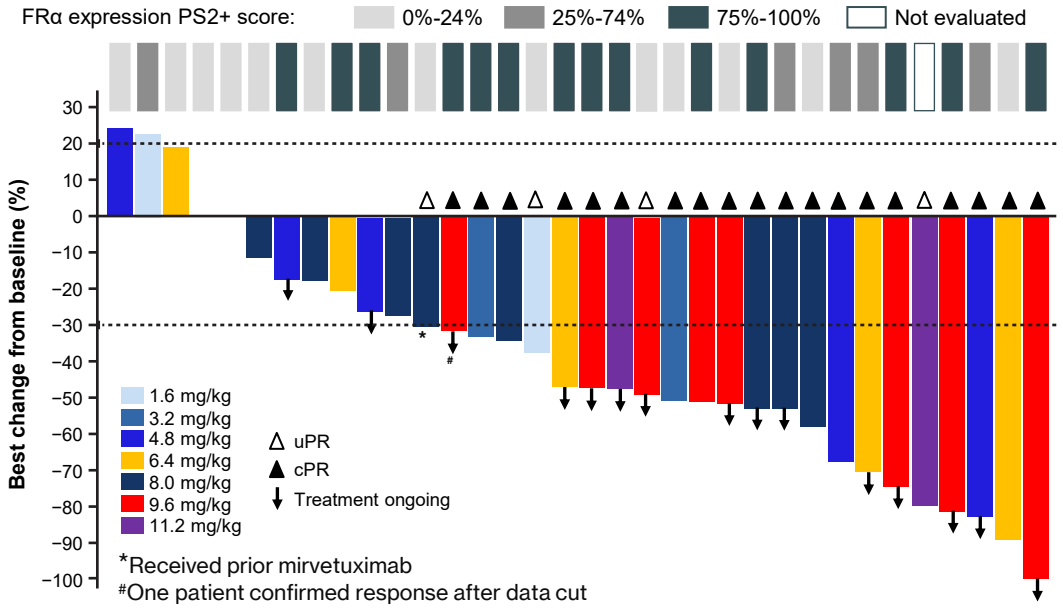
Presented at 2026 American Association of Cancer Research Annual Meeting

[a] Death due to small intestinal perforation (unrelated).
LoRusso P. et al. Abstract #CT306 presented at AACR Annual Meeting 2026
TRAE: treatment-related adverse event

ZWI-ZW191-101 | clinical results

Anti-tumor activity of ZW191 in ovarian cancer (n=34)

Data cutoff: March 9, 2026



Ovarian Cancer	6.4-9.6 mg/kg (n=23)	Total across all dose levels (n=34)
cORR#, % (95% CI)	61% (38.5, 80.3)	56% (37.9, 72.8)
DCR, % (95% CI)	100% (85.2, 100.0)	94% (80.3, 99.3)

Efficacy for response-evaluable participants with ovarian and endometrial cancer

Data cutoff: March 9, 2026

Ovarian Cancer and Endometrial Cancer	6.4-9.6 mg/kg	Total across dose levels
mTTR, mo (range)	1.4 (1.2-4.2)	1.4 (1.2-4.2)
mDOR, mo (95% CI)	NR (4.2, NR)	NR (4.2, NR)
mPFS, mo (95% CI)	7.6 (4.2, NR)	7.6 (5.5, NR)

As of data cut-off, 34 ovarian cancer participants were response-evaluable by having at least 1 post-baseline scan and were included in the efficacy analysis. Response based on RECIST v1.1 (response and progression defined as –30% and +20% change from baseline, respectively). FRα expression was assessed by immunohistochemistry using archival or newly collected formalin-fixed, paraffin-embedded biopsies with the VENTANA® FOLR1 (FOLR1-2.1) assay. The PS2+ score was defined as the percentage of tumor cells with 2+ and 3+ staining intensity and categorized as low/negative 0%-24%, intermediate 25%-74%, and high 75%-100%. Disease control rate is defined as a best response of complete response, partial response, non-complete response/non-progressive disease, or stable disease per RECIST v1.1. #One patient confirmed response after data cut
LoRusso P. et al. Abstract #CT306 presented at the 2026 AACR Annual Meeting.
CI: confidence interval; cORR: confirmed objective response rate; cPR: confirmed partial response; DCR: disease control response; FRα: folate receptor alpha; OC: ovarian cancer; RECIST v1.1: Response Evaluation Criteria in Solid Tumors, version 1.1; uPR: unconfirmed partial response. mDOR: median duration of response; mo: months; mPFS: median progression-free survival; mTTR: median time to response; NR: not reached; OC: ovarian cancer; PR: partial response.

Presented at 2026 American Association of Cancer Research Annual Meeting

ZW191 | Next steps

Data-driven development

Building confidence in our ADC platform through safety, pharmacokinetics, and efficacy with emerging clinical data

Optimization & differentiation

11.2 mg/kg dose defined as maximum tolerated dose

Randomized dose optimization began in 4Q-2025 in platinum resistant ovarian cancer at 9.6 and 6.4 mg/kg doses (~30 pts/cohort)

Phase 1 data supports best-in-class potential

Strategic growth potential

Emerging data will inform registration and combination strategies, including earlier-line opportunities

In parallel, partnership discussions are underway to further refine and accelerate development

ZW251

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

Phase 1 clinical trial underway (NCT07164313)

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]
- High tolerability in repeat dose nonhuman primate studies of up to 120mg/kg
- Preclinical tolerability profile enables high first in human dose of 3.2 mg/kg

Significant patient need

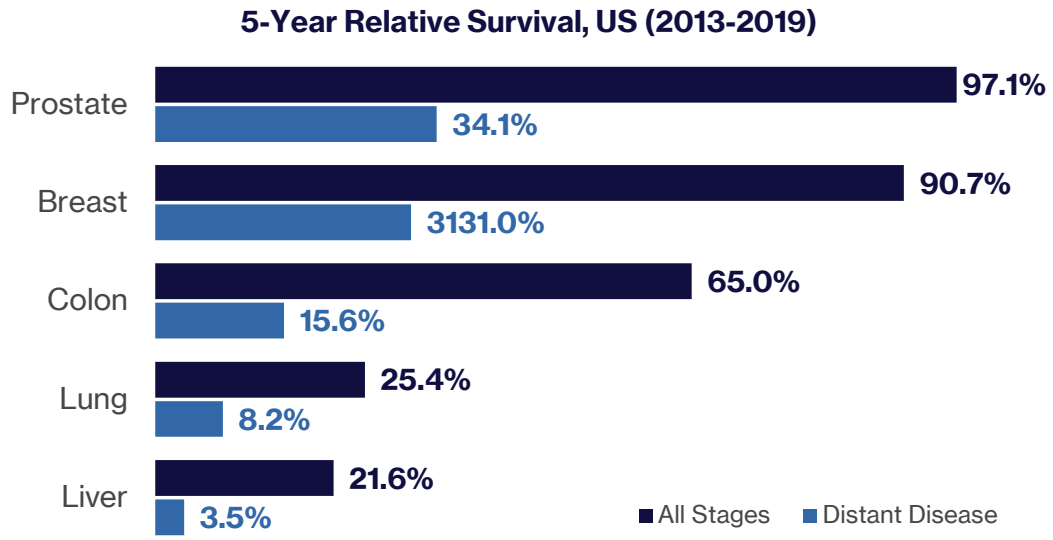
- GPC3 is expressed in 76% of HCC, with high expression observed in ~55% of HCC[2]
- HCC is the most common type of primary liver cancer and the third leading cause of cancer deaths globally[1]

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.
ADC: Antibody Drug Conjugate; GPC3: Glypican-3 MOA: Mechanism of action

Hepatocellular carcinoma epidemiology and current treatment

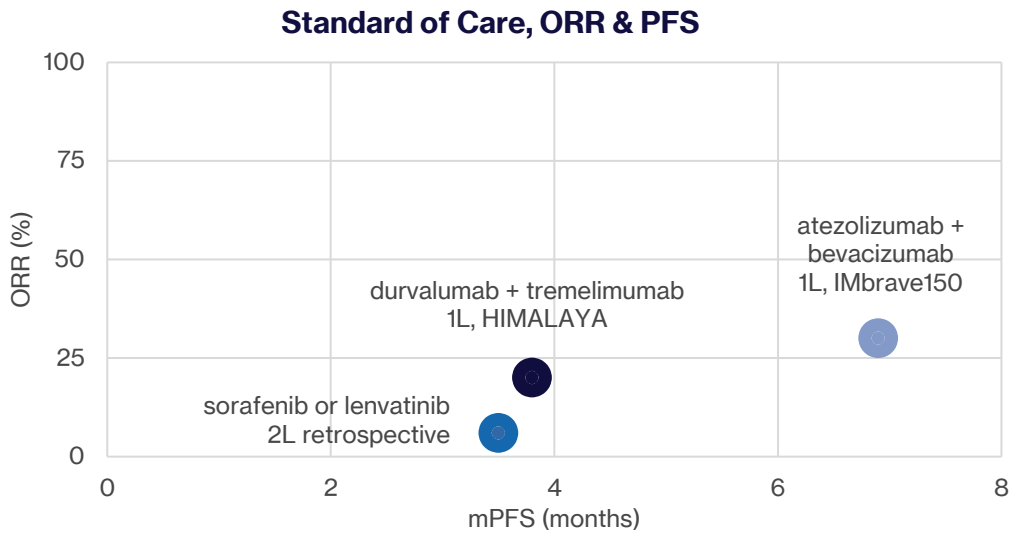
HCC BURDEN[1]

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



STANDARD OF CARE FOR SYSTEMIC HCC[2]

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



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**

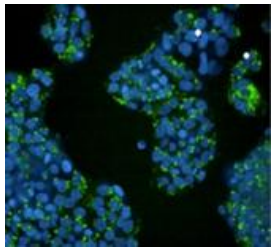
1. WHO. International Agency of Cancer Research. Cancer Today. 2020. Available at: https://gco.iarc.fr/today/home. Accessed October 2023 SEER. Cancer Stat Facts. National Cancer Institute. Available at https://seer.cancer.gov/statfacts/; 2. Finn RS et al NEJM 2020; Abou-Alfa GK et al NEJM Evid 2022; Yoo C et al Liver Cancer 2021
1L: First-line; 2L: Second-line; PFS: Progression-free survivial; ORR: Overall response rate; MOA: Mechanism of action; TOPO1: topoisomerase 1 inhibitor. HCC: Hepatocellular carcinoma; ADC: Antibody-drug conjugate.

ZW251 | potential utility in hepatocellular carcinoma

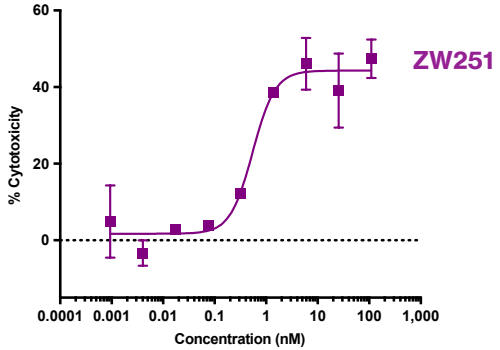
Robust ADC internalization and cytotoxicity

ZW251 internalized in HCC cell line

Internalization visualized after 24-hour treatment



Tumor spheroid cytotoxicity in HCC cell line



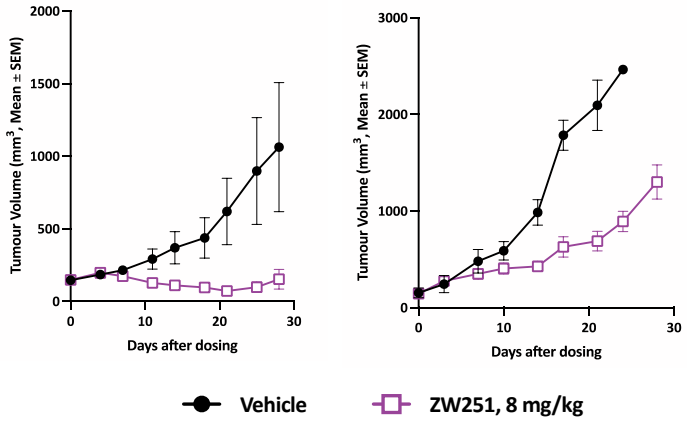
Cytotoxicity assessed by cell line spheroids (treatment over 4 days)

Differentiated modality demonstrates anti-tumor activity

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

HCC PDX
GPC3 H-Score: 288

HCC PDX
GPC3 H-Score: 84

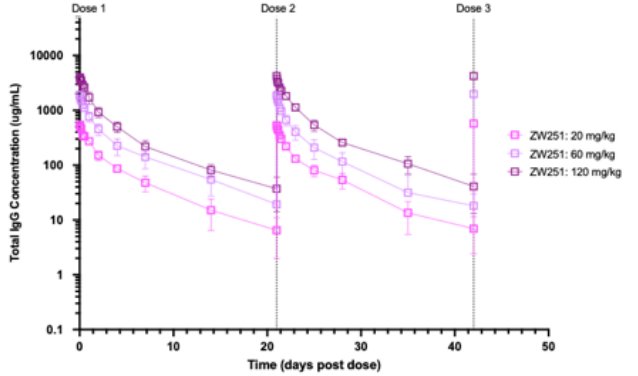


Impressive tolerability and dose-proportional PK in NHP

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



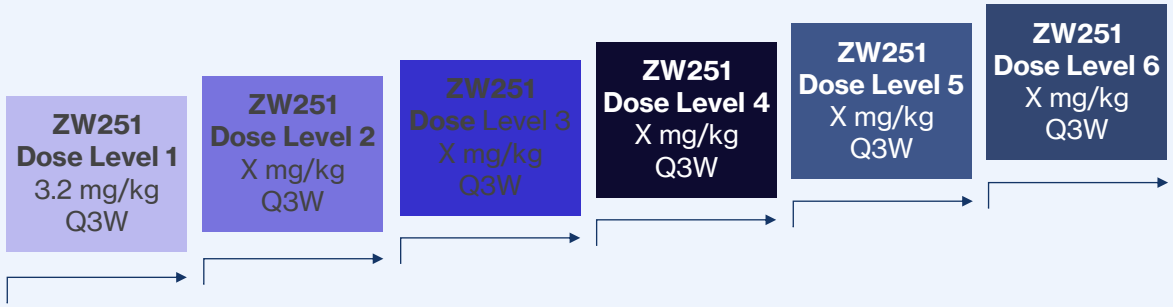
HCC: Hepatocellular carcinoma; PDX: patient derived xenograft; MTD: maximum tolerated dose; T1/2: half-life; GLP: good laboratory practice
Madera L et al., Abstract #2658 presented at AACR 2023; Madera L et al, presentation at World ADC 2023; Madera L et al., Abstract #177 presented at EORTC-NCI-AACR 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.

ZW251: Phase 1 study in glypican 3-expressing hepatocellular carcinoma (HCC) (NCT07164313)

Key Eligibility Criteria

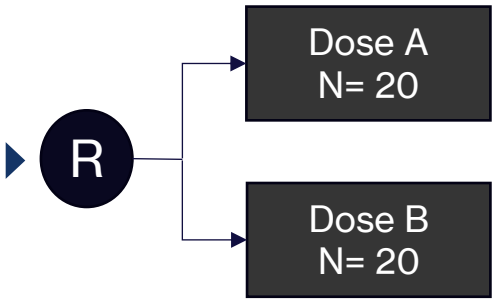
- HCC advanced or metastatic
- Germ Cell Tumors
- Squamous NSCLC
- Progressed on SOC treatment
- Measurable by RECIST 1.1
- Child-Pugh class A
- ECOG 0-1
- Adequate organ function

Part 1: Dose Escalation (~6 dose levels; n=60)



Treatment until disease progression, unacceptable toxicity, or withdrawal of consent

Part 2: Dose Optimization (n=40)



Primary Endpoints	Secondary Endpoints
• Safety and tolerability • ORR (Part 2)	• PK, ADA, • DOR, DCR, PFS, ORR (Part 1)

ADA: anti-drug antibody; BOR: best overall response; DCR: disease control rate; DOR: duration of response; ECOG: Eastern Cooperative Oncology Group performance status; NSCLC: non-small cell lung cancer; ORR: objective response rate; PD: pharmacodynamics; PK: pharmacokinetics; Q3W: every 3 weeks; RECIST: Response Evaluation Criteria in Solid Tumors; SOC: standard of care;

ZW220

ADC Designed to Target NaPi2b-Expressing Ovarian Cancer and NSCLC

IND-ready candidate

Optimized design[1]

- ADC targeting NaPi2b-expressing solid tumors
- Comprised of a humanized IgG1 antibody conjugated to a moderate potency topoisomerase 1 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 target mediated 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

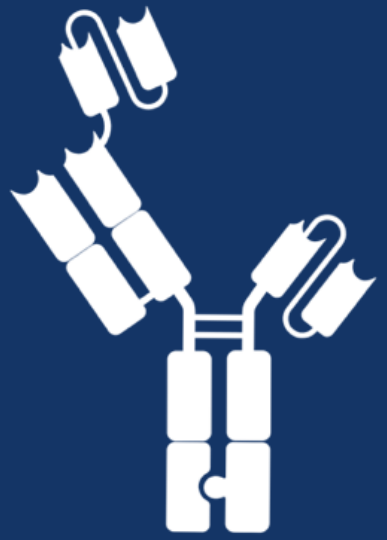
Significant patient need

- NaPi2b is found in ~83% of ovarian serous adenocarcinomas2 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

ZW209

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



Anticipated IND submission in 2026

Optimized design

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

Differentiated profile

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

Significant patient need

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

1. https://www.yalemedicine.org/conditions/small-cell-lung-cancer#:~: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.

ZW1528

Bispecific Designed to Address Respiratory Inflammation

Anticipated regulatory submission in 2027

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

Meaningful catalyst events anticipated throughout 2026

2026

- **Presented potentially practice changing and clinically meaningful mPFS and mOS in Phase 3** clinical trial of zanidatamab in 1L HER2+ GEA with our partners Jazz and BeOne at ASCO GI[1]
- **Zanidatamab Phase 3 data in 1L HER2+ GEA submitted for inclusion in the National Comprehensive Cancer Network Guidelines** by our partner Jazz
- **Ongoing royalty revenue for Ziihera®** from Jazz and BeOne
- **Additional data from Part 1 of the Phase 1 trial of ZW191** presented at the AACR Annual Meeting
- **Jazz and BeOne completed sBLA filings, in the U.S. and China respectively**, for zanidatamab for the treatment of 1L HER2+ GEA. The FDA has provided a PDUFA target action date of August 25, 2026 in the U.S.
- **An additional planned OS interim analysis** for zanidatamab plus chemotherapy from the HERIZON-GEA-01 trial is currently expected in mid-2026
- **Zymeworks has the potential to receive substantial near-term milestone** payments related to future anticipated regulatory approvals in GEA including $250.0 million in the U.S.
- **Anticipate IND submission for ZW209** (DLL3) in 2026
- **Execution of strategic initiative to compound existing royalties** through strategic transactions including partnerships and acquisitions
- **Potential to continue opportunistically executing on share repurchase program** which authorized repurchases up to an aggregate of $125.0 million in common stock

2027

- **Expected non-U.S. regulatory submission for ZW1528** (IL4R x IL-33) in 2026

Cash[2] runway forecast beyond 2028 when combined with receipt of certain anticipated regulatory milestone payments[3]

Illustrative. Key news flow only.
1. Both Ziihera plus chemotherapy and Ziihera plus Tevimbra and chemotherapy demonstrated highly statistically significant and clinically meaningful improvements in progression-free survival (PFS) compared to the control arm, trastuzumab plus chemotherapy. Ziihera plus Tevimbra and chemotherapy also demonstrated clinically meaningful and statistically significant improvements in overall survival (OS), and Ziihera plus chemotherapy demonstrated a clinically meaningful effect with a strong trend toward statistical significance for OS compared to the control arm at the time of this first analysis; 2. Cash, cash equivalents, and marketable securities; 3. Assuming the full execution of the $125.0M share repurchase plan, we currently expect our existing cash resources as of March 31, 2026, when combined with anticipated regulatory milestone payments of $440.0 million related to the potential approvals of Ziihera in GEA in the U.S., Europe, Japan, and China, to fund our planned operations beyond 2028. This anticipated cash runway does not take into account any contribution from additional future milestone payments or royalties related to Ziihera, other current licensed product candidates or contributions from future partnerships and collaborations. GEA: Gastroesophageal adenocarcinoma; 1L: first-line; sBLA: supplemental biologics license application.

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