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

OCTOBER 2026

Nasdaq: ZYME | zymeworks.com

Legal disclaimer

This presentation, and the accompanying oral commentary, includes "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 include, but are not limited to, statements that relate to anticipated milestones payments; Zymeworks' ability to utilize Irish tax attributes; Zymeworks' flexibility to invest in its R&D pipeline and pursue strategic opportunities while returning capital to stockholders; future growth of YUPELRI® sales and future royalty payments; sales and future royalty payments related to VIBATIV®; contingent milestone payments due to Theravance Biopharma from the sale of Theravance Biopharma's TRELEGY ELLIPTA® royalty interests; the repayment of the non-recourse note issued to OMERS Life Sciences; Zymeworks' expectations regarding implementation of its long-term strategy to maximize value creation; Zymeworks' and its partners' clinical development of product candidates; potential safety profile and therapeutic effects of product candidates; the commercial potential of technology platforms and product candidates; the anticipated benefits of its collaboration agreements; the Company's 2026 full year guidance and other information that is not historical information. When used herein, words such as "plan", "believe", "expect", "may", "continue", "anticipate", "potential", "will", "on track", "progress", "preserve", "intend", "could", and similar expressions 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. 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: 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; uncertainties regarding the commercial success of YUPELRI®, TRELEGY and VIBATIV®; the anticipated benefits of the acquisition may not be realized or will not be realized within the expected time period; TRELEGY may not achieve anticipated sales resulting in sales milestones not being met; Zymeworks may not achieve milestones or receive additional payments or royalties 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' business strategy related to anticipated and potential future milestones and royalty streams and existing and potential new partnerships may not be successfully implemented; Zymeworks' evolution of its business strategy may not deliver meaningful stockholder returns; Zymeworks may be unsuccessful in actively managing and/or aggregating revenue-generating assets alongside its active R&D operations; ongoing and future clinical trials may not demonstrate safety and efficacy of any of Zymeworks' or its collaborators' product candidates; data providing early validation of our antibody drug conjugate platform and next generation pipeline programs may not be replicated in future studies; Zymeworks' assumptions and estimates regarding its financial condition, future financial performance and estimated cash runway may be incorrect; inability to maintain or enter into new partnerships or strategic collaborations; the inability of Zymeworks to identify and consummate a strategic acquisition; 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. The above assumptions, risks and uncertainties are not exhaustive. Forward-looking statements are made as of the date hereof and, except as may be required by law, Zymeworks undertakes no obligation to update, republish, or revise any forward-looking statements to reflect new information, future events or circumstances, or to reflect the occurrences of unanticipated events.

Non-GAAP Financial Measures:

This presentation includes certain financial measures that were not prepared in accordance with U.S. generally accepted accounting principles ("GAAP"). The Company has elected to present Adjusted EBITDA, a non-GAAP financial measure, on a forward-looking basis. Zymeworks believes Adjusted EBITDA provides useful information regarding the Company's underlying operating performance and facilitates comparisons of operating results across periods. Adjusted EBITDA should be considered in addition to, and not as a substitute for, financial measures prepared in accordance with GAAP. Other companies may calculate Adjusted EBITDA differently or may use other measures to evaluate their performance. Investors and others are encouraged to review Zymeworks' financial information in its entirety and not rely on a single financial measure. Adjusted EBITDA is calculated as net income (loss), adjusted to exclude income tax expense or benefit, interest income and expense, depreciation and amortization, other non-operating income or expense, share-based compensation expense, and certain other items, including transaction-related costs, restructuring charges and severance costs. The Company does not provide reconciliations for forward-looking non-GAAP measures to GAAP measures due to the inherent difficulty in forecasting and quantifying certain amounts that are necessary for such reconciliation, including adjustments that could be made for changes in share-based compensation expense, transaction-related costs, restructuring and severance costs, and the effects of any discrete income tax items. For the same reasons, the Company is unable to address the probable significance of the unavailable information. The Company provides non-GAAP financial measures that it believes will be achieved; however, it cannot accurately predict all of the components of the adjusted calculations, and the GAAP measures may be materially different than the non-GAAP measures. A reconciliation of Adjusted EBITDA to net income (loss), its most directly comparable GAAP financial measure, for certain historical periods can be found on slide 16.

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**

1H 2025

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

2H 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**

1H 2026

✓ 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

2H 2026

Ziihera® received U.S. FDA approval for the treatment of HER2+ GEA resulting in **$250.0M regulatory milestone payment from Jazz**

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

2H 2026

Completed acquisition of Theravance Biopharma, providing additional durable, recurring sources of cash flow

*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
VIATRIS
APOTEX Canadian-Based Global Health Company

COMPOUND VALUE ALTERNATIVES

- Internal Programs
- Acquired Programs
- Acquired Royalties

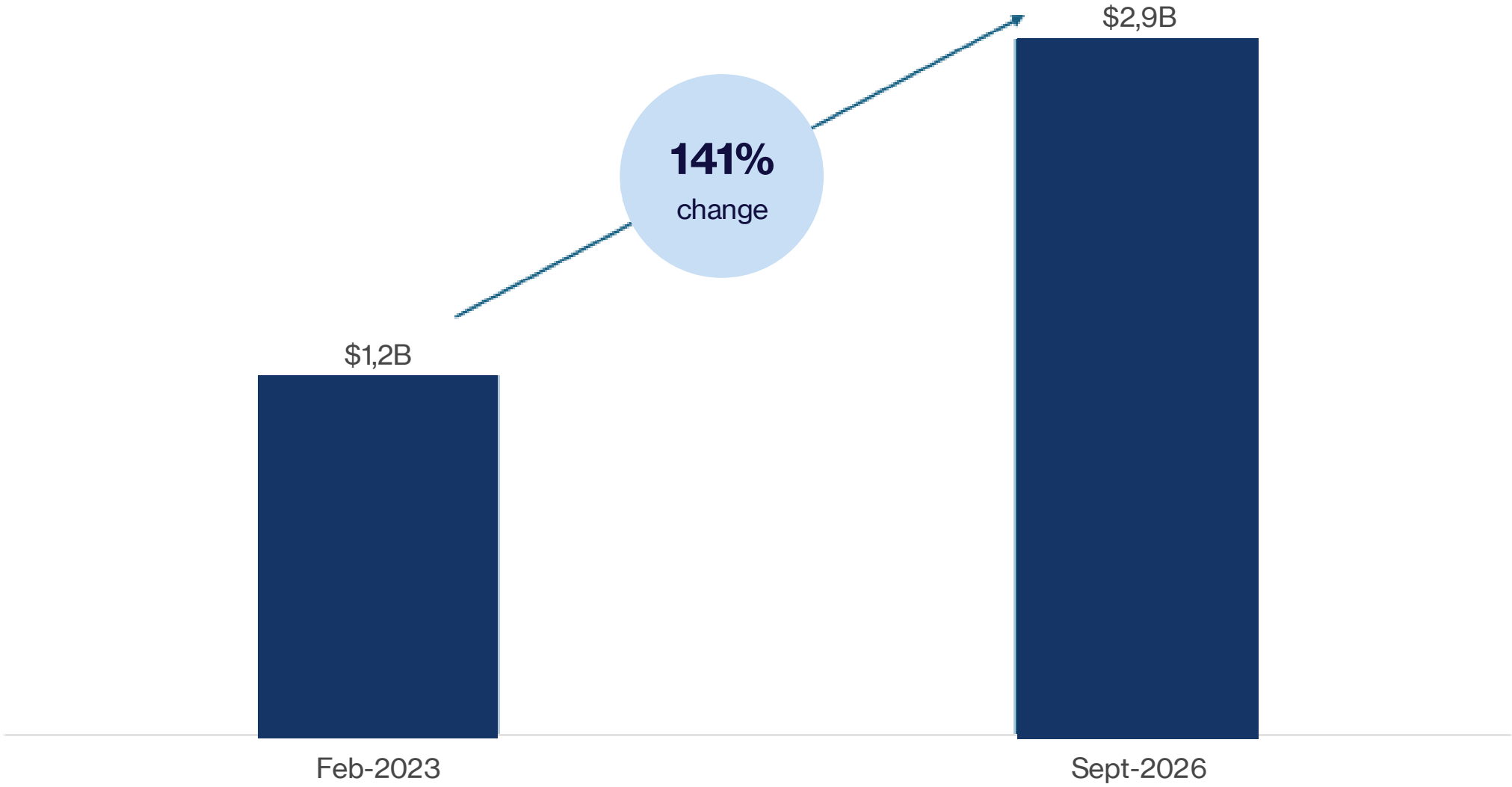
RETURN VALUE ALTERNATIVES

- 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

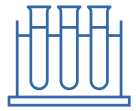
Evolution of Wall Street Consensus | 2023 vs. Now | ($ Millions)



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

Zymeworks is well-positioned with R&D and asset aggregation synergies

Transaction Component	Biotech Seller	zymeworks	Royalty Capital
	Unwilling to sell the parts: value is embedded across the company	**Underwrites the whole: evaluates every component together**	**Not optimized to buy the whole: mandate limited to the royalty line**
Commercial asset & operations	Only sellable with the company	**Ability to operate and grow**	Not optimized to own operations
Collaboration & royalty economics	Embedded, not separable	**Evaluates and structures**	Can price this line only
R&D portfolio	No standalone buyer	**Ability to develop, partner, spin-out**	Outside mandate
Tax attributes	Value lost in a break-up	**Potential to utilize**	No means to utilise
Commercial organisation	At risk in a break-up	**Ability to retain and leverage**	No operating platform

Differentiated pipeline of multifunctional therapeutics

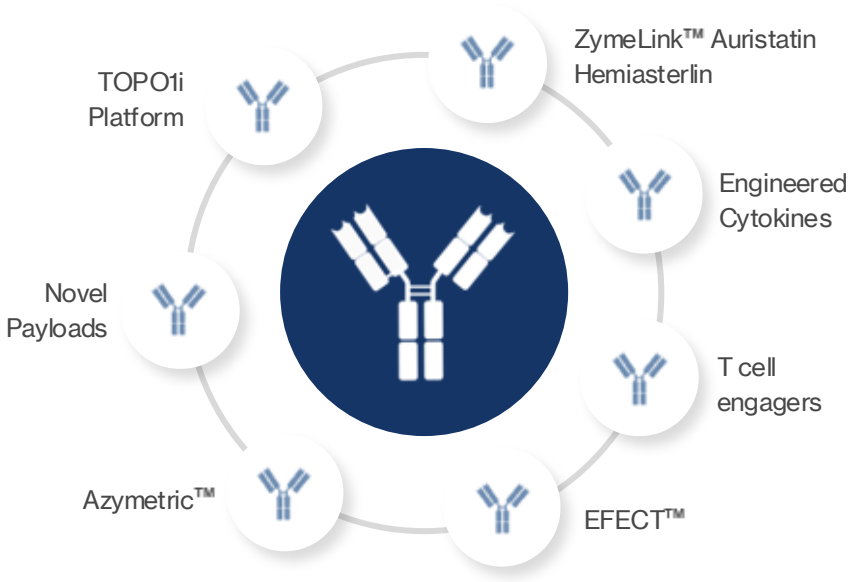
Program	Technology	Target	Indication	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
Solid Tumor Oncology: Antibody-Drug Conjugates (ADC)								
ZW191 Topo1i ADC | DAR 8 | Fc WT	ZD06519 Payload	FRα	Gynecological Thoracic			NCT06555744		
ZW251 Topo1i ADC | DAR 4 | Fc WT	ZD06519 Payload	GPC3	HCC, CGT, sqNSCLC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

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***

$3-5B

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 Launch Presentation August 25, 2026 *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

Established commercial structure with growth potential

ONCE-DAILY YUPELRI® revefenacin inhalation solution

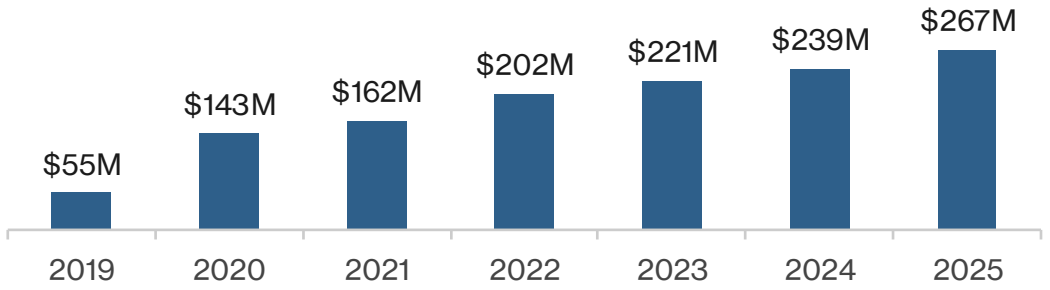
25% hospital-channel growth continues to build the clinical familiarity that supports expansion in the community setting.

Exacerbation	Hospitalization	Discharge	Outpatient
Patient presents at hospital	In-patient use of YUPELRI®	Leaves with a script	Continues in the community setting

Deepens hospital-channel use

Extends duration in community

YUPELRI® U.S. Revenue 2019-2026*



- YUPELRI® has delivered consistent growth since launch with new center activation and organic growth
- Current reports suggests a roughly 87:13 split in YUPELRI® usage between Community and Hospital settings
- Recent YUPELRI® use has increased in the hospital from both new accounts and increased utilization, while community growth remains strong

* YUPELRI® U.S. revenue rounded to the nearest million

Diverse potential revenue streams from partnerships

Program / Platform	Partner	Stage / Status	Potential Future Milestone Payments	Revenue / Royalty Rate
YUPELRI® *(revefenacin)*	*Viatris*	**Approved for COPD**	$125M	35% U.S. net profit share Double-digit tiered royalties and additional milestones on ex-U.S. net sales
VIBATIV® *(telavancin)*	*Apotex*	**Approved for MRSA and MSSA**	none	Up to 20% royalty on net sales
Ziihera® *(zanidatamab)*	*Jazz Pharmaceuticals*	**Approved for HER2+ 2L BTC and 1L GEA** *Ongoing trials in multiple indications*	Up to $1.3B	10-20% tiered royalties from Jazz sales
	BeOne Medicines		Up to $144M	High single-digit royalties from BeOne sales
pasritamig *(Azymetric and EFECT platforms)*	*J&J*	**Ph 3 trials in Prostate Cancer and mCRPC**	Up to $204.5M	Tiered worldwide royalties in the mid-single digit percentages
Bispecific antibody *(Azymetric platform)*	*GSK*	**Ph 1 started**	Up to $1.1B	Tiered worldwide royalties in the low to mid-single digit percentages
Bispecific antibody *(Azymetric and EFECT platforms)*	*Daiichi Sankyo*	**Ph 1 started**	Up to $230M	Tiered worldwide royalties from low single digit percentages up to 10%
Bispecific antibody *(Azymetric and EFECT platforms)*	*GSK*	**Preclinical**	Up to $1.1B	Tiered worldwide royalties in the low single digit percentages
Bispecific antibody *(Azymetric and EFECT platforms)*	*MERCK*	**Preclinical**	Up to $921.8M	Tiered worldwide royalties on sales

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. COPD: chronic obstructive pulmonary disease; MRSA: Methicillin-Resistant Staphylococcus aureus; MSSA: Methicillin-Susceptible Staphylococcus aureus; BTC: biliary tract cancer; GEA: gastroesophageal endenocarcinoma; mCRPR: metastatic castrate-resistant prostate cancer.

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

+$322M
Cash resources[1]

UP TO
$440M
From potential cumulative global GEA approvals

$125M
Share repurchase plan announced in November 2025

$106M
Revenues reported for 2025[2]

$278 – 292M
Total Revenue Expected in 2026[3]

$114 – 128M
2026 Expected adjusted EBITDA 3, 4

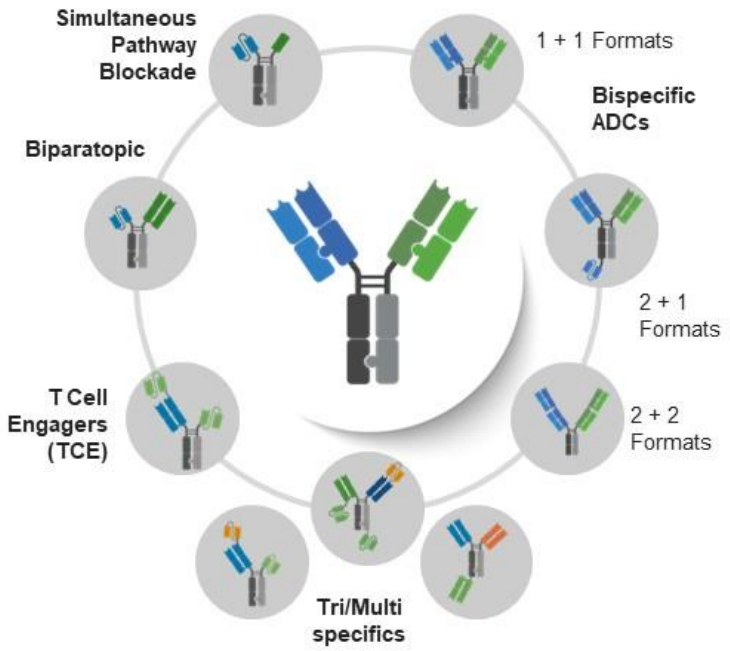
Potential to access additional non-dilutive potentially lower cost of capital financing

1. As of August 6, 2026, the Company had cash resources of approximately $322.5 million, consisting of cash, cash equivalents, and marketable securities.; 2. Revenues for 2025, reported as of December 31, 2025. 3.This guidance is as of September 28, 2026 and assumes no major unforeseen adverse events and excludes any potential contribution from transactions announced subsequent to that date. 4. Adjusted EBITDA is a non-GAAP financial measures. Refer to appendix for definition of Adjusted EBITDA and slide 16 for the GAAP to non-GAAP reconciliation.

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

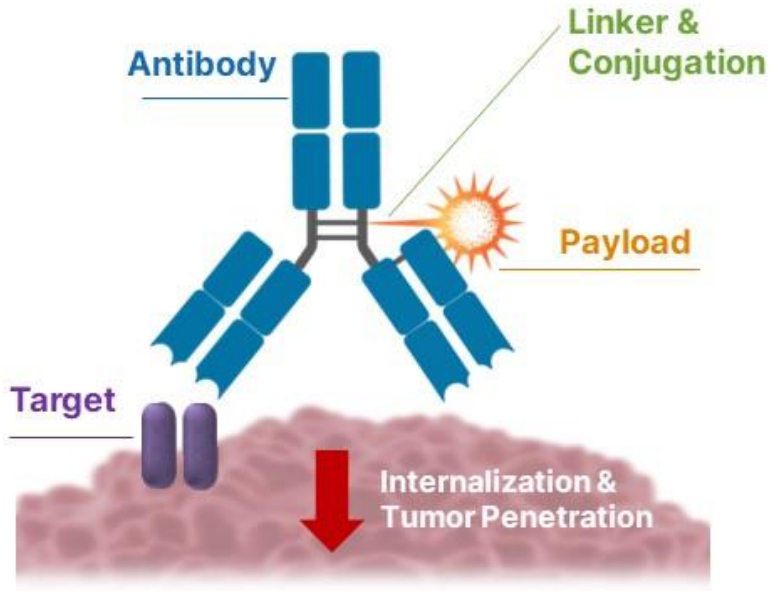
MULTISPECIFIC ANTIBODIES

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 65.2% at doses 6.4-9.6 mg/kg and 58.8% cORR across all dose levels in platinum resistant ovarian cancer (PROC)[2]
- Median progression-free survival of 7.6 months across ovarian and endometrial cancer cohorts[2]
- Opportunity to treat broader range of FRα-expressing cancers

Significant patient need

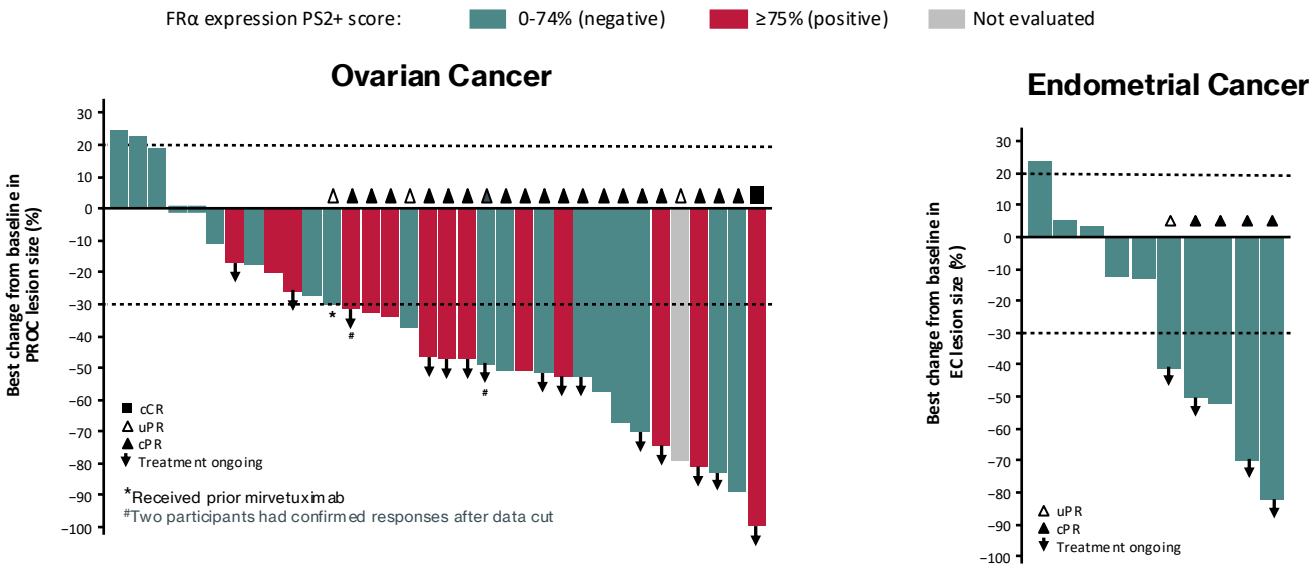
- FRα is found in ~75% of high-grade serous ovarian carcinomas[3] and ~70% of lung adenocarcinomas[4]
- The U.S. Food and Drug Administration granted Fast Track designation to ZW191 for the treatment of patients with advanced or metastatic PROC

1. Lawn S et al. Abstract # 2641 Presented at AACR 2023;
2. Hasegawa et al. Presentation #143P. Presented at ESMO Gynaecological Cancers Congress 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.

ZWI-ZW191-101 | clinical results

Presented at ESMO Gynaecological Cancers Congress 2026

Anti-tumor activity of ZW191 in ovarian cancer and endometrial cancer



Ovarian Cancer	FRα-positive (n=14)	FRα-negative (n=19)
cORR,b % (95% CI)	78.6% (49.2, 95.3)	47.4% (24.4, 71.1)
DCR, % (95% CI)	100.0% (76.8, 100.0)	89.5% (66.9, 98.7)
mTTR, months (range)	1.6 (1.2-4.2)	1.5 (1.2-5.7)

Endometrial Cancer	FRα-negative (n=10)
cORR, % (95% CI)	40.0% (12.2, 73.8)
DCR, % (95% CI)	80.0% (44.4, 97.5)
mTTR, months (range)	1.2 (1.2-1.4)

Data cutoff: March 9, 2026
As of data cutoff, 34 participants with ovarian cancer and 10 with endometrial cancer were response-evaluable and were included in the efficacy analysis. Response was based on RECIST v1.1 (response and progression defined as –30% and +20% change from baseline, respectively). PS2+ score was defined as the percentage of cells with 2+/3+ staining and categorized as FRα-negative (<75%) or FRα-positive (≥75%).

Efficacy for response-evaluable participants with ovarian and endometrial cancer

Median progression-free survival of 7.6 months across all dose levels

cCR: confirmed complete response; cPR: confirmed partial response; FRα: folate receptor alpha; PROC: platinum-resistant ovarian cancer; RECIST v1.1: Response Evaluation Criteria in Solid Tumors, version 1.1; uPR: unconfirmed partial response.

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

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

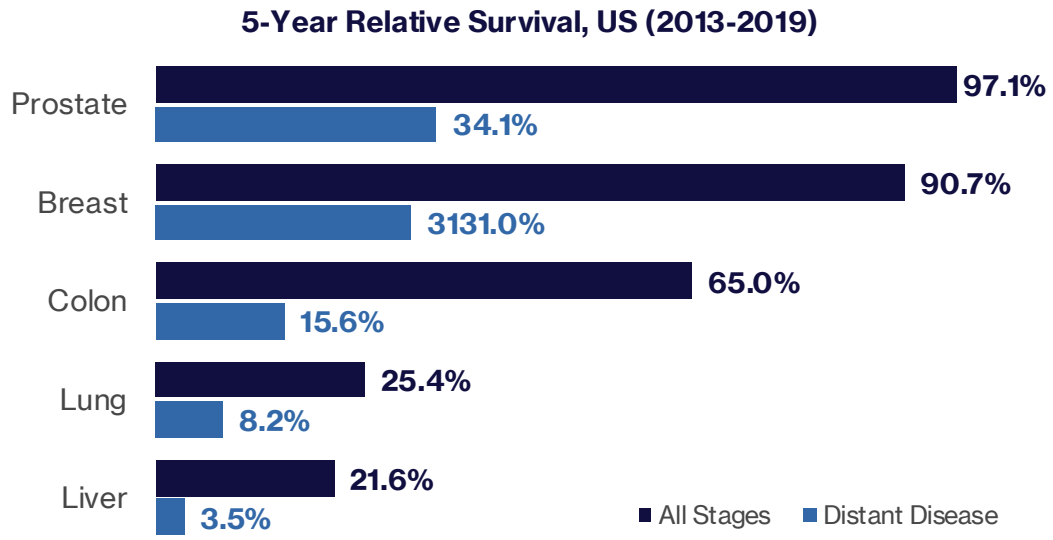
- GPC3 is expressed in 76% of HCC, with high expression observed in ~55% of HCC[2]
- HCC is the most common type of primary liver cancer and the third leading cause of cancer deaths globally[1]

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

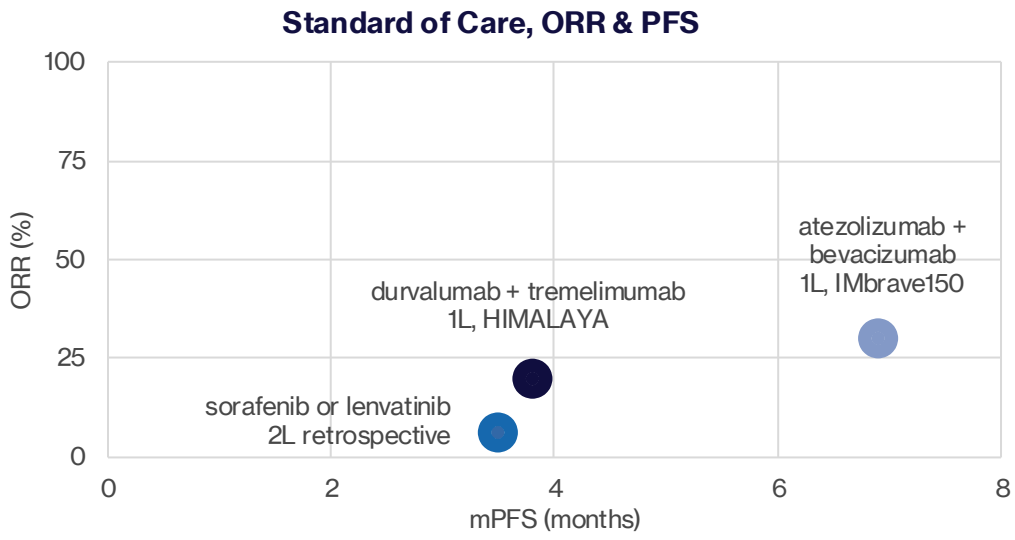
HCC BURDEN[1]

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**

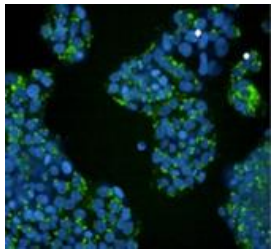
1. WHO. International Agency of Cancer Research. Cancer Today. 2020. Available at: https://gco.iarc.fr/today/home. Accessed October 2023 SEER. Cancer Stat Facts. National Cancer Institute. Available at https://seer.cancer.gov/statfacts/; 2. Finn RS et al NEJM 2020; Abou-Alfa GK et al NEJM Evid 2022; 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

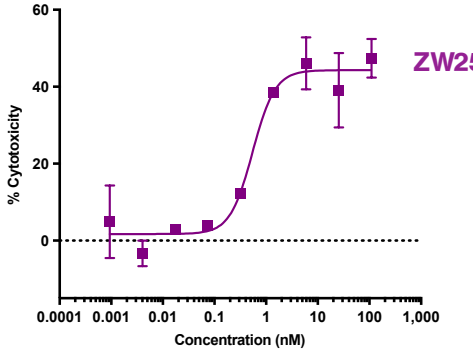
Robust ADC internalization and cytotoxicity

ZW251 internalized in HCC cell line

Internalization visualized after 24-hour treatment



Tumor spheroid cytotoxicity in HCC cell line

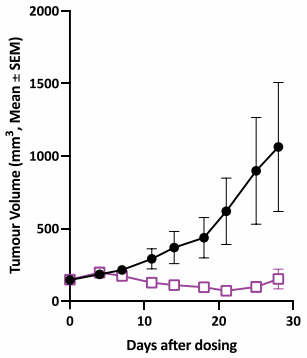


Cytotoxicity assessed by cell line spheroids (treatment over 4 days)

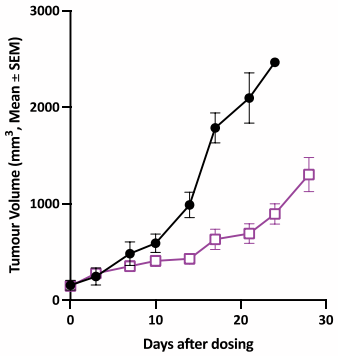
Differentiated modality demonstrates anti-tumor activity

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



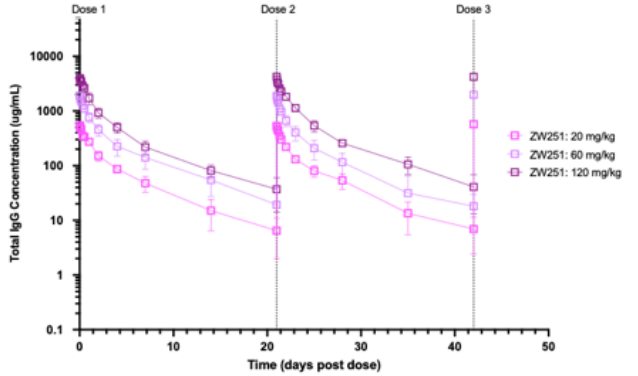
Vehicle
ZW251, 8 mg/kg

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)

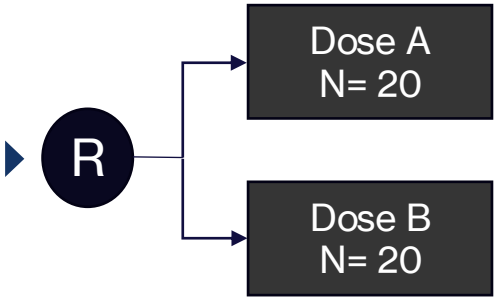
Key Eligibility Criteria

- 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

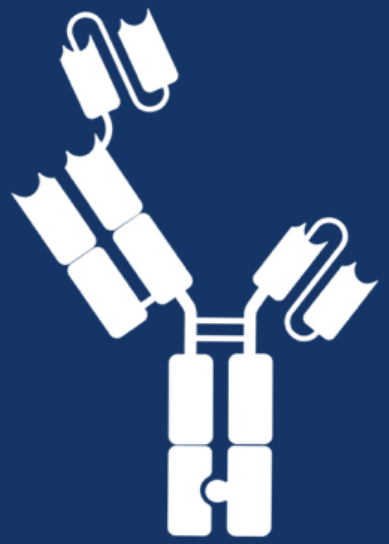
Significant patient need

- 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 and ESMO Gynaecological Cancers Congress 2026
- **The U.S. FDA approval for zanidatamab for the treatment of 1L HER2+ advanced GEA.**
- **An additional planned OS interim analysis** for zanidatamab plus chemotherapy from the HERIZON-GEA-01 trial is currently expected in Q4 2026
- **Zymeworks has the potential to receive substantial near-term milestone** payments related to future anticipated regulatory approvals for zanidatamab in GEA including $250.0 million on U.S. FDA approval
- **Anticipate IND submission for ZW209** (DLL3) in 2026
- **Execution of strategic initiative to compound existing royalties** through strategic transactions including partnerships, spinouts 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

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. GEA: Gastroesophageal adenocarcinoma; 1L: first-line; sBLA: supplemental biologics license application.

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Appendix

GAAP to Non-GAAP Reconciliation

Adjusted EBITDA
(Unaudited)

($ in millions)	Three Months Ended June 30,		Six Months Ended June 30,	
	2026	2025	2026	2025
GAAP Net income (loss)	**(45.0)**	**2.3**	**(89.2)**	**(20.3)**
Adjustments:				
Income tax (benefit)/expense	(0.3)	(0.2)	(2.5)	0.3
Interest expense / (income), net	3.3	(3.4)	2.7	(6.9)
Depreciation and amortization	1.1	2.5	2.3	5.1
Other non-operating (income) / expense	(0.2)	0.6	(0.3)	0.6
Share-based compensation expense	11.3	5.9	18.3	12.3
Transaction-related costs	3.0	—	3.0	—
Restructuring and severance costs	0.1	0.7	3.4	1.2
Adjusted EBITDA	**(26.7)**	**8.4**	**(62.3)**	**(7.7)**

Amounts may not add due to rounding.