2Q 2025 Results

Conference Call and Webcast

August 7, 2025

Nasdaq: ZYME | zymeworks.com

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This presentation and the 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; anticipated regulatory submissions and the timing thereof; the anticipated benefits of its collaboration agreements with Jazz, BeiGene and other partners, including Zymeworks’ ability to receive any future milestone payments and royalties thereunder and the anticipated timing thereof; anticipated actions by partners and the timing thereof; the potential addressable market of Zymeworks’ product candidates; the timing of and results of interactions with regulators; Zymeworks’ clinical development of its product candidates and enrollment in its clinical trials; the timing and status of ongoing and future studies and the related data; extrapolations or comparisons of results derived from independent studies which are subject to misinterpretation, assumptions or caveats of each study; anticipated preclinical and clinical data presentations; anticipated poster presentations; preclinical development progress and expectations regarding future regulatory submissions, filings and approvals and the timing thereof; the timing of and results of interactions with regulators; potential safety profile and therapeutic effects of zanidatamab and Zymeworks’ other product candidates; evolution of Zymeworks’ business strategy related to anticipated and potential future royalty streams and existing and potential new partnerships; expected financial performance and future financial position; the commercial potential of technology platforms and product candidates; 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; anticipated sufficiency of existing cash resources and certain anticipated regulatory milestone payments to fund Zymeworks’ planned operations into the second half of 2027; Zymeworks’ ability to execute new collaborations and partnerships 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”, 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: 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 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; 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; clinical trials may not demonstrate safety and efficacy of any of Zymeworks’ or its collaborators’ product candidates; 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; 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.

2Q 2025 Earnings Results Call Agenda

Leone Patterson, MBA, CPA
EVP, CBO and CFO

- Business Update
- Financial Update
- Q&A

Sabeen Mekan, MD
SVP Clinical Development

- Clinical Updates
- Q&A

Paul Moore, Ph.D.
CSO

- R&D Update
- Q&A

Ken Galbraith
Chair and CEO

- Q&A

FINANCIAL UPDATE

Leone Patterson, MBA, CPA

Executive Vice President, Chief Business and Financial Officer

Continued Progress Across Business in 2Q 2025

Pipeline Progress

Poster presentations for our wholly-owned product pipeline at:

- **ASCO Annual Congress:** ZW171 Trial in Progress Poster
- **ESMO Gynecology:** ZW191 Trial in Progress Poster
- **ATS Annual Congress:** Preclinical data presented on ZW1528, a novel IL-4Rα x IL-33 bispecific

Investigational New Drug application cleared for ZW251 with first-in-human studies planned to initiate in 2025

Zanidatamab Progress

- **Jazz presented encouraging OS data for zanidatamab** in 1L HER2+ GEA at the ASCO Annual Congress, showing median OS of 36.5 months
- **NMPA granted BeOne conditional approval of zanidatamab in China** for BTC resulting in $20M payment to Zymeworks
- **EMA granted conditional marketing approval of zanidatamab in Europe** for BTC, expanding patient access and potential future royalties payable to Zymeworks
- **Initiation of Phase 2 trial** to evaluate zanidatamab in HER2+ neoadjuvant and adjuvant breast cancer

Platform Partnership Updates

- **Bristol Myers Squibb collaboration progresses** with $7.5M option exercise payment to Zymeworks
- **J&J Innovative Medicine reported Phase 1 trial results for pasritamig** (JNJ-78278343) at the ASCO Annual Congress
- **Daiichi Sankyo, Inc. presented a Trial in Progress Poster for a Phase 1, first-in-human study of DS-2243**, a bispecific T-cell engager in patients with advanced solid tumors at the ASCO Annual Congress

Recognized ~$75M in 2025 which included ~$45M partnership-related cash milestones and option exercise fees, which significantly reduced net operating cash burn in 1H 2025 compared to 1H 2024

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1L; First Line; ATS: American Thoracic Society; ASCO: American Society of Clinical Oncology; BTC: Biliary Tract Cancer; CHMP: Committee for Medicinal Products; EMA: European Medicines Agency; ESMO: European Society for Medical Oncology; GEA: Gastroesophageal Adenocarcinoma ;HER2+: HER2-positive; OS: Overall Survival

Diverse Potential Revenue Streams from Existing Partnerships

- **Near-Term Revenue Catalysts:** Continued royalties from Jazz and initial royalties from BeOne Medicines for Ziihera® expected in 2025.
- **Long-Term Growth Potential:** Wholly-owned assets provide flexibility for future licensing and royalty opportunities.

Program & Platform	Partner	Therapeutic Indication	Current Stage[1]	Potential Future Milestone Payments	Royalty Rate
Ziihera® (zanidatamab-hrii) Azymetric | EFECT	Jazz Pharmaceuticals	HER2-expressing Cancer	Marketed in first indication (BTC)	Up to $1.36 billion	Tiered worldwide royalties between 10% to 20% other than in BeOne territories
Zanidatamab Azymetric | EFECT	BeOne	HER2-expressing Cancer	Marketed in first indication (BTC)	Up to $144 million	Tiered royalties up to 19.5% of net sales in BeOne territories[2]
Bispecific Antibody Azymetric	gsk	Infectious Disease/Undisclosed	Phase 1	Up to $1.1 billion	Tiered worldwide royalties in the low to mid-single digit percentages
JNJ-78278343 CD3 x KLK2 Bispecific Azymetric | EFECT	janssen	Castration-Resistant Prostate Cancer	Phase 1	Up to $459 million	Tiered worldwide royalties in the mid-single digit percentages
Bispecific Antibody Azymetric | EFECT	Bristol Myers Squibb	Oncology	Phase 1	Up to $313 million	Tiered worldwide royalties on sales
Bispecific Antibody Azymetric | EFECT	Daiichi-Sankyo	Immuno-Oncology	Clinical Stage	Up to $230 million	Tiered worldwide royalties from low single digit percentages up to 10%
Bispecific Antibody Azymetric | EFECT	gsk	Undisclosed	Preclinical	Up to $1.1 billion	Tiered worldwide royalties in the low single digit percentages
Bispecific Antibody Azymetric | EFECT	MERCK	Undisclosed	Preclinical	Up to $921.8 million	Tiered worldwide royalties on sales

Except as otherwise indicated, the information is provided as at June 30, 2025. The information included in the table above presents a summary of key aspects of our collaboration and licensing agreements. 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, 2024 filed with the SEC on March 5, 2025, and the other information included in the Quarterly Report on Form 10-Q for the quarter ended June 30, 2025.

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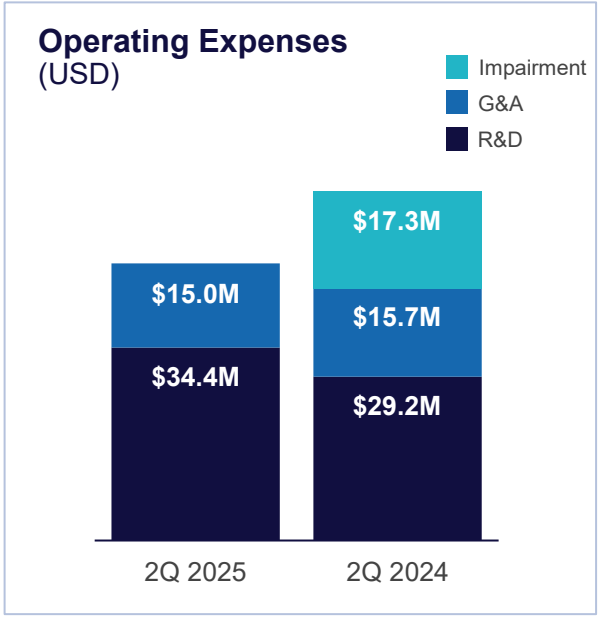
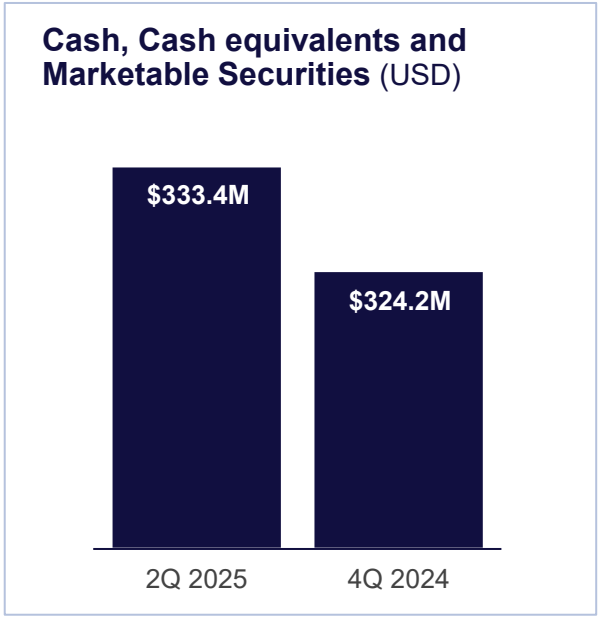
[1]Current stage represents the current preclinical, clinical or commercial stage of development for the particular program, as applicable.
[2]Tiered royalties of up to 19.5% of net sales in BeOne territories, increasing to up to 20% when cumulative amounts forgone as a result of a royalty reduction of 0.5% reaches a cap in the low double-digit millions of dollars.

2Q 2025 Revenues, Operating Expenses and Cash Resources

- $45.8M of milestone, option exercise and related deferred revenue, recognized in 2Q-2025 from BeOne and BMS.



- Decrease due to 2Q-2024 impairment charge and reduced spend for zanidatamab zovodotin and ZW220, partially offset by higher ZW171, ZW191 and other preclinical research costs.



- Increase of $9.2M in cash resources for 2Q-2025 YTD.
- Cash position benefited from milestone revenues during 2025 and favorable movements in working capital.

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CLINICAL DEVELOPMENT UPDATE

Sabeen Mekan, MD

SVP Clinical Development

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

Open-label, FIH, dose-escalation study (N~160)

21-day DLT evaluation period

Part 1: Dose Escalation (N=~40)

Advanced Ovarian cancer and NSCLC malignancies.

ZW171 administered weekly on Day 1, 8 and 15 of a 21-day cycle

Expected dose levels:

- ZW171 Dose Level 1 4.2μg (Day 1), 12.6μg (Day 8), 38μg (Day 15)
- ZW171 Dose Level 2 QW Day 1, 8, 15
- ZW171 Dose Level 3 QW Day 1, 8,15
- ZW171 Dose Level 4 QW Day 1, 8,15
- ZW171 Dose Level 5 QW Day 1, 8,15
- ZW171 Dose Level 6 QW Day 1, 8,15

MTD/RD determined

Part 2: Dose Optimization and Expansion

Dose Optimization		Dose Expansion	
Cohort 1:	Ovarian Cancer • Dose Level A (N=20) • Dose Level B (N=20)	Cohort 2:	NSCLC (N=40)
		Cohort 3:	Basket Cohort (e.g., Endometrial, Pancreatic) (N=40)

Cycle 1 day 1 ZW171 dose

Screening assessments (occur within 28 days prior to cycle 1 day 1)

21-day cycles

Every 6 or 9 Weeks[a] CT/MRI

Follow-up 30 days post last dose of ZW171

Screening | **Treatment period** | **Follow-up**

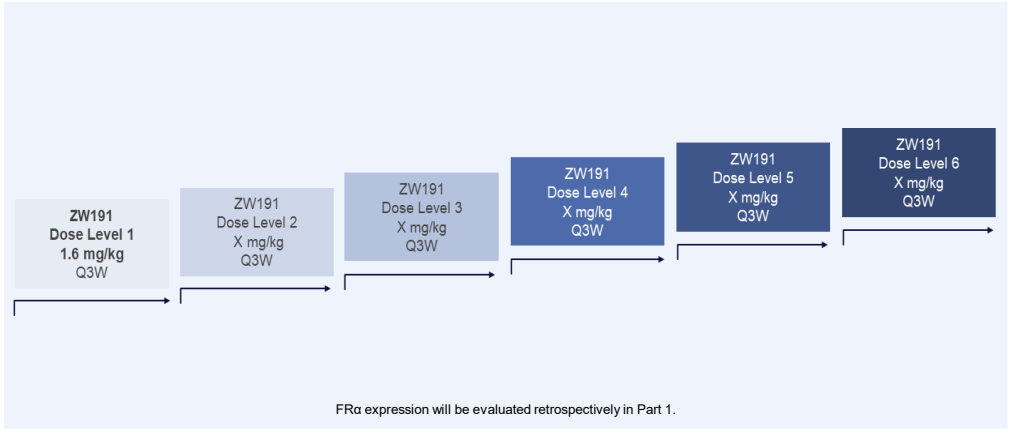
Treatment until disease progression, unacceptable toxicity, or withdrawal of consent

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.
[a]Timed from cycle 1 day 1. Q6W (every 6 weeks) for the first 4 assessments and then Q9W (every 9 weeks) thereafter.
CT/MRI: computed tomography/magnetic resonance imaging; DLT: Dose Limiting Toxicity; FIH: First-in-human; MTD: maximum tolerated dose; MSLN = mesothelin; NSCLC: non-small cell lung cancer; RD: Recommended Dose..

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

Open-label, FIH, dose-escalation study (N~145)

Part 1: Dose Escalation



MTD/RD determined

Part 2: Dose Optimziation/Expansion

Part 2a: Dose Optimization

Ovarian cancer[a]

Cohort 1: Ovarian[a]	Ovarian cancer Randomized 1:1 into 2 Dose Levels Dose Level A (n=20) Dose Level B (n-=20)

Part 2b: Dose Expansion

Endometrial cancer and non-squamous NSCLC

Cohort 2: Endometrial	n=20 FRα expressing (+). Dose Level TBD
Cohort 3: Nonsquamous NSCLC	n=20 FRα expressing (+). Dose Level TBD

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

[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..

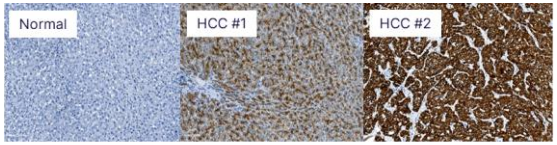
RESEARCH & DEVELOPMENT UPDATE

Paul Moore, Ph.D.

Chief Scientific Officer

IND Clearance for ZW251: A Potential First-in-Class ADC Against GPC3

GPC3 is prevalent and highly expressed in hepatocellular carcinoma (HCC)

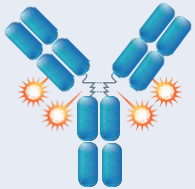


HCC % Positivity	Intensity	Reference
87%	57% IHC2+/3+	Abou-Alfa et al. 2016. J Hepatol
96%	75% '++', 3% '+++'	Wang et al. 2016. Oncotarget
84%	84% '++'	Yamauchi et al. 2005. Mod Pathol
76%	N.D.	Wang et al. 2008. Arch Pathol Lab Med

GPC3 is an oncofetal glycoprotein which is important in fetal development but downregulated in adult tissues.

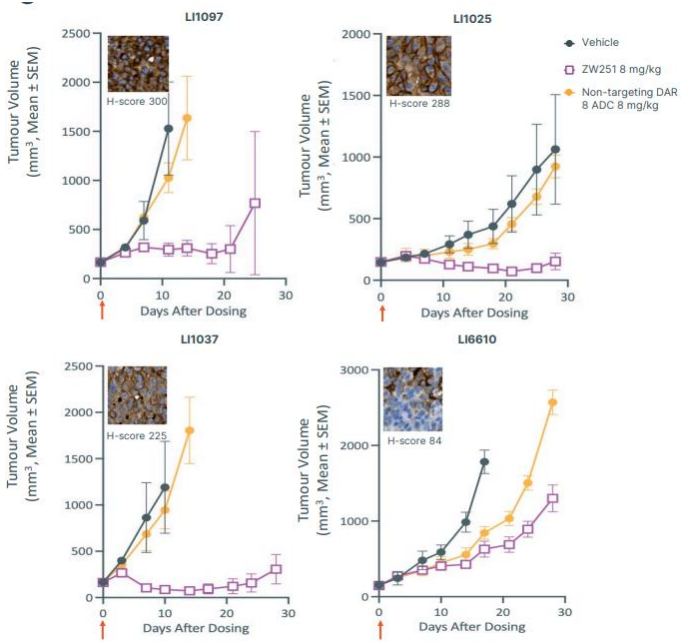
This makes GPC3 a validated and highly selective approach to treat HCC, which has also been seen in the clinic.

ZW251
A Novel GPC3-targeting ADC



- Novel TOPOi1 inhibitor payload, ZD06519 with drug-to-antibody ratio ~4
- ZD06519 has demonstrated an encouraging profile from the Phase 1 study of ZW191
- ZW251 has shown strong cytotoxicity across a range of solid tumor indications and is well-tolerated in non-GLP NHP studies with a MTD of 120 mg/kg and favorable PK
- We plan to commence Phase 1 clinical studies for ZW251 in 2025.

ZW251 demonstrates compelling pre-clinical efficacy against models of HCC



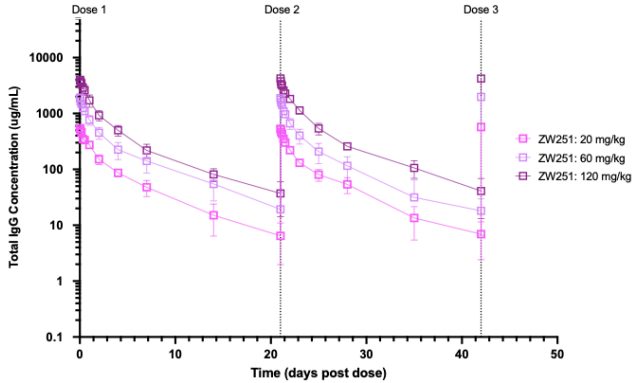
Anti-tumor activity observed in models with H-scores as low as 84

Madera, L. et al., Abstract #177 presented at ENA 2024

GPC3:Glypican-3; MTD: Maximum Tolerated Dose; NHP: Non-human primates; Non-GLP: Non-Good Laboratory Practice; PK: Pharmacokinetics; TOPOi1: Topoisomerase 1; NHP: Non-Human Primate.

ZW251 is Well-Tolerated in a Repeat Dose Non-GLP Non-Human Primate Toxicology Study with a Maximum Tolerated Dose of 120 mg/kg and Favorable PK

Dose (mg/kg)	Schedule	Mortality	Clinical observations	Histo-pathology	Clinical Chemistry	Hematology	MTD	$T_{1/2}$ (day)
20	q3wx3	None	None	None	None	Decreased reticulocytes	120 mg/kg	4.6
60								4.8
120			Fecal abnormalities (loose feces)	Decreased cellularity in thymus and lymph node				5.4



- Dose proportional pharmacokinetics observed for ZW251 (total antibody assay)
- Treatment-related lower mean reticulocyte counts observed in all groups and deemed non-adverse
- Non-adverse decreased thymus cellularity and mesenteric lymph node cellularity seen with microscopic observation in one animal administered 120 mg/kg
- **No mortality or adverse clinical observations, body weight effects, food consumption observed**

Compelling tolerability observed in non-human primates suggests potential for high human dosing of ZW251

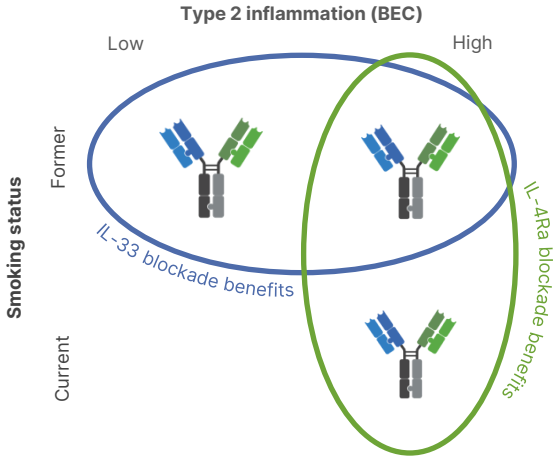
Madera *et al.* ENA 2024 Poster.
PK: Pharmacokinetics; Q3Wx3: three times a week for three weeks.

ZW1528: IL-4Ra x IL33 Bispecific Designed to Address Respiratory Inflammation

Potential novel therapeutic for COPD

COPD occurs in adults; smoking is a major risk factor

- Anti-IL-4Rα: effective in Type 2 COPD subset
- Anti-IL-33: blocks tissue alarmin driving both Type 2 and non-Type 2 responses and implicated in COPD

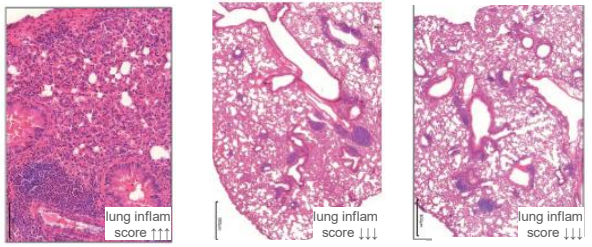


ZW1528
IL-4Rα x IL-33 Bispecific

- In-house antibody discovery of novel anti-IL4Rα and IL-33 paratopes
- Native IgG-like geometry; highly manufacturable, compatible with half-life extending Fc modifications
- Clinically-validated targets; core arm mediates complete, prolonged IL-4Rα blockade. Second arm adds inhibition of IL-33 - an upstream cytokine involved in perpetuating chronic inflammation

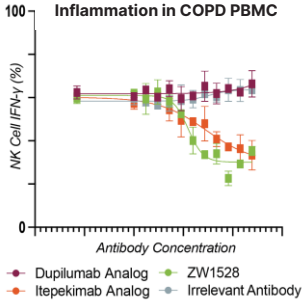
Compelling pre-clinical activity

Inhibition of Type 2 lung inflammation in murine house dust mite model (HDM)

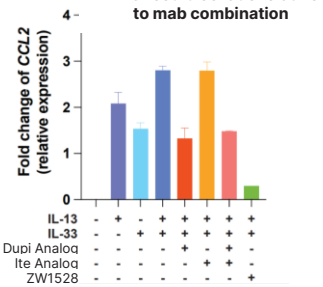


HDM alone | HDM + Dupilumab analog 3 mg/kg | HDM + ZW1528 3 mg/kg

Inhibition of Type I Inflammation in COPD PBMC



Enhanced blockade relative to mab combination



ZW1528 combines effect of two mabs to benefit a broader set of patients and potentially provide better efficacy in mixed type COPD

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Poffenberger et al., Abstract #2982 presented at ATS 2025
COPD: Chronic obstructive pulmonary disease; BEC: Blood eosinophil count;

Meaningful Catalyst Events Anticipated Throughout 2025 & 2026

2025

- **EMA and NMPA granted approval of zanidatamab for BTC,** expanding patient access and potential royalties payable to Zymeworks
- **Initial royalty revenue for Ziihera®** from Jazz collected
- **IND cleared for ZW251** (GPC3) with first-in-human studies planned to initiate in 2025
- **Initial royalty revenue for Ziihera®** from BeiGene collected
- **Pivotal Phase 3 top-line PFS data readout in 1L GEA for zanidatamab** targeted by our partner Jazz in 4Q 2025

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 the U.S. in 2026 pending regulatory approval

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

Q&A

Ken Galbraith
Chair & CEO

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