Q2 2024 Results
Conference Call and Webcast

August 1, 2024

Nasdaq: ZYME | zymeworks.com

Forward-Looking Statements

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; 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; 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; anticipated preclinical and clinical data presentations; expectations regarding future regulatory 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; 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; expectations for future investigational new drug and foreign equivalent applications submissions and 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", "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; 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; 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).

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Q2 Earnings Results Call Agenda

Bijal Desai, MBA
VP, Finance & Strategy

- Financial Update
- Q&A

Paul Moore, Ph.D.
CSO

- R&D Update
- Q&A

Ken Galbraith
Chair and CEO

- Q&A

Bijal Desai, MBA

VP, Finance & Strategy

2H 2024 Key Completed Milestones

- **FDA granted our partner Jazz Priority Review of the biologics license application (BLA) for zanidatamab** as second-line (2L) treatment for HER2+ biliary tract cancers (BTC) in the United States with target action date of November 29, 2024
- **The European Medicines Agency (EMA) has validated the Marketing Authorization Application (MAA)** for zanidatamab in 2L BTC by our partner Jazz
- **Recognized $8 million milestone payment** under the terms of Zymeworks' Asia-Pacific license and collaboration agreement with BeiGene for zanidatamab BLA acceptance in China
- **First-ever overall survival (OS) findings from the Phase 2b HERIZON-BTC-01** clinical trial for zanidatamab presented at the American Society of Clinical Oncology (ASCO) annual meeting by our partner, Jazz
- **Our partner Jazz initiated the Phase 3 EmpowHER trial** for zanidatamab in late-line HER2+ breast cancer
- **Investigational new drug (IND) applications cleared by FDA for ZW191 and ZW171** with first-in-human studies planned to initiate in 2H 2024
- **Review and refocus of R&D pipeline** resulting in the discontinuation of zanidatamab zovodotin development program

Q2 2024YTD Financial Results

In millions USD	Q2 2024YTD	Q2 2023YTD
Revenue	$29.3	$42.6
R&D Expense	$61.2	$85.3
G&A Expense	$31.5	$38.7
Impairment	$17.3	-
Net Loss	$(69.3)	$(75.5)
	June 30, 2024	December 31, 2023
Cash Resources[1]	$395.9	$456.3

- **Revenue** decreased in Q2 2024YTD primarily due to lower development support payments from Jazz and lower revenue from our partners for research support and other payments compared to Q2 2023YTD, partially offset by milestone revenue from BeiGene.
- **R&D Expense** decreased primarily due to a decrease in expenses for zanidatamab as a result of transfer of this program to Jazz. This decrease was partially offset by an increase expense with respect to product candidates ZW171, ZW251 and ZW220. Salaries and benefits expenses decreased due to a decrease in non-recurring severance expenses partially offset by an increase in stock-based compensation expense compared to Q2 2023YTD.
- **G&A Expense** decreased primarily due to a decrease in external consulting expenses for information technology, insurance costs, legal spend, expenses for advisory services and depreciation and amortization expenses compared to Q2 2023YTD, partially offset by expenses due to an office lease termination.
- **Impairment** expense recognized because of our decision to discontinue the zanidatamab zovodotin clinical development program which utilized the technology represented by acquired in-process research and development assets.
- **Net loss** of $0.91 per diluted share in Q2 2024YTD compared to net loss of $1.13 per diluted share in Q2 2023YTD.
- **Cash Resources**[1], together with receipt of certain anticipated regulatory milestones, are anticipated to fund our planned operations into 2H 2027.

G&A: general and administrative; USD: United States dollar.
1. Cash resources consist of cash, cash equivalents, and marketable securities.
Note: All financial results are as-reported for the six months ended June 30, 2024, and 2023, respectively.

Projected Cash Runway Supports R&D Priorities into 2H 2027

Current Financial Status:

- Cash resources[1] of approx. $395.9M (as of June 30, 2024)
- Cash resources does not include an $8 million milestone payment under the terms of Zymeworks' Asia-Pacific license and collaboration agreement with BeiGene for the development and commercialization of zanidatamab for the BLA acceptance in China, which was received in July 2024
- Anticipated cash runway into 2H 2027, which includes certain anticipated regulatory milestone payments

Potential sources to extend cash runway beyond 2H 2027:

- Additional regulatory approval and commercial milestones for zanidatamab from Jazz and BeiGene
- Tiered royalties between 10-20% from Jazz and 10-19.5% from BeiGene sales (up to 20% when royalty reduction of 0.5% reaches cap in the low double-digit millions of dollars)
- Additional payments from legacy technology platform collaborations
- Potential new partnerships/collaborations to provide upfront payments and committed R&D funding

1. Cash resources consist of cash, cash equivalents, and marketable securities.

Paul Moore, Ph.D.

Chief Scientific Officer

Diversified Portfolio of Wholly-Owned Candidates

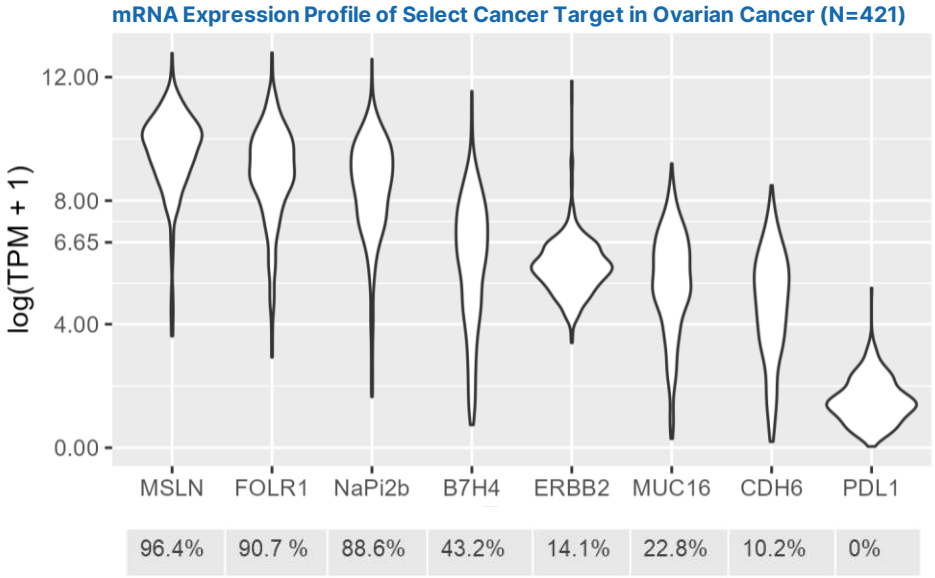
Designing next-generation antibody-drug conjugates (ADC) and T cell engagers (TCE) on targets with evidence of clinical activity and addressing areas of unmet therapeutic potential

Research and Early-Development Portfolio	Target	Late-Discovery / IND-Enabling / Phase 1 / Phase 2 / Phase 3	Anticipated Milestone
ZW191 TOPO1i ADC Program	FRα	OVCA, other GYNE CA, NSCLC	Phase 1 studies expected in 2H 2024
ZW171 2+1 CD3-Engager Program	MSLN	OVCA, NSCLC, MSLN-expressing CA	Phase 1 studies expected in 2H 2024
ZW220 TOPO1i ADC Program	NaPi2b	OVCA, NSCLC	Expected IND 2025
ZW251 TOPO1i ADC Program	GPC3	HCC	Expected IND 2025
Tri-TCE (Co-Stim) Trispecific T cell Engagers	CLDN18.2 x CD3 x CD28 DLL3 x CD3 x CD28	TBD	Expected IND 1H 2026
Tri-TCE (CPI) Trispecific T cell Engagers	TAA x PD-L1 x CD3	TBD	Pilot toxicology studies

FRα: folate receptor alpha, GPC3: glypican-3; HCC: hepatocellular carcinoma; IND: investigational new drug; MSLN: mesothelin; NaPi2b: sodium-dependent phosphate transporter 2B; NSCLC: non-small cell lung cancer; OVCA: ovarian cancer; TAA: tumor associated antigen; TBD: to be determined; TriTCE: trispecific T cell engager

*Please note these indications are at varying stages of late-stage development. Please refer to our full pipeline presented in our full corporate presentation on our website.

Targeting FRα Provides Strategic Diversification: Balancing ADC and TCE Portfolios Across Therapeutic Area of Focus



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

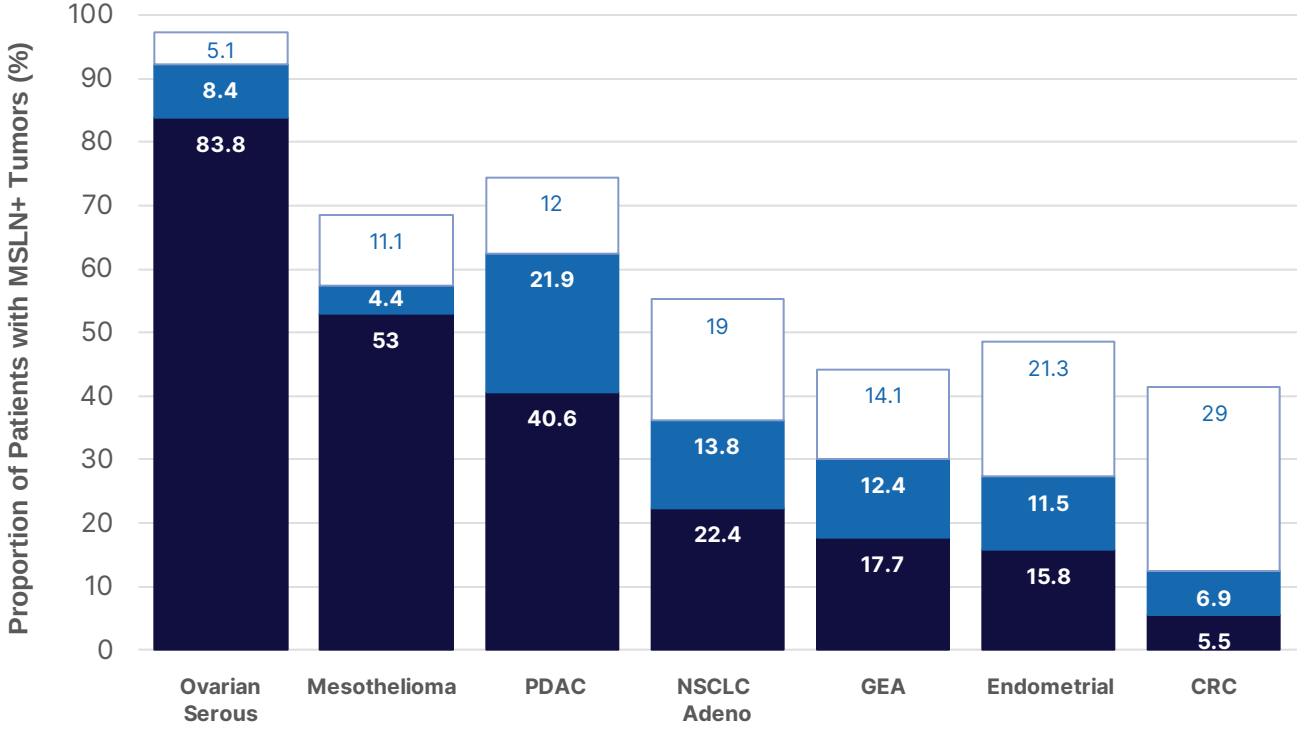
FOLR1, NaPi2b, and MSLN Expressed at Relatively Higher Level Than Other Targets (inc. B7-H4, CDH6) Pursued in Ovarian Cancer

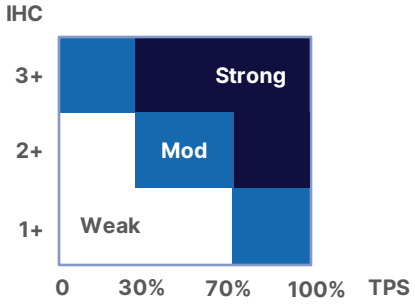
TCGA bulk RNA-sequencing data were obtained from TCGA-OV, workflow STAR – Counts from https://portal.gdc.cancer.gov/ repository. The median TPM (Transcript per Million) for each gene in each patient was plotted on a violin plot using ggplot2[1]. This dataset contains 421 samples (patients) from Ovarian Serous Cystadenocarinoma (OV). The width of the shape/violins indicates the density of samples

TPM: transcripts per million

1. Wickham H (2016). ggplot2: Elegant Graphics for Data Analysis. Springer-Verlag New York. ISBN 978-3-319-24277-4, https://ggplot2.tidyverse.org. OVCA: Ovarian Cancer

Moderate to Strong Expression of MSLN is Frequent in Ovarian Cancer, Pancreatic Cancer, NSCLC, and Endometrial Cancer





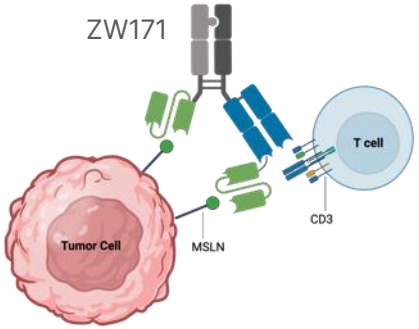
MSLN is expressed at strong/moderate levels in ovarian cancers with nonserous histology

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

Designed with a 2+ 1 Antibody Format to Enhance Safety and Anti-Tumor Activity

What is the 2+1 Antibody Format in ZW171 ?

- 2 anti-MSLN paratopes to enable avid tumor selective binding
- 1 anti-CD3 paratope to ensure MSLN dependent redirected T cell activation and tumor cell killing

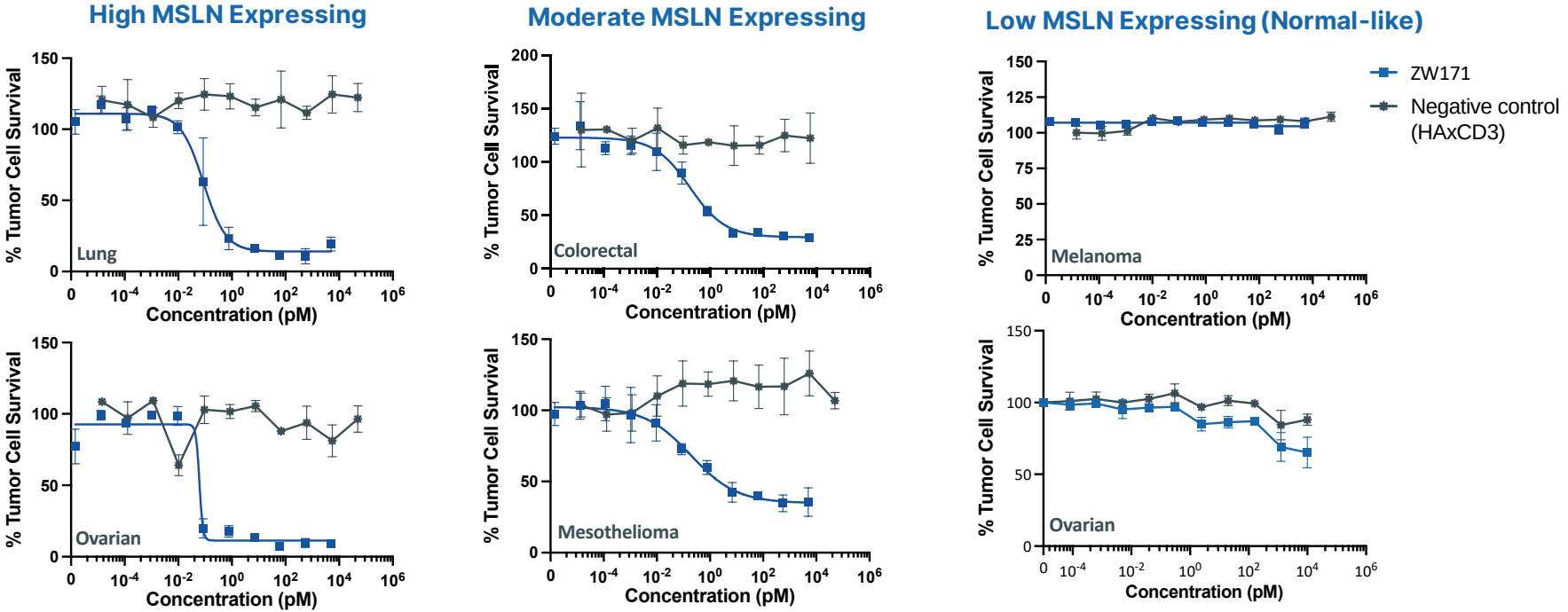


Benefits of ZW171 2+1 Antibody Format

Challenge		Expected Benefit of ZW171 2+1 Antibody Format
Safety	Normal tissue expression and off tumor toxicity	• Tumor selective binding that spares normal tissues • Binding and cytotoxicity directed at high/moderate MSLN-expressing cancer cells
	T cell engagement and cytokine release	• Anti-MSLN scFv paratope proximity to anti-CD3 Fab functions to further reduce T cell binding
Anti-tumor Activity	Circulating soluble MSLN	• Maintains potency in presence of soluble MSLN
	Limited anti-tumor activity	• Unique 2+1 format with two anti-MSLN scFv and one anti-CD3 Fab optimized for enhanced anti-tumor activity compared to other 2+1 formats and MSLNxCD3 bispecifics

ZW171 Mediates Cytotoxicity Against High and Moderate MSLN-Expressing Tumor Cells

ZW171 exhibits MSLN-dependent cytotoxicity in MSLN-expressing lung, ovarian, colon, and mesothelioma cancer cell lines

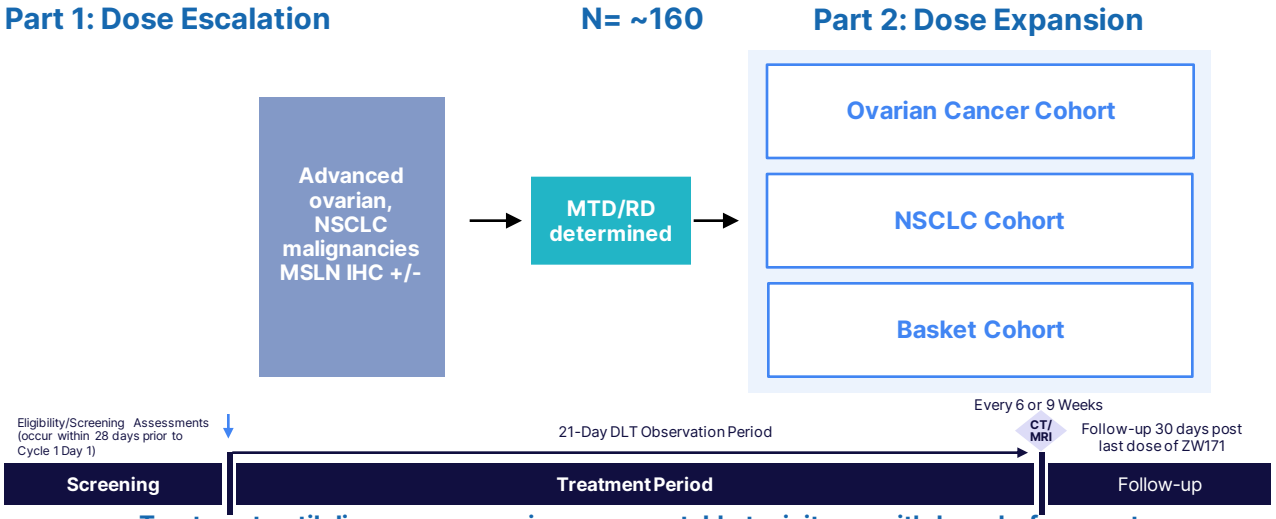


Human pan T cells and tumor cells were co-cultured at an effector-to-target ratio of 5:1 in the presence of ZW171 or negative control for 72 hours. H292 and OVCAR8 MSLNhigh; HCT116 and H2452 MSLNmod; OVTOKO and A375 MSLNlow cell lines

Afacan N, et al. Presented at: AACR. 2023 (abstr #2942)

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

Open-label, FIH, dose-escalation study



Part 1: Dose Escalation		Part 2: Dose Expansion	
Primary Endpoint	**Secondary Endpoints**	**Primary Endpoints**	**Secondary Endpoints**
• Safety and tolerability • MTD/MAD	• PK, ADA • cORR (RECIST)	• OBD • Safety and tolerability • cORR	• PK, ADA • PFS • DOR • OS

KEY ELIGIBILITY CRITERIA

Inclusion criteria

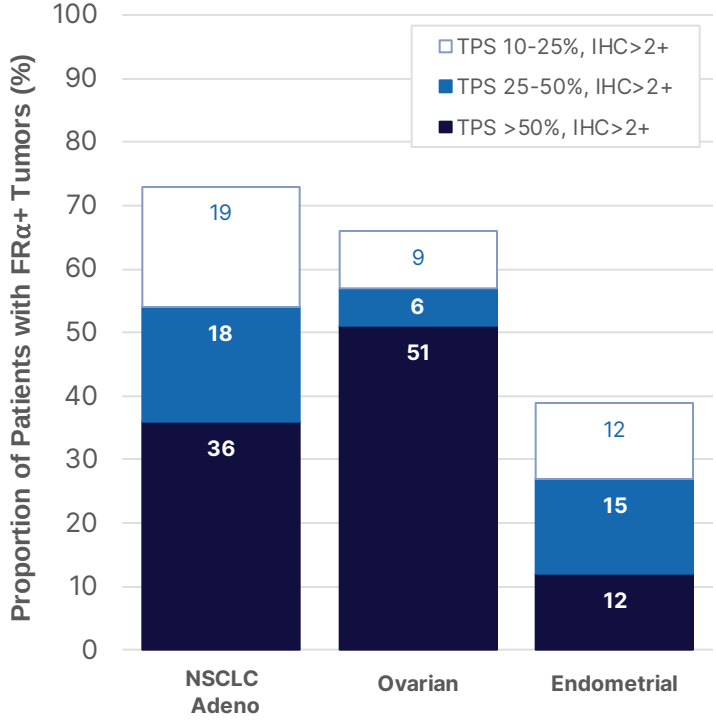
- Pathologically confirmed cancers with evidence of locally advanced (unresectable) and/or metastatic disease. Cancers that are refractory to all available SOC treatment, cancers for which no SOC treatment is available, or the participant cannot tolerate or refuses SOC therapy
- ECOG PS 0 or 1
- Adequate organ function

Exclusion criteria

- Known additional malignancy that is progressing or that has required active treatment
- Ongoing clinically significant toxicity (Grade ≥2)
- Advanced/metastatic, symptomatic, visceral spread, at risk of life-threatening complications in the short-term

ADA: anti-drug antibodies; cORR: confirmed objective response rate; DL: dose level; DOR: duration of response; ECOG: Eastern Cooperative Oncology Group; FIH: first in human; GEA: gastrointestinal adenocarcinomas; IHC: immunohistochemistry; MAD: maximum administered dose; MTD: maximum tolerated dose; MSLN: mesothelin; mTPI: modified toxicity probability interval; NSCLC: non-small cell lung cancer; OBD: optimal biological dose; OS: overall survival; PFS: progression-free survival; PK: pharmacokinetics; pts: patients; PS: preferred status; Q3W: every 3 weeks; RD: recommended dose; SC: subcutaneous; SOC: standard of care; TBC: to be confirmed

FRα is Frequently Overexpressed in Non-Small Cell Lung Cancer, Ovarian Cancer, and Endometrial Cancer



Ovarian Cancer, PS2+ Scoring

- **~35% of PROC tumors score as FRα-High** (TPS≥75%, IHC≥2+)
- **~80% of PROC tumors express some FRα** (TPS≥25%, IHC≥1+)

Endometrial Cancer, PS2+ Scoring

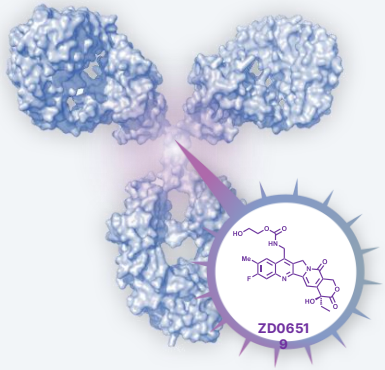
- **~15% of tumors score as FRα-High** (TPS≥75%, IHC≥2+)
- **~ 3% of tumors score as FRα-Positive** (TPS≥50%, IHC≥2+)

Adapted from Gymnopoulos M et al. Poster presented at AACR 2023.
NSCLC: non-small cell lung cancer; TPS: tumor proportion score; IHC: immunohistochemistry.

IMGN corporate presentation Jul 2023; STRO corporate presentation Sep 2023; Porter RL et al. Oral presentation at AACR 2024

ZD06519 was Designed in Alignment with our Understanding of ADC Mechanisms Featuring Moderate Potency and "Sweet Spot" Linker Stability

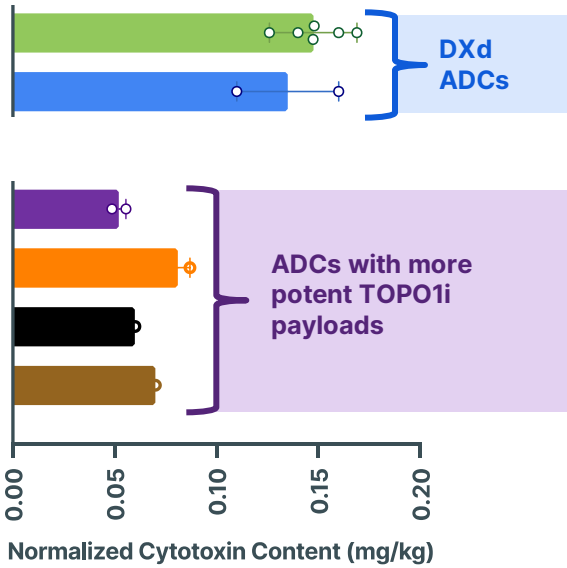
- A **combination of moderate potency** and **"sweet spot" stability is expected to enable a high protein dose**
- Hypothesis **supported by limited doses reached by exatecan** and other potent TOPO1i ADCs



ZD06519 was designed and selected to potentially allow high antibody dose in humans[1]

DAR	Target	Payload potency	Ab-Linker stability	ADC
8	HER2, HER3, CDH6	Mid	Mid	DXd-ADC*
4	B7H3	Mid	Mid	I-DXd#
8	FRα	High	Mid/high	BAT8006^
8	FRα	High	Mid	PRO1184^
6	cMET	High	High	ABBV-400
4	CLDN18.2	High	High	IBI-343^

*T-DXd, HER3-DXd, R-DXd
#Dato-DXd has lower MTD due to on-target off-tumor toxicities
^Exatecan payload

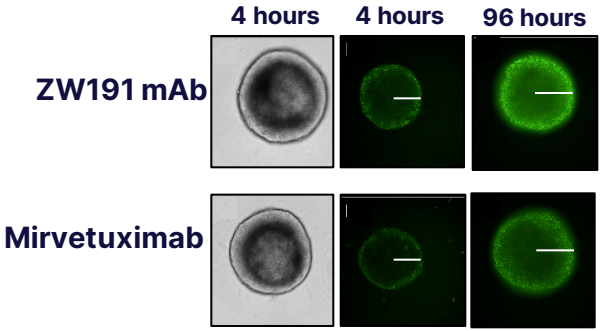


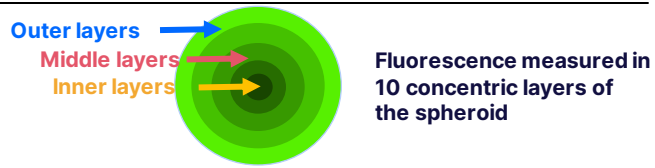
1. M. Petersen et al. Molecular Cancer Therapeutics, 2024, 23, 606–618; T-DXd approved dose: 5.4 and 6.4 mg/kg; HER3-DXd RP2D: 5.6 mg/kg, R-DXd dose expansion 4.8, 5.6, and 6.4 mg/kg; I-DXd dose expansion: 8-12 mg/kg; BAT8006 dose expansion: 2.1 and 2.4 mg/kg; PRO1184 dose expansion: 120-140 mg/m2; ABBV-400 MTD: 3 mg/kg; IBI-343 phase 3 dose: 6 mg/kg; Normalized Cytotoxin Content = DoseADC*DAR*MWpayload/MWADC

ZW191 Demonstrates Effective 3D Tumor Model Penetration

Tumor Spheroid Penetration

High FRα Expression, JEG3 Cell Line, 50 nM

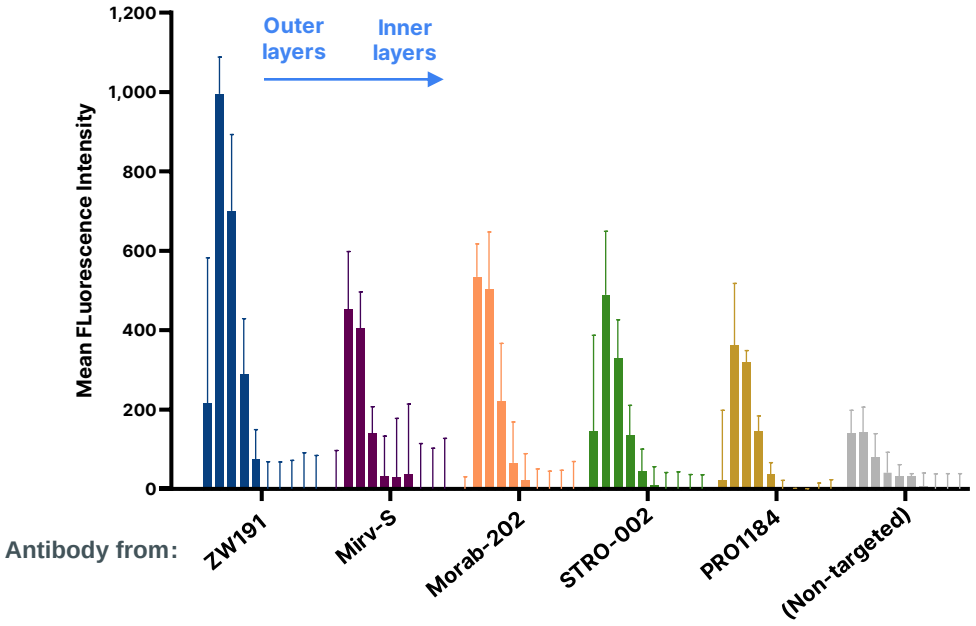




Fluorescence measured in 10 concentric layers of the spheroid

Tumor Spheroid Penetration

High FRα Expression, JEG3 Cell Line, 50 nM, 24hours



Zymeworks: A Differentiated Product Pipeline Built on Unique Capabilities in Antibody Engineering and Medicinal Chemistry

Seeking to address unmet patient needs in HER2+ GI Cancers

zanidatamab
(HER2 bispecific antibody)

- **Licensed to Jazz and BeiGene**
- **BTC 2L:** FDA has accepted and granted Priority Review of the BLA for zanidatamab. The EMA validated the MAA for zanidatamab in 2L BTC.
- **GEA 1L**: Based on an updated blinded assessment of progression events, Jazz estimates top-line PFS data will be available in 2Q25.

5 new INDs planned
Focus on Gyn CA, Lung CA, & GI CA

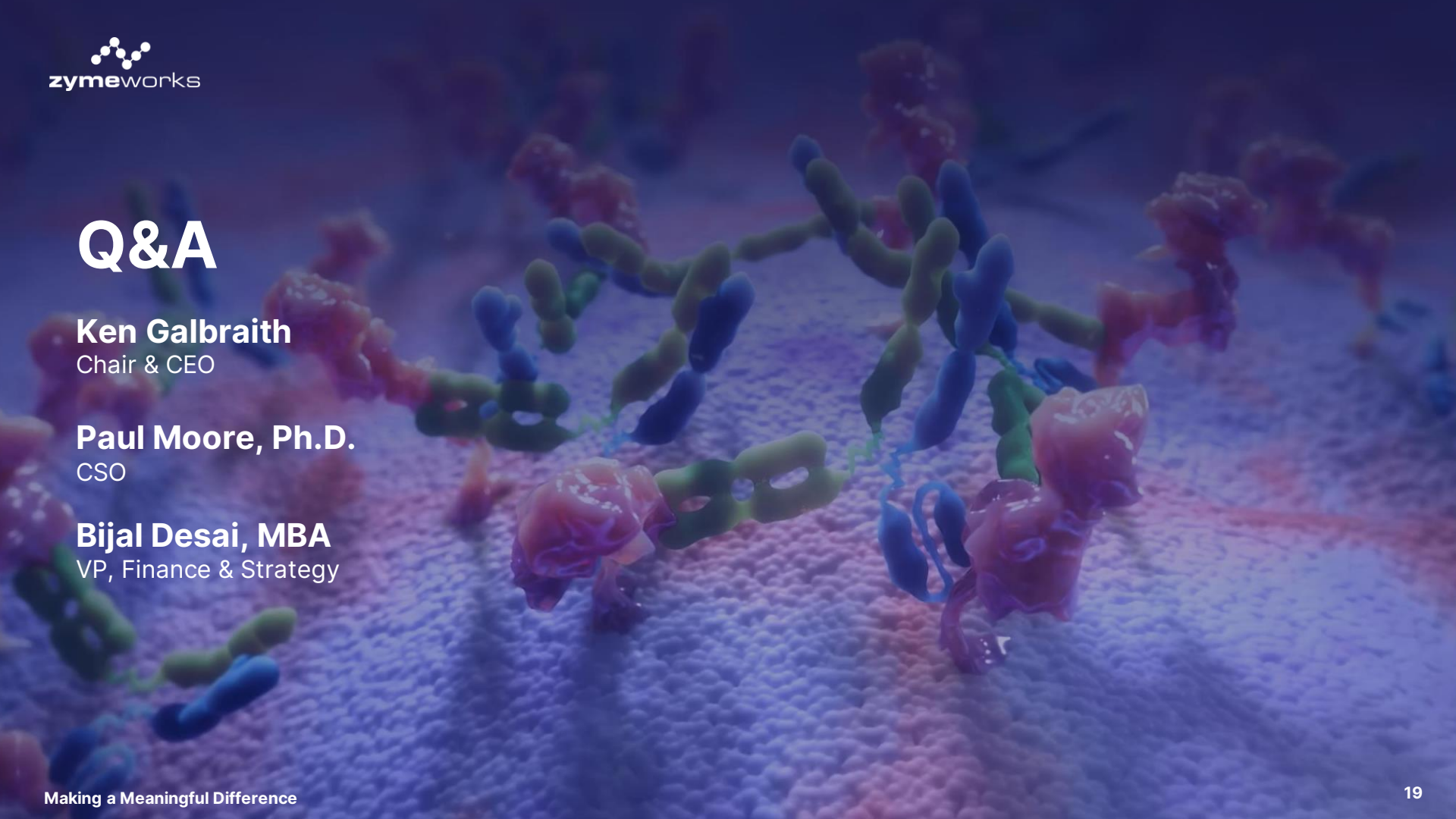
- **ZW171 (IND cleared)**
  MSLN x CD3 bispecific antibody
- **ZW191 (IND cleared)**
  FRα TOPO1i ADC
- **ZW220 (IND 2025)**
  NaPi2b TOPO1i ADC
- **ZW251 (IND 2025)**
  GPC3 TOPO1i ADC
- **Candidate 5 TBD (IND 2026)**
  Pre-clinical TriTCE candidate nomination expected in 2H 2024

Pipeline Events

- **Jazz initiated a Phase 3 trial to evaluate zanidatamab** in patients with HER2-positive breast cancer whose disease has progressed on previous trastuzumab deruxtecan (T-DXd) treatment
- **Nomination of Tri-TCE product candidate**
- **Jazz estimates top-line PFS data will be available in 2Q25**
- **PDUFA date of November 29, 2024** for zanidatamab in 2L HER2+BTC in the USA

Expanding product pipeline with potential near-term approval and launch of zanidatamab.
Cash runway forecast into 2H 2027, including receipt of certain assumed anticipated regulatory milestone payments.

1L: first-line (treatment); 2L: second-line (treatment); ADC: antibody-drug conjugate; BLA: Biologics License Application; BTC: biliary tract cancers; CD3: cluster of differentiation 3 protein complex and T cell co-receptor; FRα: folate receptor alpha; FDA: U.S. Food and Drug Administration; GEA: gastroesophageal adenocarcinoma; GI CA: gastrointestinal cancer; GPC3: glypican-3; Gyn CA: gynecological cancer; HER2: human epidermal growth factor receptor 2; IND: investigational new drug (application); Lung CA: lung cancer; MSLN: mesothelin; NaPi2b: sodium-dependent phosphate transporter 2b; NSCLC: non-small cell lung cancer; PDUFA: Prescription Drug User Fee Act; TOPO1i: topoisomerase 1 inhibitor.



Q&A

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