zymeworks

Q3 2024 Results Conference Call and Webcast

October 31, 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; preclinical development progress and 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).

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.

Q3 2024 Earnings Results Call Agenda

Leone Patterson, MBA, CPA
EVP, CBO and CFO

- Business Update
- Financial Update
- Q&A

Paul Moore, Ph.D.
CSO

- R&D Update
- Q&A

Ken Galbraith
Chair and CEO

- Q&A

Leone Patterson, MBA, CPA

EVP, CBO and CFO

Recent Developments

Aug 2024
IND applications cleared by the US FDA for ZW191 and ZW171

Sep 2024
Updated Phase 2 data for zanidatamab demonstrating increased mPFS in HER2+ mGEA at ESMO 2024

Sep 2024
Recognized revenue of $2.5m research **milestone payment from GSK**

Oct 2024
First patient dosed in the Phase 1 trial (NCT06523803) of ZW171

Oct 2024
Preclinical data on ZW251 demonstrating compelling preclinical activity in hepatocellular carcinoma model bearing a topoisomerase I inhibitor payload

Preclinical data on ZW220 demonstrating compelling preclinical activity in NSCLC, ovarian and uterine cancer models, with a favorable toxicology profile in non-human primates

Oct 2024
Completion of initial $30M of share repurchase program

ESMO: European Society of Medical Oncology; FDA: U.S. Food and Drug Administration; HER2+: HER2-positive; IND: investigational drug application; mGEA: metastatic gastroesophageal adenocarcinoma; mPFS: median progression-free survival; NSCLC: non-small cell lung cancer

Stock Repurchase Program

- On August 1, 2024, we adopted a stock repurchase program (the “Repurchase Program”), whereby the Company may repurchase up to $60.0M of the Company’s outstanding common stock, with an initial authorized phase of $30.0M.
- As of September 30, 2024, we had completed the repurchase of 1,818,530 shares of our common stock under the Repurchase Program at an average price per share of $11.32 for a cost of $20.6 million.
- As of October 31, 2024, we have completed the initial $30.0 million of the Repurchase Program through the purchase of 2,545,402 shares of common stock at an average price per share of $11.79.

Q3 2024YTD Financial Results

In millions USD	Q3 2024YTD	Q3 2023YTD
Revenue	$45.3	$59.1
R&D Expense	$97.6	$118.1
G&A Expense	$45.3	$55.6
Impairment	$17.3	-
Net Loss	$(99.2)	$(104.2)
	Sept 30, 2024	December 31, 2023
Cash Resources[1]	$374.9	$456.3

- **Revenue** decreased in Q3 2024YTD primarily due to lower development support payments from Jazz partially offset by milestone revenue from BeiGene and GSK.
- **R&D Expense** decreased primarily due to a decrease in expenses for zanidatamab as a result of transfer of this program to Jazz and a decrease in expenses for ZW171 and ZW191. This decrease was partially offset by an increase in expense with respect to product candidates ZW220 and ZW251 and other preclinical and research activities. Stock-based compensation expense increased compared to Q3 2023YTD due to a lower expense in 2023 as a result of the transfer of employees to Jazz in 2023.
- **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 Q3 2023YTD, partially offset by expenses due to an office lease termination and an increase in stock-based compensation expense.
- **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 $1.30 per diluted share in Q3 2024YTD compared to net loss of $1.53 per diluted share in Q3 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 nine months ended Sept 30, 2024, and 2023, respectively.

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

Current Financial Status:

- Cash resources[1] of approx. $375M (as of Sept 30, 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.

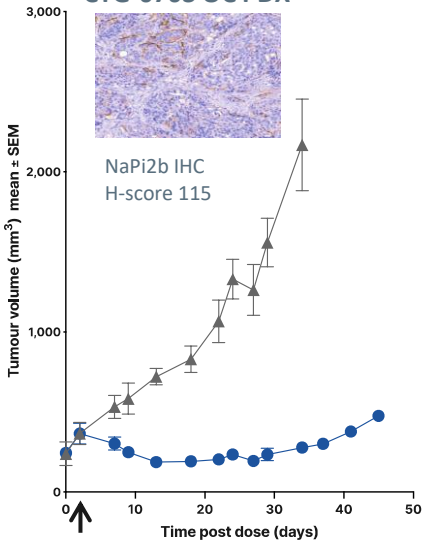
Paul Moore, Ph.D.

Chief Scientific Officer

ZW220 Demonstrates Anti-tumor Efficacy In NaPi2b-expressing Ovarian, Endometrial and NSCLC *in vivo* Models

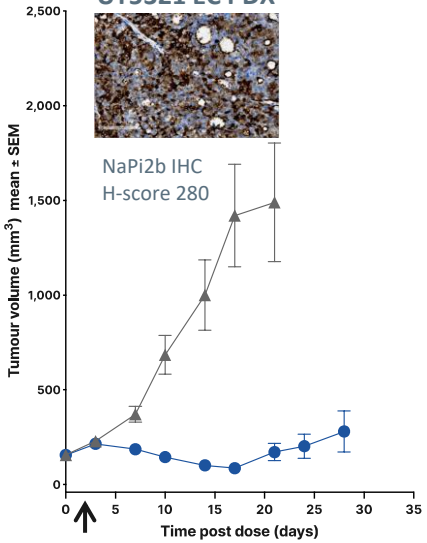
Ovarian

CTG-0703 OC PDX



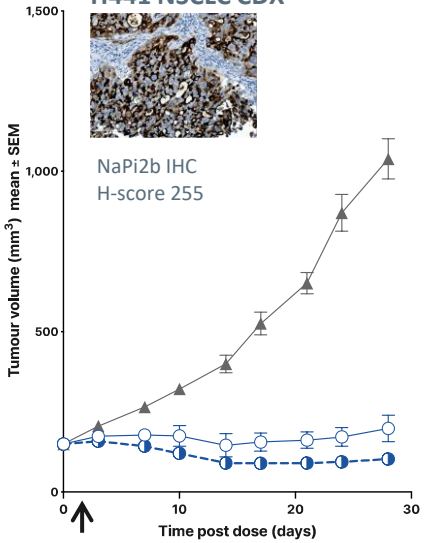
Endometrial

UT5321 EC PDX



Lung

H441 NSCLC CDX



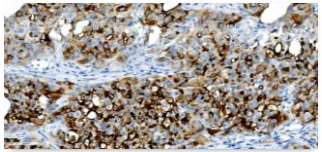
ZW220 was active at 6 mg/kg in a majority of ovarian, endometrial and NSCLC models tested

- 4 to 8 models evaluated per indication. Representative models shown
- 6 mg/kg is considered a conservative dose for ZW220 based on tolerability data.

Antitumor activity in patient derived xenograft (PDX) models of ovarian cancer, uterine (endometrial) cancer, and non-small cell lung cancer (NSCLC), n=3 mice/cohort. IV administration on Day 0. Immunohistochemistry (IHC) images from same study tissues stained using a commercial anti-NaPi2b antibody. H-scores determined by pathologist.

ZW220 Displays Bystander-Mediated Killing Activity

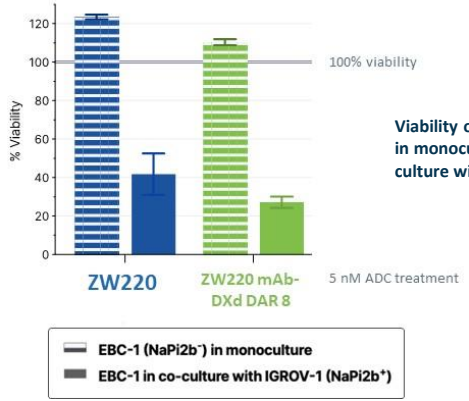
NaPi2b expression heterogeneity



low/no NaPi2b staining — strong NaPi2b staining

Commercial anti-NaPi2b antibody used for immunohistochemistry (IHC) staining of lung cell line-derived xenograft (CDX) model, archival sample.

ZW220 exhibits bystander-mediated killing in vitro

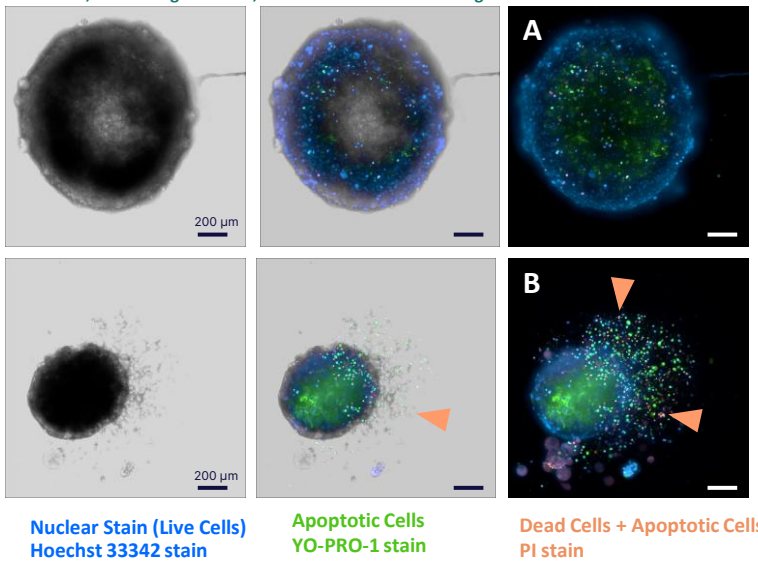


Viability of EBC-1 cells (NaPi2b⁻) in monoculture alone of in co-culture with IGROV-1 (NaPi2b⁺)

ZW220 exhibits comparable bystander activity to ZW220 mAb-DXd DAR 8 ADC control. Bystander activity, as shown by the decreased viability of NaPi2b- cells when co-cultured with NaPi2b+ cells, was assessed in a co-culture assay with IGROV-1 and EBC-1 cells, stably and homogenously expressing GFP by lentiviral transduction, 4-night incubation with ADCs, dead cell exclusion with YO-PRO-3, viability analysis by flow cytometry..

ZW220 is highly active and demonstrates bystander killing *in vitro*, with significant size reduction of heterogeneous NaPi2b spheroids

HCC-78, NaPi2b-high cell line, co-cultured with NaPi2b-negative carcinoma cell line 1:1



Minimal cell death

Compact morphology

Reduction in spheroid size compared to untreated

↑ Apoptotic core and dead cells

Nuclear Stain (Live Cells) Hoechst 33342 stain

Apoptotic Cells YO-PRO-1 stain

Dead Cells + Apoptotic Cells PI stain

Representative images of heterogeneous NaPi2b-expressing spheroids treated with ZW220, free TOPO1i payload, or untreated (blank medium). Spheroids were formed by 1:1 co-culture of NaPi2b-negative cell line (ZW220-insensitive under monoculture conditions) and HCC78 NSCLC cell line (NaPi2b-high, ZW220-sensitive in monoculture) and treated with test article for 6 days. Following incubation, spheroids were stained with fluorescent viability and cytotoxicity markers and imaged and analyzed by high content imaging, using Operetta instrument.

ZW220 is Well Tolerated in Preclinical Toxicology Models

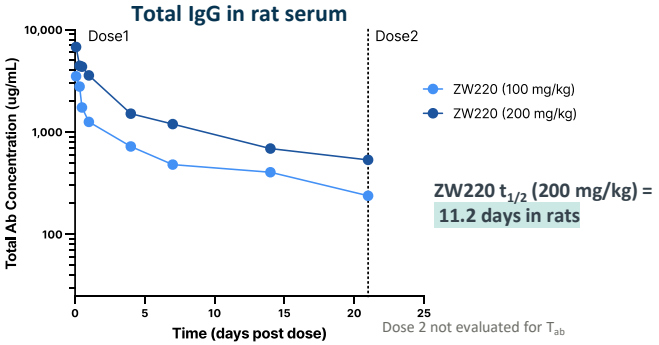
Rat toxicology (non-GLP)

2-dose non-GLP Rat toxicology study ZW220, Q3Wx2

Dose levels:
100 mg/kg
200 mg/kg

Dose 1 Day 1 → Dose 2 Day 22 → Terminal necropsy day 28

4F + 4M per group



Rat MTD ≥ 200 mg/kg

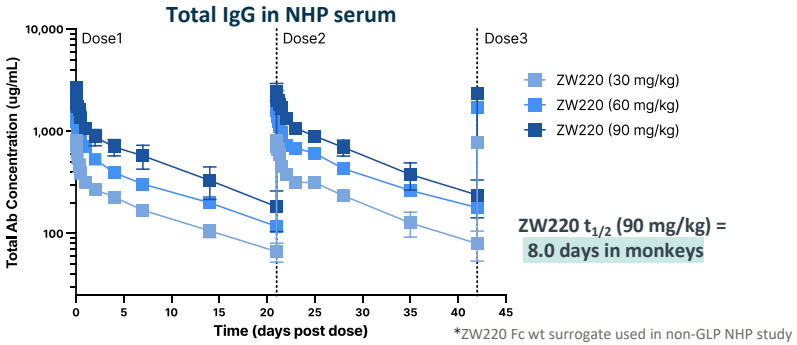
Non-human primate (NHP) toxicology (non-GLP)

3-dose non-GLP NHP toxicology study ZW220*, Q3Wx3

Dose levels:
30 mg/kg
60 mg/kg
90 mg/kg

Dose 1 Day 1 → Dose 2 Day 22 → Dose 3 Day 43 → Terminal necropsy day 50

3M per group



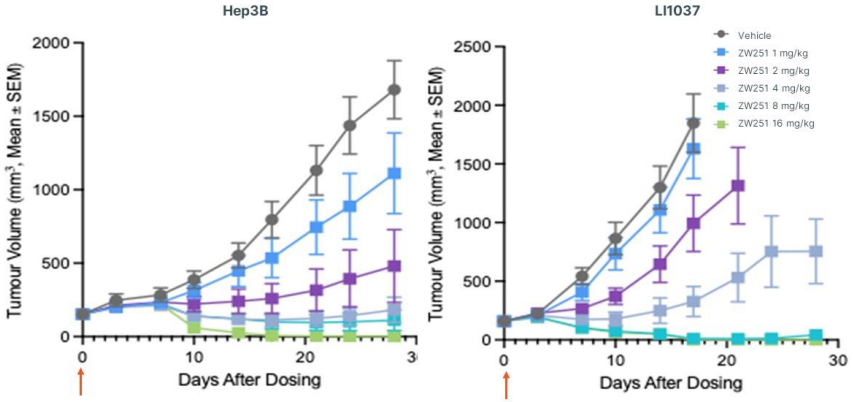
*ZW220 Fc wt surrogate used in non-GLP NHP study

NHP MTD =≥ 90 mg/kg

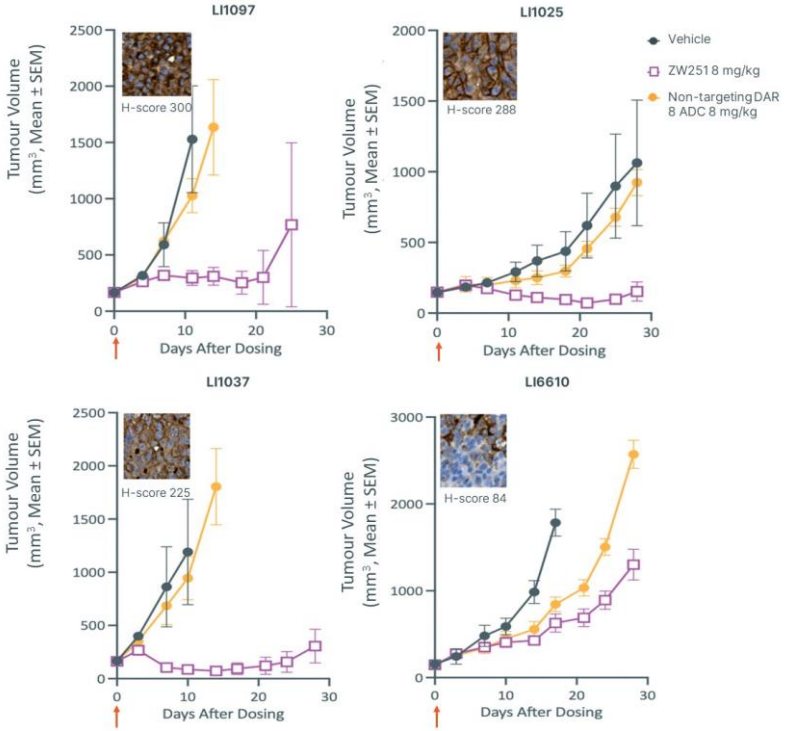
Relevant study design and result parameters from repeat dose non-GLP toxicology studies in male cynomolgus monkeys and male + female rats, performed to assess the tolerability and pharmacokinetic profile of ZW220 (n=3 monkeys/group and n=6 female + 6 male rats/group). Circulating antibody levels in NHP determined by ligand binding assay (MSD) measuring human IgG in serum following single intravenous dosing of ADC, following 1st, 2nd and 3rd dose (1st time point only) for monkey study and following 1st dose only for rat study. Half life (T1/2) and clearance rate calculated from total IgG (Tab) data.

ZW251 Demonstrates Robust in Vivo Anti-Tumor Activity in HCC Xenograft Models

Dose Response Activity



Representative HCC PDX Model Activity



Breadth of Activity

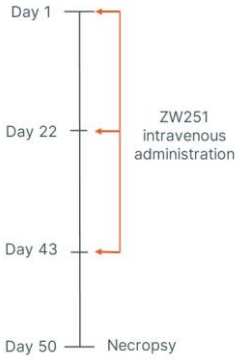
	GPC3 Expression		
ZW251 Anti-Tumor Activity >50%	H-score > 200	H-score < 200	TBD*
	82% (9/11 models)	50% (2/4 models)	100% (3/3 models)

*Assessment of GPC3 expression ongoing

Breadth of ZW251 anti-tumor activity across all tested CDX/PDX models of HCC. Anti-tumor activity at 8 mg/kg was determined by %tumor growth inhibition calculated as $[(1-TV_{treatment}/TV_{vehicle}) \times 100]$ at Day 21, or at the closest evaluable time point. GPC3 expression was determined by IHC using codrituzumab followed by pathologist scoring.

ZW251 Well Tolerated in Repeat Dose Non-Human Primate Toxicology Study and Exhibits Dose-Proportional Pharmacokinetics

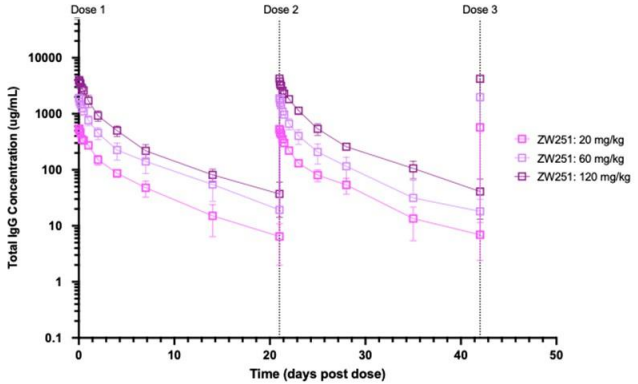
A



B

Test article	Dose	Mortality	Clinical observations	Histopathology	Clinical Chemistry	Hematology	MTD	$T_{1/2}$ (day)
ZW251 DAR 4	20 mg/kg	None	None	None	None	Decreased reticulocytes	120 mg/kg	4.6
	60 mg/kg	None	None	None	None	Decreased reticulocytes		4.8
	120 mg/kg	None	Fecal abnormalities (loose feces)	Thymus and Lymph node	None	Decreased reticulocytes		5.4

C

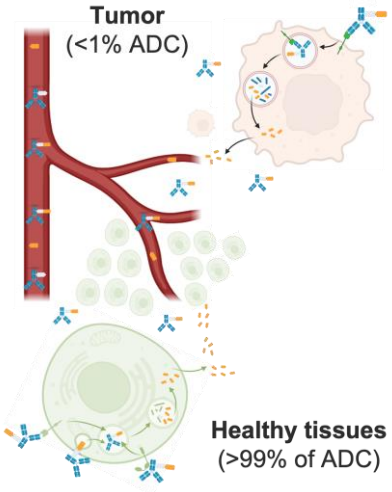


(A) Study design of a repeat dose non-GLP toxicology study in cynomolgus monkeys performed to assess the tolerability and pharmacokinetic profile of ZW251. **(B)** Toxicology results of non-human primates administered with ZW251. **(C)** Total human antibody levels in non-human primate serum as measured by ELISA

- Dose proportional pharmacokinetics observed with total antibody levels in non-human primate serum in a multi-dose study
- Treatment-related lower mean reticulocyte counts observed and deemed non-adverse in all dose groups; 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; no on-target toxicity observed
- **Observed tolerability in non-human primates of ZW251 up to 120 mg/kg suggests potential for high first-in-human dosing of ZW251**

ADC Designed to Simultaneously Enhance Efficacy and Tolerability

	Efficacy	Tolerability
Payload	Moderate potency should enable **high protein dose** and drive better tumor penetration and target engagement. **Bystander activity and systemic payload exposure** may contribute to efficacy.	Moderate potency may limit damage where conjugated drug accumulates in some normal tissues
Linker	ADCs with increased antibody-linker stability have not improved efficacy at tolerated doses to date	ADCs with increased antibody-linker stability often exhibit a worse overall toxicity profile. Moderate antibody-linker instability may **limit normal tissue exposure to conjugated drug.**
Antibody	Antibodies that favor internalization, tumor penetration, and target saturation may lead to improved payload enrichment in the tumor and positively contribute to efficacy	Improved antibody properties and enhanced tumor-to-normal tissue ratio for payload disposition may reduce off-target toxicity.

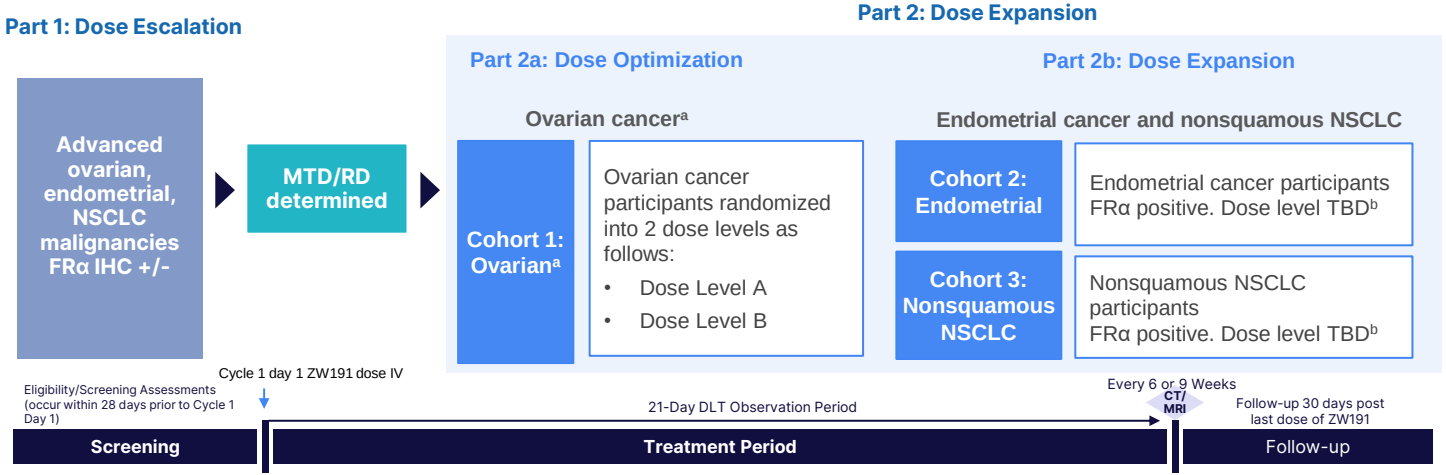


ADC Candidate	NHP HNSTD
ZW191	60 mg/kg
ZW220	≥90 mg/kg
ZW251	120 mg/kg

ADC: antibody-drug conjugate, HNSTD: highest non-severely toxic dose, NHP: non-human primates

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

Open-label, FIH, dose-escalation study N= ~145



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

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 ovarian cancer, endometrial cancer, NSCLC
- Progressive disease refractory to all SOCs that confer clinical benefit
- Measurable disease per RECIST v1.1
- ECOG PS 0-1
- 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

[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.

ADA: anti-drug antibody; ADC: antibody-drug conjugate; AE: adverse event; AESI: adverse event of special interest; CNS: central nervous system; CT/MRI: computed tomography/magnetic resonance imaging; ECOG PS: Eastern Cooperative Oncology Group performance status; FRα: folate receptor alpha; IHC: immunohistochemistry; IV: intravenous; MTD: maximum tolerated dose; NSCLC: non-small cell lung cancer; ORR: objective response rate; PD: pharmacodynamics; PK: pharmacokinetics; Q3W: every 3 weeks; RDE: recommended dose for expansion; RECIST: Response Evaluation Criteria in Solid Tumors; SAE: serious adverse event; SMC: safety monitoring committee; SOC: standard of care; TBD: to be determined; TOPO1i: topoisomerase-1 inhibitor.

ZW171 Clinical Development Progress

NA **North America**

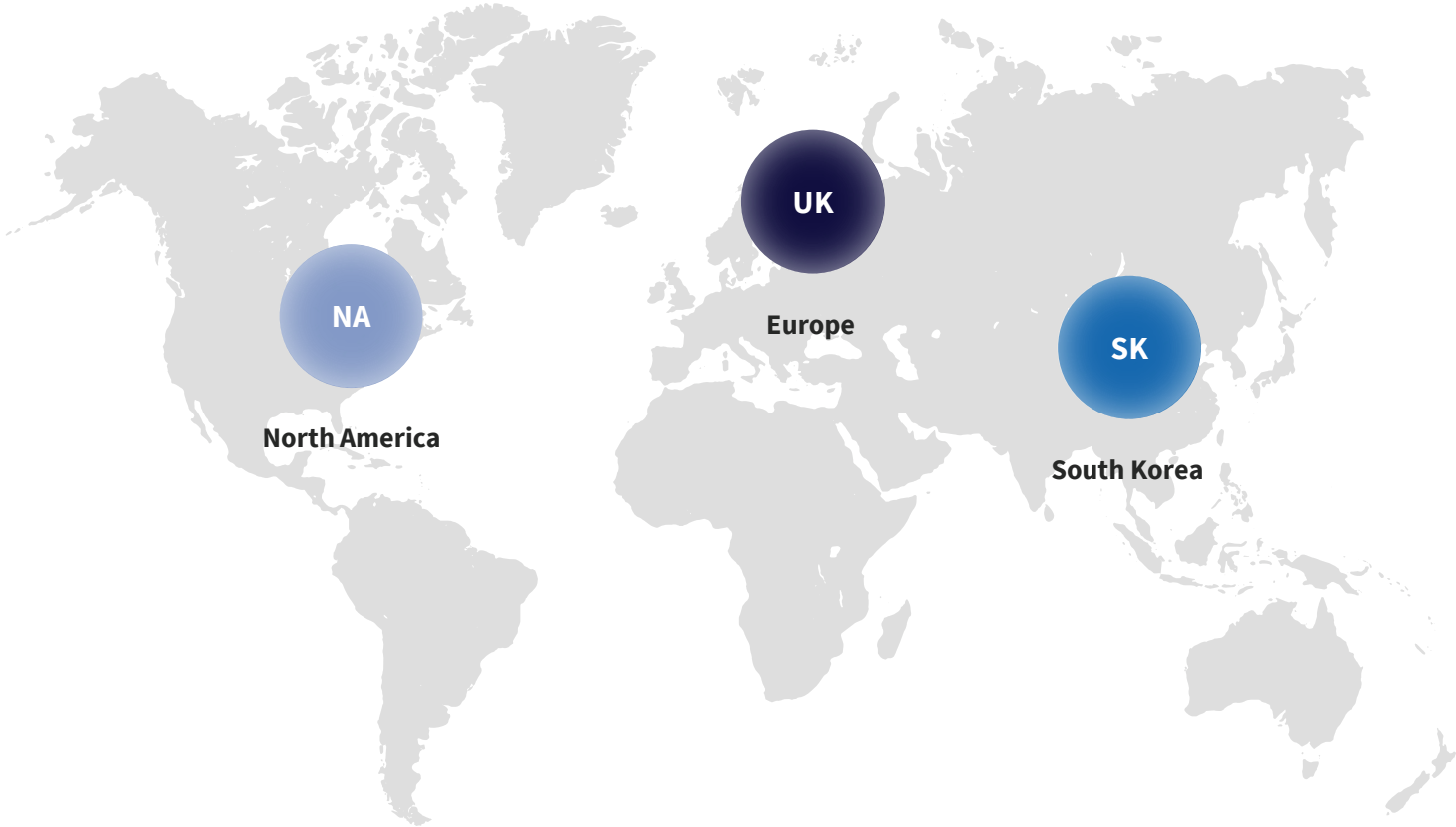
US FDA Approval
First Sites Activated

UK **United Kingdom**

MHRA Approval

SK **South Korea**

MFDS Approval



EMA: European Medicines Agency; US FDA:U.S. Food and Drug Administration; MFDS: Ministry of Food and Drug Safety; MHRA: Medicines and Healthcare Products Regulatory Agency

Zymeworks R&D Day 2024: Thursday, December 12, 2024

Date: Thursday, December 12, 2024
Time: 7:30 am - 1:00 pm ET
Location: Lotte Palace New York, 455 Madison Avenue at 50th Street, New York, NY 1002

Breakfast & Registration
7:30 am - 8:30 am ET

Event & Livestream Begins
8:30 am ET

Formal Presentations and Q&A Session
8:30 am - 12:00 pm ET

Livestream Concludes
12:00 pm ET

Lunch & Breakout Sessions with Presenters and Zymeworks Management Team (optional)
12:00 pm - 1:00 pm ET

Event Concludes
1:00 pm ET

About the Event:

The event will be led by Dr. Paul Moore, Chief Scientific Officer and other members of our Research and Development team, and will include:

- Updates on our portfolio of solid tumor targeting antibody-drug conjugates (ADCs) and T-cell engager (TCE) molecules, featuring key opinion leaders from these therapeutic areas who will join our management team to discuss ongoing R&D and clinical activities;
- Candidate nomination from our Trispecific TCE platform as the last product candidate selected in our '5 by 5' R&D strategy; and
- Strategy and rationale for expansion into new therapeutic areas in hematological cancers and autoimmune and inflammatory diseases (AIID) and preclinical development progress on potential IND filings for new product candidates in 2026 and beyond.

A live question and answer session will follow each formal presentation.

Please RSVP by **Friday, November 15, 2024.**

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**: Trial ongoing; Jazz has estimated top-line PFS data will be available in 2Q25

Focus on Gyn CA, Lung CA, & GI CA

- **ZW171 (Actively recruiting)**
  MSLN x CD3 bispecific antibody
- **ZW191 (Actively recruiting)**
  FRα TOPO1i ADC
- **ZW220 (IND 1H 2025)**
  NaPi2b TOPO1i ADC
- **ZW251 (IND 2H 2025)**
  GPC3 TOPO1i ADC
- **Candidate 5 TBD (IND 1H 2026)**
  Pre-clinical TriTCE candidate nomination expected in 2H 2024

Pipeline Events

- **Anticipated nomination of Tri-TCE product candidate during R&D day**
- **Jazz initiated a Phase 3 trial (EmpowHER-BC-303) to evaluate zanidatamab** in patients with HER2-positive breast cancer whose disease has progressed on previous trastuzumab deruxtecan (T-DXd) treatment
- **Jazz estimates top-line 1L GEA 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

Ken Galbraith
Chair & CEO

Paul Moore, Ph.D.
CSO

Leone Patterson, MBA, CPA
EVP, CBO and CFO