Q1 2024 Results
Conference Call and Webcast

May 2, 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 zanidatamab; 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' preclinical 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).

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.

Q1 Earnings Results Call Agenda

Ken Galbraith
Chair and CEO

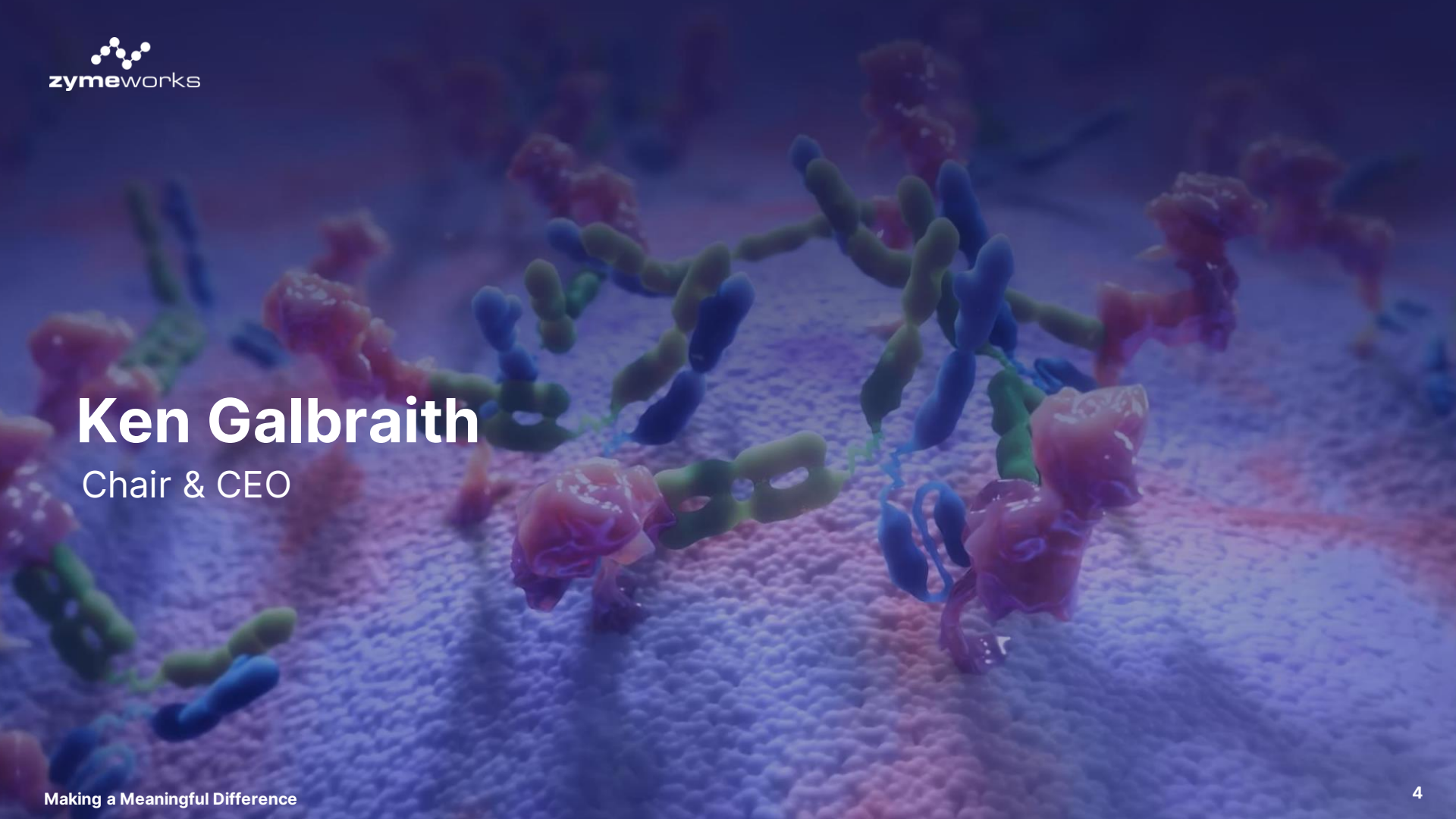
- Financial Update
- Q&A

Paul Moore, Ph.D.
CSO

- R&D Update
- Q&A

Bijal Desai, MBA
VP, Finance & Strategy

- Q&A



Ken Galbraith

Chair & CEO

Key Developments for 2024 and Expected News Flow

1H 2024

- Our partner Jazz **completed the U.S. regulatory submission** for zanidatamab seeking accelerated approval in 2L BTC
- Jazz initiated a **Phase 3 global confirmatory trial** for zanidatamab in 1L BTC
- Jazz guided that their plans to submit an MAA to the EMA for zanidatamab in BTC are proceeding
- **Expected IND submission** for first 5x5 product candidate
- Strengthened board of directors with the addition of Dr. Neil Gallagher

- **5 poster presentations at AACR** including:
  - Additional preclinical data for ZW191
  - Next Generation CD28 Co-Stimulatory Trispecific T Cell Engager program for Claudin 18.2 and DLL3
  - Platform capabilities for designing bispecific ADCs
  - Development of 3D spheroid models to evaluate cytotoxic activity of ADCs
- Upcoming **poster presentation for zanidatamab featuring updated data** from HERIZON-BTC-01 at ASCO by Jazz

2H 2024

- Pivotal **Phase 3 top-line data readout in GEA** 1L targeted by our partner Jazz in late 2024
- Expected **BLA submission in China** by our partner BeiGene for zanidatamab in 2L BTC
- Jazz expects to **initiate a Phase 3 trial** for zanidatamab in 2H24 in patients who have progressed on previous T-DXd treatment

- **Expected IND submission** for second 5x5 product candidate
- Expected nomination of 5th product candidate in 5x5 R&D portfolio
- **R&D day** planned for 4Q 2024 to highlight future progress and strategy
- **Continued preclinical data readouts** at multiple scientific conferences throughout 2024

1L: first-line (treatment); 2L: second-line (treatment); AACR: American Association for Cancer Research; ADC: antibody-drug conjugate; ASCO: American Society of Clinical Oncology; BLA: biologics license application; BTC: biliary tract cancers; CD28: cluster of differentiation 28; DLL3: delta-like ligand 3; EMA: European Medicines Agency; GEA: gastroesophageal adenocarcinoma; IND: investigational new drug (application); MAA: marketing authorization application; R&D: research and development; T-Dxd: trastuzumab deruxtecan.

Q1 2024 Financial Results

In millions USD	Q1 2024	Q1 2023
Revenue	$10.0	$35.6
R&D Expense	$32.0	$45.9
G&A Expense	$15.8	$16.9
Net Loss	$(31.7)	$(24.4)
	March 31, 2024	December 31, 2023
Cash Resources[1]	$420.5	$456.3

- **Revenue** decreased in Q1 2024 primarily due to lower development support payments from Jazz and lower revenue from our partners for research support and other payments compared to Q1 2023.
- **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, compared to Q1 2023, was partially offset by an increase in preclinical expenses, primarily with respect to preclinical product candidates ZW171, ZW191, and ZW220. Salaries and benefits expenses decreased due to lower headcount in Q1 2024, partially offset by an increase in stock-based compensation expense compared to Q1 2023.
- **G&A Expense** decreased primarily due to a decrease in insurance costs and external legal spend compared to Q1 2023.
- **Net loss** of $0.42 per diluted share in Q1 2024 compared to net loss of $0.37 per diluted share in Q1 2023.
- **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 three months ended March 31, 2024, and 2023, respectively.

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

Current Financial Status:

- Cash resources[1] of approx. $420.5M (as of March 31, 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
- Additional payments from legacy technology platform collaborations
- Potential new partnerships/collaborations to provide upfront payments and committed R&D funding

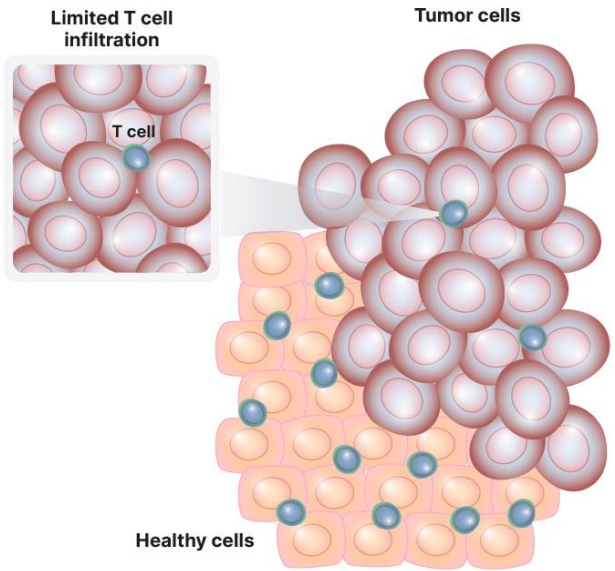
1. Cash resources consist of cash, cash equivalents, and marketable securities.

Paul Moore, Ph.D.

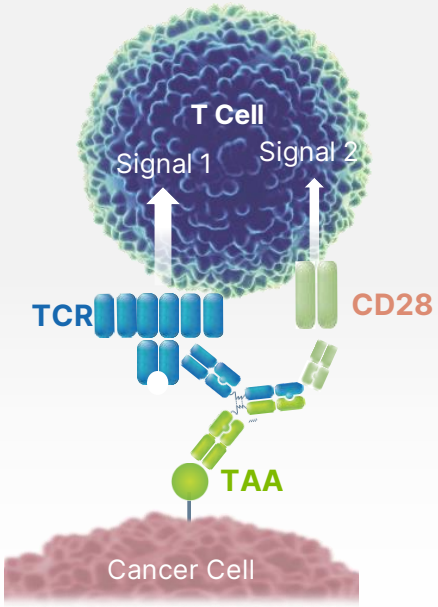
Chief Scientific Officer

Zymeworks Trispecific Co-Stimulatory TCE: Overcoming Lack of Efficacy and Durability of Responses in Solid Tumors by Optimization of Signal 1 and 2

Low T cell infiltration and T cell anergy remain challenges in the treatment of solid tumors



Zymeworks Trispecific Co-Stimulatory Program



Provides Signal 1 (CD3) and Signal 2 (CD28) in one molecule **to increase T cell activation and proliferation**

Engineered to balance signal 1 and 2 for optimized **TAA-dependent T cell activation** and expansion

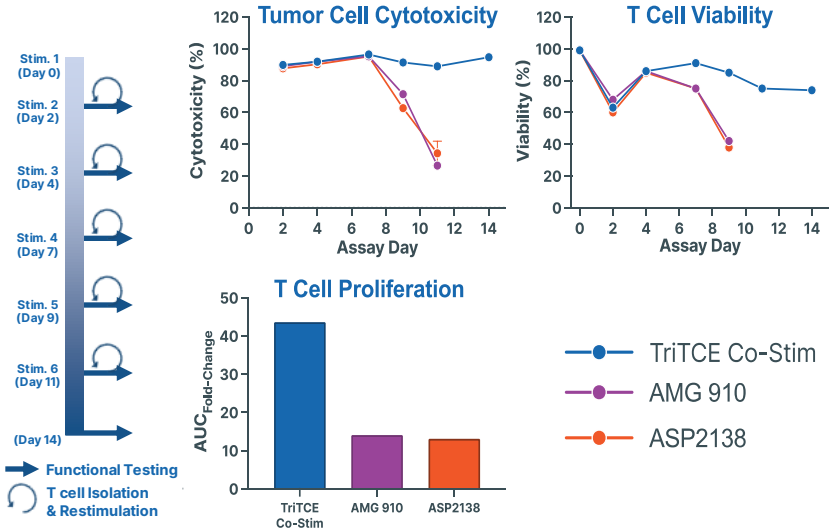
TriTCE Co-stim has the potential **to provide more durable responses** and reinvigorate T cell responses in 'cold' tumors with lower T cell infiltration

CD3: cluster of differentiation 3 protein complex and T cell co-receptor; TAA: tumor associated antigen; TCE: T cell engager; TCR: T cell receptor; TriTCE Co-Stim: trispecific T cell engager co-stimulatory program.
Arvedson T et al. Ann Rev Cancer Biol 2022.

TriTCE Co-Stim: A Next Generation Trispecific T Cell Engager Platform

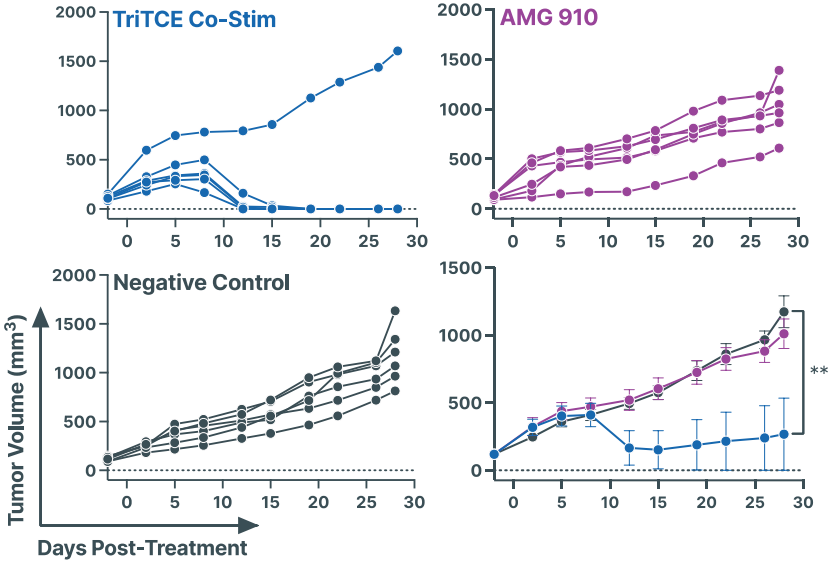
- Designed to enhance T cell activity and provide more durable anti-tumor control
- CLDN 18.2 used as a model tumor antigen and activity benchmarked against clinical stage bispecifc TCEs

Sustained T cell Cytotoxicity and T cell Fitness



CLDN18.2 TriTCE Co-Stim displays sustained T cell fitness and anti-tumor activity in a serial, repeat challenge assay. T cells were stimulated with SNU 601 cells (**5:1 E:T**) and test article (1 nM). For each subsequent round of stimulation, T cells are isolated from the T cell:tumor cell co-culture, counted, and re-stimulated with fresh SNU 601 target cells (5:1 E:T) and fresh test article (1 nM). Schematic of T cell restimulation. Following each round of stimulation, T cell: tumor cell co-cultures were assessed for tumor cell cytotoxicity, T cell viability, and T cell proliferation. Data are representative of two individual donors and are presented as mean ± SD. Insufficient T cells for continued stimulation with AMG 910 and ASP2138 following stimulation 5. Viability and proliferation data for AMG 910 and ASP2138 were excluded for stimulation 5 due to technical error (tumor cell carryover).

Enhanced Anti-Tumor Activity in Established Gastric Cancer Humanized Xenograft Model



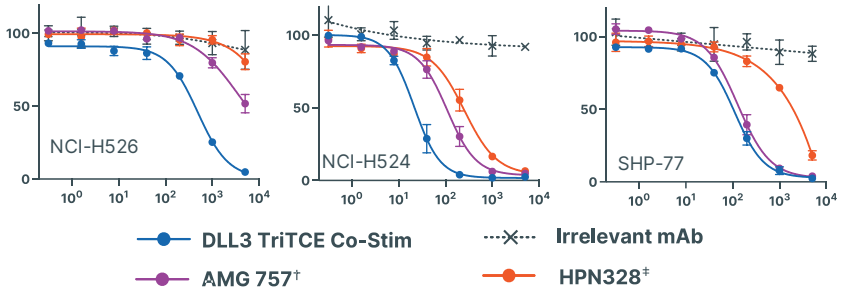
In vivo efficacy following treatment with CLDN18.2 TriTCE Co-Stim. NCG mice (n=6) were injected SC with SNU 620 (gastric) target cells, engrafted with human PBMCs, and treated IV with 0.05 mg/kg of test article qTwx4. Mice were assessed for tumor volume. Data are presented as mean ± SEM. ** p<0.01

CLDN: claudin; E:T: Effector to Target ratio; NCG: nude, complement deficient, gamma-irradiated; nM: nanomolar; PBMC: peripheral blood mononuclear cells; SC: subcutaneous.
AMG 910 (CLDN18.2/CD3 Bispecific T cell engager) & ASP2138 (CLDN18.2/CD3 2+1 bispecific antibody) replicas produced in-house.
Newhook L et al., Abstract #6719 presented at AACR Annual Meeting 2024.

DLL3 TriTCE Co-Stim: A Next Generation Trispecific T Cell Engager

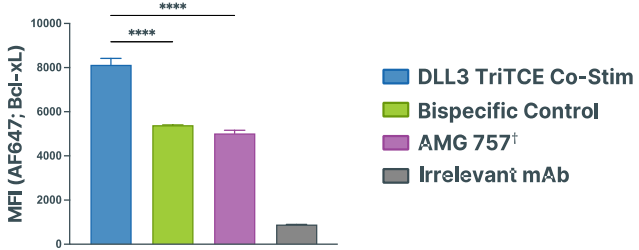
- Designed to incorporate CD28 co-stimulation to improve activity beyond conventional DLL3 x CD3 bispecifics by enhancing T cell activity and providing more durable responses in poorly infiltrated 'cold' tumors

Enhanced T Cell Cytotoxicity (SCLC)



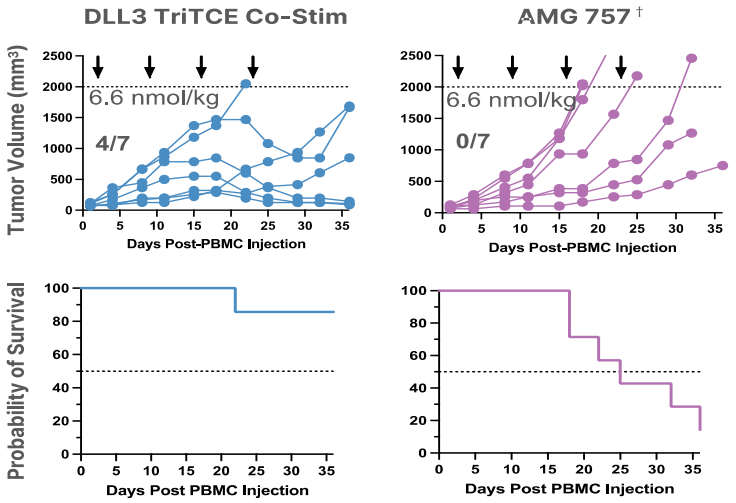
DLL3 TriTCE Co-Stim displays superior in vitro cytotoxicity relative to clinical benchmarks across multiple DLL3-positive SCLC tumor cell lines. Test articles were incubated with T cells co-cultured with DLL3-expressing tumor cell lines (E:T =1:2) for 7 days and evaluated for cytotoxicity.

Improved T Cell Survival Compared To Bispecific TCEs



DLL3 TriTCE Co-Stim increases T cell proliferation and upregulation of anti-apoptotic marker Bcl-xL. Test articles (5 nM) were incubated with T cells co-cultured with NCI-H82 cells for 48 hours and evaluated for Bcl-xL expression by flow cytometry. **** p<0.0001

Superior Anti-Tumor Activity in Established SCLC Humanized Xenograft Model



DLL3 TriTCE Co-Stim efficacy in vivo. SHP-77 cells were injected s.c. in NCG mice. Following PBMC humanization, mice were treated IV with test article q1w x 4. Tumor volume over time of mice treated with DLL3 TriTCE Co-Stim (6.6 nmol/kg), AMG 757 (6.6 nmol/kg). Full or partial tumor regression was observed in 4/7 mice treated with DLL3 TriTCE Co-Stim. Arrows indicate treatment days. Kaplan-Meier curves showing probability of survival of tumor-bearing mice treated with DLL3 TriTCE Co-Stim (blue), AMG 757 (purple, MS = 25 days). Death events represent euthanized animals due to reaching experimental endpoint (TV ≥ 2000 mm3).

mAb: monoclonal antibody; SCLC: small cell lung cancer.
† AMG 757 (DLL3/CD3 bispecific T cell engager) produced in-house.
Repenning P et al., Abstract #6716 Presented at AACR Annual Meeting 2024.

TriTCE Co-Stim: Differentiated Co-Stimulatory (CD28) Platform vs. Clinical Competitors

Co-Stimulatory (CD28) TCE Strategies	Zymeworks' Potential Advantage and Limitations of Alternative Strategies
Zymeworks TriTCE Co-Stim	✓ Zymeworks TriTCE Co-Stim provides **balanced CD3 and CD28 activation** to prevent overactivation of T cells[1,2] ✓ **Tumor Target-dependent activity** associated with sustained T cell viability and cytotoxicity resulting in improved anti-tumor activity in preclinical models compared to bispecific TCEs[1,2,3,4,5] ✓ **No CD28 binding in absence of CD3 engagement**, lowering risk of CD28-mediated immune related adverse events (irAEs); well-tolerated in both in vivo CRS models[1,2] and non-human primates[3]
CD28xTAA Bispecific (e.g. Regeneron, Xencor)	❑ Optimized for strong CD28 agonism, potentially difficult to optimize by dose adjustment[6,7] ❑ Dependent on presence of signal 1 primed T cells in TME[6,7] ❑ Potential for severe irAEs in combination with anti-PD-1, similar to CPI toxicities[8,9,10,11,12]
CD3xTAA + CD28xTAA Bispecific Combinations (e.g. Regeneron, Janssen, Roche)	❑ Increased development and challenging dose optimization requirements for two molecules[13] ❑ Potential for CD28 bispecific irAEs[9] ❑ Challenging TAA pairs or non-overlapping epitope targets requirements[6]
CD28xCD3xTAA Trispecific (Sanofi)	❑ High affinity CD3 and CD28 paratopes, activation of peripheral T cells[14,15] ❑ T cell binding and TMDD observed in the periphery[14,15] ❑ CD28 paratope based on CD28 super-agonist, potentially limiting application[14,15]

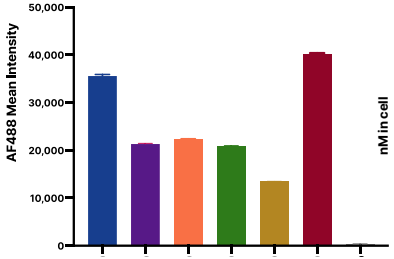
CPI: checkpoint inhibitor; PD-1: programmed cell death protein 1; TMDD: tumor mediated drug disposition; TME: tumor microenvironment.

1. Newhook et al., Cancer Res. (2023); 2. Newhook et al., JITC (2023); 3. Newhook L et al., Abstract #6719 presented at AACR Annual Meeting 2024; 4. Repenning P et al., Abstract #6716 Presented at AACR Annual Meeting 2024. 5. Newhook et al., SITC (2023); 6. Skokos et al., Sci. Transl. Med. (2020); 7. Dragovich et al., Cancer Research (2023); 8. Stein et al., Journal Clinical Oncology (2023); 9. Martins et al., Nature Reviews Clin Oncol (2019); 10. Eastwood et al., BJP (2010); 11. Roemer et al., Blood (2011); 12. Hui et al., Science (2017); 13. Humphrey et al. (2011) J Natl Cancer Inst. 14. Seung et al., Nature (2022); 15. Promsote et al., Nature Communications (2023).

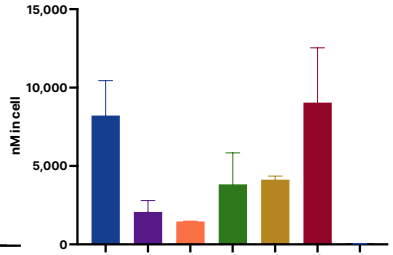
ZW191: Key Design Considerations; On Track for Clinical Studies in 2024

ZW191's Novel mAb Drives Superior Internalization, Payload Delivery, and Tissue Penetration

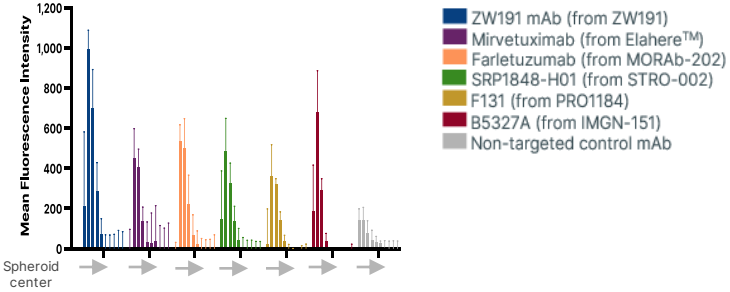
Internalization



Payload Delivery



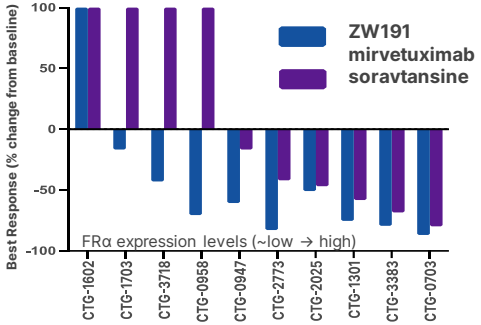
Tumor Spheroid Penetration

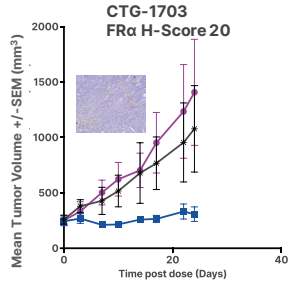


In vitro functional assessment of the antibody properties of ZW191 and other FRα-targeted ADCs and a non-targeted control mAb (all WT Fc to facilitate comparison). Internalization of AF488 labelled antibodies to KB-Hela cells after 24 hrs at 100 nM; Mass-spec. quantification of internalized payload following 24-hour treatment of IGROV-1 cells with 10 nM of ADCs comprising ZW191 mAb or other FRα-targeted mAbs conjugated to ZymeLink® Auristatin (ZLA); Penetration of AF488 labelled antibodies as quantified by high content imaging of spheroid layers at 24 hours post-treatment at 50 nM.

Anti-Tumor Activity Across Multiple Tumor Types And Range of FRα Expression (PDX models)

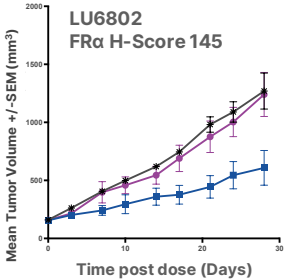
Ovarian Cancer



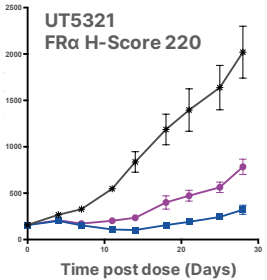


In vivo efficacy of ZW191 and mirvetuximab soravtansine was assessed in Nude or NOD/SCID mice, n=3 per group, single dose 6mg/kg.

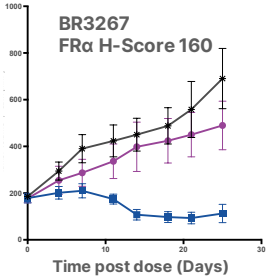
NSCLC



Endometrial



TNBC



Fc: fragment crystallizable region of antibody; FRα: folate receptor alpha; NSCLC: non-small cell lung cancer; PDX: patient derived xenografts; TNBC: triple-negative breast cancer; WT: wildtype.

Wong J et al., Abstract #3127 presented at American Association for Cancer Research annual meeting 2024; Lawn S. et al. Abstract # 1862 presented at American Association for Cancer Research annual meeting 2024.

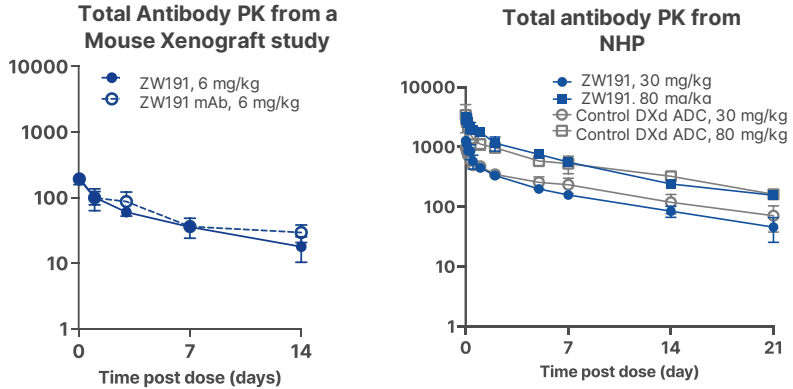
ZW191: Novel and Proprietary TOPO1i Payload Well-Tolerated

ZW191 Shows a Compelling Tolerability Profile of 60 mg/kg in NHP[1]

Dose mg/kg	Clinical observations	Histopathology	Clinical Chemistry	Hematology & coagulation	Adverse effects	HNSTD
10	None	None	↑ AST, ALT (n=1)	No effects	None	60 mg/kg
30	Emesis/vomitus	↓ Thymic lymphocytes, ↓ PACS	↑ AST, ALT			
60	Liquid/discolored feces Emesis/vomitus ↓ activity level (n=1)	↓ Thymic lymphocytes, ↓ PACS	↑ AST, ALT ↑ CK			

- No mortality or body weight effects
- No ophthalmic effects
- All effects were non-adverse and reversible
- HNSTD in NHP of 60 mg/kg presents a compelling profile, enabling expectation of achieving efficacious dose level

ZW191 Has a Favorable Pharmacokinetic (PK) Profile[2]



- **ZW191 displays favorable PK** and is **well tolerated in NHP at exposure levels** above those projected to be efficacious
- GMP process development is underway to support an expected 2024 IND filing

ALT: alanine aminotransferase; AST: aspartate aminotransferase; CK: creatine kinase; GMP: good manufacturing practices; HNSTD: highest non-severely toxic dose; MTD: maximum tolerated dose; NHP: non-human primates; PACS: pancreatic acinar cell secretion.

1. Lawn S. et al. ZW191 – a FRα-targeting antibody-drug conjugate with strong preclinical activity across multiple FRα-expressing indications. Abstract # 1862 presented at American Association for Cancer Research annual meeting 2024.
2. Lawn S et al. ZW191, a novel FRa-targeting antibody drug conjugate bearing a topoisomerase-I inhibitor payload. Abstract # 2641 presented at American Association for Cancer Research annual meeting 2023.

Milestone Opportunities in 2024 & 2025

Cash resources* as of March 31, 2024 **$420.5M**

Several opportunities for business development with unencumbered global rights for novel compounds

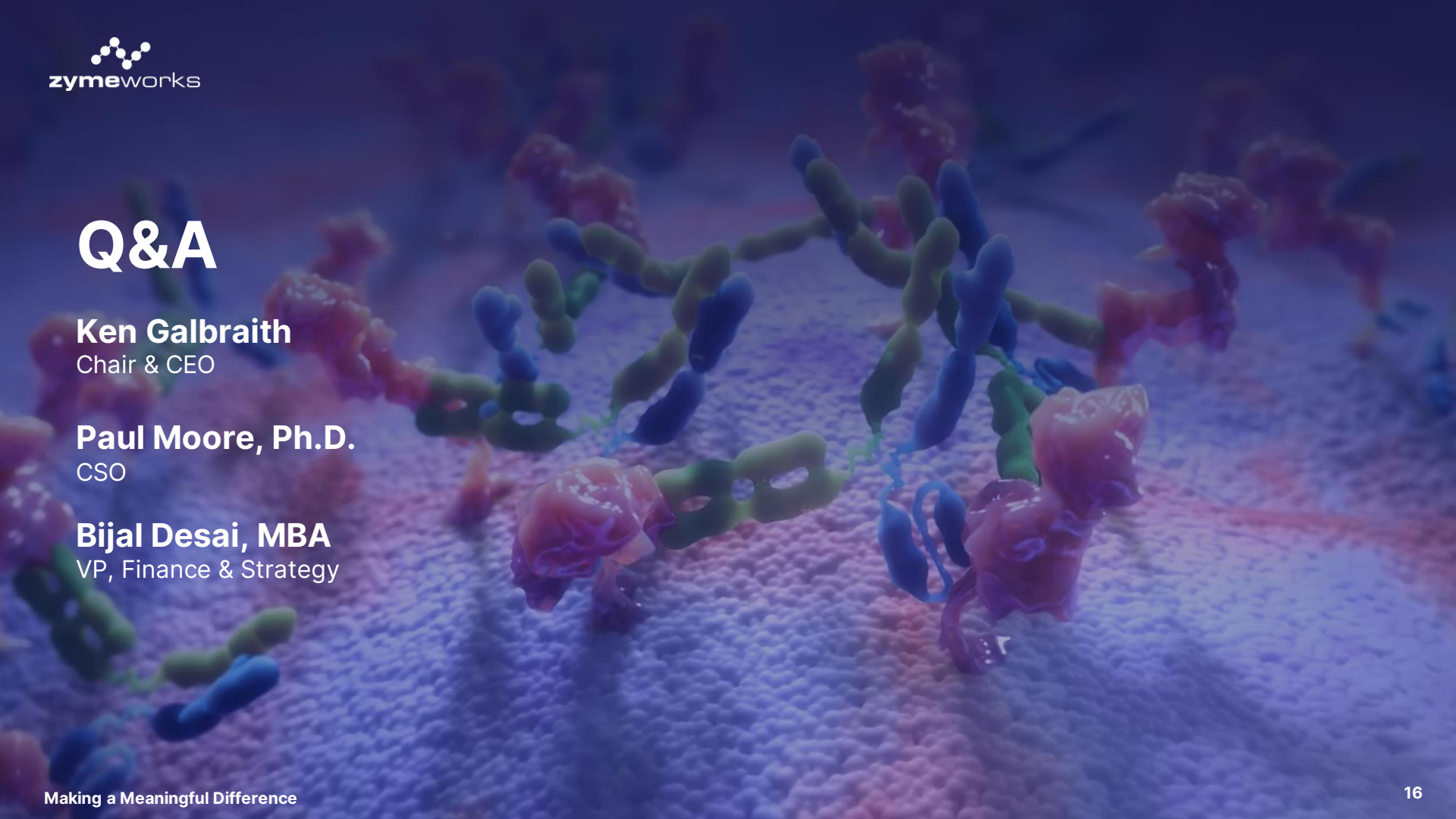
Current cash runway projected to support development goals into the **second half of 2027**.

Multiple value generating opportunities expected in 2024 and 2025, with **5 IND submissions expected by 2026**

Potential to nominate 2 IND candidates every year from 2027+

- **Top-line data from HERIZON-GEA-01** targeted for late 2024
- **Potential U.S. and China approval** for zanidatamab in 2L BTC during or before 2025

*includes cash, cash equivalents and marketable securities.



Q&A

Ken Galbraith
Chair & CEO

Paul Moore, Ph.D.
CSO

Bijal Desai, MBA
VP, Finance & Strategy