zymeworks

4Q & FY 2023 Results Conference Call and Webcast

March 6, 2024

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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; our 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 cash resources and other potential sources of cash to fund Zymeworks' planned operations into the second half of 2027, and potentially beyond; 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, including its Annual Report on Form 10-K for its year ended December 31, 2023 (a copy of which may be obtained at www.sec.gov and www.sedar.com).

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.

Q4 Earnings Results Call Agenda

Chris Astle, PhD
SVP & CFO

- Financial Update
- Q&A

Paul Moore, PhD
CSO

- R&D Update
- Q&A

Ken Galbraith
Chair and CEO

- Q&A

Chris Astle, PhD

Senior Vice President & Chief Financial Officer

2023 in Review: Selected Key Milestones

1H 2023

- **Positive results from Phase 2 study in 1L GEA** for zanidatamab (zani) at ASCO GI
- **11 poster presentations** at AACR including additional preclinical data supporting the potential therapeutic benefit of product candidates in our '5x5' program
- **Positive pivotal trial data from the Phase 2b** HERIZON-BTC-01 trial for zani at ASCO
- Inclusion in the **Russell Indices**

2H 2023

- **ZW220** announced as preclinical product candidate for an IND submission in 2025
- Updated results at ESMO for zani including **QoL outcomes in BTC trial**
- **ZW251** announced as preclinical product candidate for an IND submission in 2025
- Inclusion in the Nasdaq Biotechnology Index **(NBI)**
- Private Placement and projected **runway extension** into 2H 2027

Ongoing

- On track for anticipated **IND submissions for ZW171 and ZW191**
- **Multiple data catalysts** highlighting the innovation within our early-stage pipeline
- **Targeting late 2024 for Phase 3 top-line readout** from HERIZON-GEA-01. Enrollment for OS to be increased from 714 to 918
- Jazz initiates **rolling BLA** submission for zani's accelerated approval in 2L BTC and announces commencement of **confirmatory trial** in 1L BTC
- **Pursuing expansion of global footprint** in Dublin, California, and Singapore, and **additions to the BoD and leadership team** to support acceleration of pipeline development

1L: first-line (treatment); 2L: second-line (treatment); AACR: American Association for Cancer Research; ASCO: American Society of Clinical Oncology; ASCO GI: ASCO Gastrointestinal Cancers Symposium; BLA: biologics license application; BTC: biliary tract cancers; ESMO: European Society for Medical Oncology; GEA: gastroesophageal adenocarcinoma; IND: investigational new drug (application); OS: overall survival; QoL: quality of life

Zanidatamab: $2B+ Peak Sales Potential*

1

Expect to enter market first in BTC (pending regulatory approval)[1]

- Rolling BLA submission for accelerated approval in 2L BTC
- Confirmatory Phase 3 trial initiated in 1L metastatic BTC

Represents ~12,000 HER2+ cases annually[2] In USA, Europe[3], and Japan

2

Path to approval in 1L GEA with sBLA

- HER2+/PD-L1 negative: opportunity to address unmet need and replace trastuzumab
- HER2+/PD-L1 positive: opportunity to replace trastuzumab as HER2-targeted therapy of choice[1]
- Opportunity to explore potential in neoadjuvant populations[1]

Represents larger patient opportunity with ~63,000 HER2+ cases annually[2] in USA, Europe[3] , and Japan

3

Expanded opportunity across lines of Breast Cancer (BC)[1]

- Early lines of therapy (neoadjuvant)
- Post T-DXd
- Novel combinations[1]

Ongoing trials in early breast cancer:

- I-SPY2 Trial[4]
- MD Anderson collaboration

Considerable market opportunity with more than 150,000 cases annually[5] in USA, Europe[3], and Japan

4

Broad potential beyond BTC, GEA, and BC in multiple HER2-expressing indications[6]

- Colorectal
- NSCLC
- Ovarian
- Endometrial
- Pancreatic
- Bladder
- Salivary Gland
- Ampullary
- And other HER2-expressing solid tumors

*Adapted from Jazz Pharmaceuticals' Guidance

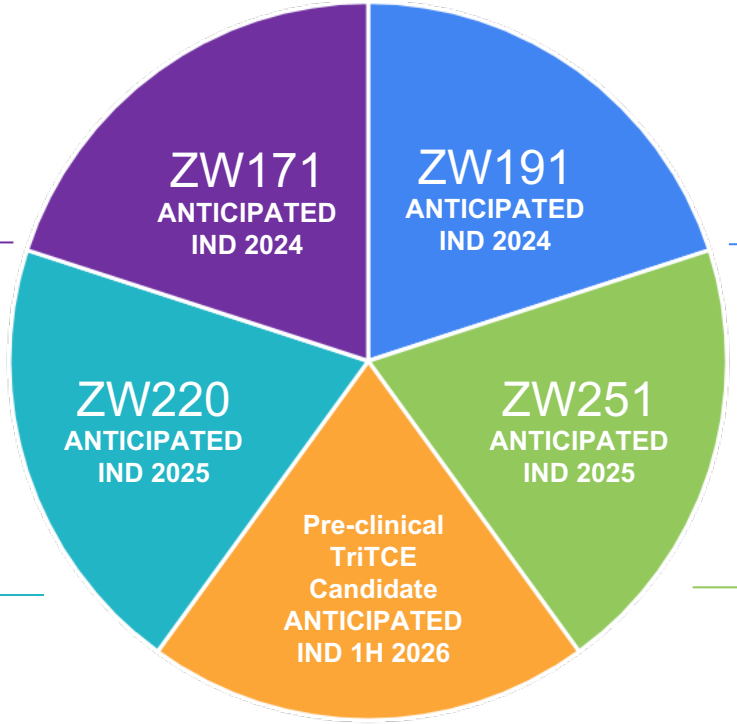
FDA: U.S. Food and Drug Administration; HER2: human epidermal growth factor receptor 2; HCP: healthcare provider; NSCLC: non-small cell lung cancer; PD-L1: programmed cell death ligand 1; sBLA: supplemental biologics license application; T-DXd: trastuzumab deruxtecan.

[1] Pending regulatory approvals, [2] Incidence sources: Kantar reports, ToGA surveillance report; SEER, cancer.gov; ClearView Analysis; GLOBOCAN, Data on file, [3] Major markets, U.K, France, Germany, Spain, Italy, [4] NCT01042379, [5] Incidence source estimates derived from multiple sources: Decision Resources Group, Kantar Health, Jazz Market Research, data on file, [6] Funda Meric-Bernstam et al, Zanidatamab, a novel bispecific antibody, for the treatment of locally advanced or metastatic HER2-expressing or HER2-amplified cancers: a phase 1, dose-escalation and expansion study, The Lancet Oncology, Volume 23, Issue 12, 2022, Pages 1558-1570, ISSN 1470-2045, https://doi.org/10.1016/S1470-2045(22)00621-0.

5x5 R&D Strategy: Diversified Portfolio Beyond Zanidatamab with Multiple Opportunities for Success

ZW171 (MSLN)
Bispecific T-Cell Engager (2+1) targeting ovarian, NSCLC, and other mesothelin-expressing cancers

ZW220 (NaPi2b)
Antibody-Drug Conjugate targeting NaPi2b-expressing non-small cell lung cancer and ovarian cancer



ZW191 (FRα)
Antibody-Drug Conjugate targeting folate receptor alpha expressing tumors including ovarian, other gynecological, and non-small cell lung cancers

ZW251 (GPC3)
Antibody-Drug Conjugate targeting GPC3-expressing hepatocellular carcinoma

FRa: folate receptor alpha; GPC3: glypican-3; MSLN: mesothelin; NaPi2b: sodium-dependent phosphate transporter 2b; TriTCE: trispecific t cell engager.

Full Year 2023 Financial Results

In millions USD	Full Year 2023	Full Year 2022
Revenue	$76.0	$412.5
R&D Expense	$143.6	$208.6
G&A Expense	$70.4	$73.4
Net (Loss) Income	$(118.7)	$124.3
	December 31, 2023	December 31, 2022
Cash Resources[1]	$456.3	$492.2

- **Revenue** decrease in 2023 primarily driven by primarily due to a non-recurring upfront fee of $375.0M from Jazz in 2022. This was partially offset by higher development support and drug supply revenue from Jazz in 2023 due to the impact of the Original and Amended Jazz Collaboration Agreements.
- **R&D Expense** decrease primarily due to a decrease in expenses for zanidatamab as a result of transfer of this program to Jazz. This decrease, compared to 2022, was partially offset by an increase in preclinical expenses, primarily with respect to preclinical product candidates ZW171 and ZW191, and in higher zanidatamab zovodotin program costs. In addition, salaries and benefits expenses decreased compared to the same period in 2022, due to lower headcount in 2023 and lower non-recurring severance expenses.
- **G&A Expense** decrease primarily due to a decrease in salaries and benefits expenses due to lower headcount and due to lower non-recurring severance expenses in 2023, as well as due to a decrease in expenses for professional services. This was partially offset by an increase in other expenses related to higher depreciation on facilities and higher technology spend in 2023.
- **Net loss** of $1.72 per diluted share compared to net income of $1.90 per diluted share in 2022.
- **Cash Resources**[1] together with receipt of certain anticipated regulatory milestones are anticipated to fund our planned operations through at least 2H 2027, and potentially beyond.

R&D: research and development; 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 years ended December 31, 2022 and December 31, 2023, respectively.

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

Current Financial Status:

- Cash resources[1] of approx. $456.3M (as of December 31, 2023)
- Includes recent private placement of $50M to EcoR1 Capital
- Anticipated cash runway into 2H 2027, which includes certain regulatory milestones

Potential sources to extend cash runway beyond 2H 2027:

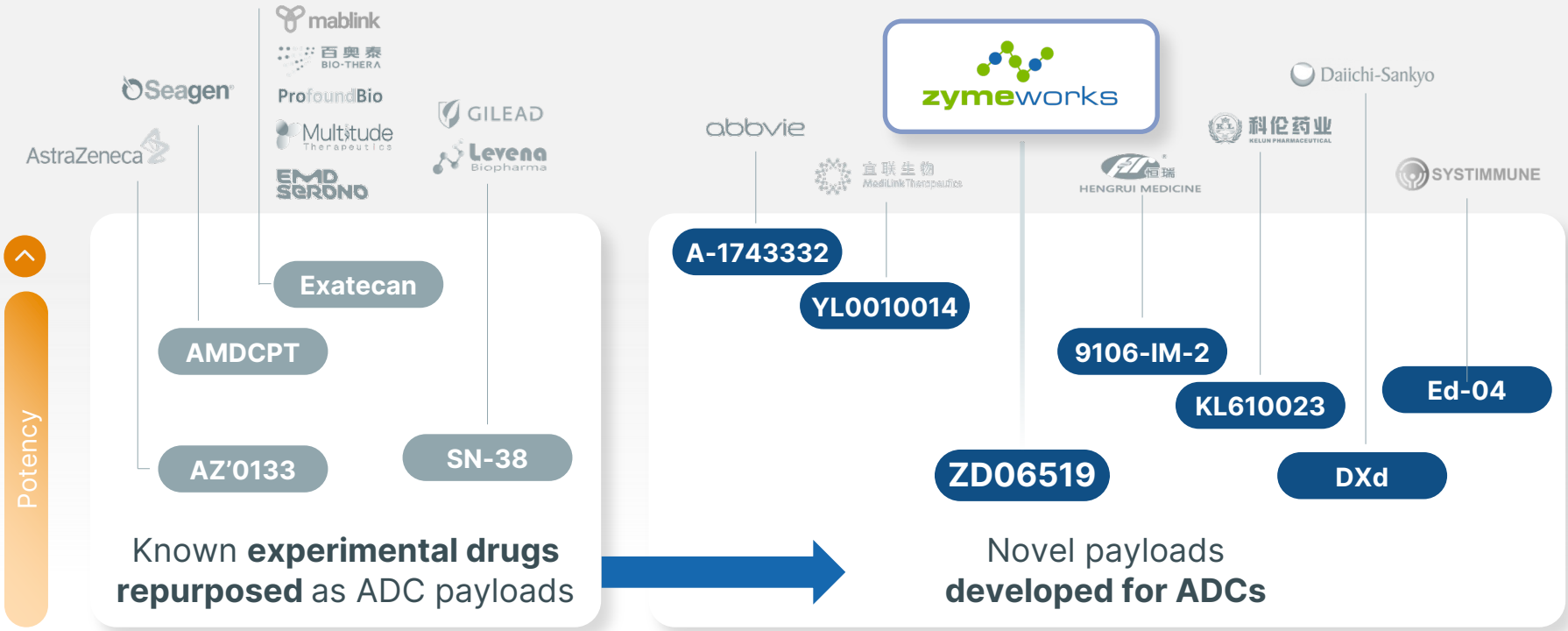
- Additional regulatory approval and commercial milestones for zanidatamab from Jazz and BeiGene
- Tiered royalties between 10-20% from Jazz and 10-19.5% from BeiGene sales (up to 20% when royalty reduction of 0.5% reaches cap in the low double-digit millions of dollars)
- Additional payments from legacy 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, PhD

Chief Scientific Officer

Zymeworks Novel Camptothecin Payload was Selected with ADCs in Mind



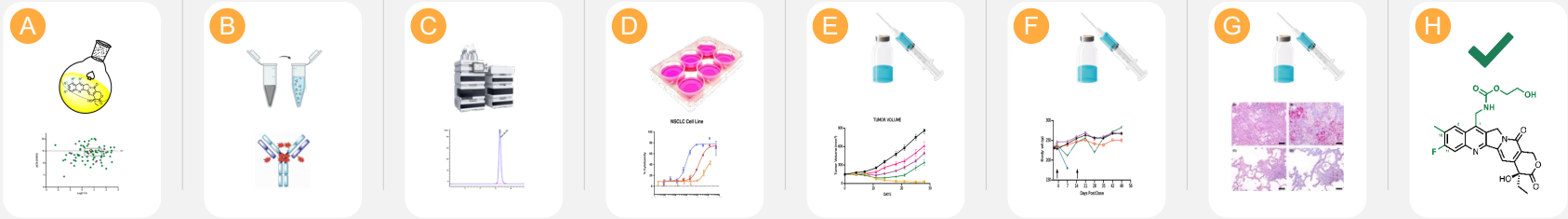
Design of novel payloads enables incorporation of properties tailored for ADC mechanism

ADC: antibody-drug conjugate

Robust Interrogation Yields Pipeline Ready TOPO1i ADC Platform

From concept to platform:

Payload synthesis & screening	Conjugation of select payloads	ADC biophysical characterization	In vitro potency & stability	In vivo anti-tumor activity & PK	Rodent tolerability	Non-human primate toxicology & TK	Lead selection
A	B	C	D	E	F	G	H



From platform to pipeline:

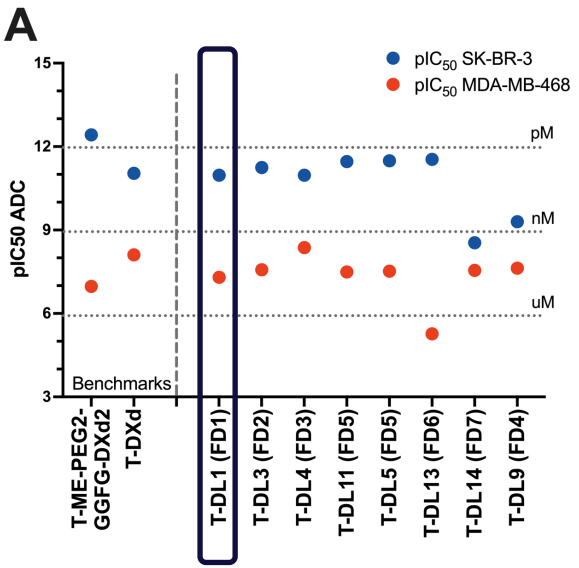
8	80	>25	>25	3	5
Tumor targets	Cell lines	CDX models	PDX models	PK studies	Tox & TK studies

3 Pipeline programs
ZW191, ZW220, ZW251

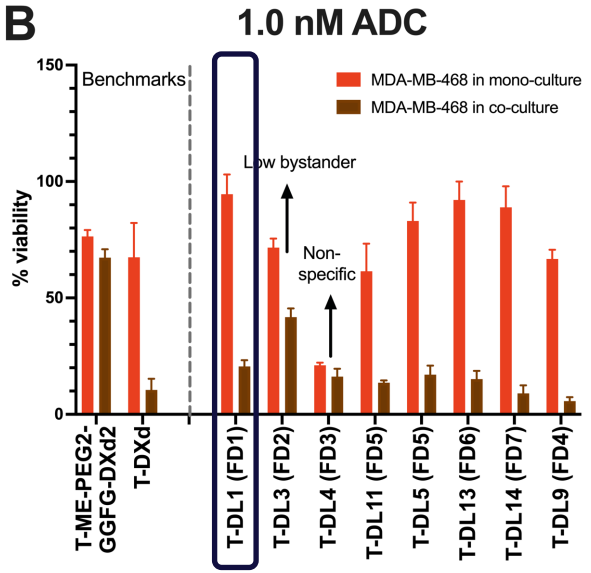
Additional early-stage assets

CDX: cell derived xenografts; PDX: patient derived xenografts; PK: pharmacokinetic; TK: Toxicokinetic; Topo1i: topoisomerase-I inhibitor

Majority of ADCs Showed Optimal Potency and Bystander Activity



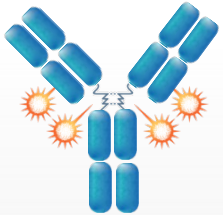
Target-dependent activity

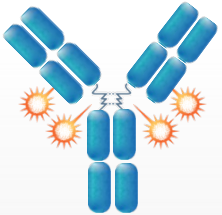


Bystander active payloads

nM: nanomolar

ZD06519 Payload is Being Utilized in Multiple Pipeline Programs





	ZW191	ZW220	ZW251
Target	**FRα**	**NaPi2b**	**GPC3**
Format/Technology	Monospecific/TOPO1i ADC	Monospecific/TOPO1i ADC	Monospecific/TOPO1i ADC
Potential Indications	Ovarian cancer, other gynecological cancers, and other solid tumors	Ovarian cancer, NSCLC	Hepatocellular carcinoma
DAR	8	4	4
Stage	IND-enabling	IND-enabling	IND-enabling
Next Milestone	On track for 2024 IND	On track for 2025 IND	On track for 2025 IND

Additional early-stage assets in development

Extensive Expected News Flow over 2024 and 2025

1H 2024

PIPELINE EVENTS

- Expect to complete USA regulatory submission for zanidatamab in 2L BTC
- Initiation of Phase 3 confirmatory trial for zanidatamab in 1L BTC
- Expected IND submission for first 5x5 candidate

PUBLICATIONS & CONFERENCES

- ASCO GI (January 18-20)
- JSMO (February 22-24)
- World ADC London (March 12-15)
- AACR (April 5-10)
- PEGS (May 13-17)

2H 2024

PIPELINE EVENTS

- Pivotal Phase 3 top-line data readout in GEA 1L targeted in late 2024
- Expected BLA submission in China for zanidatamab in 2L BTC
- Expected IND submission for second 5x5
- Nomination of 5th product candidate in 5x5

PUBLICATIONS & CONFERENCES

- ASCO (May 31-June 4)
- WCGQ (July 3-6)
- ESMO (September 13-17)
- EORTC-NCI-AACR (October 23-25)
- SITC (November 6-10)
- SABCS (December 10-14)

Manuscripts: Overview of ZD06519 (TOPO1i payload)

2025

PIPELINE EVENTS

- Potential USA and China launch for zanidatamab in 2L BTC and initial royalty revenue from partners Jazz and BeiGene
- Expected IND submission for ZW220 (NaPi2b)
- Expected IND submission for ZW251 (GPC3)

Illustrative. Key news flow only. EORTC-NCI-AACR: EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics; JSMO: Japanese Society of Medical Oncology; PEGS: Protein Engineering Summit; SABCS: San Antonio Breast Cancer Symposium; SITC: Society for Immunotherapy of Cancer; World ADC: World Antibody-Drug Conjugates Summit; WCGI: World Congress on Gastrointestinal Cancer

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**: rolling USA regulatory submission underway with breakthrough designation
- **GEA 1L**: Targeting pivotal Phase 3 top-line data readout in late 2024
- Additional ongoing and planned clinical studies beyond BTC and GEA

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

- **ZW171 (IND 2024)**
  MSLN x CD3 bispecific antibody
- **ZW191 (IND 2024)**
  FRα TOPO1i ADC
- **ZW220 (IND 2025)**
  NaPi2b TOPO1i ADC
- **ZW251 (IND 2025)**
  GPC3 TOPO1i ADC
- **Candidate5 TBD (IND 2026)**
  Pre-clinical TriTCE candidate nomination expected in 2H 2024

Continuing to innovate and move beyond oncology

- Unique/differentiated platform to build nextgen **ADC**'s and **TriTCE**'s
- Therapeutic focus to be expanded into **autoimmune and inflammatory disease (AIID)**
- Research scope to potentially expand into multifunctional engineered cytokines and dual checkpoint inhibitors

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

CD3: cluster of differentiation 3 protein complex and T cell co-receptor; GI: gastrointestinal; GI CA: gastrointestinal cancer; Gyn CA: gynecological cancer; Lung CA: lung cancer

Milestone Opportunities in 2024 & 2025

Cash resources as of December 31, 2023 **$456.3M***

Several opportunities for business development with global rights for novel compounds

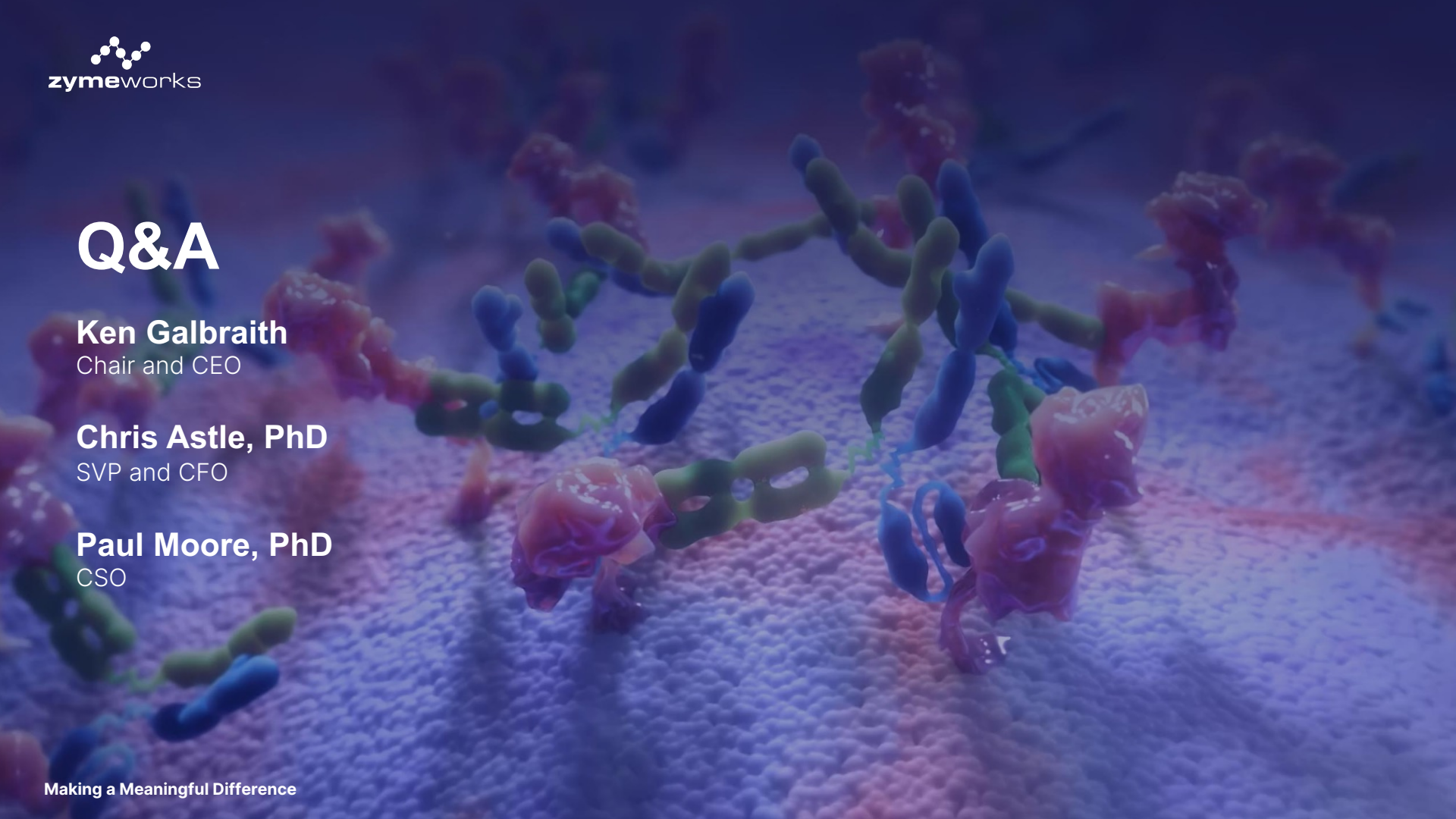
Current cash runway projected to support development goals into the second half of **2027 and potentially beyond**

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

Potential to nominate 2 candidates every year from in-house drug discovery platform

- **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

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Chair and CEO

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