zymeworks

Third Quarter 2023 Results Conference Call and Webcast

November 7, 2023

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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; potential 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; 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 through at least the end of 2026, 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 Quarterly Report on Form 10-Q for its quarter ended September 30, 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.

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Non-GAAP Financial Measures

In addition to reporting financial information in accordance with generally accepted accounting principles ("GAAP") in this presentation, Zymeworks is also reporting selected non-GAAP, or adjusted, financial measures, including adjusted research and development expenses and adjusted general and administrative expenses. These non-GAAP financial measures are in addition to, and not as a substitute for or superior to measures of financial performance prepared in accordance with GAAP and are not defined by GAAP and should not be considered as alternatives to any other indicator of Zymeworks' performance required to be reported under GAAP. In addition, other companies, including companies in our industry, may calculate similarly titled non-GAAP or adjusted measures differently or may use other measures to evaluate their performance, all of which could reduce the usefulness of our non-GAAP, or adjusted, measures as tools for comparison. Investors and others are encouraged to review Zymeworks' financial information in its entirety and not rely on a single financial measure. As defined by Zymeworks, adjusted expenses represent total research and development expenses and general and administrative expenses adjusted for non-cash stock-based compensation expenses for equity and liability classified equity instruments as well as expenses incurred in relation to the restructuring program implemented in 2022.

Adjusted expenses are non-GAAP measures that Zymeworks believes may be helpful to investors because they provide consistency and comparability with past financial performance.

See the appendix for a reconciliation of those measures to the most directly comparable GAAP measures.

Q3 Earnings Results Call Agenda

Chris Astle, PhD
SVP & CFO

- Financial Update
- Q&A

Paul Moore, PhD
CSO

- ZW251
- R&D Update
- Q&A

Ken Galbraith
Chair and CEO

- Q&A

Chris Astle, Ph.D.

Senior Vice President & Chief Financial Officer

Q3 2023 Financial Results – Nine Months Ended

In millions USD	Nine months ended Sept 30, 2023	Nine months ended Sept 30, 2022
Revenue	$59.1	$10.0
Non-GAAP R&D Expense[1]	$117.4	$148.8
Non-GAAP G&A Expense[1]	$51.8	$41.9
Net Income (Loss)	$(104.2)	$(185.1)

	Sept 30, 2023	Dec 31, 2022
Cash Resources[2]	$390.2	$492.2

- **Revenue** increased by $49.1 million which included development support and drug supply revenue from Jazz, net of a credit issued to Jazz for amendments to our partnership agreement, and research support and other payments from our partners.
- **Non-GAAP R&D Expense** decreased by $31.4 million, primarily due to a decrease in expenses for zanidatamab due to the transfer of this program to Jazz, partially offset by an increase in preclinical expenses and in higher zanidatamab zovodotin program costs compared to the same period in 2022. In addition, salaries and benefits expenses decreased due to lower headcount compared to the same period in 2022.
- **Non-GAAP G&A Expense** increased by $9.9 million primarily due to an increase expenses for professional services, IT and depreciation, partially offset by lower salaries and benefits due to lower headcount as compared to the same period in 2022.
- **Net Loss** decreased by 44%, primarily driven by higher revenue and interest income relative to the same period in 2022.
- **Cash Resources[2]** are anticipated to fund our planned operations through the end of 2026, and potentially beyond.

R&D: research and development; G&A: general and administrative; USD: United States dollar
1. Non-GAAP measure. Refer to "Appendix: Q3 2023 Financial Results – Reconciliation of Non-GAAP Measures" for reconciliation to our GAAP reported financial information.
2. Cash resources consist of cash, cash equivalents, and marketable securities.

Note: All financial results are as-reported for the nine months ended September 30, 2023, and September 30, 2022, respectively.

Paul Moore, Ph.D.

Chief Scientific Officer

Zanidatamab: Clinical Takeaways from ESMO

Phase 1b/2 study for zanidatamab plus chemo and tislelizumab in GEA

Updated Results Presented by BeiGene (ESMO 2023)

- Confirmed ORR of 75.8% (95% CI: 57.7, 88.9)
- Median PFS of 16.7 months (95% CI: 8.2, NE)
- Median duration of response of 22.8 months (95% CI: 7.4, NE)
- A Phase 3 trial (NCT05152147) evaluating this regimen is ongoing with top-line data from HERIZON-GEA-01 expected to be reported in 2024

Phase 1b/2 data as reported at ESMO by partner BeiGene | October 2023

Quality of life outcomes from the Phase 2b HERIZON-BTC-01 study on health-related quality of life ("HRQoL")

Results Presented by Jazz (ESMO 2023)

- HRQoL outcomes were exploratory endpoints and were assessed using patient-reported 5-Level EQ-5 Dimension (EQ-5D-5L) descriptive system questionnaire
- Patients with HER2-positive BTC who responded to zanidatamab reported improved HRQoL compared with baseline
- Overall, zanidatamab showed positive results that support its potential to reduce disease burden and potentially result in improved patient HRQoL compared with baseline
- As previously reported from the Phase 2b study, zanidatamab as monotherapy in this patient population had a confirmed ORR of 41.3% (51.6% in the IHC3+ patients) and a median PFS of 5.5 months

Phase 2b data as reported at ESMO by partner Jazz | October 2023

Zanidatamab has shown **broad activity in HER2-expressing cancers** and **path forward for indications beyond BTC and GEA** to be determined by ongoing development efforts

5x5 R&D Strategy: Diversified Portfolio Provides Multiple Opportunities for Success

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

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

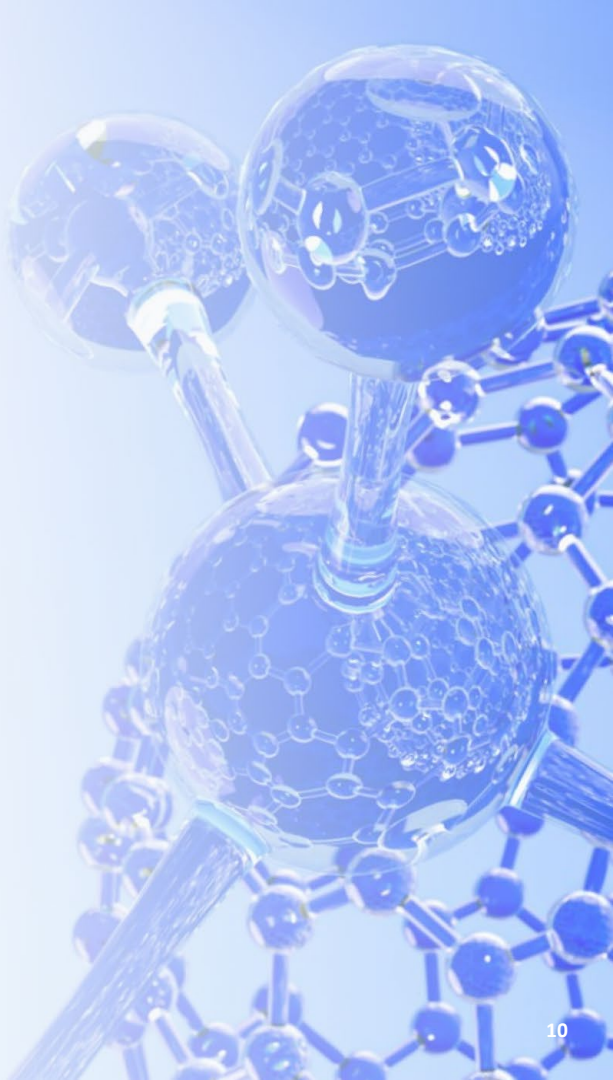
ZW191
Antibody Drug Conjugate targeting folate receptor alpha expressing tumors including ovarian, other gynecological, and non-small cell lung cancers

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

IND: investigation new drug; NaPi2b: sodium-dependent phosphate transporter; TriTCE: trispecific t cell engager

ZW251

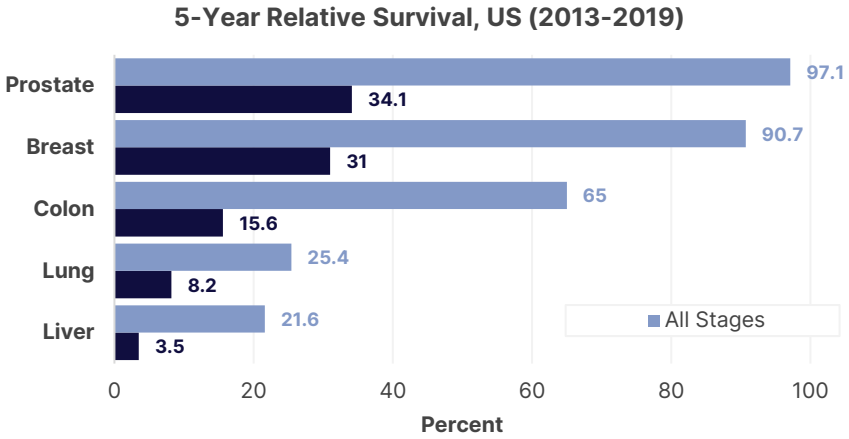
A potential **first-in-class** GPC3-targeting topoisomerase I inhibitor ADC



HCC Epidemiology and Current Treatment

HCC Burden

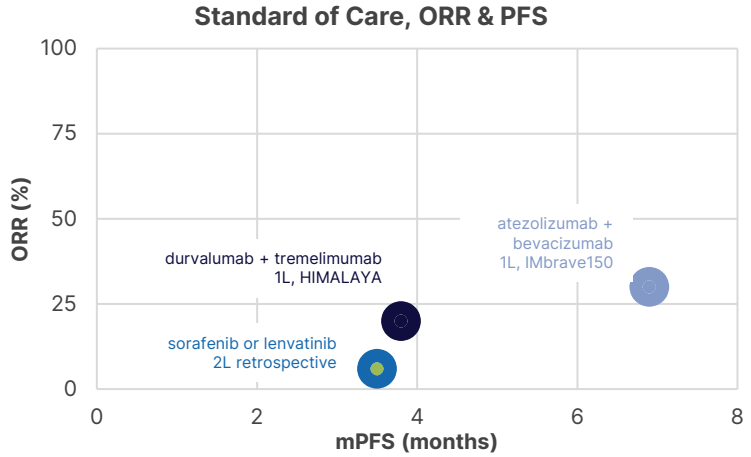
- Globally 6th most common cancer and third most common cause of death from cancer



WHO. International Agency of Cancer Research. Cancer Today. 2020. Available at: https://gco.iarc.fr/today/home. Accessed October 2023 SEER. Cancer Stat Facts. National Cancer Institute. Available at https://seer.cancer.gov/statfacts/

Standard of Care for Systemic HCC

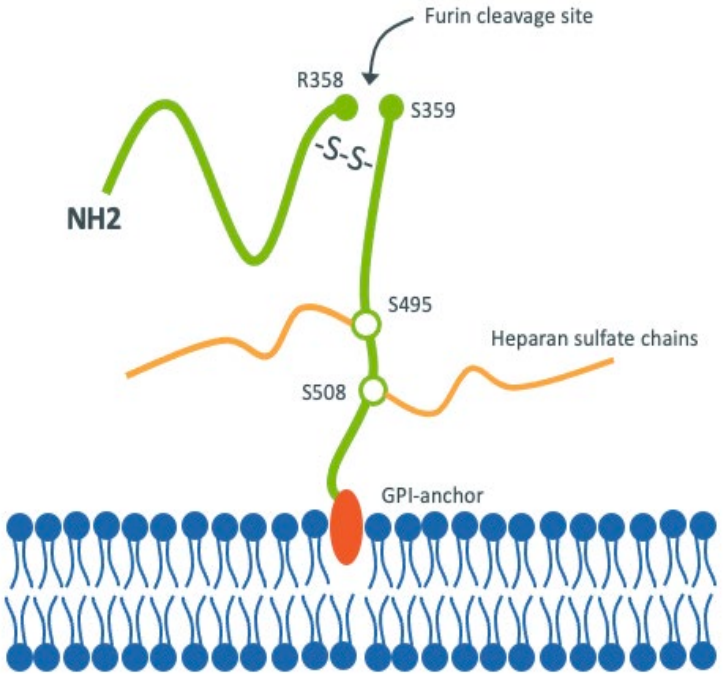
- In the US, most patients receive IO-VEGF or IO-IO combinations in 1L; multi-targeted TKIs are a 2L option



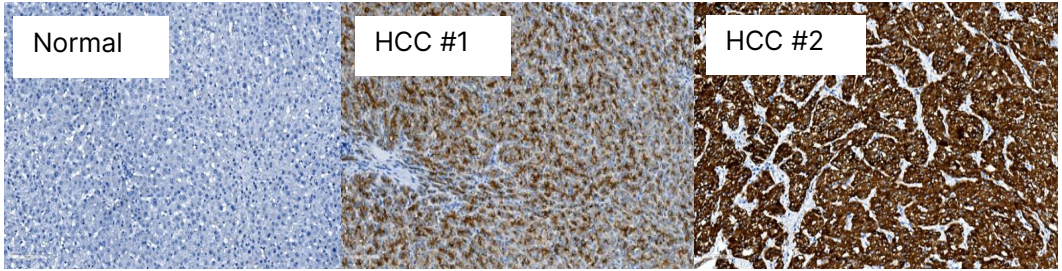
Finn RS et al NEJM 2020; Abou-Alfa GK et al NEJM Evid 2022; Yoo C et al Liver Cancer 2021

As a first-in-class TOPO1-based ADC for HCC, ZW251 offers the potential of a **new MOA** for patients, and an **opportunity to improve upon the current standard of care**

GPC3 is prevalent and highly expressed in hepatocellular carcinoma



Cell-surface GPI-anchored oncofetal glycoprotein

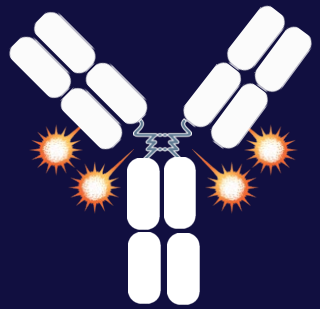


HCC % Positivity	Intensity	Reference
87%	57% IHC2+/3+	Abou-Alfa et al. 2016. J Hepatol
96%	75% '++', 3% '+++'	Wang et al. 2016. Oncotarget
84%	84% '++'	Yamauchi et al. 2005. Mod Pathol
76%	N.D.	Wang et al. 2008. Arch Pathol Lab Med

N.D. – not determined

ZW251

Glypican 3-targeting ADC



Glypican 3 exhibits limited expression in healthy tissues and is expressed in 76% of hepatocellular carcinomas (HCC) with high expression observed in ~55% of HCC[1]

Design

- An IgG1 **antibody** designed for potential optimization of ADC characteristics
- Topoisomerase 1 inhibitor **mechanism of action**
- **Moderate potency** payload with **bystander** activity (ZD06519)
- Intermediate **drug-to-antibody ratio** ~ 4
- Validated **peptide cleavable linker** sequence

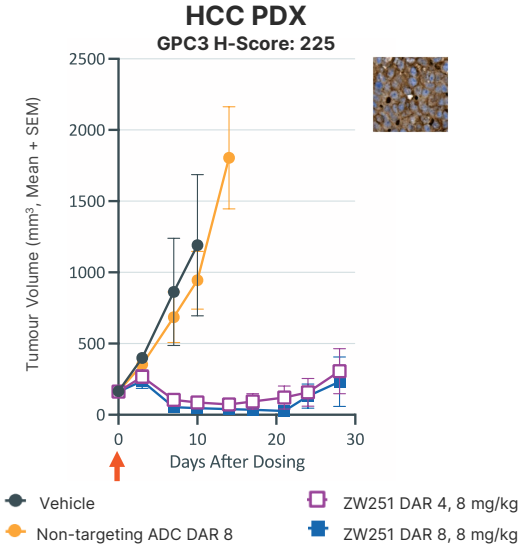
Profile

- **Strong preclinical activity** in models with a breadth of GPC3 expression[2]
- Noteworthy **tolerability in repeat dose** non-human primate toxicology studies[2]
- **First in class** ADC potential for HCC
- IND planned for H2 2025

ADC: antibody drug conjugate; DAR: drug to antibody ratio; GPC3: glypican-3; HCC: hepatocellular carcinoma
1. Wang HL et al., Arch Pathol Lab Med 2008 2.Madera L et al., Abstract #2658 presented at AACR 2023

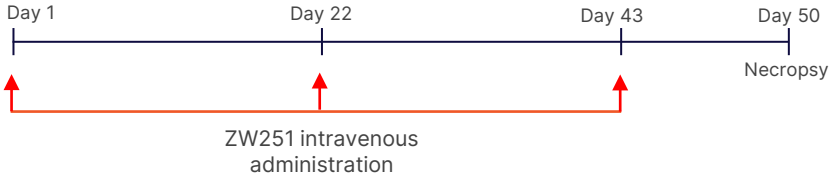
ZW251: Potent Antitumor Activity and Favorable Safety Profile in Preclinical Models

Differentiated Modality Demonstrates Anti-Tumor Activity in HCC models



Strong activity observed across a broad range of GPC3 expression

ZW251 Is Well-Tolerated In A Repeat Dose Non-Human Primate Toxicology Study



Test Article	Doses		
ZW251 DAR 8	10 mg/kg	30 mg/kg	60 mg/kg
ZW251 DAR 4	20 mg/kg	60 mg/kg	120 mg/kg

- Minimal changes in body weight, hematology parameters, and clinical chemistry parameters in all treatment groups
- **No mortality observed in any treatment group**

DAR: drug-to-antibody ratio; NHP: non-human primate; mAb: monoclonal antibody; PK: pharmacokinetics

Madera L et al., ZW251, a novel glypican-3-targeting antibody drug conjugate bearing a topoisomerase 1 inhibitor payload. Abstract #2658 presented at American Association for Cancer Research annual meeting 2023.

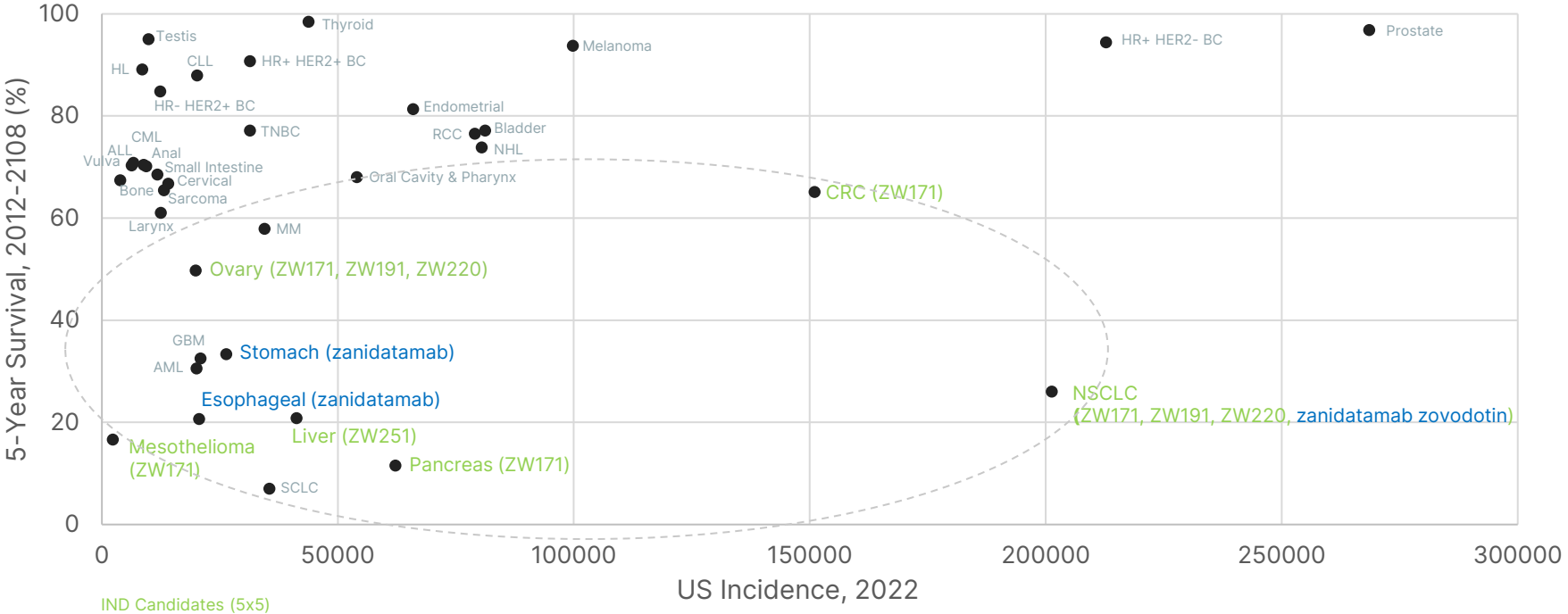
Integrated Platforms Help Drive Growing Product Candidate Pipeline

Research and Early-Development Portfolio	Target	Late-Discovery / IND-Enabling / Phase 1 / Phase 2 / Phase 3	Anticipated Milestone
Zanidatamab	HER2	BTC, GEA, BC, and other solid tumors*	Expected GEA pivotal data 2024
Zanidatamab Zovodotin (ZW49)	HER2	NSCLC	Expected Phase 2 initiation 2024
ZW191 TOPO1i ADC Program	FRα	Gynecological, NSCLC, TNBC	Expected IND 2024
ZW171 2+1 CD3-Engager Program	MSLN	Pancreatic, OVCA, CRC	Expected IND 2024
ZW220 TOPO1i ADC Program	NaPi2b	OVCA, NSCLC	Expected IND 1H 2025
ZW251 TOPO1i ADC Program	GPC3	HCC	Expected IND 2H 2025
Tri-TCE (CPI, Co-Stim) Trispecific T Cell Engagers	Solid Tumors	TBD	

BC: breast cancer; BTC: biliary tract cancer; CRC: colorectal cancer, FR: folate receptor, GEA: gastroesophageal adenocarcinoma; GPC3: glypican-3; HCC: hepatocellular carcinoma; HER2: human epidermal growth factor 2; IND: investigational new drug; MSLN: mesothelin; NaPi2b: sodium-dependent phosphate transporter 2B; NSCLC: non-small cell lung cancer; OVCA: ovarian cancer; TBD: to be determined; TNBC: triple-negative breast cancer; TriTCE: trispecific t-cell engager

*Please note these indications are at varying stages of late-stage development. Please refer to our full pipeline within the appendix of this presentation.

On A Mission to Improve the Standard of Care For Difficult to Treat Diseases



SEER*Explorer, accessed 10 Oct 2022

Long-term Expansion of R&D Strategy Beyond "5x5"

R&D Strategy

- Focus on developing new product candidates with the potential for two new IND's annually from 2027+
- Seek to expand therapeutic focus into autoimmune and inflammatory disease
- Seek to expand research interests into multifunctional engineered cytokines and dual checkpoint inhibitors

Therapeutic Optionality

- ADC development to focus on novel payloads and bispecific/biparatopic binding
- MSAT development to focus on novel trispecific platforms, including dual TAA's

Financial Structure

Combination of internally-funded and partnered development programs

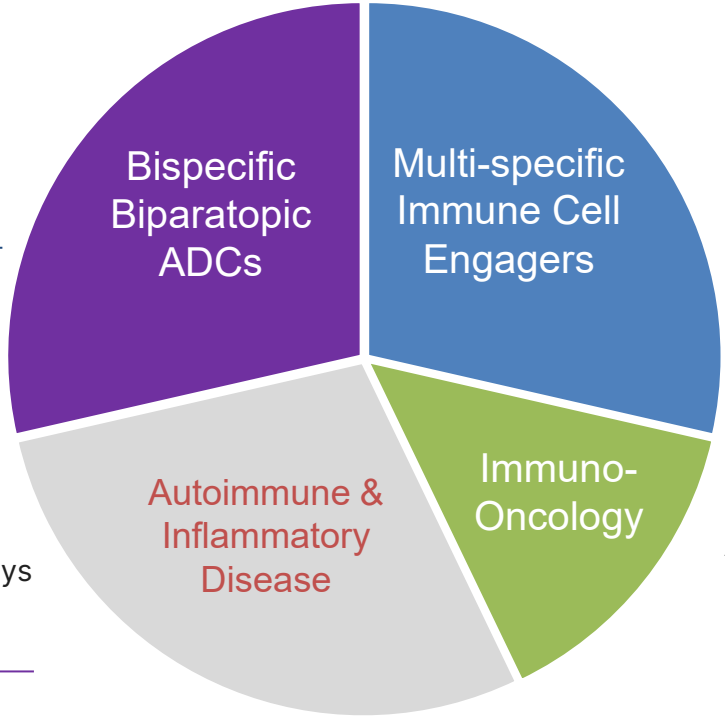
ADC: antibody drug conjugate; IND: investigational new drug; MSAT: multi-specific antibody therapeutic; TAA: tumor associated antigen

AD-VAN-CE Beyond 5 x 5

- Advancing design of ADCs and Multi-specifics to address complex disease states
- Continue to apply technology to hard-to-treat cancers and expand utility to additional therapeutic applications

ADCs
- Bispecific/Biparatopic(s)
- Novel Payload(s)
- Dual Payloads
- Solid tumors/Hem Onc

AIID
- Bispecifics
- Dual cytokines or disease pathways
- Existing platform technology application



Multi-specific Cell Engagers
- Next Gen T Cell Engagers
- Alternative Immune Cell recruitment
- Dual Tumor Associated Antigens
- Solid Tumors/Hem Onc

Additional IO
- Cytokine Engineering
- Multifunctional Immune Modulators

Milestone Opportunities in 2024 & 2025

Cash resources as of September 30, 2023 **$390.2M***

Several opportunities for business development with global rights for novel compounds

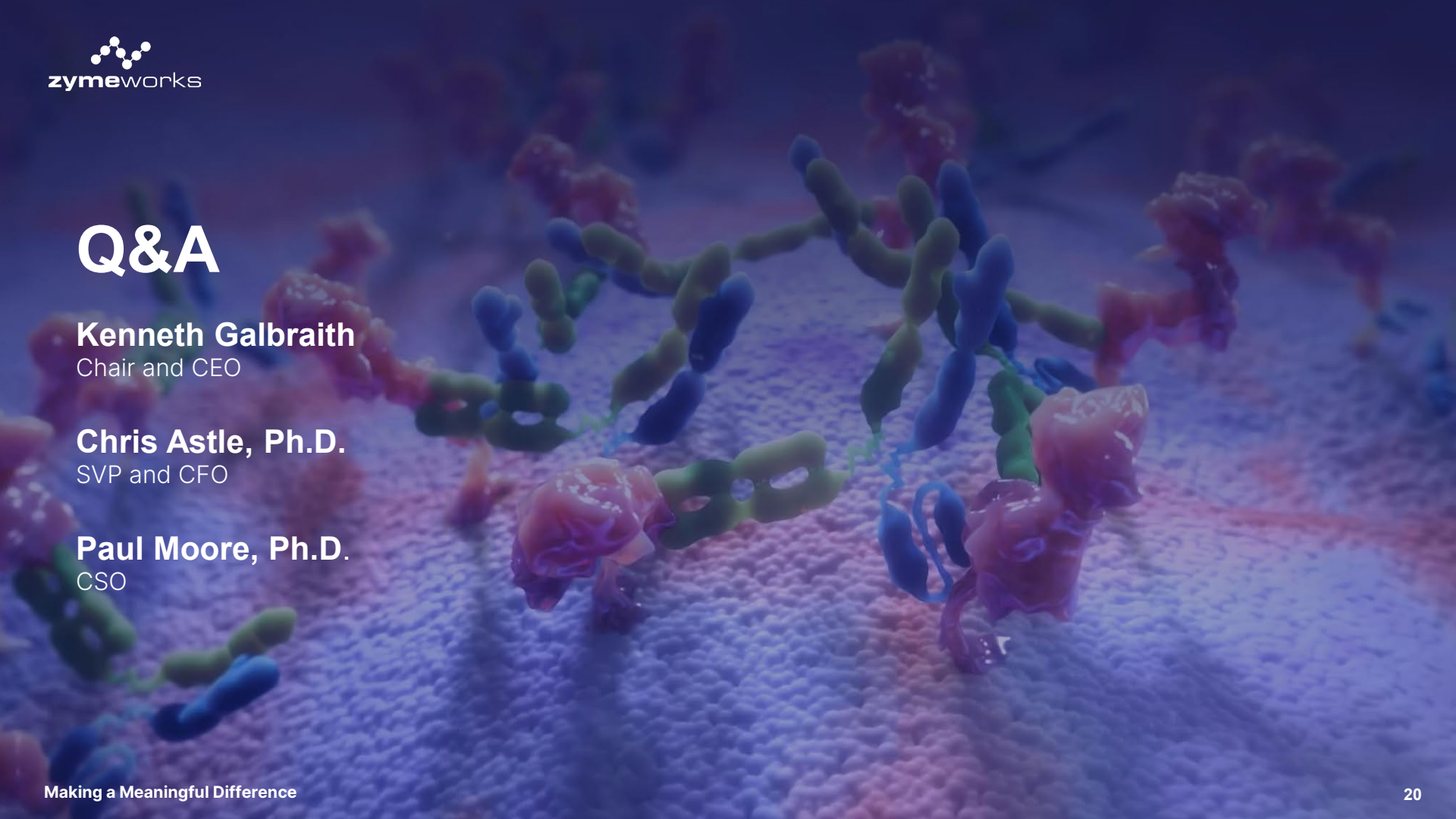
Current cash runway anticipated to support development goals through the end of **2026 and potentially beyond**

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 expected to be reported in 2024

*includes cash, cash equivalents and marketable securities.



Q&A

Kenneth Galbraith
Chair and CEO

Chris Astle, Ph.D.
SVP and CFO

Paul Moore, Ph.D.
CSO

Appendix

Q3 2023 Financial Results – Reconciliation of Non-GAAP Measures

In millions USD	Nine months ended Sept 30, 2023	Nine months ended Sept 30, 2022
R&D expenses	$118.1	$155.6
Stock-based compensation expense equity classified instruments	(0.7)	(1.5)
Stock-based compensation recovery for liability classified instruments	-	0.8
Restructuring expense	-	(6.1)
Adjusted R&D expenses (Non-GAAP basis)	$117.4	$148.8

In millions USD	Nine months ended Sept 30, 2023	Nine months ended Sept 30, 2022
G&A expenses	$55.6	$43.2
Stock-based compensation expense equity classified instruments	(4.9)	(1.5)
Stock-based compensation recovery for liability classified instruments	1.1	3.0
Restructuring expense	-	(2.8)
Adjusted G&A (Non-GAAP basis)	$51.8	$41.9

R&D: research and development; G&A: general and administrative; USD: United States dollar

Appendix

Differentiated Development of Multi-Specific Antibody Therapeutics

Versatile multi-specific antibody therapeutics optimizing potency and precision with proven track record and robust clinical pipeline

Program	Potential Indication	Target(s)	Preclinical / Phase 1 / Phase 2 / Pivotal	Collaboration Partners
Zanidatamab Bispecific	BTC	HER2 x HER2	HERIZON-BTC-01	Jazz Pharmaceuticals, BeiGene
	GEA	HER2 x HER2	HERIZON-GEA-01	Jazz Pharmaceuticals, BeiGene
	BC and other solid tumors	HER2 x HER2	8+ ongoing Phase 1 & Phase 2 trials (view)	Jazz Pharmaceuticals, BeiGene
ZW171 Bispecific T-Cell Engager	Pancreatic, OVCA, CRC	MSLN x CD3 (2+1)	On track for IND filing in 2024	
TriTCE Co-Stimulatory Trispecific T cell engager	Under active evaluation	CLDN18.2 x CD3 x CD28	Pilot toxicology studies	
TriTCE Checkpoint Inhibition Trispecific T cell engager	Under active evaluation	TAA x PD-L1 x CD3	Pilot toxicology studies	
Selected Partnered Programs				
JNJ-78278343 Bispecific	Castration-Resistant Prostate Cancer	CD3 x KLK2	Azymetric™ | EFECT™	Johnson & Johnson Innovation
Undisclosed Bispecific	Oncology	Undisclosed	Azymetric™ | EFECT™	Bristol Myers Squibb[1]

[1]Original Agreement with Celgene (now a Bristol-Myers Squibb company).
BC: breast cancer; BTC: biliary tract cancer; CLDN: claudin; CRC: colorectal cancer, GEA: gastroesophageal adenocarcinoma; HER2: human epidermal growth factor 2; IND: investigational new drug; MSLN: mesothelin; OVCA: ovarian cancer; TAA: tumor associated antigen; TriTCE: trispecific t-cell engager

Appendix

Differentiated Development of Antibody Drug Conjugates

Designing next-generation antibody drug conjugates (ADCs) on targets with evidence of clinical activity and addressing areas of unmet therapeutic potential

Program	Potential Indication	Target(s)	Payload	DAR (Range)	Preclinical	Phase 1	Phase 2	Pivotal	Collaboration Partners
Zanidatamab zovodotin ADC	NSCLC	HER2	Auristatin (ZD02044)	2	NCT03821233				
ZW191 ADC	Gynecological cancers, NSCLC, TNBC	FRα	Topoisomerase 1 Inhibitor (ZD06519)	8	On track for IND filing in 2024				
ZW220 ADC	OVCA, NSCLC	NaPi2b	Topoisomerase 1 Inhibitor (ZD06519)	4	On track for IND filing in 2025				
ZW251 ADC	Hepatocellular carcinoma	GPC3	Topoisomerase 1 Inhibitor (ZD06519)	4-8	Lead format under evaluation				
Selected Partnered Program									
XB002 (ICON-2) ADC	Solid tumors	Tissue Factor	Auristatin	Undisclosed	NCT04925284				EXELIXIS[1] mid-single digit royalt

[1] Agreement with Iconic; XB002 in-licensed by Exelixis

DAR: drug to antibody ratio; FR: folate receptor, GPC3: glypican-3; HER2: human epidermal growth factor receptor 2; NaPi2b: sodium-dependent phosphate transporter 2B; NSCLC: non-small cell lung cancer; OVCA: ovarian cancer; TNBC: triple-negative breast cancer