



2023 Bloom Burton & Co. Healthcare Investor Conference

Kenneth Galbraith, Chair & CEO
April 25, 2023

Nasdaq: ZYME | zymeworks.com



Legal Disclaimer



This presentation includes “forward-looking statements” within the meaning of the U.S. Private Securities Litigation Reform Act of 1995 and “forward-looking information” within the meaning of Canadian securities laws, or collectively, forward-looking statements. Forward-looking statements in this press release include, but are not limited to, statements that relate to Zymeworks’ expectations regarding implementation of its corporate goals, Zymeworks’ clinical development of its product candidates, related clinical trials, anticipated clinical data presentations and the timing thereof, potential therapeutic effects of zanidatamab and its other product candidates, expected benefits of the new executive leadership team of Zymeworks, 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 2026 and potentially beyond, Zymeworks’ ability to execute new collaborations and partnerships and other information that is not historical information. Forward-looking statements can often be identified by the use of terminology such as “future,” “potential,” “progress,” “subject to,” “anticipate,” “plan,” “expect,” “estimate,” “project,” “may,” “will,” “could,” “can,” the negatives thereof, variations thereon and similar expressions, or by discussions of strategy. 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, including, without limitation, Zymeworks’ examination of historical operating trends, are based upon our current expectations and various assumptions. 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: the impact of the COVID-19 pandemic 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, may be more severe and more prolonged than currently anticipated; clinical trials may not demonstrate safety and efficacy of any of Zymeworks’ or its collaborators’ product candidates; 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; regulatory agencies may impose additional requirements or delay the initiation of clinical trials; the impact of new or changing laws and regulations; market conditions; Zymeworks’ assumptions regarding its financial condition or future financial performance may be incorrect; Zymeworks may not recognize the anticipated cost savings of its reduction in workforce; inability to maintain or enter into new partnerships or strategic collaborations; and the factors described under “Risk Factors” in Zymeworks’ quarterly and annual reports and other sections of our public filings with the Securities and Exchange Commission and Canadian securities regulators.

These forward-looking statements are made only as of the date hereof, and Zymeworks Inc. undertakes no obligation to update or revise the forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.



Multifunctional Antibody Therapeutics for Oncology (and Beyond)

Integrated R&D Engine

**Multispecific
Antibody
Therapeutics
(MSAT)**

**Antibody Drug
Conjugates
(ADC)**



Focus on indications with poor patient prognosis (e.g., lowest 5-year OS)

Desired Product Profile

**First and
Second-line**

market
opportunities

**Accelerated
Approval**

regulatory pathway
allows potential of
early market entry



Pursue lead indications with global peak sales potential >\$500MM per product

Elements of Enterprise Value Framework



Our Strategy

Zymeworks is well positioned to build upon our key priorities and enhance shareholder value through focusing on our Enterprise Value Framework

Enterprise value framework focuses on delivering progress across all five key elements through 2023 and 2024

All elements of our framework are focused on our proven ability in ADC's and MSAT's

Goal of optimizing value as measured by per share returns for shareholders over the long-term



**Zanidatamab
Collaboration
with Jazz
Pharmaceuticals**



**Zanidatamab
Collaboration with
BeiGene (in APAC)**



**Zanidatamab
Zovodotin**

**Research and
Early
Development
Programs**

**Legacy
Technology
Licensing
Portfolio**

Key Priorities for 2023 and 2024



- 1 Financial Transformation**
 Transformation of financial position **ensures funding of key priorities** for multiple years and ability to opportunistically fund R&D engine
- 2 Purposeful Development**
 Further **evaluate zanidatamab zovodotin in key indications**, as monotherapy and in combination, to provide potential rationale for future registrational studies and potential US commercialization/ex-US partnering
- 3 Drive Value**
 Continue to **aggressively pursue** and **drive value** through partnerships and collaborations
- 4 Collaborate**
Maximize value of zanidatamab brand through support of key commercialization partners, Jazz and BeiGene

KEY PRIORITIES	STATUS/TARGET
Zanidatamab Commercialization Support	
Continue to report additional zanidatamab data	1H23
Update on development pathway in key indications	Ongoing
Updated timing on requisite regulatory filings	Ongoing
Research and Early Development Programs	
Submit IND for two lead preclinical programs (ZW171 / ZW191)	2024
Nominate additional preclinical product candidate for 2025 IND	2023
Continue actively presenting and publishing key scientific data	April - AACR
Aggressively pursue collaboration and partnerships	Ongoing
Zanidatamab Zovodotin	
Present additional data from Ph1 clinical study	2023
Initiate multiple Ph 2 clinical studies – NSCLC & mBC	2023
Legacy Platform Licensing Portfolio	
Earn additional milestone payments from existing agreements	Ongoing
Evaluate potential for monetization or expansion	Ongoing

AACR: American Association of Cancer Research; IND: investigational new drug application; mBC: metastatic breast cancer; NSCLC: non-small cell lung cancer; R&D: research and development; RP2D: Recommended Phase 2 dose



Novel Platforms Enable Unique and Differentiated Product Portfolio



Platforms Driving the Next Generation of Antibody Based Therapeutics

Azymetric™



Multispecific Antibody Generation

- Biparatopic/Bispecifics
- Trivalent/Trispecifics
- T-cell engager technology
- Fc-Fusions
- IgG1-like biophysical, manufacturing, and purification protocols

Drug Conjugate Platforms



Fit-For Purpose ADC Candidate Creation

- ZymeLink™ Auristatin
- ZymeLink™ Hemiasterlin
- TOPO1i Technology
- Cysteine-Insertion Conjugation Technology
- Immune Stimulating (TLR7)

EFACT™



Tailored Immune Function Modulation

- Tailored sets of Fc modifications that can modulate immune cell recruitment and function
- Enhance or eliminate immune effector function to optimize therapeutics

ProTECT™



Tumor-Specific Immune Co-stimulation

- Tumor-specific activity via conditional blocking to reduce off-tumor toxicities
- Functional block adds co-stimulation or checkpoint modulation to enhance efficacy

Enable New Biology



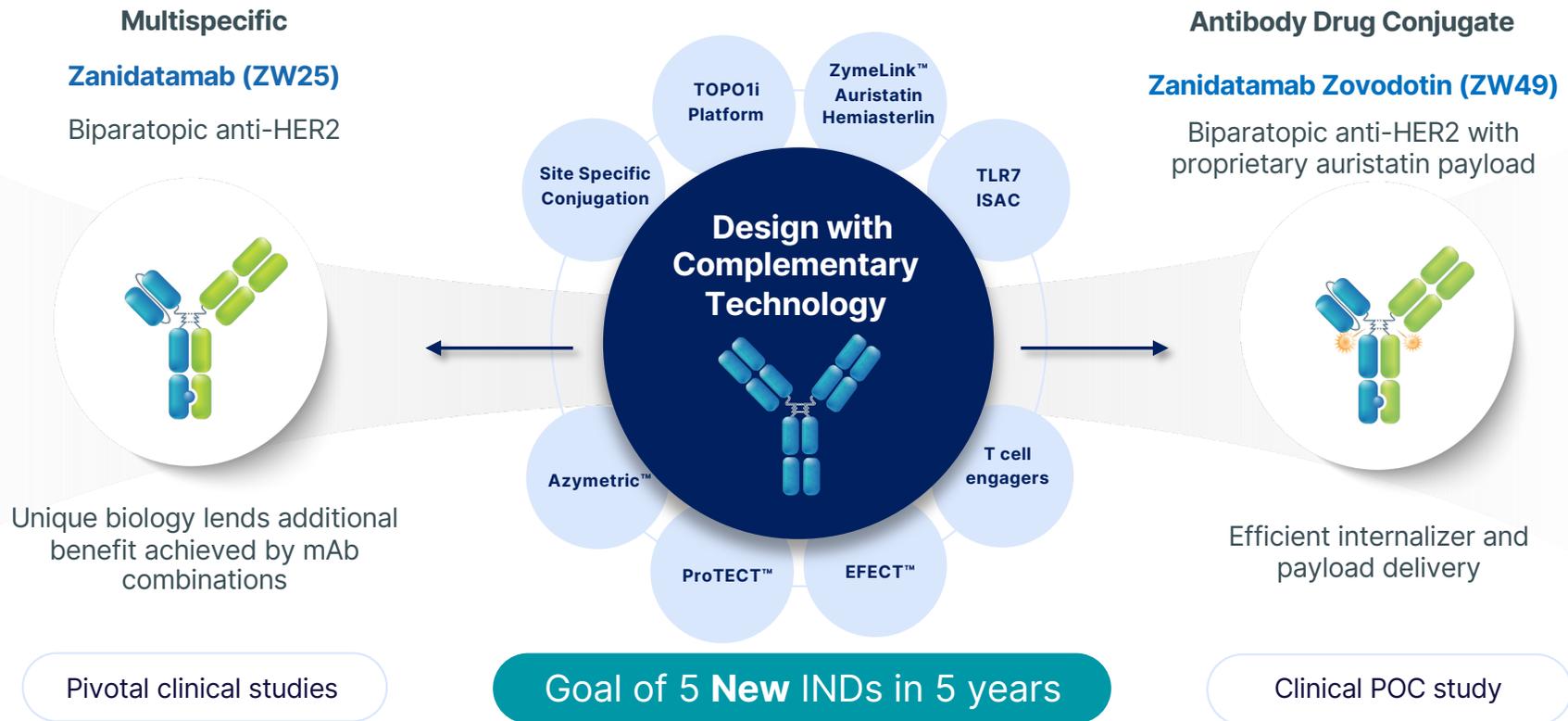
Modular



Scalable



Zymeworks Technology Platforms Proven to Generate Differentiated and Clinically-Validated Therapeutics



DAR: drug to antibody ratio; Fc: fragment crystallizable region of antibody; HER2: human epidermal growth factor receptor 2; IND: investigational new drug application; ISAC: Immunostimulatory Drug Conjugate; MOA: mechanism of action; POC: proof of concept

A Growing Product Candidate Pipeline of Potential Best-in-Class Therapeutics



Zanidatamab	Preclinical	Phase 1	Phase 2	Pivotal	Collaboration Partner
1st-Line Gastroesophageal Adenocarcinomas HERIZON-GEA-01 Chemotherapy Combination	[Progress bar spanning Preclinical, Phase 1, and Phase 2]				BeiGene Jazz Pharmaceuticals
2nd-Line Biliary Tract Cancers HERIZON-BTC-01 Monotherapy	[Progress bar spanning Preclinical, Phase 1, and Phase 2]				BeiGene Jazz Pharmaceuticals
1st-Line Gastrointestinal Cancers Gastroesophageal Adenocarcinoma, Biliary Tract Cancer, and Colorectal Cancer Chemotherapy Combination	[Progress bar spanning Preclinical and Phase 1]				BeiGene Jazz Pharmaceuticals
Zanidatamab Monotherapy & Chemotherapy Combination	[Progress bar spanning Preclinical]				BeiGene Jazz Pharmaceuticals



A Growing Product Candidate Pipeline of Potential Best-in-Class Therapeutics



Research and Early-Development Portfolio

Preclinical

Phase 1

Phase 2

Pivotal

Partner

Zanidatamab Zovodotin¹

HER2-Expressing Cancers
Indications: NSCLC, mBC



ZW191

Folate Receptor- α Targeted Topoisomerase 1 Inhibitor Antibody Drug Conjugate
Indications: OVCA, Gynecological, NSCLC, TNBC



On track for 2024 IND

ZW171

2+1 MSLN x CD3 Bispecific Antibody
Indications: Pancreatic, OVCA, CRC



On track for 2024 IND

ZW251

Glypican-3 Targeted Topoisomerase 1 Inhibitor Antibody Drug Conjugate
Indications: Hepatocellular carcinoma



ZW220

NaPi2b Targeted Topoisomerase 1 Inhibitor Antibody Drug Conjugate
Indication: OVCA, NSCLC, other solid tumors



¹ Phase 2 studies anticipated to begin in 2023

CRC: Colorectal cancer; GEA: gastroesophageal adenocarcinoma; mBC: metastatic breast cancer; NSCLC: non-small cell lung cancer; OVCA: ovarian cancer; TNBC: triple negative breast cancer





RESEARCH & DEVELOPMENT

Platforms and Product Candidates

11 AACR Poster Presentations Showcased Focused R&D Strategy



Date	Time	Title	Abstract #	Session: Category, Title, Location & Poster Board #	Presenter
April 17	9:00 am – 12:30 pm ET	Revisiting the dogma of antibody drug conjugates (ADCs): Emerging data challenge the benefit of linker stability and the primacy of payload delivery	1538	Category: Experimental and Molecular Therapeutics Title: Antibody Drug Conjugates Location: Section 14 Poster Board: 18	Raffaele Colombo
		ZW220, a novel NaPi2b-targeting antibody drug conjugate bearing a topoisomerase 1 inhibitor payload	1533	Category: Experimental and Molecular Therapeutics Title: Antibody Drug Conjugates Location: Section 14 Poster Board: 13	Andrea Hernandez Rojas
	1:30 – 5:00 pm ET	ZW270, a conditionally masked IL-12 cytokine fusion protein displaying potent anti-tumor activity absent systemic toxicity	2935	Category: Immunology Title: Therapeutic Antibodies 2 Location: Section 23 Poster Board: 13	Nichole Escalante
		PROTECT™, a novel trispecific antibody masking platform with integrated immune modulation displays unique activity and differentiated modes of action	2926	Category: Immunology Title: Therapeutic Antibodies 2 Location: Section 23 Poster Board: 4	Anna von Rossum & Genevieve Desjardins
		TriTCE CPI, next generation trispecific T cell engagers with integrated checkpoint inhibition (CPI) for the treatment of solid tumors	2982	Category: Immunology Title: Therapeutic Antibodies 3 Location: Section 24 Poster Board: 29	Maya Poffenberger
		ZW171, a T cell-engaging, bispecific antibody for the treatment of mesothelin-expressing solid tumors	2942	Category: Immunology Title: Therapeutic Antibodies 2 Location: Section 23 Poster Board: 20	Nicole Afacan
		ZW191, a novel FRa-targeting antibody drug conjugate bearing a topoisomerase1 inhibitor payload	2641	Category: Experimental and Molecular Therapeutics Title: Antibody Technologies Location: Section 13 Poster Board: 9	Sam Lawn
		ZW251, a novel glypican-3-targeting antibody drug conjugate bearing a topoisomerase 1 inhibitor payload	2658	Category: Experimental and Molecular Therapeutics Title: Antibody Technologies Location: Section 13 Poster Board: 26	Laurence Madera
		Zanidatamab zovodotin (ZW49) induces hallmarks of immunogenic cell death and is active in patient-derived xenograft models of gastric cancer	2633	Category: Experimental and Molecular Therapeutics Title: Antibody Technologies Location: Section 13 Poster Board: 1	Stuart Barnscher
April 18	1:30 – 5:00 pm ET	TriTCE Co-stim, next generation costimulatory trispecific T cell engagers for the treatment of solid tumors	5121	Category: Immunology Title: Combination Immunotherapies 2 Location: Section 22 Poster Board: 24	Lisa Newhook
		RBB2 amplification detected in ctDNA as a surrogate for tumor tissue FISH analysis of HER2 status in a phase 1, study with zanidatamab for the treatment of locally advanced or metastatic HER2 expressing cancers	CT278	Session Title: Phase I Clinical Trials 2 Location: Section 47. Poster Board 18:	Diana Shpektor

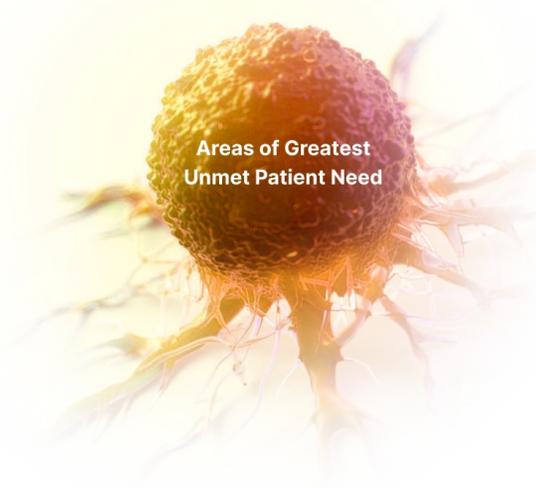


ADC and Multispecific Modalities Driving Our Pipeline

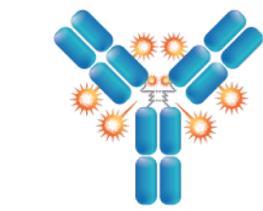
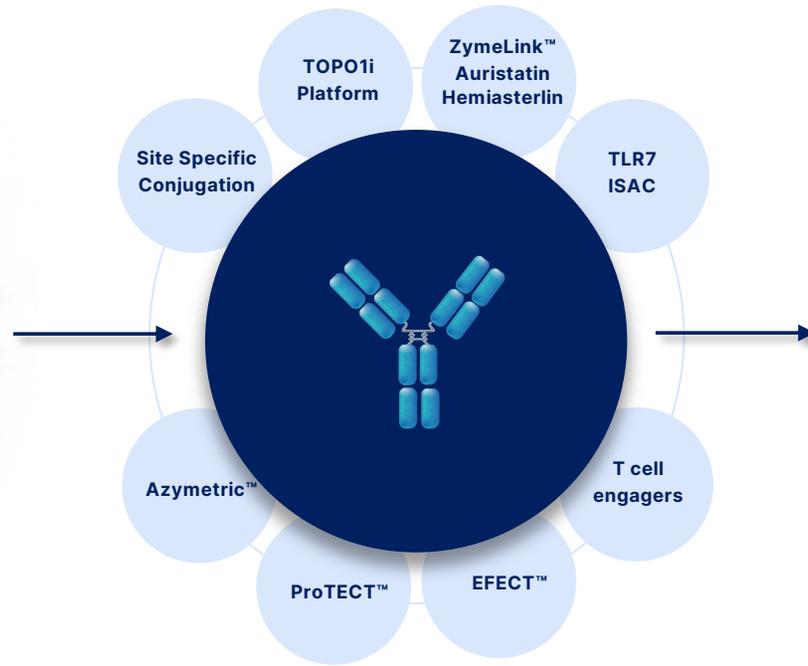
Select Difficult-to-Treat Cancers & Target

Design with Complementary Technology

Optionality with Two Foundational Fit-for-Purpose Modalities

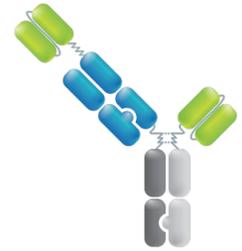


Areas of Greatest Unmet Patient Need



Antibody Drug Conjugates
 Customization:

- Antibody properties
- Antibody format
- Payload
- DAR



Multispecifics
 Customization:

- Multiple MOA in single molecule
- Synergistic biology
- Precision targeting through multivalency

DAR: drug to antibody ratio; ISAC: immune stimulating antibody conjugate; MOA: mechanism of action



Zymeworks Multispecific T Cell Engager Strategy: Utilizing Azymetric™ to Build Differentiated & Next Generation Multispecific T Cell Engagers



Biological Problem

- 1** Narrow therapeutic window and toxicity due to CRS associated with Gen 1 TCE in solid tumors
- 2** Limited T cell intratumoral availability and T cell anergy in solid tumors
- 3** Immunosuppressive tumor microenvironment limiting T cell responses in solid tumors

Zymeworks Solution

2+1 T Cell Engager (ZW171)

Mitigate cytokine release syndrome with low affinity T cell binding and enhanced efficacy and selectivity with avidity-driven tumor antigen binding

TriTCE Co-stimulation

Increase T cell fitness, activation and proliferation via tumor-dependent T cell co-stimulation

TriTCE Checkpoint Inhibitor

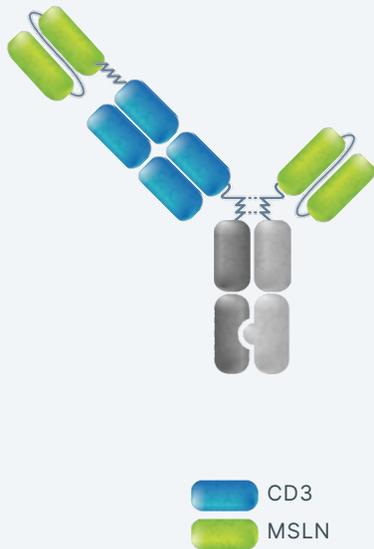
Increase T cell responses through simultaneous checkpoint blockade and avidity-driven binding

TCE: t cell engager

ZW171: 2+1 Bispecific MSLN x CD3 T Cell Engaging Antibody

Lead MSAT Preclinical Product Candidate

ZW171



MSLN Targeted

Antibody targets mesothelin (MSLN), a glycoprotein that is elevated in many cancers including pancreatic, mesothelioma and ovarian cancer

Target is clinically validated, indications have high unmet clinical need

CD3 Targeted

Targeting CD3 receptor to redirect T cell cytotoxicity towards cancerous cells

Anti-CD3 antibody targeting novel epitope that mediates low T cell binding and cytokine release and potent tumor cell lysis

Format Engineering

Extensive assessment of different formats with different valences & geometries

2+1 dual scFv identified as avidity-driven format with optimal activity and safety profile

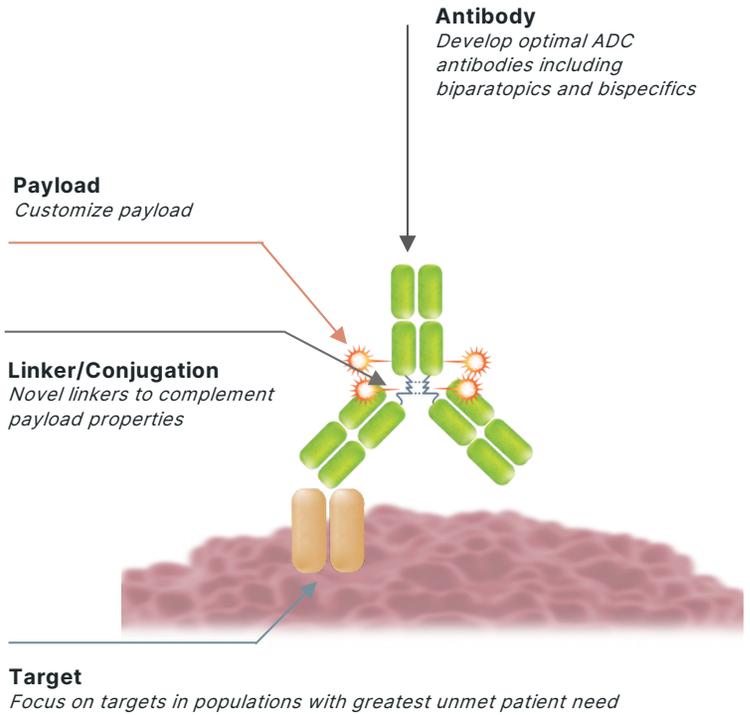
Progress

Pilot NHP toxicology and PK
On track for anticipated IND filing in 2024

NHP: non-human primate; PK: pharmacokinetics; scFv: single-chain variable fragment

Designing Fit-for-Purpose ADC Candidates

	Zymeworks Strategy Today	Zymeworks Strategy Tomorrow
Target	Focus on targets with evidence of clinical activity in indications of unmet need	Explore novel targets
Antibody	Develop optimal ADC antibodies	Leverage bispecific and biparatopic expertise to develop optimal ADC antibodies
Linker/Conjugation	Leverage validated peptide-cleavable linkers & stochastic conjugation	Design novel linkers to complement payload properties
Payload	Focus on novel TOPO1i ADC technology	Develop novel payloads by adapting MoAs with clinical validation to novel ADC application



ADC: antibody drug conjugate; MOA: mechanism of action; TOPO1i: topoisomerase inhibitor

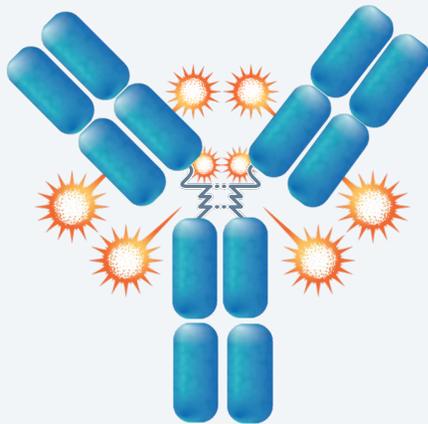


ZW191: Folate Receptor Alpha Topoisomerase-1 Inhibitor ADC

Lead ADC Preclinical Product Candidate



ZW191



Target

Folate receptor alpha (FR α , FOLR1) is a clinically validated ADC target. FR α is over-expressed on the cell surface of ovarian cancer, other gynecological cancers, and additional high incidence solid tumors with unmet medical need (NSCLC, TNBC, etc.)

Antibody

Internally discovered, novel IgG1 monospecific antibody. Designed for optimal internalization, payload delivery, and tumor penetration.

Drug Linker

Cysteine conjugated, DAR8, protease cleavable, traceless drug-linker. Novel bystander-active topoisomerase-1 inhibitor.

Progress

Robust anti-tumor activity in patient-derived xenograft models of ovarian cancer with low levels of FR α .

On track for anticipated IND filing in 2024

ADC: antibody-drug conjugate; DAR: drug-to-antibody ratio; IND: investigational new drug; IgG1: immunoglobulin G1; NSCLC: non small cell lung cancer; TNBC: triple negative breast cancer

Zymeworks Moving Forward “5 by 5”



Goal of 5 new product candidates planned for IND filing by 2027

2017-2022

Select Product Pipeline



Platform Technologies & Tools



2022-2027

Accelerate Product Pipeline

5 New Molecules in Clinic in 5 Years

Select Product Partnerships





ZANIDATAMAB

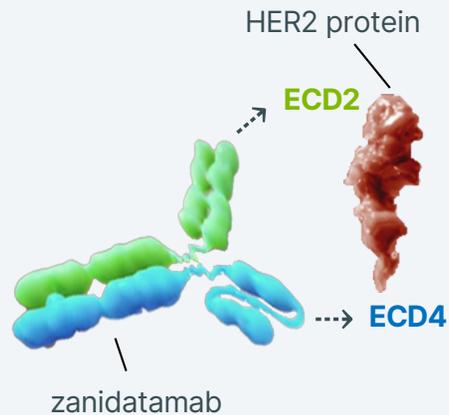
Commercial Collaborations

Transactions allow zanidatamab to reach a broad group of patients globally and may improve patient outcomes beyond the current standards of care, pending regulatory approval

Zanidatamab: A Bispecific Antibody for HER2-Expressing Cancers



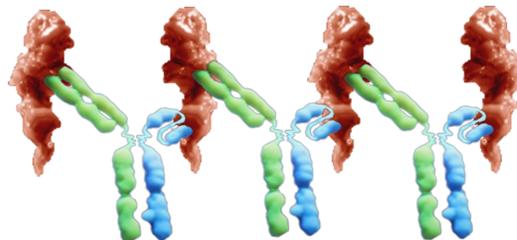
Zanidatamab



Zanidatamab's Unique Binding Geometry Promotes:

- Biparatopic – targets two distinct HER2 epitopes and results in HER2 binding across a range of expression levels (low to high)
- HER2-receptor cross-linking, clustering, internalization, and downregulation
 - Enhanced receptor clustering on cell surface (cluster internalization, receptor downregulation)
 - Inhibition of cellular proliferation
- Fc-mediated cytotoxicity: ADCC, ADCP, CDC

Dual HER2-Binding of Zanidatamab Drives Unique MOA



The geometry of zanidatamab prevents it from binding to the same HER2 molecule

Note: Zanidatamab has been granted Breakthrough Therapy designation by the FDA for patients with previously-treated HER2 gene-amplified BTC as well as two Fast Track designations, one for previously treated or recurrent HER2-positive BTC and another for first-line GEA in combination with standard of care chemotherapy. Zanidatamab also received Orphan Drug designation for the treatment of BTC and GEA in the United States and for gastric cancer and BTC in the European Union.

ADCC: antibody-dependent cellular cytotoxicity; ADCP: antibody-dependent cellular phagocytosis; CDC: complement-dependent cytotoxicity; ECD: extracellular domain; Fc: fragment crystallizable region of antibody; HER2: human epidermal growth factor receptor 2

Key Financial Terms of Licensing Agreement with Jazz



Licensing Agreement Terms¹

Counterparty	 Jazz Pharmaceuticals.
Upfront Payments	\$375,000,000 received in 4Q22
Regulatory Milestones	Up to \$525,000,000
Commercial Milestones	Up to \$862,500,000
Royalties	Tiered royalties of 10 to 20% of net sales
Current R&D Spend	Costs for ongoing clinical studies to be reimbursed by Jazz ²
Territories	US, EU, Japan and all other territories except those in Asia Pacific not covered by BeiGene agreement
Future R&D Spend	Jazz to fund 100% of costs for future studies

Key Benefits to Zanidatamab Licensing Agreement:

- **Meaningful improvement to financial position and reduction in future expenditures** allows focus on growth of exciting early-stage pipeline while zanidatamab advances to commercialization
- **Accelerate and expand R&D programs** (early R&D and ZW49) while maintaining anticipated cash runway through at least 2026 with a goal of advancing **5 new programs into clinical studies in 5 years**
- **Continued management** of existing zanidatamab program by Zymeworks, in partnership with Jazz, including first BLA, **leveraging existing internal expertise to progress programs rapidly**, with future zanidatamab-related clinical studies, regulatory filings, and commercialization to be managed and funded by Jazz
- **Substantial potential milestone payments** based on global regulatory milestones for zanidatamab in BTC and GEA with further upside from royalties and commercial milestones
- **Leverage** Jazz's global commercial infrastructure together with BeiGene's complementary strengths in APAC regions to **optimize commercialization of zanidatamab without requirement for investment in commercial infrastructure** within Zymeworks

¹ All dollar values in US Dollars

² Costs related to ongoing clinical studies incurred after signing of the agreement to be reimbursed 100% by Jazz, includes approximately \$24M in reimbursable amounts from 4Q22

Key Financial Terms of Asia Pacific Licensing Agreement with BeiGene



Licensing Agreement Terms¹

Counterparty



Upfront Payments

\$40,000,000

Development and Commercial Milestones

Up to \$390,000,000

Royalties

Tiered royalties of up to 20% of net sales in BeiGene territories

Territories

Asia-Pacific region (excluding Japan and India)

Co-development Funding

Currently for BTC and GEA global development

Additional Details:

- Received \$40MM upfront payment in 2018 and \$20MM in milestones to-date
- BeiGene has development and commercial rights to zanidatamab and zanidatamab zovodotin
- Collaborate on certain global studies including HERIZON-BTC-01 and HERIZON-GEA-01 with BeiGene responsible for clinical and regulatory activities in their territory
- Co-development funding agreed for any global studies

¹All dollar values in US Dollars



Advancing Pivotal Studies in BTC and GEA



HERIZON-BTC-01

A Global Pivotal Study in Second-Line
HER2-Amplified BTC

Population: PATIENTS WITH HER2-AMPLIFIED BTC WHO RECEIVED
PRIOR GEMCITABINE

N = 100

Cohort 1: 75 with IHC 2+ or 3+

Cohort 2: 25 with IHC 0 or 1+

Regimen: 28 Day Cycles

Day 1: Zanidatamab, 20 mg/kg IV

Day 15: Zanidatamab, 20 mg/kg IV

Every 8 Weeks CT/MRI

Locations: Canada, USA, Chile, France, Italy, Spain, United Kingdom,
China, South Korea

Primary End Points: ORR

Secondary End Points: Proportion of patients with DOR \geq 16 weeks, DOR,
DCR, PFS, OS, safety

Additional Details: topline data presented late 2022 with full data readout
anticipated in 1H23

HERIZON-GEA-01

A Global Pivotal Study in First-Line
HER2-Positive GEA

Population: PATIENTS WITH HER2-POSITIVE ADVANCED OR METASTATIC GEA
N = 714

Regimen: 21 Day Cycles

ARM 1: Trastuzumab + SOC chemotherapy, N=238

ARM 2: Zanidatamab + SOC chemotherapy, N=238

ARM 3: Zanidatamab + tislelizumab + SOC chemotherapy, N=238

Assessment Every 6 weeks for first 54 weeks, Every 9 weeks thereafter

Locations: Australia, China, India, Malaysia, South Korea, Singapore, Taiwan, Thailand,
Belgium, Czech Republic, Estonia, France, Italy, Georgia, Germany, Greece, Ireland,
Netherlands, Poland, Portugal, Romania, Serbia, South Africa, Spain, Turkey, Ukraine
and United Kingdom, Canada, Mexico, Guatemala, Argentina, Brazil, Chile
Peru

Primary End Points: PFS, OS

Secondary End Points: ORR, Frequency and Severity of AEs, Change in HRQOL from
baseline

Additional Details: anticipate top-line readout in 2024

^aSOC (standard of care) chemotherapy: CAPOX or FP; ^bresponse assessments until progression per BICR or withdrawal of consent BICR: Blind independent central review; GEA: gastroesophageal adenocarcinoma; PFS: Progression-free survival; OS: overall survival



ZANIDATAMAB ZOVIDOTIN

Phase 2 Clinical Development

Zanidatamab Zovodotin: A Bispecific ADC for HER2-Targeted Therapy



Data Highlights and Catalysts

Clinical Data Highlights

- Differentiated tolerability profile amongst HER2-targeted ADCs with the majority of adverse events being grade 1 or 2 and manageable
- Confirmed ORR of 31%, disease control rate of 72% observed across 29 response-evaluable patients treated with zanidatamab zovodotin at 2.5 mg/kg Q3W
- Clear single-agent activity in heavily pretreated patients with potential go-forward regimen of 2.5 mg/kg dosed every three weeks
- Weekly dosing regimen continues to enroll with dose escalation at 1.75 mg/kg and an expansion cohort at 1.5 mg/kg

Expected Catalysts

- Update on progression of weekly expansion and escalation cohorts in 2023
- Expansion of Phase 2 to begin 2023
- Expect to commence enrollment before the end of 2023



Unique mechanism of action, tolerability profile, and clear single-agent activity support measured and incremental future development strategy

Phase 1 data (NCT03821233) as reported at ESMO | Sep 2022; ORR: objective response rate

Zanidatamab Zovodotin: Focused and Strategic Development Path



Zanidatamab zovodotin

has shown single-agent activity in multiple tumor types with a differentiated tolerability profile amongst other HER2-targeted ADCs and has multiple pathways for development

Planned Phase 2 Studies

Non-Small Cell Lung Cancer (NSCLC)

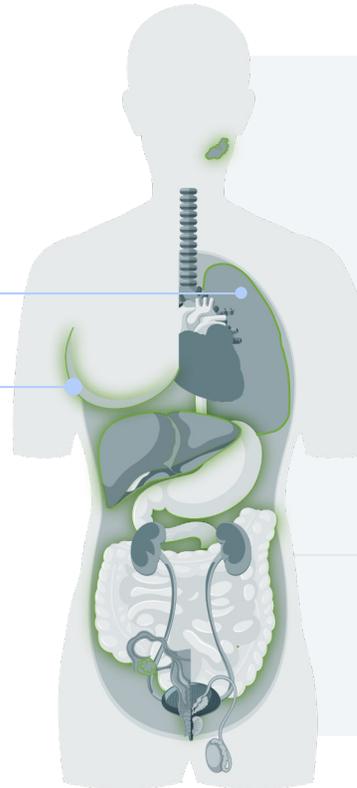
HER2-targeted NSCLC

Metastatic Breast Cancer (mBC)

HER2-positive mBC after progression with T-DXd
HER2-low mBC

Path Forward

- Phase 1 dose escalation to continue in Japan
- Present additional Phase 1 data in 2023
- Initiate separate Phase 2 clinical studies, expect study start in 2023
- Confirm ex-US partnership prior to start of registrational pathway by end of 2025



DIFFERENTIATED STRATEGY

Differentiated tolerability profile with no interstitial lung disease, no significant neuropathy, and no significant neutropenia noted to date

Single-agent activity across multiple HER2-expressing tumor types

Strategy to combine with standards of care across indications, with no known overlapping toxicities

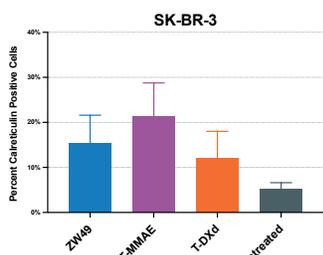
Incrementally staged investment in clinical development to **preserve and maintain** cash runway

Phase 1 data (NCT03821233) as reported at ESMO | Sep 2022

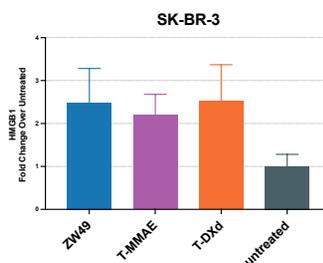
Mechanistic Rationale for Zanidatamab Zovodotin Combination with Anti-PD1



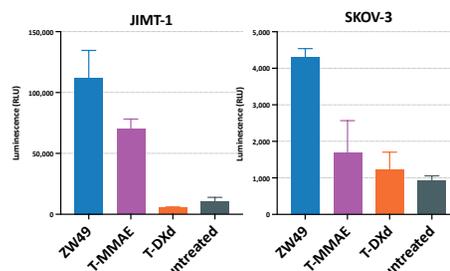
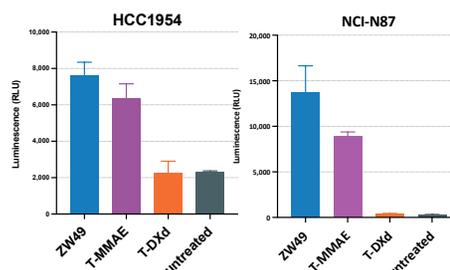
Calreticulin



HMGB1



Extracellular ATP



ADC	Antibody	Drug-linker (payload)	DAR
Zani Zo	zanidatamab (ZW25)	zovodotin (ZD02044)	2
T-MMAE	trastuzumab	vedotin (MMAE)	4
T-DXd	trastuzumab	deruxtecan (DXd)	8

- Zanidatamab zovodotin (zani zo) induces hallmarks of Immunogenic cell death (ICD) with preclinical evidence of enhanced activity compared to trastuzumab-based ADCs with either DXd or MMAE payloads
- ADCs that induce ICD may have a mechanistic advantage when combined with an anti-PD1
- Continued development ongoing with planned Phase 2 studies in NSCLC and mBC anticipated to begin in 2023

DXd: deruxtecan; mBC: metastatic breast cancer; MMAE: Monomethyl auristatin E; NSCLC: non-small cell lung cancer



Legacy Technology License Portfolio

Legacy Partnerships & Collaborations Validate Zymeworks' Technology



Programs & Platforms	Preclinical	Phase 1	Phase 2	Phase 3	Commercial Rights
Bispecific Antibody Azymetric EFECT	Oncology				Bristol Myers Squibb ¹
XB002 (ICON-2) Tissue Factor ADC ZymeLink	Solid Tumors				EXELIXIS ²
JNJ-78278343 CD3 x KLK2 Bispecific Azymetric EFECT	Castration-Resistant Prostate Cancer				Johnson & Johnson INNOVATION
Antibody Drug Conjugate ZymeLink	Oncology				ATRECA
Bispecific Antibody Azymetric EFECT	Undisclosed				MERCK
Bispecific Antibody Azymetric EFECT	Immuno-Oncology				Daiichi-Sankyo
Bispecific Antibody Azymetric EFECT	Infectious Disease/Undisclosed				gsk
Bispecific Antibody Azymetric EFECT	Dermatology				L E O
Bispecific Antibody Azymetric EFECT	Undisclosed				BeiGene

Over \$180MM³ in milestones received to-date

¹Original Agreement with Celgene (which is now a Bristol-Myers Squibb company)

²Original Agreement with Iconic; XB002 in-licensed by Exelixis

³Excludes Upfront Payments and milestones received in association with zanidatamab partnerships



CORPORATE SUMMARY

Building Long-Term Enterprise Value

Strong Financial Position to Fund Broad Product Portfolio



Updated Financial Guidance:

2023 Net operating cash burn of between \$90 and \$120 million¹

Cash runway through at least 2026, and potentially beyond

Cash balance of \$492.2 million⁴ as of YE22 allows Zymeworks to **fund planned operations through at least 2026**, and potentially beyond

Cash Runway Guidance **Includes:**

- Receipt of \$375MM in upfront payments from Jazz and existing cash resources²
- Ongoing funding from Jazz for zanidatamab development³
- Certain anticipated regulatory milestones from BeiGene and Jazz related to BTC and GEA
- Expansion of zanidatamab zovodotin Phase 1 and advancement into registrational studies
- Advancement of preclinical product candidates for two new INDs by 2024, plus one annually thereafter, and first-in-human studies for lead product candidates (ZW171 and ZW191)

Cash Runway Guidance **Excludes:**

- Proceeds from additional partnerships
- Proceeds from legacy platform licensing portfolio
- Potential additional regulatory milestones for zanidatamab from BeiGene and Jazz
- Potential commercial milestones for zanidatamab
- Potential royalties for zanidatamab from BeiGene and Jazz

¹ Net operating cash burn includes planned capital expenditures of \$15MM for 2022

² Zymeworks has unaudited existing cash resources of approximately \$490MM as of 12/31/2022

³ Ongoing funding for zanidatamab related development expenses incurred by Zymeworks and reimbursed by Jazz Pharmaceuticals will be recorded as revenues

⁴ Cash balance as of 12/31/2022 and excludes approximately \$24 million from zanidatamab related reimbursements for R&D expenses incurred from 10/19/2022 through 12/31/2022

Key Anticipated Events & Milestones Opportunities Throughout Product Pipeline



2023

- **Phase 2 1L GEA Follow-Up (presented January 19 at ASCO GI)**
zanidatamab + chemotherapy
- **Additional publications** on preclinical development candidates **(presented at AACR)**
- **HERIZON-BTC-01 (1H23)**
Full data presentation
- **Present additional Phase 1 data** for zanidatamab zovodotin **(2H23)**
- **Expand zanidatamab zovodotin into Phase 2** studies in key expansion areas: non-small cell lung cancer, and breast cancer
- **Earn additional milestone payments** for expansion or extension of existing legacy platform agreements
- **Nomination of next product candidate** for Preclinical Development **(2H23)** with target IND filing in 2025

2024

- **Submit 2 IND Applications**
for ZW171 and ZW191
- **HERIZON-GEA-01**
Anticipate Top-Line Data
- **Continue leveraging platforms** to generate preclinical product candidates and partnerships
- **Earn additional milestone payments** for expansion or extension of existing legacy platform agreements
- **Nominate additional potential product candidate** for preclinical development with target IND filing in 2026

IND: investigational new drug



Thank You



Company Contacts

Investor Relations

Jack Spinks

Director, Investor Relations

ir@zymeworks.com

(604) 678-1388

Media Relations

Diana Papove

Director, Corporate Communications

media@zymeworks.com

(604) 678-1388



Nasdaq: ZYME | zymeworks.com

