

41st Annual J.P. Morgan Healthcare Conference

Kenneth Galbraith Chair and CEO

Nasdaq: ZYME | zymeworks.com

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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)





P.

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



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

Corporate Value Framework – Elements of Enterprise Value



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

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

🚺 BeiGene Jazz Pharmaceuticals. Zanidatamab Zanidatamab Collaboration with Collaboration with BeiGene Jazz Zanidatamab Zovodotin Pharmaceuticals Research and Early Legacy Technology Development Licensing Portfolio Programs

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Key Priorities for 2023 and 2024



Financial Transformation

Transformation of financial position **ensures funding of key priorities** for multiple years and ability to opportunistically fund R&D engine

Purposeful Development

Further **evaluate zanidatamab zovodotin in key indications**, as monotherapy and in combination, to provide potential rationale for future registrational studies

3 Drive Value

Continue to **aggressively pursue** and **drive value** through partnerships and collaborations

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 preclinical data	2023
Aggressively pursue collaboration and partnerships	Ongoing
Zanidatamab Zovodotin	
Present additional data from Ph1 clinical study	2023
Expand ZW49 Ph1 study in key indications of interest	Ongoing
Legacy Platform Licensing Portfolio	
Earn additional milestone payments from existing agreements	Ongoing
Evaluate potential for monetization or expansion	Ongoing

IND: investigational new drug application; R&D: research and development; RP2D: Recommended Phase 2 dose

Focused on Making a Meaningful Difference For Patients

Our Mission

To discover, develop, and commercialize novel medicines that can **make a meaningful difference in the lives of patients** around the world who are impacted by difficult-to-treat cancers and other serious diseases

Our Vision

Using our innovative approach to multifunctional therapeutics to improve the lives of patients with difficult-to-treat cancers and other serious diseases



Platforms Driving the Next Generation of Antibody Based Therapeutics



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)



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



Tumor-Specific Immune Costimulation

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

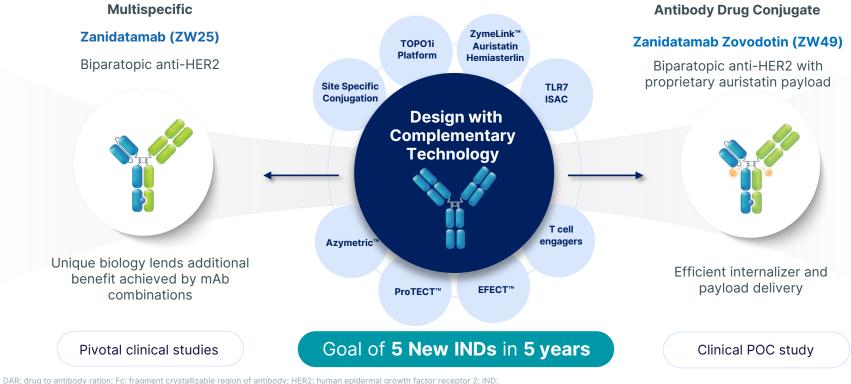
Enable New Biology

Modular

Scalable 🚽

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





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					Jazz Pharmaceuticals.
2nd-Line Biliary Tract Cancers HERIZON-BTC-01 Monotherapy					Jazz Pharmaceuticals.
1st-Line Gastrointestinal Cancers Gastroesophageal Adenocarcinoma, Biliary Tract Cancer, and Colorectal Cancer Chemotherapy Combination					Jazz Pharmaceuticals.
Zanidatamab Monotherapy & Chemotherapy Combination					Jazz Pharmaceuticals.



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



Early Development and Early R&D	Preclinical	Phase 1	Phase 2	Pivotal	Collaboration Partner
Zanidatamab Zovodotin HER2-Expressing Cancers Indications: NSCLC, GEA, CRC, OVCA, BC					🔁 BeiGene
ZW191 Folate Receptor-α Targeted Topoisomerase 1 Inhibitor Antibody Drug Conjugate Indications: OVCA, Gynecological, NSCLC					
ZW171 2+1 MSLN x CD3 Bispecific Antibody Indications: Pancreatic, OVCA, CRC					
ZW251 Glypican-3 Targeted Topoisomerase 1 Inhibitor Antibody Drug Conjugate Indications: OVCA, NSCLC					
ZW220 NaPi2b Targeted Topoisomerase 1 Inhibitor Antibody Drug Conjugate Indication: Hepatocellular Carcinoma					

BC: breast cancer; CRC: Colorectal cancer; GEA: gastroesophageal adenocarcinoma; NSCLC: non-small cell lung cancer; OVCA: ovarian cancer

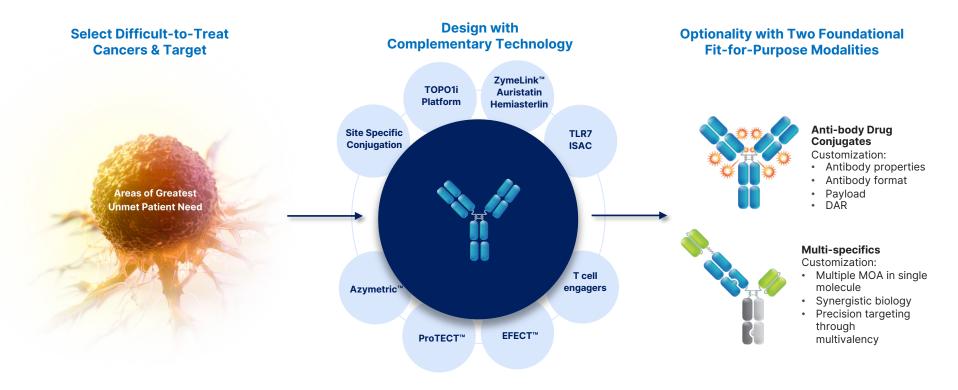


RESEARCH & DEVELOPMENT

Platforms and Product Candidates

ADC and Multispecific Modalities Driving Our Pipeline

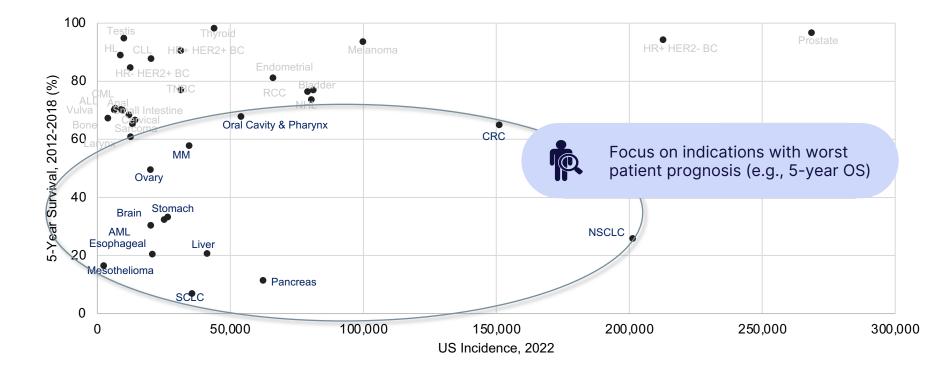
zymeworks



DAR: drug to antibody ration; MOA: mechanism of action

Goal: Focus on Cancer Indications with Greatest Unmet Patient Need





SEER*Explorer, accessed 10 Oct 2022

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



Biological Problem

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

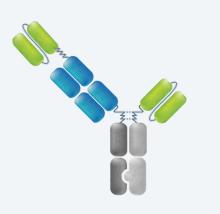
TCE: t cell engager

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



Lead 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

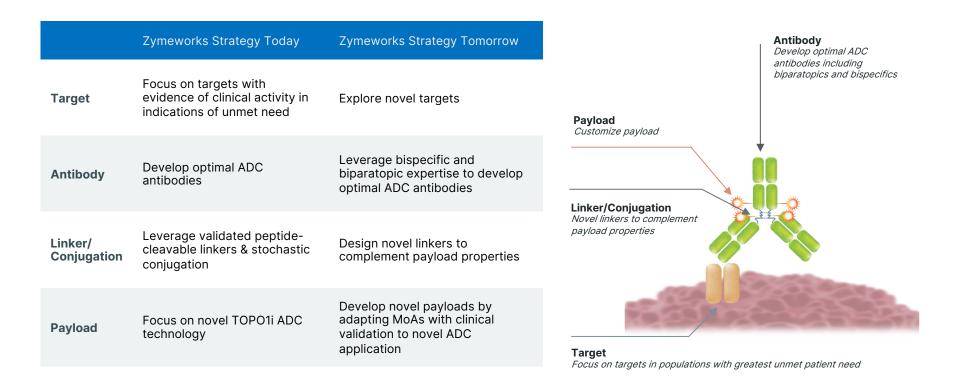
Validation

In preclinical development Targeting 2024 IND



Designing Fit-for-Purpose ADC Candidates





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

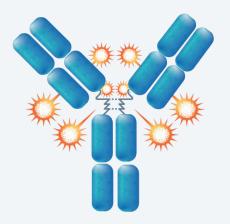


ZW191: Folate Receptor Alpha Topoisomerase-1 Inhibitor ADC



Lead Preclinical Product Candidate





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 Optimal internalization, payload delivery and tumor penetration

Drug Linker

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

Status

 $MTD \ge 30 \text{ mg/kg}$ in two dose non-human primate (NHP) toxicology study, with favorable PK

Strong anti-tumor activity in models with a range of expression

Targeting 2024 IND

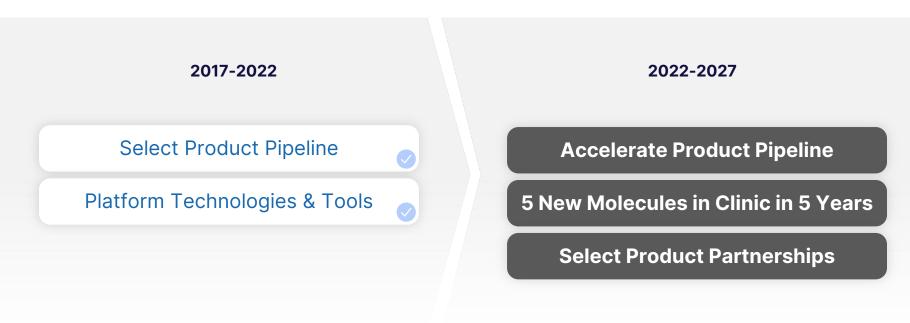
ADC: antibody-drug conjugate; DAR: drug-to-antibody ratio; NSCLC: non small cell lung cancer; MTD: maximum tolerable dose; TNBC: triple negative breast cancer



Zymeworks Moving Forward "5 by 5"



5 new product candidates planned for IND's over next 5 years







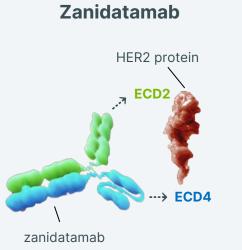
ZANIDATAMAB

Commercial Collaborations

Transactions allow zanidatamab 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'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

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Key Financial Terms of Licensing Agreement with Jazz



	Licensing Agreement Terms ¹
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	All costs for ongoing clinical studies to be reimbursed 100% 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 of 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, excludes approximately \$30MM in potential reimbursable amounts in 4Q22

Key Financial Terms of Asia Pacific Licensing Agreement with BeiGene



Licensing Agreement Terms ¹				
Counterparty	🛛 BeiGene			
Upfront Payments	\$40,000,000			
Development and Commercial Milestones	Up to \$390,000,000			
Royalties	Tiered royalties on 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

All dollar values in US Dollars

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 ≥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 chemotherapya, N=238 ARM 2: Zanidatamab + SOC chemotherapya, N=238 ARM 3: Zanidatamab + tislelizumab + SOC chemotherapya, 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 full data readout in 2024

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





ZANIDATAMAB ZOVODOTIN

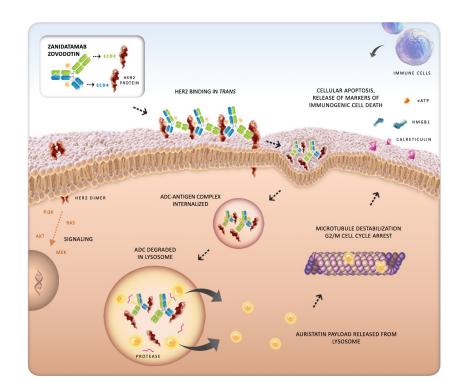
Clinical Development

Zanidtamab Zovodotin: A Bispecific ADC for HER2-Targeted Therapy



Unique Mechanism of Action^{1,2,3}

- IgG1-like biparatopic antibody backbone directed against ECD4 & ECD2 of HER2
- Antibody sequence identical to zanidatamab
- Proprietary auristatin payload covalently linked to the antibody via a protease-cleavable linker
- Average drug-to-antibody ratio (DAR) of 2
- Biparatopic antibody-induced internalization with increased auristatin-mediated cytotoxicity and immunogenic cell death
- Potential to address unmet need in cancers with high and low levels of HER2 expression and HER2-mutations



ADC, antibody-drug conjugate; AKT, serine-threonine protein kinase family; eATP, extracellular adenosine 5'triphosphate; ECD, extracellular domain; HER, human epidermal growth factor receptor; HMGB1, high mobility group box 1; G2/M, second gap phase/mitotic phase; MEK, mitogen-activated protein kinase; RAS, rat sarcoma pathway Kinase; RAS, rat sarcoma pathway

1. Hamblett et al., #3914 Poster Presentation at AACR 2018; 2. Davies et al., #3912, Poster Presentation at AACR 2018; 3. Data on file



Zanidtamab Zovodotin: Differentiated HER2-Targeted ADC



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

Non-Small Cell Lung Cancer (NSCLC)

HER2-amplified NSCLC

Metastatic Breast Cancer (mBC)

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

Gastroesophageal Adenocarcinoma (GEA)

Previously treated HER2-positive GEA

Colorectal Cancer (CRC)

HER2-amplified CRC

Pan Tumor Indications

Ovarian and endometrial



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

Potential combinability 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



Zanidtamab Zovodotin: A Bispecific ADC for HER2-Targeted Therapy

Data Highlights and Catalysts

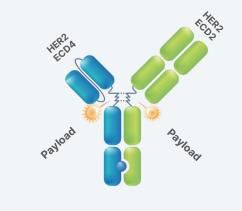
Clinical Data Highlights

- 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 responseevaluable patients treated with zanidatamab zovodotin at 2.5 mg/kg Q3W
- Clear single-agent activity in heavily pretreated patients with RP2D 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 1 into six key patient cohorts

Zanidatamab zovodotin



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

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







Legacy Technology License Portfolio

Legacy Partnerships & Collaborations Validate Zymeworks' Technology



Programs & Platforms	Preclinical	Phase 1	Phase 2	Commercial Rights
Bispecific Antibody Azymetric EFECT	Oncology			(^{III}) Bristol Myers ¹ Squibb [™]
XB002 (ICON-2) Tissue Factor ADC ZymeLink	Solid Tumors			EXELIXIS ²
JNJ-78278343 CD3 x KLK2 Bispecific Azymetric EFECT	Castration-Resistant Prosta	ate Cancer		Johmon-Johmon INNOVERON
JNJ-78306358 CD3 x HLA-G Bispecific Azymetric EFECT	Solid Tumors			Johmon-Johmon Intervence
ATRC-301 EphA2 Targeting ADC ZymeLink	Oncology			
Bispecific Antibody Azymetric EFECT	Undisclosed			
Bispecific Antibody Azymetric EFECT	Immuno-Oncology			Dailchi-Saniyo
Bispecific Antibody Azymetric EFECT	Infectious Disease/Undisclosed			gsk
Bispecific Antibody Azymetric EFECT	Dermatology			
Bispecific Antibody Azymetric EFECT	Undisclosed			🔁 BeiGene
	Over \$180MM ³ in I	milestones receiv	ed to-date	

Making a Meaningful Difference

Original Agreement with Celgene (which is now a Bristol-Myers Squibb company)
 Original Agreement with Iconic; XB002 in-licensed by Exelixis
 Excludes Upfront Payments and milestones received in association with zanidatamab partners



CORPORATE SUMMARY

Building Long-Term 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

Unaudited **cash balance of ~\$490 million**⁴ 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

4 Cash balance is unaudited as of 12/31/2022 and excludes approximately \$30 million from zanidatamab related reimbursements for R&D expenses incurred in 4Q22



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

Key Expected Events & Milestones Throughout the Product Pipeline



2023

- Phase 2 1L GEA Follow-Up (January 19 at ASCO GI) (zanidatamab + chemotherapy)
- HERIZON-BTC-01 (1H23)
 Study Completion
- Additional publications on preclinical development candidates (1H23)
- Present additional Phase 1 data for zanidatamab zovodotin
- Expand zanidatamab zovodotin Phase 1 in key expansion areas: non-small cell lung cancer, GEA, ovarian cancer, colorectal 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)

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

HR+: Hormone receptor positive; IND: investigational new drug; OS: overall survival; PFS: progression-free survival

Key Investment Highlights



Near-term commercialization of zanidatamab

supported by collaboration agreements with Jazz and BeiGene; pending necessary regulatory approvals

Future product pipeline and R&D engine

driven by expected progress of ZW49, ZW171, ZW191 and next-generation ADC and multispecific technologies

Enterprise Value Framework

Driving value from all five key areas of focus

Execution on new and existing partnerships as continued strategy for non-dilutive funding and continued advancement of product pipeline

Improved financial position provides ability to **rapidly advance** product candidates with a **focus** on next-generation ADC and multispecific technologies Strategic priorities underpinned by experienced management team, improved financial position with cash runway through at least 2026, and portfolio of existing partnership and collaborations



